Light at Night, Human Health - references with abstracts

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Many of these papers were cited in the following summary reports:

International Agency for Research on Cancer (IARC)
Monographs on the Evaluation of Carcinogenic Risks to Humans
Volume 98 (2010) Shiftwork, 563-754

http://monographs.iarc.fr/ENG/Monographs/vol98/mono98-8.pdf

European Commission, Directorate-General for Health & Consumers
Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)
Report entitled: Health Effects of Artificial Light (July 18, 2011)

http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_033.pdf

Institute of Medicine, Washington, DC: The National Academies Press
National Academy of Sciences, 3-29 - 3-30
Report entitled: Breast Cancer and the Environment: A life course (2012)

http://www.nap.edu/catalog.php?record_id=13263

Abe M, Herzog ED, Yamazaki S et al. ***Year*** 2002

Authors Michikazu Abe, Erik D. Herzog, Shin Yamazaki, Marty Straume, Hajime Tei, Yoshiyuki Sakaki,

Report Name Circadian rhythms in isolated brain regions.

Publication J Neurosci

Issue-page numbers 22:350–356. PMID:11756518

URL http://www.jneurosci.org/content/22/1/350.full.pdf

Abstract

The suprachiasmatic nucleus (SCN) of the mammalian hypothalamus has been referred to as the master circadian pacemaker that drives daily rhythms in behavior and physiology. There is, however, evidence for extra-SCN circadian oscillators. Neural tissues cultured from rats carrying the Per-luciferase transgene were used to monitor the intrinsic Per1 expression patterns in different brain areas and their response to changes
in the light cycle. Although many Per-expressing brain areas were arrhythmic in culture, 14 of the 27 areas examined were rhythmic. The pineal and pituitary glands both expressed rhythms that persisted for 3 d in vitro, with peak expression during the subjective night. Nuclei in the olfactory bulb and the ventral hypothalamus expressed rhythmicity with peak expression at night, whereas other brain areas were either weakly rhythmic and peaked at night, or arrhythmic. After a 6 hr advance or delay in the light cycle, the pineal, paraventricular nucleus of the hypothalamus, and arcuate nucleus each adjusted the phase of their rhythmicity with different kinetics.
Together, these results indicate that the brain contains multiple, damped circadian oscillators outside the SCN. The phasing of these oscillators to one another may play a critical role in coordinating brain activity and its adjustment to changes in the light cycle.

Keywords suprachiasmatic nucleus; pineal; pituitary; olfac-bulb; arcuate nucleus; Per; luciferase; entrainment; jet lag

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Ackermann K, Sletten TL, Revell VL, et al. ***Year*** 2009

Authors Katrin Ackermann, Tracey L. Sletten, Victoria L. Revell, Simon N. Archer and Debra J. Skene

Report Name Blue-light phase shifts PER3 gene expression in human leukocytes

Publication Chronobiology International

Issue-page numbers 2009, Vol. 26, No. 4 , Pages 769-779 (doi:10.1080/07420520902929045)

URL http://informahealthcare.com/doi/abs/10.1080/07420520902929045

Abstract The timing of clock gene expression in human leukocytes was investigated following a phase-advancing light stimulus to determine whether the response is wavelength- and/or age-dependent. PERIOD3 (PER3) clock gene expression in leukocytes and plasma melatonin were analyzed before and after monochromatic blue and green light exposure. Significant phase advances were observed in the peak timing of both PER3 expression and melatonin following blue but not green light. The amplitude of the PER3 rhythm at baseline was significantly reduced with age. However, age did not affect the response of the PER3 rhythm to light.

Keywords PERIOD3, Phase shift, Melatonin, Leukocytes, Blue light

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Ackermann K, Stehle JH ***Year*** 2006

Authors Katrin Ackermann and Dr. Jörg H. Stehle

Report Name Melatonin Synthesis in the Human Pineal Gland: Advantages, Implications, and Difficulties

Publication Chronobiology International

Issue-page numbers 23:1-2, 369-379

URL http://informahealthcare.com/doi/abs/10.1080/07420520500464379

Abstract Rhythms in the mammalian pineal organ depend on afferent information that is derived from the endogenous clock residing in the hypothalamic suprachiasmatic nucleus (SCN). The best characterized function of the pineal gland is the nocturnally elevated synthesis of the hormone melatonin, which provides the body with the signal of the duration of the night period. The rate-limiting enzyme for melatonin synthesis is arylalkylamine N-acetyltransferase (AANAT). In contrast to the transcriptional regulation of the Aanat gene in rodents, a post-translational shaping of the melatonin pattern is indicated in the human pineal gland. Despite the fact that melatonin levels can be determined easily in various body fluids, the molecular elements involved in shaping the rhythmic hormone synthesis cannot be analyzed experimentally in the living organism. However, the use of post-mortem pineal material seems to constitute a valid approach to decipher the regulation of human melatonin synthesis.

Keywords AANAT, mRNA, Degradation, Post-Mortem, HIOMT, Melatonin Circadian Rhythm, Human Beings

Adrian W, Bhanji A — *Year* 1992

Authors Adrian, W., Bhanji, A.

Report Name Fundamentals of disability glare: A formula to describe stray light in the eye as a function of glare angle and age.

Publication Proceedingsof the First International Symposium on Glare. New York: Lighting Research Institute.

Issue-page numbers pp. 185-193. (1992)

URL http://my.epri.com/portal/server.pt?space=CommunityPage&cached=true&parentname=ObjMgr&parentid=2&control=SetCommunity&CommunityID=404&RaiseDocID=0000000

Abstract N/A

Keywords Glare

Adrian WK — *Year* 1968

Authors Adrian, W. K.

Report Name The Priniciples of Disability and Discomfort Glare

Publication Proceeding of the First Annual Symposium on Visibility in the Driving Task

Issue-page numbers Texas A and M University, 1 (1968), pp 75-95

URL http://www.worldcat.org/wcpa/ow/219522212

Abstract

Keywords glare, visibility

Authors Jacopo Aguzzi, Nicole M Bullock, Gianluca Tosini

Report Name Spontaneous internal desynchronization of locomotor activity and body temperature rhythms from plasma melatonin rhythm in rats exposed to constant dim light

Publication Journal of Circadian Rhythms (2006)

Issue-page numbers Volume: 4, Publisher: BioMed Central, Pages: 6

URL http://www.mendeley.com/research/spontaneous-internal-desynchronization-locomotor-activity-body-temperature-rhythms-plasma-melatonin-rhythm-rats-exposed-constant-dim-li

Abstract Background: We have recently reported that spontaneous internal desynchronization between the locomotor activity rhythm and the melatonin rhythm may occur in rats (30% of tested animals) when they are maintained in constant dim red light (LLdim) for 60 days. Previous work has also shown that melatonin plays an important role in the modulation of the circadian rhythms of running wheel activity (Rw) and body temperature (Tb). The aim of the present study was to investigate the effect that desynchronization of the melatonin rhythm may have on the coupling and expression of circadian rhythms in Rw and Tb. Methods: Rats were maintained in a temperature controlled (2324C) ventilated lightproof room under LLdim (red dim light 1 W/cm2 5 Lux, lower wavelength cutoff at 640 nm). Animals were individually housed in cages equipped with a running wheel and a magnetic sensor system to detect wheel rotation; Tb was monitored by telemetry. Tb and Rw data were recorded in 5-min bins and saved on disk. For each animal, we determined the mesor and the amplitude of the Rw and Tb rhythm using waveform analysis on 7-day segments of the data. After sixty days of LLdim exposure, blood samples (80100 M) were collected every 4 hours over a 24-hrs period from the tail artery, and serum melatonin levels were measured by radioimmunoassay. Results: Twenty-one animals showed clear circadian rhythms Rw and Tb, whereas one animal was arrhythmic. Rw and Tb rhythms were always strictly associated and we did not observe desynchronization between these two rhythms. Plasma melatonin levels showed marked variations among individuals in the peak levels and in the night-to-day ratio. In six rats, the night-to-day ratio was less than 2, whereas in the rat that showed arrhythmicity in Rw and Tb melatonin levels were high and rhythmic with a large night-to-day ratio. In seven animals, serum melatonin levels peaked during the subjective day (from CT0 to CT8), thus suggesting that in these animals the circadian rhythm of serum melatonin desynchronized from the circadian rhythms of Rw and Tb. No significant correlation was observed between the amplitude (or the levels) of the melatonin profile and the amplitude and mesor of the Rw and Tb rhythms. Conclusion: Our data indicate that the free-running periods and the amplitude of Rw and Tb were not different between desynchronized and non-desynchronized rats, thus suggesting that the circadian rhythm of serum melatonin plays a marginal role in the regulation of the Rw and Tb rhythms. The present study also supports the notion that in the rat the circadian rhythms of locomotor activity and body temperature are controlled by a single circadian pacemaker.

Keywords

Akerstedt T, Palmblad J, de la Torre B et al. **Year** 1980

Authors Akerstedt T, Palmblad J, de la Torre B et al.

Report Name Adrenocortical and gonadal steroids during sleep deprivation

Publication Sleep

Issue-page numbers 3:23–30. PMID:6781027

URL http://www.ncbi.nlm.nih.gov/pubmed/6781027

Abstract Twelve healthy males were exposed to 48 hr of sleep deprivation under conditions of strictly controlled activity and of food and drink intake. During the experiment the subjects were isolated from external time cures, i.e. no daylight, clocks, etc. Plasma samples were obtained before and at the end of the vigil, as well as after 5 days of recovery. Samples were analyzed for adrenal and gonadal steroid hormones and for follicle-stimulating (FSH) and luteinizing hormones (LH). The levels of all unconjugated steroids studied (cortisol, 17-hydroxypregnenolone, 17-hydroxyprogesterone, androstenedione, dihydrotestosterone) were significantly lower at the end of the sleep deprivation period. Self-ratings of fatigue were significantly higher at the end of the deprivation period. After recovery, all values returned to base line. No changes were observed in the levels of FSH, LH, or most conjugated steroids. It was concluded that the results were not consistent with the view that sleep deprivation induces an emergency reaction with increased activation, but rather that it results in lower levels of both psychological and physiological activation.

Keywords

Akhtar RA, Reddy AB, Maywood ES et al. **Year** 2002

Authors Ruth A. Akhtar6, 1, Akhilesh B. Reddy6, 2, Elizabeth S. Maywood2, Jonathan D. Clayton1, Verdun M. King3, Andrew G. Smith4, Timothy W. Gant4, Michael H. Hastings2 and Cl

Report Name Circadian cycling of the mouse liver transcriptome, as revealed by cDNA microarray, is driven by the suprachiasmatic nucleus.

Publication Curr Biol

Issue-page numbers 12:540–550 doi:10.1016/S0960-9822(02)00759-5. PMID:11937022

URL http://www.cell.com/current-biology/abstract/S0960-9822%2802%2900759-5

Abstract Background: Genes encoding the circadian pacemaker in the hypothalamic suprachiasmatic nuclei (SCN) of mammals have recently been identified, but the molecular basis of circadian timing in peripheral tissue is not well understood. We used a custom-made cDNA microarray to identify mouse liver transcripts that show circadian cycles of abundance under constant conditions.Results: Using two independent tissue sampling and hybridization regimes, we show that ~9% of the 2122 genes studied show robust circadian cycling in the liver. These transcripts were categorized by their phase of abundance, defining clusters of day- and night-related genes, and also by the function of their products. Circadian regulation of genes was tissue specific, insofar as novel rhythmic liver genes were not necessarily rhythmic in the brain, even when expressed in the SCN. The rhythmic transcriptome in the periphery is, nevertheless, dependent on the SCN because surgical ablation of the SCN severely dampened or destroyed completely the cyclical expression of both canonical circadian genes and novel genes identified by microarray analysis.Conclusions: Temporally complex, circadian programming of the transcriptome in a peripheral organ is imposed across a wide range of core cellular functions and is dependent on an interaction between intrinsic, tissue-specific factors and extrinsic regulation by the SCN central pacemaker.

Keywords

Albers A, Duriscoe D **Year** 2001

Authors Albers A, Duriscoe D.

Report Name Modeling Light Pollution From Population Data and Implications for National Park Service Lands

Publication The George Wright Forum

Issue-page numbers 2001;18:56-68

URL http://www.georgewright.org/184albers.pdf

Abstract There are many factors that affect nighttime sky brightness, both natural and human-made. It is useful to think of what the main light sources are and how this light is scattered. The natural sources come from stars, the Milky Way, airglow, and moonlight. Human-made sources include streetlights and other outdoor lights, concentrated largely in towns and cities. Light is scattered by air molecules, natural and anthropogenic particulates, and haze (an enlargement of these particulates related to atmospheric moisture). The result of all these factors is what we see at night in terms of the sky brightness. To help clarify the further discussion, some simplifications will be helpful. We will assume no moonlight and relatively low levels of particulates and haze—in other words, that we are looking at the night sky under conditions that are among the best for a given location. We also neglect things such as surface albedo, which affects how much light is directed upward from city lights. The main remaining factor is city lights, whose effect is approximately related to population, and natural airglow (a continuous aurora-like glow) that actually varies during the course of the sunspot cycle. The darkest sites on earth have a brighter glow than those in outer space for two main reasons: the scattering of starlight by the atmosphere, and airglow.

Keywords light pollution

Albrecht U, Sun ZS, Eichele G, Lee CC **Year** 1997

Authors Urs Albrecht1, ||, Zhong Sheng Sun2, ||, Gregor Eichele1, 3 and Cheng Chi Lee

Report Name A differential response of two putative mammalian circadian regulators, mper1 and mper2, to light.

Publication Cell

Issue-page numbers 91:1055–1064 doi:10.1016/S0092-8674(00)80495-X. PMID:9428527

URL http://www.cell.com/abstract/S0092-8674%2800%2980495-X

Abstract A mouse gene, mper1, having all the properties expected of a circadian clock gene, was reported recently. This gene is expressed in a circadian pattern in the suprachiasmatic nucleus (SCN). mper1 maintains this pattern of circadian expression in constant darkness and can be entrained to a new light/dark cycle. Here we report the isolation of a second mammalian gene, mper2, which also has these properties and greater homology to Drosophila period. Expression of mper1 and mper2 is overlapping but asynchronous by 4 hr. mper1, unlike period and mper2 , is expressed rapidly after exposure to light at CT22. It appears that mper1 is the pacemaker component which responds to light and thus mediates photic entrainment.

Keywords

Authors Peter D. Alfinito* and Ellen Townes-Anderson

Report Name Activation of mislocalized opsin kills rod cells: a novel mechanism for rod cell death in retinal disease

Publication Proc Natl Acad Sci U S A

Issue-page numbers 2002; 99:5655-6

URL http://www.pnas.org/content/99/8/5655.full.pdf

Abstract

Rod photoreceptors are highly compartmentalized sensory neurons
that maintain strict ultrastructural and molecular polarity.
Structural subdivisions include the outer segment, inner segment,
cell body, and synaptic terminal. The visual pigment rhodopsin is
found predominantly in membranes of the rod cell outer segment
but becomes mislocalized, appearing throughout the plasma membrane
of the cell in many retinal diseases and injuries. Currently,
there is no known link between rhodopsin redistribution and rod
cell death. We propose that activation of mislocalized rhodopsin
kills rod cells by stimulating normally inaccessible signaling pathways.
This hypothesis was tested in primary retinal cell cultures,
which contain photoreceptors. In rod photoreceptors, opsin immunofluorescence
occurred throughout the rod cell plasma membrane.
Activation of this mislocalized opsin by photostimulation
after formation of isorhodopsin or by incubation with -ionone
(opsin agonist) killed 19–30% of rod cells. Rod cell death was
apoptotic, as indicated by marked chromatin condensation and the
requirement for caspase-3 activation. Rod cell death could be
induced by forskolin (adenylate cyclase agonist), and conversely,
-ionone-induced cell death could be blocked by cotreatment with
SQ22536 (an adenylate cyclase inhibitor). Pertussis toxin (a G
protein inhibitor) also blocked -ionone-induced cell death. The
data support a mechanism by which activation of mislocalized
opsin initiates apoptotic rod cell death through G protein stimulation
of adenylate cyclase.

Keywords

Algvere PV, Marshall J, Seregard S **Year** 2006

Authors Peep V. Algvere, John Marshall and Stefan Seregard

Report Name Age-related maculopathy and the impact of blue light hazard

Publication ACTA OPHTHALMOLOGICA SCANDINAVICA

Issue-page numbers 84: 4–15

URL http://www.healingtheeye.com/Articles/maculopathy_blue_light_hazard.pdf

Abstract

The pathogenesis of age-related maculopathy (ARM), the most common cause of visual loss after the age of 60 years, is indeed a complicated scenario that involves a variety of hereditary and environmental factors. The pathological cellular and molecular events underlying retinal photochemical light damage, including photoreceptor apoptosis, have been analysed in experimental animal models. Studies of agerelated alterations of the retina and photoreceptors, the accumulation of lipofuscin in retinal pigment epithelium (RPE) cells, and the formation of drusen have greatly contributed to our knowledge. A new concept of an inflammatory response to drusen has emerged, suggesting immunogenic and systemic reactions in Bruch's membrane and the subretinal space. Oxidative stress and free radical damage also impact on the photoreceptors and RPE cells in the ageing eye. Based on the photoelectric effect, a fundamental concept in quantum physics, the consequences of high-energy irradiation have been analysed in animal models and cell culture. Short-wavelength radiation (rhodopsin spectrum), and the blue light hazard (excitation peak 440 nm), have been shown to have a major impact on photoreceptor and RPE function, inducing photochemical damage and apoptotic cell death. Following cataract surgery, there is a dramatic change in ocular transmittance. In aphakic or pseudophakic eyes (with clear intraocular lenses), high-energy (blue) and ultraviolet-A radiation strikes the retina. Epidemiological data indicate a significantly increased 5-year incidence of late ARM in non-phakic eyes compared with phakic eyes. In recent years, putative prophylactic measures against ARM have emerged. The implantation of 'yellow' intraocular lenses (IOLs) that absorb high-energy blue radiation is, from a theoretical point of view, the most rational approach, and, from a practical point of view, is easy to accomplish. With increasing age, RPE cells accumulate lipofuscin (chromophore A2E). It is noteworthy that the yellow IOL not only protects A2E-laden human RPE cells from blue light (peak 430 nm) damage, but also alleviates the detrimental effects of green (peak 550 nm) and white light. A prophylactic treatment using antioxidants is aimed at counteracting oxidative stress and free radical cellular damage. The Age-Related Eye Disease Study (AREDS), a randomized clinical trial, showed a significantly lower incidence of late ARM in a cohort of patients with drusen maculopathy treated with high doses of antioxidants than in a placebo group. In recent years, considerable progress in retinal research has been achieved, creating a platform for the search for new prophylactic and therapeutic measures to alleviate or prevent photoreceptor and RPE degeneration in ARM.

Keywords age-related maculopathy – short-wavelength radiation – blue light hazard

Altimus CM, Güler AD, Alam NM, et al. **Year** 2010

Authors Cara M Altimus, Ali D Güler, Nazia M Alam, A Cyrus Arman, Glen T Prusky, Alapakkam P Sampath & Samer Hattar

Report Name Rod photoreceptors drive circadian photoentrainment across a wide range of light intensities

Publication Nature Neuroscience

Issue-page numbers 13, Pages: 1107–1112 Year published: (2010) doi:10.1038/nn.2617

URL http://www.nature.com/neuro/journal/v13/n9/full/nn.2617.html

Abstract In mammals, synchronization of the circadian pacemaker in the hypothalamus is achieved through direct input from the eyes conveyed by intrinsically photosensitive retinal ganglion cells (ipRGCs). Circadian photoentrainment can be maintained by rod and cone photoreceptors, but their functional contributions and their retinal circuits that impinge on ipRGCs are not well understood. Using mice that lack functional rods or in which rods are the only functional photoreceptors, we found that rods were solely responsible for photoentrainment at scotopic light intensities. Rods were also capable of driving circadian photoentrainment at photopic intensities at which they were incapable of supporting a visually guided behavior. Using mice in which cone photoreceptors were ablated, we found that rods signal through cones at high light intensities, but not at low light intensities. Thus, rods use two distinct retinal circuits to drive ipRGC function to support circadian photoentrainment across a wide range of light intensities.

Keywords

Amalric R, Gautherie M, Hobbins WB et al. **Year** 1981

Authors Amalric R, Gautherie M, Hobbins WB, Stark A, Thierree RA.

Report Name [The future of women with isolated abnormal infrared thermogram of the breast (author's transl)]

Publication Nouv Presse Med

Issue-page numbers 10:3153–3155. PMID:7290978

URL http://www.ncbi.nlm.nih.gov/pubmed/7290978

Abstract Abnormal infra-red thermograms of the breast are called "isolated" when they are not accompanied by other clinical or paraclinical abnormalities. They occur in asymptomatic women systematically examined or in women consulting for mammary symptoms other than palpable nodules. Their incidence is about 10-15%. They are usually considered as "false-positive" findings, but when these women are regularly followed up breast cancers are found to occur with a frequency ranging from 5% to 38%. "False-positive" thermograms therefore imply a high risk of breast cancer. Extremely prolonged clinical surveillance with periodical radiothermic tests and, if necessary, guided biopsies are required for early detection of small-size or even impalpable mammary carcinomas.

Keywords

Authors An M, Huang J, Shimomura Y, Katsuura T.

Report Name Time-of-day-dependent effects of monochromatic light exposure on human cognitive function

Publication J Physiol Anthropol

Issue-page numbers Sep;28(5):217-23.

URL http://www.ncbi.nlm.nih.gov/pubmed/19823003

Abstract

Light elicits non-visual effects on a wide range of biological functions and behavior. These effects are mediated by a melanopsin-based photoreceptor system that is very sensitive to blue light (440-480 nm) relative to the three-cone visual photopic system. The aim of the current study was to assess the time-of-day-dependent effects of two different wavelength monochromatic lights at 458 nm and 550 nm on human cognitive function. We conducted an experiment in the daytime and nighttime on different days. Twelve subjects were selected, none of whom was either morning-type or evening-type, as assessed by a translated version of the morningness/eveningness questionnaire. The cognitive function was measured by event-related potential (ERP) using an oddball task, and arousal level was measured by the Alpha Attenuation Test (AAT). We found that 458 nm light exposure caused a significantly larger P300 amplitude than occurred with 550 nm light. There was a significant interaction among wavelength, time of day, and electrode site. Exposure to 458 nm light induced a larger P300 amplitude at nighttime than in the daytime at the Fz electrode site. The Alpha Attenuation Coefficient (AAC) at nighttime was higher than in the daytime. Our results suggest that short wavelength monochromatic light can affect the circadian rhythms of cognitive functions, and indicate that these effects are mediated by a melanopsin-based photoreceptor system. This study has extended previous findings in terms of time of day, and higher cognitive function by using an endogenous ERP component, P300.

Keywords

Ancoli-Israel S, Cole R, Alessi C, et al. ***Year*** 2003

Authors Sonia Ancoli-Israel, Roger Cole, Cathy Alessi, Mark Chambers, William Moorcroft, Charles P. Pollak

Report Name The Role of Actigraphy in the Study of Sleep and Circadian Rhythms

Publication SLEEP

Issue-page numbers 2003;26(3):342-92.

URL http://wakemate.com/media/docs/actigraphy.pdf

Abstract

ACTIGRAPHY HAS BEEN USED TO STUDY SLEEP/WAKE PATTERNS FOR OVER 20 YEARS. The advantage of actigraphy over traditional polysomnography (PSG) is that actigraphy can conveniently record continuously for 24-hours a day for days, weeks or even longer. In 1995, Sadeh et al.,1 under the auspices of the American Sleep Disorders Association (now called the American Academy of Sleep Medicine, AASM), reviewed the current knowledge about the role of actigraphy in the evaluation of sleep disorders. They concluded that actigraphy does provide useful information and that it may be a “cost-effective method for assessing specific sleep disorders...[but that] methodological issues have not been systematically addressed in clinical research and practice.” Based on that task force’s report, the AASM Standards of Practice Committee concluded that actigraphy was not indicated for routine diagnosis or for assessment of severity or management of sleep disorders, but might be a useful adjunct for diagnosing insomnia, circadian rhythm disorders or excessive sleepiness.2 Since that time, actigraph technology has improved, and many more studies have been conducted. Several review papers have concluded that wrist actigraphy can usefully approximate sleep versus wake state during 24 hours and have noted that actigraphy has been used for monitoring insomnia, circadian sleep/wake disturbances, and periodic limb movement disorder.3,4 This paper begins where the 1995 paper left off. Under the auspices of the AASM, a new task force was established to review the current state of the art of this technology.

Keywords

Andersen M, Mardaljevic J, Lockley SW **Year** 2012

Authors M Andersen, J Mardaljevic, SW Lockley

Report Name A framework for predicting the non-visual effects of daylight – Part I: photobiology- based model

Publication Lighting Research and Technology

Issue-page numbers March 2012 vol. 44 no. 1 37-53

URL http://lrt.sagepub.com/content/44/1/37.short

Abstract This paper investigates the formulation of a modelling framework for the non-visual effects of daylight, such as entrainment of the circadian system and maintenance of alertness. The body of empirical data from photobiology studies is now sufficient to start developing preliminary non-visual lighting evaluation methods for lighting design. Eventually, these non-visual effects have the potential to become a relevant quantity to consider when assessing the overall daylighting performance of a space. This paper describes the assumptions and general approach that were developed to propose a modeling framework for occupant exposure to non-visual effects of light, and presents a novel means of visualising the 'circadian potential' of a point in space. The proposed approach uses current outcomes of photobiology research to define – at this point static – threshold values for illumination in terms of spectrum, intensity and timing of light at the human eye. These values are then translated into goals for lighting simulation, based on vertical illuminance at the eye, that – ultimately – could become goals for building design. A new climate-based simulation model has been developed to apply these concepts to a residential environment. This will be described in Part 2 of this paper.

Keywords

Anderson G, Beischlag TV, Vinciguerra M, Mazzoccoli G **Year** 2013

Authors George Anderson, Timothy V. Beischlag, Manlio Vinciguerra, Gianluigi Mazzoccoli

Report Name The circadian clock circuitry and the AHR signaling pathway in physiology and pathology

Publication Biochemical Pharmacology

Issue-page numbers Volume 85, Issue 10, 15 May 2013, Pages 1405–1416

URL http://www.sciencedirect.com/science/article/pii/S0006295213001263

Abstract Life forms populating the Earth must face environmental challenges to assure individual and species survival. The strategies predisposed to maintain organismal homeostasis and grant selective advantage rely on anticipatory phenomena facing periodic modifications, and compensatory phenomena facing unpredictable changes. Biological processes bringing about these responses are respectively driven by the circadian timing system, a complex of biological oscillators entrained to the environmental light/dark cycle, and by regulatory and metabolic networks that precisely direct the body's adjustments to variations of external conditions and internal milieu. A critical role in organismal homeostatic functions is played by the aryl hydrocarbon receptor (AHR) complex, which senses environmental and endogenous compounds, influences metabolic responses controlling phase I/II gene expression, and modulates vital phenomena such as development, inflammation and adaptive immunity. A physiological cross-talk between circadian and AHR signaling pathways has been evidenced. The alteration of AHR signaling pathway deriving from genetic damage with polymorphisms or mutations, or produced by exogenous or endogenous AHR activation, and chronodisruption caused by mismatch between the body's internal clock and geophysical time/social schedules, are capable of triggering pathological mechanisms involved in metabolic, immune-related and neoplastic diseases. On the other hand, the molecular components of the circadian clock circuitry and AHR signaling pathway may represent useful tools for preventive interventions and valuable targets of therapeutic approaches.

Keywords AHR;

Authors Anderson JL, Glod CA, Dai J, Cao Y, Lockley SW.

Report Name Lux vs. wavelength in light treatment of Seasonal Affective Disorder

Publication Acta Psychiatr Scand

Issue-page numbers Sep;120(3):203-12. Epub 2009 Feb 3.

URL http://www.optimalhealthpartner.com/A_Archive/Anderson_LuxVsWavelength.pdf

Abstract

OBJECTIVE:

Published dosing guidelines for treatment of Seasonal Affective Disorder (SAD) refer to photopic lux, which is not appropriate for short-wavelength light. Short wavelengths are most potent for many non-visual responses to light. If SAD therapy were similarly mediated, standards utilizing lux risk overestimating necessary dose. We investigated antidepressant responses to light using two light-emitting diode (LED) sources, each emitting substantial short-wavelength light, but <2500 lux.
METHOD:

A randomized, double-blind trial investigated 3-week 45 min/day out-patient treatment with blue-appearing (goLITE) or blue-enriched white-appearing light in 18 moderately-depressed adults (12F, 49.1 +/- 9.5 years). Equivalent numbers of photons within the short-wavelength range were emitted, but the white source emitted twice as many photons overall and seven-fold more lux.
RESULTS:

Depression ratings (SIGH-ADS; http://www.cet.org) decrease averaged 82% (SD = 17%) from baseline (P < 0.0001) in both white- and blue-light groups. Both sources were well tolerated.
CONCLUSION:

Short-wavelength LED light sources may be effective in SAD treatment at fewer lux than traditional fluorescent sources.

Keywords

Anderson LE, Morris JE, Sasser LB, Stevens RG — ***Year*** 2000

Authors Anderson LE, Morris JE, Sasser LB, Stevens RG

Report Name Effect of constant light on DMBA mammary tumorigenesis in rats

Publication Cancer Lett

Issue-page numbers 148:121–126 doi:10.1016/S0304-3835(99)00320-1. PMID:10695987

URL http://www.sciencedirect.com/science/article/pii/S0304383599003201

Abstract A study of light, and mammary tumorigenesis was conducted in rats. One-hundred female Sprague–Dawley rats were divided by weight into two groups. One group was exposed to constant light (LL) from 26 days of age, and the second group was exposed to 8 h light and 16 h dark per day (LD). Both groups received an 8 mg dose of a chemical carcinogen, dimethylbenzanthracene (DMBA) at 52 days of age. At 13 weeks post-DMBA, there were significantly fewer mammary tumors in the LL group compared with the LD group. Constant light was clearly demonstrated to have a profound effect on mammary tissue development. Although virgin, the majority of the LL rats (29/50) had gross evidence of lactation at 141 days of age. None of the LD rats (0/50) showed evidence of milk production. These results suggest that constant light not only substantially accelerated mammary gland development, but pushed development of the tissue past the stage normally observed in virgin animals (to the lactation stage).

Keywords Mammary gland development; Light exposure; Mammary cancer; Dimethylbenzanthracene; Carcinogenesis; Rats

Anderson TD, Arceco R, Hayes TJ — ***Year*** 1993

Authors Anderson TD, Arceco R, Hayes TJ

Report Name Comparative toxicity and pathology associated with administration of recombinant HuIL-1 alpha to animals.

Publication Int Rev Exp Pathol

Issue-page numbers 34 Pt A;9–36. PMID:8454419

URL http://www.ncbi.nlm.nih.gov/pubmed/8454419

Abstract N/A

Keywords

Anderson TJ, Ferguson DJP, Raab GM **Year** 1982

Authors Anderson TJ, Ferguson DJP, Raab GM

Report Name Cell turnover in the “resting” human breast: influence of parity, contraceptive pill, age and laterality.

Publication Br J Cancer

Issue-page numbers 46:376–382. PMID:7126427

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2011125/pdf/brjcancer00432-0065.pdf

Abstract Summary. -Morphological identification of cell multiplication (mitosis) and cell deletion (apoptosis) within the lobules of the "resting" human breast is used to assess the response of the breast parenchyma to the menstrual cycle. The responses are shown to have a biorhythm in phase with the menstrual cycle, with a 3-day separation of the mitotic and apoptotic peaks. The study fails to demonstrate significant differences in the responses between groups defined according to parity, contraceptive-pill use or presence of fibroadenoma. However, significant differences are found in the apoptotic response according to age and laterality. The results highlight the complexity of modulating influences on breast parenchymal turnover in the
"resting" state, and prompt the investigation of other factors as well as steroid hormones and prolactin in the promotion of mitosis. The factors promoting apoptosis in the breast are still not clear.

Keywords

Anisimov VN **Year** 2003

Authors Vladimir N. Anisimov

Report Name The role of pineal gland in breast cancer development

Publication Critical Reviews in Oncology/Hematology

Issue-page numbers Volume 46, Issue 3, June 2003, Pages 221-234

URL http://www.sciencedirect.com/science/article/pii/S1040842803000210

Abstract The role of the modulation of the pineal gland function in development of breast cancer is discussed in this review. An inhibition of the pineal function with pinealectomy or with the exposure to the constant lightnext term regimen stimulates mammary carcinogenesis, whereas the previous termlightnext term deprivation inhibits the carcinogenesis. Epidemiological observations on increased risk of breast cancer in night shift workers, flight attendants, radio and telegraph operators and on decreased risk in blind women are in accordance with the results of experiments in rodents. Treatment with pineal indole hormone melatonin inhibits mammary carcinogenesis in pinealectomized rats, in animals kept at the standard previous termlightnext term/dark regimen (LD) or at the constant illumination (LL) regimen. Pineal peptide preparation Epithalamin and synthetic tetrapeptide Epitalon (Ala–Glu–Asp–Gly) are potent inhibitors of mammary carcinogenesis in rodents and might be useful in the prevention of breast cancer in women at risk.

Keywords

Anisimov VN, Baturin DA, Popovich IG, et al. ***Year*** 2004

Authors Vladimir N. ANISIMOV, Dmitri A. BATURIN, Irina G. POPOVICH, Mark A. ZABEZHINSKI, Kenneth G. MANTON, Anna V. SEMENCHENKO and Anatoly I. YASHIN

Report Name Effect of exposure to light-at-night on life span and spontaneous carcinogenesis in female CBA mice

Publication Int J Cancer

Issue-page numbers 2004;111:475-479

URL http://www.demogr.mpg.de/publications/files/1712_1189699323_1_IJC-CBA-light.pdf

Abstract

The effect of constant illumination on the development of spontaneous tumors in female CBA mice was investigated. Fifty female CBA mice starting from the age of 2 months were kept under standard light/dark regimen (12 hr light: 12hr dark; LD) and 50 CBA mice of similar age were kept under constant illumination (24 hr a day, 2,500 Lux, LL). Exposure to the LL regimen decreased food consumption but did not influence body weight, significantly accelerated age-related disturbances in estrous function, and was followed
by a significant increase in spontaneous tumor incidence in female CBA mice. Tumor incidence as well as the number of total or malignant tumors was significantly increased in the LL group compared to the LD group ($p < 0.001$). The incidence of lung adenocarcinomas, leukemias and hepatocarcinomas was 7/50; 6/50 and 4/50 in the LL group and 1/50; 0/50 and 0/50 in the LD group. Mice from the
LL groups had shorter life spans then those from the LD group. The data demonstrate, for the first time, that exposure to constant illumination was followed by increases in the incidence of spontaneous lung carcinoma, leukemias and hepatocarcinoma in female CBA mice.

Keywords light-at-night; spontaneous tumors; life span; CBA mice

Authors Anisimov VN, Vinogradova IA, Panchenko AV, Popovich IG, Zabezhinski MA.

Report Name Light-at-night-induced circadian disruption, cancer and aging.

Publication Curr Aging Sci.

Issue-page numbers 2012 Dec;5(3):170-7.

URL http://www.ncbi.nlm.nih.gov/pubmed/23237593

Abstract

Light-at-night has become an increasing and essential part of the modern lifestyle and leads to a number of health problems, including excessive body mass index, cardiovascular diseases, diabetes, and cancer. The International Agency for Research on Cancer (IARC) Working Group concluded that "shift-work that involves circadian disruption is probably carcinogenic to humans" (Group 2A) [1]. According to the circadian disruption hypothesis, light-at-night might disrupt the endogenous circadian rhythm and specifically suppress nocturnal production of the pineal hormone melatonin and its secretion into the blood. We evaluated the effect of various light/dark regimens on the survival, life span, and spontaneous and chemical carcinogenesis in rodents. Exposure to constant illumination was followed by accelerated aging and enhanced spontaneous tumorigenesis in female CBA and transgenic HER-2/neu mice. In male and female rats maintained at various light/dark regimens (standard 12:12 light/dark [LD], the natural light [NL] of northwestern Russia, constant light [LL], and constant darkness [DD]) from the age of 25 days until natural death, it was found that exposure to NL and LL regimens accelerated age-related switch-off of the estrous function (in females), induced development of metabolic syndrome and spontaneous tumorigenesis, and shortened life span both in male and females rats compared to the standard LD regimen. Melatonin given in nocturnal drinking water prevented the adverse effect of the constant illumination (LL) and natural light (NL) regimens on the homeostasis, life span, and tumor development both in mice and rats. The exposure to the LL regimen accelerated colon carcinogenesis induced by 1,2-dimethylhydrazine (DMH) in rats, whereas the treatment with melatonin alleviated the effects of LL. The maintenance of rats at the DD regimen inhibited DMH-induced carcinogenesis. The LL regimen accelerated, whereas the DD regimen inhibited both mammary carcinogenesis induced by N-nitrosomethylurea and transplacental carcinogenesis induced by N-nitrosoethylurea in rats. Treatment with melatonin prevented premature aging and tumorigenesis in rodents. The data found in the literature and our observations suggest that the use of melatonin would be effective for cancer prevention in humans at risk as a result of light pollution.

Keywords

Anjum B, Singh RB, Verma N, et al. **Year** 2012

Authors B. Anjum, R.B. Singh, Narsingh Verma, Ranjana Singh, A.A. Mahdi, R.K. Singh,

Report Name Associations of Circadian Disruption of Sleep and Nutritional Factors with

Publication The Open Nutraceuticals Journal

Issue-page numbers 2012, 5, 124-135

URL http://benthamscience.com/open/tonutraj/articles/V005/124TONUTRAJ.pdf

Abstract

Background: Daily entrainment of the human circadian clock is important for good human health. In previous studies, shift work has been linked to higher risk of chronic diseases, including certain types of cancers. Exposure to light at night suppresses the physiologic production of melatonin, a hormone that has antiproliferative effects on intestinal cancers. In the present review, we examine the available evidence on sleep disruption, changes in nutrient intake and nutritional factors and risk of cancers.
Methods: Internet search of PubMed and discussion with colleagues.
Results: Recent studies indicate that night shift work appears to have independent influence on the function of the endocrine system, gastrointestinal tract and circadian brain function. Sleep disruption enhances cortisol secretion and ghrelin release from the stomach and decreases melatonin and leptin which interfere with functioning of beta cells of pancreas. Apart from biological dysfunctions, behavioral changes, increased intake of refined carbohydrates, w-6 fats and low w-3 fats, physical inactivity, excess of tobacco and alcoholism appear to be common among night shift workers. Leptin signals the brain to feel satiety whereas ghrelin, produced in the stomach, signals hunger. Recent studies also indicate that sleep-deprived individuals with hormonal changes have greater cravings for sweet and fatty foods. Apart from this, stress hormone cortisol, which increases with sleep deprivation also contribute to hunger. In addition to altered hormone levels, late night awakening provides greater opportunity to eat, smoke and drink alcohol and eating often includes high-caloric foods. Epidemiological studies indicate that sleep disruption may be associated with obesity and other chronic diseases including cancers. Since electric light at night has adverse effects among night shift workers compared to day shift workers, it has been proposed that a portion of the high and rising risk of breast and prostate cancer worldwide may be because of night shift work. The suppression of melatonin by exposure to light at night may be one reason for the higher rates of breast, prostate and colorectal cancers in the developed world. Suppression of nocturnal melatonin by exposure to light at night results in lack of protection by melatonin on cancer cell receptor sites which allows the uptake of linoleic acid (LA) which in turn enhances the growth of cancer cells. Melatonin is a protective, oncostatic hormone and strong antioxidant having evolved in all plants and animals over the millennia. It is possible that rotating night shift at least three nights per month for 15 or more years may increase the risk of colorectal cancer and other cancers.
Conclusions: Experimental evidence and limited human evidence allowed the International Agency for Research on Cancer (IARC) to classify circadian disruption of sleep, as a probable human carcinogen, group 2A. Behavioral changes, intake of fast foods, physical inactivity, excess of tobacco and alcoholism are common among night shift workers which may also apart from deficiency of melatonin.

Keywords Light at night, night shift, melatonin, diet, nutrient.

ANSES *Year* 2010

Authors The French Agency for Food, Environmental and Occupational Health & Safety (ANSES)

Report Name ANSES publishes its expert assessment of health issues related to lighting systems using light-emitting diodes (LEDs)

Publication Web Release http://www.afssa.fr/Documents/PRES2010CPA14EN.pdf

Issue-page numbers

URL http://osha.europa.eu/en/news/fr-anses-publishes-its-expert-assessment-of-health-issues-related-to-lighting-systems-using-light-emitting-diodes-leds

Abstract The principal characteristic of diodes sold for lighting purposes is the high proportion of blue in the white light emitted and their very high luminance ("brightness"). The issues of most concern identified by the ANSES concern the eye due to the toxic effect of blue light and the risk of glare. The blue light necessary to obtain white LEDs causes toxic stress to the retina. Children are particularly sensitive to this risk, as their crystalline lens is still developing and is unable to filter the light efficiently. These new lighting systems can produce "intensities of light" up to 1000 times higher than traditional lighting systems, thus creating a risk of glare. The strongly directed light they produce, as well as the quality of the light emitted, can also cause visual discomfort.
ANSES recommends that only LEDs belonging to Risk Groups similar to those of traditional lighting systems be accessible to the general public, with higher-risk lighting systems being reserved for professional use under conditions in which it is possible to guarantee the safety of workers. ANSES has made various recommendations concerning consumer information, modifications to and implementation of the standards in force and the need for further knowledge of health issues surrounding artificial lighting.

Keywords LED, toxic, eye, glare, blue

Antle MC, Smith VM, Sterniczuk R, et al. *Year* 2009

Authors Michael C. Antle, Victoria M. Smith, Roxanne Sterniczuk, Glenn R. Yamakawa and Brooke D. Rakai

Report Name Physiological responses of the circadian clock to acute light exposure at night

Publication Reviews in Endocrine & Metabolic Disorders

Issue-page numbers Volume 10, Number 4, 279-291, DOI: 10.1007/s11154-009-9116-6

URL http://www.springerlink.com/content/y252n14q1400l166/

Abstract Circadian rhythms in physiological, endocrine and metabolic functioning are controlled by a neural clock located in the suprachiasmatic nucleus (SCN). This structure is endogenously rhythmic and the phase of this rhythm can be reset by light information from the eye. A key feature of the SCN is that while it is a small structure containing on the order of about 20,000 cells, it is amazingly heterogeneous. It is likely that anatomical heterogeneity reflects an underlying functional heterogeneity. In this review, we examine the physiological responses of cells in the SCN to light stimuli that reset the phase of the circadian clock, highlighting where possible the spatial pattern of such responses. Increases in intracellular calcium are an important signal in response to light, and this increase triggers many biochemical cascades that mediate responses to light. Furthermore, only some cells in the SCN are actually endogenously rhythmic, and these cells likely do not receive strong direct input from the retina. Therefore, this review also considers how light information is conveyed from the retinorecipient cells to the endogenously rhythmic cells that track circadian phase. A number of neuropeptides, including vasoactive intestinal polypeptide, gastrin-releasing peptide and substance P, may be particularly important in relaying such signals, but other neurochemicals such as GABA and nitric oxide may participate as well. A thorough understanding of the intracellular and intercellular responses to light, as well as the spatial arrangements of such responses may help identify important pharmacological targets for therapeutic interventions to treat sleep and circadian disorders.

Keywords VIP - GRP - SP - PKC - PKG - PKA - MAPK - CamKII - Kinase

Authors Kenneth Appleman, Mariana G. Figueiro, Mark S. Rea

Report Name Controlling light–dark exposure patterns rather than sleep schedules determines circadian phase

Publication Sleep Medicine

Issue-page numbers Volume 14, Issue 5, May 2013, Pages 456–461

URL http://www.sciencedirect.com/science/article/pii/S1389945713000075

Abstract

Objective
To examine, in a field study circadian phase changes associated with two different light–dark exposures patterns, one that was congruent with a phase advanced sleep schedule and one that was incongruent with an advanced schedule.
Methods

Twenty-one adults (mean age ± standard deviation = 22.5 ± 3.9 years; 11 women) participated in the 12 day study. After a five-day baseline period, participants were all given individualized, fixed, 90-minute advanced sleep schedules for one week. Participants were randomly assigned to one of two groups, an advance group with a light–dark exposure prescription designed to advance circadian phase or a delay group with light–dark exposure prescription designed to delay circadian phase. The advance group received two morning hours of short-wavelength (blue) light (λmax ≈ 476 ± 1 nm, full-width-half-maximum ≈ 20 nm) exposure and three evening hours of light restriction (orange-filtered light, λ < 525 nm = 0). The delay group received blue light for three hours in the evening and light restriction for two hours in the morning. Participants led their normal lives while wearing a calibrated wrist-worn light exposure and activity monitor.
Results

After seven days on the 90-minute advanced sleep schedule, circadian phase advanced 132 ± 19 minutes for the advance group and delayed 59 ± 7.5 minutes for the delay group.
Conclusions

Controlling the light–dark exposure pattern shifts circadian phase in the expected direction irrespective of the fixed advanced sleep schedule.

Keywords Circadian phase; Dim light melatonin onset; Personal light exposure; Subjective sleepiness

Authors Archer SN, Robilliard DL, Skene DJ et al.

Report Name A length polymorphism in the circadian clock gene Per3 is linked to delayed sleep phase syndrome and extreme diurnal preference.

Publication Sleep

Issue-page numbers 26:413–415. PMID:12841365

URL http://www.journalsleep.org/Articles/260401.pdf

Abstract

SLEEP TIMING AND STRUCTURE ARE STRONGLY INFLUENCED BY THE CIRCADIAN SYSTEM,1 which anticipates day length and generates daily rhythms from a master pacemaker in the suprachiasmatic nuclei.2 Every day, environmental photic time cues are processed via retinal input pathways to synchronize (entrain) the circadian pacemaker to the 24-hour day. In the absence of external time cues, the free-running endogenous circadian period ƒÑ is expressed. Diurnal preference, as determined by the Horne-Ostberg (HO) questionnaire3, a validated quantitative tool, has been shown to correlate with ƒÑ.4 The relatively
rare conditions known as advanced and delayed sleep phase syndromes (ASPS/DSPS) have been described as pathologic extremes of diurnal preference and may be linked to extremely short or long ƒÑ,
respectively.5 The accepted model for the molecular machinery that generates circadian
rhythms involves a number of clock genes and their products.6 The Period (Per) gene family is a central component in this mechanism, providing negative auto-feedback on its own expression. Per transcripts and
PER proteins oscillate with period lengths correlated to the observed ƒÑ.7 Phosphorylation targets PER for degradation, imposing a rate-limiting step on the amount of PER protein available for dimerization and subsequent nuclear translocation. A mutation in Per2 has been reported to associate with ASPS, potentially by disrupting a target site for phosphorylation by casein kinase 1 (CK1) ƒÃ. Here, we report a novel link between a length polymorphism in Per3
and diurnal preference in humans. Homozygous Per3 knockout mice
display a free-running ƒÑ 30 minutes shorter than the wildtype.8 Five Per3
polymorphisms have been reported in a Japanese population, occurring
in four haplotypes.9 One of these haplotypes was reported to be more
frequent in DSPS subjects, although the association between the five
polymorphisms within this haplotype and the disorder were not determined. Taking a different approach, we focused specifically on a lengthpolymorphic repeat region composed of either 4 or 5 units, which is
described, but not specifically analyzed, in the previous paper. The prevalence of this polymorphism was studied both in subjects with extreme diurnal preference and in DSPS patients.

Keywords

Authors G B Arden, S Jyothi, C H Hogg, Y F Lee and S Sivaprasad

Report Name Regression of early diabetic macular oedema is associated with prevention of dark adaptation

Publication Eye

Issue-page numbers (21 October 2011) | doi:10.1038/eye.2011.264

URL http://www.nature.com/eye/journal/vaop/ncurrent/full/eye2011264a.html

Abstract

Hypothesis

Dark-adapted rods consume oxygen at high rates and light adaptation decreases this oxygen burden and can have therapeutic effects on diabetic macular oedema (DMO).

Methods

Patients with mild non-proliferative diabetic retinopathy (DR) and early, untreated non-sight-threatening DMO slept for 6 months wearing masks that illuminated the eyelid of one closed eye by 505 nm light. Exclusion criteria were any concomitant eye disease, DR >ETDRS grade 35, and other systemic diseases. Primary outcome: change of OCT retinal thickness in the local region where oedema was present.

Results

A total of 34 out of 40 patients completed the study. Mean baseline OCT macular cube thickness was equivalent for study and fellow eyes. But study eyes had a greater mean thickness in the central subfield zone 1 (282±53 μm) vs (256±19 μm) the fellow eyes. Twenty-eight study eyes showed intraretinal cysts compared with nine in the fellow eyes. At 6 months, only 19 study eyes had cysts while cysts were seen in 20 fellow eyes. After 6 months, the worst affected ETDRS zone and the central subfield zone 1 reduced in thickness in study eyes only by 12 μm (95% CI 20 to −7, P=0.01). The secondary outcomes of change in visual acuity, achromatic contrast sensitivity, and microperimetric thresholds improved significantly in study eyes and deteriorated in fellow eyes.

Conclusions

Sleeping in dim light that can keep rods light adapted may reverse the changes of DMO.

Keywords

Arendt J

Year 2012

Authors Josephine Arendt

Report Name Biological Rhythms During Residence in Polar Regions

Publication Chronobiology International

Issue-page numbers May 2012, Vol. 29, No. 4 , Pages 379-394 (doi:10.3109/07420528.2012.668997)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2012.668997

Abstract

At Arctic and Antarctic latitudes, personnel are deprived of natural sunlight in winter and have continuous daylight in summer: light of sufficient intensity and suitable spectral composition is the main factor that maintains the 24-h period of human circadian rhythms. Thus, the status of the circadian system is of interest. Moreover, the relatively controlled artificial light conditions in winter are conducive to experimentation with different types of light treatment. The hormone melatonin and/or its metabolite 6-sulfatoxymelatonin (aMT6s) provide probably the best index of circadian (and seasonal) timing. A frequent observation has been a delay of the circadian system in winter. A skeleton photoperiod (2 × 1-h, bright white light, morning and evening) can restore summer timing. A single 1-h pulse of light in the morning may be sufficient. A few people desynchronize from the 24-h day (free-run) and show their intrinsic circadian period, usually >24 h. With regard to general health in polar regions, intermittent reports describe abnormalities in various physiological processes from the point of view of daily and seasonal rhythms, but positive health outcomes are also published. True winter depression (SAD) appears to be rare, although subsyndromal SAD is reported. Probably of most concern are the numerous reports of sleep problems. These have prompted investigations of the underlying mechanisms and treatment interventions. A delay of the circadian system with “normal” working hours implies sleep is attempted at a suboptimal phase. Decrements in sleep efficiency, latency, duration, and quality are also seen in winter. Increasing the intensity of ambient light exposure throughout the day advanced circadian phase and was associated with benefits for sleep: blue-enriched light was slightly more effective than standard white light. Effects on performance remain to be fully investigated. At 75°S, base personnel adapt the circadian system to night work within a week, in contrast to temperate zones where complete adaptation rarely occurs. A similar situation occurs on high-latitude North Sea oil installations, especially when working 18:00–06:00 h. Lack of conflicting light exposure (and “social obligations”) is the probable explanation. Many have problems returning to day work, showing circadian desynchrony. Timed light treatment again has helped to restore normal phase/sleep in a small number of people. Postprandial response to meals is compromised during periods of desynchrony with evidence of insulin resistance and elevated triglycerides, risk factors for heart disease. Only small numbers of subjects have been studied intensively in polar regions; however, these observations suggest that suboptimal light conditions are deleterious to health. They apply equally to people living in temperate zones with insufficient light exposure.

Keywords Antarctic, Arctic, Circadian, Light, Melatonin, Polar, Sleep

Arendt J

Year 2006

Authors Josephine Arendt

Report Name Melatonin and Human Rhythms

Publication Chronobiology International

Issue-page numbers 23:1-2, 21-37

URL http://informahealthcare.com/doi/abs/10.1080/07420520500464361

Abstract Melatonin signals time of day and time of year in mammals by virtue of its pattern of secretion, which defines 'biological night.' It is supremely important for research on the physiology and pathology of the human biological clock. Light suppresses melatonin secretion at night using pathways involved in circadian photoreception. The melatonin rhythm (as evidenced by its profile in plasma, saliva, or its major metabolite, 6-sulphatoxymelatonin [aMT6s] in urine) is the best peripheral index of the timing of the human circadian pacemaker. Light suppression and phase-shifting of the melatonin 24 h profile enables the characterization of human circadian photoreception, and circulating concentrations of the hormone are used to investigate the general properties of the human circadian system in health and disease. Suppression of melatonin by light at night has been invoked as a possible influence on major disease risk as there is increasing evidence for its oncostatic effects. Exogenous melatonin acts as a 'chronobiotic.' Acutely, it increases sleep propensity during 'biological day.' These properties have led to successful treatments for serveal circadian rhythm disorders. Endogenous melatonin acts to reinforce the functioning of the human circadian system, probably in many ways. The future holds much promise for melatonin as a research tool and as a therapy for various conditions.

Keywords Melatonin, Light, Circadian and Circaanual Rhythms, Chronobiotic, Sleep, Sleep Disorders, Photoperiodism

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Arendt J

Year 2010

Authors Arendt J

Report Name Shift work: coping with the biological clock.

Publication Occup Med (Lond)

Issue-page numbers 2010 Jan;60(1):10-20

URL http://www.ncbi.nlm.nih.gov/pubmed/20051441

Abstract The internal circadian clock adapts slowly, if at all, to rapid transitions between different shift schedules. This leads to misalignment (desynchrony) of rhythmic physiological systems, such as sleep, alertness, performance, metabolism and the hormones melatonin and cortisol, with the imposed work-rest schedule. Consequences include sleep deprivation and poor performance. Clock gene variants may influence tolerance of sleep deprivation. Shift work is associated with an increased risk of major disease (heart disease and cancer) and this may also, at least in part, be attributed to frequent circadian desynchrony. Abnormal metabolism has been invoked as a contributory factor to the increased risk of heart disease. There is recent evidence for an increased risk of certain cancers, with hypothesized causal roles of light at night, melatonin suppression and circadian desynchrony. Various strategies exist for coping with circadian desynchrony and for hastening circadian realignment (if desired). The most important factor in manipulating the circadian system is exposure to and/or avoidance of bright light at specific times of the 'biological night'.

Keywords

Arendt J

Year 1985

Authors Josephine Arendt

Report Name Mammalian pineal rhythms

Publication Pineal Res Rev

Issue-page numbers 3:161–213

URL N/A

Abstract N/A

Keywords

Arendt J

Year 1986

Authors Josephine Arendt

Report Name Role of the pineal gland and melatonin in seasonal reproductive function in mammals.

Publication Oxf Rev Reprod Bi

Issue-page numbers 8:266–320. PMID:3540805

URL http://www.ncbi.nlm.nih.gov/pubmed/3540805

Abstract N/A

Keywords

Arendt J — *Year* 1998

Authors Josephine Arendt

Report Name Melatonin and the pineal gland: influence on mammalian seasonal and circadian physiology

Publication Reviews of Reproduction

Issue-page numbers (1998) 3, 13-22

URL http://ror.reproduction-online.org/cgi/reprint/3/1/13.pdf

Abstract The pineal hormone melatonin is secreted with a marked circadian rhythm. Normally, maximum production occurs during the dark phase of the day and the duration of secretion reflects the duration of the night. The changing profile of secretion as a function of daylength conveys photoperiodic information for the organization of seasonal rhythms in mammals. The role of melatonin in mammalian circadian physiology is less clear. However, exogenous melatonin can phase shift, and in some cases entrain, circadian rhythms in rodents and humans. It can also lower body temperature and induce transient sleepiness. These properties indicate that melatonin can be used therapeutically in circadian rhythm disorder. Successful outcomes have been reported, for example in jet lag and shift work, and with cyclic sleep disorder of some blind subjects. Melatonin receptors of several subtypes are found in the brain, the retina, the pituitary and elsewhere. They are currently under intense investigation. Melatonin agonists and antagonists are under development.

Keywords melatonin, pineal gland, circadian

Arendt J — *Year* 1988

Authors Josephine Arendt

Report Name Melatonin

Publication Clin Endocrinol (Oxf)

Issue-page numbers 29:205–229 doi:10.1111/j.1365-2265.1988.tb00263.x. PMID:3073883

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1988.tb00263.x/abstract

Abstract N/A

Keywords

Arendt J

Year 2000

Authors Josephine Arendt

Report Name Melatonin, circadian rhythms, and sleep.

Publication N Engl J Med

Issue-page numbers 343:1114–1116 doi:10.1056/NEJM200010123431510. PMID:11027748

URL http://www.nejm.org/doi/full/10.1056/NEJM200010123431510

Abstract Disturbances in circadian rhythms often result in disturbances in sleep. Examples include syndromes in which sleep time is delayed or advanced, the sleeping problems associated with jet lag and shift work, and the sleep disorders that occur in totally blind persons with free-running circadian rhythms (i.e., rhythms that are not synchronized to the 24-hour day).1 The hormone melatonin can be used both to characterize and to treat such disorders.

The circadian rhythm of melatonin secretion is generated by the central pacemaker, or “clock,” in the suprachiasmatic nuclei of the hypothalamus, and like many other circadian rhythms, it is synchronized to . . .

Keywords

Arendt J

Year 2005

Authors Josephine Arendt

Report Name Melatonin: characteristics, concerns, and prospects.

Publication J Biol Rhythms

Issue-page numbers 20:291–303 doi:10.1177/0748730405277492. PMID:16077149

URL http://isites.harvard.edu/fs/docs/icb.topic197607.files/Due_Wk_10_Nov_19/Arendt_Melatonin_review.pdf

Abstract Melatonin is of great importance to the investigation of human biological rhythms. Its rhythm in plasma or saliva provides the best available measure of the timing of the internal circadian clock. Its major metabolite 6-sulphatoxymelatonin is robust and easily measured in urine. It thus enables long-term monitoring of human rhythms in real-life situations where rhythms may be disturbed, and in clinical situations where invasive procedures are difficult. Melatonin is not only a “hand of the clock”; endogenous melatonin acts to reinforce the functioning of the human circadian system, probably in many ways. Most is known about its relationship to sleep and the decline in core body temperature and alertness at night. Current perspectives also include a possible influence on major disease risk, arising from circadian rhythm disruption.
Melatonin clearly has the ability to induce sleepiness and lower core body temperature during “biological day” and to change the timing of human rhythms when treatment is appropriately timed. It can entrain free-running rhythms and maintain entrainment in most blind and some sighted people. Used therapeutically
it has proved a successful treatment for circadian rhythm disorder, particularly the non-24-h sleep wake disorder of the blind. Numerous other clinical applications are under investigation. There are, however, areas of controversy, large gaps in knowledge, and insufficient standardization of experimental conditions
and analysis for general conclusions to be drawn with regard to most situations. The future holds much promise for melatonin as a therapeutic treatment. Most interesting, however, will be the dissection of its effects on human genes.

Keywords melatonin, light, rhythms, human

Arendt J

Year 1995

Authors Josephine Arendt

Report Name Melatonin and the Mammalian Pineal Gland

Publication Book

Issue-page numbers Chapman and Hall, London 1995

URL http://www.amazon.com/Melatonin-Mammalian-Pineal-Josephine-Arendt/dp/0412536005

Abstract Book

Keywords melatonin, pineal gland

Arendt J

Year 1978

Authors Josephine Arendt

Report Name Melatonin assays in body fluids.

Publication J Neural Transm Suppl

Issue-page numbers (13):265–278. PMID: 288853

URL http://www.ncbi.nlm.nih.gov/pubmed/288853

Abstract A variety of methods now exist for the assay of melatonin in body fluids. Their relative merits are compared and the validation of one in particular (RIA) described. Physiological studies of melatonin by RIA have shown probable modulation of its secretion by gonadal steroids. The circadian activity maximum in the dark phase of one of the pineal melatonin synthesizing enzymes, N-acetyltransferase, is reflected in peripheral melatonin levels. Man, like all other species studied so far, has a dark phase rise in circulating melatonin. During the menstrual cycle, melatonin shows a luteal phase rise. Further evidence of pineal rhythmicity is found in seasonal melatonin variations in man. The study of the rhythmic properties of peripheral melatonin in man may provide important information on central nervous function.

Keywords

Arendt J, Bojkowski C, Franey C et al. **Year** 1985

Authors Arendt J, Bojkowski C, Franey C et al.

Report Name Immunoassay of 6-hydroxymelatonin sulfate in human plasma and urine: abolition of the urinary 24-hour rhythm with atenolol

Publication J Clin Endocrinol Metab

Issue-page numbers 60:1166–1173 doi:10.1210/jcem-60-6-1166. PMID:3998065

URL http://jcem.endojournals.org/content/60/6/1166.short

Abstract An assessment of the rhythmic characteristics of melatonin secretion in manand other species requires the determination of 24-h secretion profiles. Measurement of a major excreted metabolite would allow noninvasive study of pineal function, applicablein particular to pediatric and long term circadian rhythm studies. This report describesa simple and rapid RIA for 6-hydroxymelatonin sulfate in human plasma and urine. Physiological studies revealed that both plasma and urinary levels of 6-hydroxymelatonin sulfate were closely related to plasma melatonin, and that the urinary 24-h rhythm was abolished by the β1-adrenergic anagonist atenolol.

Keywords

Arendt J, Borbely AA, Franey C, Wright J **Year** 1984

Authors Arendt J, Borbely AA, Franey C, Wright J

Report Name The effects of chronic, small doses of melatonin given in the late afternoon on fatigue in man: a preliminary study.

Publication Neurosci Lett

Issue-page numbers 45:317–321 doi:10.1016/0304-3940(84)90245-3. PMID:6728321

URL http://www.sciencedirect.com/science/article/pii/0304394084902453

Abstract In a double-blind cross-over study, melatonin (2 mg) or placebo, was administered daily for 4 weeks to 12 volunteers (10 men and 2 women) at 17.00 h during February and March. Self-rated fatigue (tiredness) was significantly increased in the evening during melatonin treatment. No other consistent effects on sleep ratings or mood parameters were observed and the dose was well tolerated.

Keywords melatonin; fatigue

Arendt J, Broadway J

Year 1987

Authors Josephine Arendt and James Broadway

Report Name Light and Melatonin as Zeitgebers in Man

Publication Chronobiology International

Issue-page numbers 4:2, 273-282

URL http://informahealthcare.com/doi/abs/10.3109/07420528709078534

Abstract N/A

Keywords Light, melatonin

Arendt J, Labib MH, Bojkowski C et al.

Year 1989

Authors Arendt J, Labib MH, Bojkowski C et al.

Report Name Rapid decrease in melatonin production during treatment of delayed puberty with oestradiol in a case of craniopharyngioma.

Publication Lancet

Issue-page numbers 333:1326. doi:10.1016/S0140-6736(89)92716-5

URL N/A

Abstract N/A

Keywords

Year 2008

Authors Josephine Arendt, Shantha M. W. Rajaratnam

Report Name Melatonin and its agonists: an update

Publication Br J Psychiatry

Issue-page numbers Oct;193(4):267-9.

URL http://bjp.rcpsych.org/content/193/4/267.abstract

Abstract

The pineal hormone melatonin is able to shift the timing of circadian rhythms, including the sleep–wake cycle, and to promote sleep. Melatonin agonists with similar properties have therapeutic potential for the treatment of circadian rhythm sleep disorders. Depression is specifically targeted by agomelatine, which is also a serotonin-2C (5-HT2C) antagonist.

Keywords

Authors Ariznavarreta C, Cardinali DP, Villanúa MA et al.

Report Name Circadian rhythms in airline pilots submitted to long-haul transmeridian flights

Publication Aviat Space Environ Med

Issue-page numbers 73:445–455. PMID:12014603

URL http://www.ncbi.nlm.nih.gov/pubmed/12014603

Abstract

BACKGROUND:

Circadian rhythms shift out of phase after transmeridian flights. Desynchronization between body rhythms and the environment is linked to jet lag, which depends on age, flight direction, and number of time zones crossed.
METHODS:

To investigate this problem in airline pilots, we performed a multivariate analysis of their circadian systems during Madrid-Mexico-Madrid flights (-7 time zones, n = 12) and Madrid-Tokyo-Madrid flights (+8 time zones, n = 21). Telemetry was used to record pilots' activity, skin temperature, and heart rate, obtaining 6 d of continuous data, including 2 d before the flight, the flights themselves, 2 d at the stopover, and 1 d after the return flight. Time series were analyzed by cosinor, and the resulting parameters of the rhythms were compared by ANOVA and Tukey contrasts in every category formed by the age groups (under and over 50 yr old) and flight direction groups. Subjective time estimation of short, intermediate, and long intervals was recorded. Other psychological variables were measured, including anxiety, tiredness, and performance.
RESULTS AND CONCLUSIONS:

Activity/rest and heart rate rhythms appeared to be linked to a "weak oscillator." Temperature rhythms manifested a rigid response after the phase shifts of the light/dark cycle, closely related to the biological clock. Subjective time appreciation tended to be overestimated without exhibiting a clear circadian component, but attributable to fatigue and stress. Psychometric evaluation showed that desynchronization affected all the pilots. Some results showed an age-related variability with a more marked influence in younger pilots. No consistent effects regarding flight direction were found.

Keywords

Armstrong BK, Kricker A

Year 2001

Authors Bruce K Armstrong, Anne Kricker

Report Name The epidemiology of UV induced skin cancer

Publication Journal of Photochemistry and Photobiology B: Biology

Issue-page numbers Volume 63, Issues 1-3, October 2001, Pages 8-18

URL http://www.sciencedirect.com/science/article/pii/S1011134401001981

Abstract There is persuasive evidence that each of the three main types of skin cancer, basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma, is caused by sun exposure. The incidence rate of each is higher in fairer skinned, sun-sensitive rather than darker skinned, less sun-sensitive people; risk increases with increasing ambient solar radiation; the highest densities are on the most sun exposed parts of the body and the lowest on the least exposed; and they are associated in individuals with total (mainly SCC), occupational (mainly SCC) and non-occupational or recreational sun exposure (mainly melanoma and BCC) and a history of sunburn and presence of benign sun damage in the skin. That UV radiation specifically causes these skin cancers depends on indirect inferences from the action spectrum of solar radiation for skin cancer from studies in animals and the action spectrum for dipyrimidine dimers and evidence that presumed causative mutations for skin cancer arise most commonly at dipyrimidine sites. Sun protection is essential if skin cancer incidence is to be reduced. The epidemiological data suggest that in implementing sun protection an increase in intermittency of exposure should be avoided, that sun protection will have the greatest impact if achieved as early as possible in life and that it will probably have an impact later in life, especially in those who had high childhood exposure to solar radiation.

Keywords Basal cell carcinoma; Squamous cell carcinoma; Cutaneous malignant melanoma; UVA; UVB

Ashkenazi L, Haim A

Year 2012

Authors Lilach Ashkenazi and Abraham Haim

Report Name Light Interference (LI) as a possible stressor altering HSP70 and its gene expression levels in brain and liver tissues of Golden Spiny Mice

Publication J Exp Biol

Issue-page numbers First posted online August 29, 2012 doi: 10.1242/jeb.073429

URL http://jeb.biologists.org/content/early/2012/08/21/jeb.073429.short

Abstract Light at Night (LAN) and light interference (LI) are part of modern life, which disrupt the natural light/dark cycle, causing alteration at physiological and molecular levels, partly by suppressing melatonin (MLT) secretion at night. Heat shock proteins (HSP) are activated by various stressors. We assessed HSP70 changes and gene expression in brain tissue (BT) and hepatic tissue (HT) of Golden spiny mice (Acomys russatus), acclimated to LI for 2(sLI), 7 (mLI) and 21(lLI) nights. The effect of MLT treatment on LI-mice was also assessed. HSP70 levels increased in BT and HT after sLI, while after mLI and lLI, HSP70 decreased to basic levels. Changes in HSP70 levels as a response to MLT occurred after sLI only in the HT. However, hsp70 expression following sLI increased in BT, but not in HT. MLT treatment and sLI caused decrease in hsp70 levels in BT and increase in hsp70 in HT. sLI-acclimation elicited stress response in A. russatus as expressed by increased HSP70 levels and gene expression. Longer acclimation decreases protein and gene expression to their basic levels. We conclude, that for BT and HT of A. russatus LI is a short-termed stressor, our results also revealed that A. russatus can acclimate to LI, possibly because of its circadian system plasticity, which allows it to behave both as a nocturnal and as a diurnal rodent. To the best of our knowledge, this is the first study showing the effect of LI as a stressor on the cellular level, by activating HSP70.

Keywords

Ashkenazi L, Haim A — **Year** 2013

Authors Lilach Ashkenazi, Abraham Haim

Report Name Effect of Light at Night on oxidative stress markers in Golden spiny mice (Acomys russatus) liver

Publication Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology

Issue-page numbers Volume 165, Issue 3, July 2013, Pages 353–357

URL http://www.sciencedirect.com/science/article/pii/S1095643313001037

Abstract Light at Night (LAN) suppresses melatonin (MLT) production, and effects metabolism, hormone secretion, gene expression and enzyme activity. Changes in antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase (SOD), can be used as an indication for oxidative stress level. We assayed activity and expression of these enzymes in the liver of Acomys russatus exposed to LAN and treated with MLT. Short day (SD)-acclimated A. russatus, was exposed to 30 min of LAN for two, seven or 21 nights. MLT impact was assessed simultaneously with two and seven nights of LAN exposure. GPx and SOD activities were measured. Gpx1 expression was evaluated by RT-PCR. There was a significant increase in GPx activity following LAN exposure for all acclimation durations, GPx activity was elevated after two nights of LAN and MLT treatment, Gpx1 expression was elevated by MLT after seven nights of LAN. SOD activity increased after two nights of LAN in MLT-treated A. russatus, GPx activity increased with the duration of LAN acclimation, indicating changes in liver redox status. Our results suggest that LAN is a stressor that influences oxidative stress. As in the other studies, MLT increases antioxidant activities, presumably attenuating stress response, in order to restore homeostasis.

Keywords

Aubert C, Janiaud P, Lecalvez J — **Year** 1980

Authors Aubert C, Janiaud P, Lecalvez J.

Report Name Effect of pinealectomy and melatonin on mammary tumor growth in Sprague-Dawley rats under different conditions of lighting.

Publication J Neural Transm

Issue-page numbers 1980;47(2):121-30.

URL http://www.springerlink.com/content/j2555m31j6u045j2/

Abstract Stress modifies the neurohormonal balance of biogenic amines (catecholamines and indoleamines such as serotonin and melatonin). An experimental approach for investigation of the possible role of such neurohormonal balances on tumor induction and tumor growth can be achieved by administration of melatonin, by pinealectomy or by varying the nycthemeral cycle of lighting. In the case of mammary tumors induced in female Sprague-Dawley rats by per os administration of 7.12 DMBA, two important observations were made: the carcinogenic compound alters the levels of pituitary serotonin, particularly at the level of the intermediary lobe, and melatonin seems to play a role in restricting tumor development.
These results indicate that neuro-hormonal balances, implicated in pineal-hypothalamo-pituitary hormonal regulation, play a role in tumor induction and tumor growth of mammary tumors in female rats, probably by modifying peripheral hormone secretion. The stress induced by modification of a nycthemeral cycle can, under certain experimental conditions, modify tumor response and development.

Keywords melatonin, tumor growth, rats, lighting

Aubert C, Prade M, Bohuon C **Year** 1970

Authors Aubert C, Prade M, Bohuon C

Report Name [Effect of pinealectomy on the melanic tumours of the golden hamster induced by administration (per os) of a single dose of 9,10-dimethyl-1,2-benzanthracene]

Publication C R Acad Sci Hebd Seances Acad Sci D

Issue-page numbers 271:2465–2468. PMID:4995225

URL http://www.ncbi.nlm.nih.gov/pubmed/4995225

Abstract N/A

Keywords

Aubrecht TG, Weil ZM, Magalang UJ, Nelson RJ **Year** 2013

Authors Taryn G Aubrecht, Zachary M Weil, Ulysses J. Magalang, and Randy J. Nelson

Report Name Dim Light at Night Interacts with Intermittent Hypoxia to Alter Cognitive And Affective Responses.

Publication AJP - Regu Physiol

Issue-page numbers Published online before print May 8, 2013, doi: 10.1152/ajpregu.00100.2013

URL http://ajpregu.physiology.org/content/early/2013/05/03/ajpregu.00100.2013.abstract

Abstract Obstructive sleep apnea (OSA) and dim light at night (dLAN) have both been independently associated with alterations in mood and cognition. We aimed to determine whether dLAN would interact with intermittent hypoxia (IH), a condition characteristic of OSA, to alter behavioral, cognitive, and affective responses. Adult male mice were housed in either standard lighting conditions (14:10; 150 lux:0 lux) or dLAN (150 lux:5 lux). Mice were then exposed to IH (15 cycles/h, 8 h/day, FIO2 nadir of 5%) for 3 weeks, then tested in assays of affective and cognitive responses; brains were collected for dendritic morphology and PCR analysis. Exposure to dLAN and IH increased anxiety-like behaviors as assessed in the open field, elevated plus maze, and the light/dark box. dLAN and IH increased depressive-like behaviors in the forced swim test. IH impaired learning and memory performance in the passive avoidance task, however, no differences were observed in spatial working memory as assessed by y-maze or object recognition. IH combined with dLAN decreased cell body area in the CA1 and CA3 regions of the hippocampus. Overall, IH decreased apical spine density in the CA3, whereas dLAN decreased spine density in the CA1 of the hippocampus. TNF-alpha gene expression was not altered by IH or lighting condition whereas VEGF expression was increased by dLAN. The combination of IH and dLAN provokes negative effects on hippocampal dendritic morphology, affect, and cognition, suggesting that limiting nighttime exposure to light in combination with other established treatments may be of benefit to patients with OSA.

Keywords Intermittent Hypoxia, light at night, anxiety, depression, learning and memory

Auger RR, Burgess HJ, Dierkhising RA, et al. **Year** 2011

Authors R. Robert Auger, Helen J. Burgess, Ross A. Dierkhising, Ruchi G. Sharma, and Nancy L. Slocumb

Report Name Light Exposure Among Adolescents With Delayed Sleep Phase Disorder: A Prospective Cohort Study

Publication Chronobiology International

Issue-page numbers Dec., 2011, Vol. 28, No. 10 , Pages 911-920

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.619906

Abstract The objective of this study was to compare light exposure and sleep parameters between adolescents with delayed sleep phase disorder (DSPD; n = 16, 15.3 ± 1.8 yrs) and unaffected controls (n = 22, 13.7 ± 2.4 yrs) using a prospective cohort design. Participants wore wrist actigraphs with photosensors for 14 days. Mean hourly lux levels from 20:00 to 05:00 h and 05:00 to 14:00 h were examined, in addition to the 9-h intervals prior to sleep onset and after sleep offset. Sleep parameters were compared separately, and were also included as covariates within models that analyzed associations with specified light intervals. Additional covariates included group and school night status. Adolescent delayed sleep phase subjects received more evening ($p < .02$, 22:00–02:00 h) and less morning ($p < .05$, 08:00–09:00 h and 10:00–12:00 h) light than controls, but had less pre-sleep exposure with adjustments for the time of sleep onset ($p < .03$, 5–7 h prior to onset hour). No differences were identified with respect to the sleep offset interval. Increased total sleep time and later sleep offset times were associated with decreased evening ($p < .001$ and $p = .02$, respectively) and morning ($p = .01$ and $p < .001$, respectively) light exposure, and later sleep onset times were associated with increased evening exposure ($p < .001$). Increased total sleep time also correlated with increased exposure during the 9 h before sleep onset ($p = .01$), and a later sleep onset time corresponded with decreased light exposure during the same interval ($p < .001$). Outcomes persisted regardless of school night status. In conclusion, light exposure interpretation requires adjustments for sleep timing among adolescents with DSPD. Pre- and post-sleep light exposures do not appear to contribute directly to phase delays. Sensitivity to morning light may be reduced among adolescents with DSPD.

Keywords Adolescents, Circadian, Delayed sleep phase disorder, Light, Sleep

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Axelrod J, Weissbach H **Year** 1960

Authors Axelrod J, Weissbach H

Report Name Enzymatic O-methylation of N-acetylserotonin to melatonin

Publication Science

Issue-page numbers 131:1312 doi:10.1126/science.131.3409.1312. PMID:13795316

URL http://www.sciencemag.org/content/131/3409/1312.abstract?sid=a20b9ad5-5ab2-49c7-b27f-ae46ab172e45

Abstract An enzyme, hydroxyindole-O-methyl transferase, that can transfer the methyl group of S-adenosylmethionine to the hydroxy group of N-acetylserotonin to form the hormone melatonin is described. This enzyme, which is highly localized in the pineal gland, also O-methylates serotonin.

Keywords

Baba K, Pozdeyev N, Mazzoni F, et al. **Year** 2009

Authors Kenkichi Baba, Nikita Pozdeyev, Francesca Mazzoni, Susana Contreras-Alcantara, Cuimei Liu, Manami Kasamatsu, Theresa Martinez-Merlos, Enrica Strettoi, P. Michael Iuvone

Report Name Melatonin modulates visual function and cell viability in the mouse retina via the MT1 melatonin receptor

Publication PNAS

Issue-page numbers August 14, 2009, doi: 10.1073/pnas.0904400106

URL http://www.pnas.org/content/early/2009/08/13/0904400106

Abstract A clear demonstration of the role of melatonin and its receptors in specific retinal functions is lacking. The present study investigated the distribution of MT1 receptors within the retina, and the scotopic and photopic electroretinograms (ERG) and retinal morphology in wild-type (WT) and MT1 receptor-deficient mice. MT1 receptor transcripts were localized in photoreceptor cells and in some inner retinal neurons. A diurnal rhythm in the dark-adapted ERG responses was observed in WT mice, with higher a- and b-wave amplitudes at night, but this rhythm was absent in mice lacking MT1 receptors. Injection of melatonin during the day decreased the scotopic response threshold and the amplitude of the a- and b-waves in the WT mice, but not in the MT1−/− mice. The effects of MT1 receptor deficiency on retinal morphology was investigated at three different ages (3, 12, and 18 months). No differences between MT1−/− and WT mice were observed at 3 months of age, whereas at 12 months MT1−/− mice have a significant reduction in the number of photoreceptor nuclei in the outer nuclear layer compared with WT controls. No differences were observed in the number of cells in inner nuclear layer or in ganglion cells at 12 months of age. At 18 months, the loss of photoreceptor nuclei in the outer nuclear layer was further accentuated and the number of ganglion cells was also significantly lower than that of controls. These data demonstrate the functional significance of melatonin and MT1 receptors in the mammalian retina and create the basis for future studies on the therapeutic use of melatonin in retinal degeneration.

Keywords electroretinogram, neuroprotection, visual sensitivity, glaucoma

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Baehr EK, Fogg LF, Eastman CI **Year** 1999

Authors Erin K. Baehr, Louis F. Fogg, and Charmane I. Eastman

Report Name Intermittent bright light and exercise to entrain human circadian rhythms to night work

Publication AJP - Regu Physiol

Issue-page numbers December 1999 vol. 277 no. 6 R1598-R1604

URL http://ajpregu.physiology.org/content/277/6/R1598.full

Abstract Bright light can phase shift human circadian rhythms, and recent studies have suggested that exercise can also produce phase shifts in humans. However, few studies have examined the phase-shifting effects of intermittent bright light, exercise, or the combination. This simulated night work field study included eight consecutive night shifts followed by daytime sleep/dark periods (delayed 9 h from baseline). There were 33 subjects in a 2 × 2 design that compared1) intermittent bright light (6 pulses, 40-min long each, at 5,000 lx) versus dim light and2) intermittent exercise (6 bouts, 15-min long each, at 50–60% of maximum heart rate) versus no exercise. Bright light and exercise occurred during the first 6 h of the first three night shifts. The circadian phase marker was the demasked rectal temperature minimum. Intermittent bright-light groups had significantly larger phase delays than dim-light groups, and 94% of subjects who received bright light had phase shifts large enough for the temperature minimum to reach daytime sleep. Exercise did not affect phase shifts; neither facilitating nor inhibiting phase shifts produced by bright light.

Keywords body temperature, sleep, shift work, work-schedule tolerance

Baer RL, Harber LC

Year 1965

Authors Baer RL, Harber LC.

Report Name Photobiology of lupus erythematosus

Publication Arch Dermatol

Issue-page numbers 92: 124-128

URL http://www.ncbi.nlm.nih.gov/pubmed/11850910

Abstract Ultraviolet radiation in the 2850 to 3150 angstrom range can produce abnormal cutaneous reactions and exacerbation of systemic manifestations in some cases of subacute and acute systemic lupus erythematosus. It may also be responsible for cutaneous lesions and systemic involvement in rare cases of chronic discoid lupus erythematosus--probably those with disseminated lesions. The pathophysiological mechanism producing these photobiological effects in lupus erythematosus remains unknown.

Keywords

Baigent SM

Year 2001

Authors Baigent SM

Report Name Peripheral corticotropin-releasing hormone and urocortin in the control of the immune response

Publication Peptides

Issue-page numbers 22:809–820 doi:10.1016/S0196-9781(01)00395-3. PMID:11337095

URL http://www.sciencedirect.com/science/article/pii/S0196978101003953

Abstract Immunological and cellular stress signals trigger the release of corticotropin-releasing hormone (CRH) from the spleen, thymus and inflamed tissue. In vivo and in vitro studies generally suggest that peripheral, immune CRH has pro-inflammatory effects and acts in a paracrine manner by binding to CRH-R1 and CRH-R2 receptors on neighboring immune cells. However, it now seems likely that some of the suggested pro-inflammatory actions of CRH may be attributed to novel CRH-like peptides or to the related peptide, urocortin, which is also present in immune cells and has especially high affinity for CRH-R2 receptors.

Keywords CRH; Urocortin; CRH-like peptides; CRH receptors; Peripheral immune system; Inflammation

Authors Archna Bajaj, Bernard Rosner, Steven W. Lockley, and Eva S. Schernhammer

Report Name Validation of a Light Questionnaire with Real-life Photopic Illuminance Measurements: the Harvard Light Exposure Assessment Questionnaire

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers July 2011 20; 1341 doi: 10.1158/1055-9965.EPI-11-0204

URL http://cebp.aacrjournals.org/content/20/7/1341.short

Abstract

Background: Shift work, which necessitates light exposure at night, is now considered a probable carcinogen. To study the effects of light on chronic diseases like cancer, methods to measure light exposure in large observational studies are needed. We aimed to investigate the validity of self-reported current light exposure.

Methods: We developed a self-administered semiquantitative light questionnaire, the Harvard Light Exposure Assessment (H-LEA) questionnaire, and compared photopic scores derived from this questionnaire with actual photopic and circadian measures obtained from a real-life 7-day light meter application among 132 women (85 rotating night shift workers and 47 day workers) participating in the Nurses' Health Study II.

Results: After adjustment for age, body mass index (BMI), collection day, and night work status, the overall partial Spearman correlation between self-report of light exposure and actual photopic light measurements was 0.72 ($P < 0.001$; Kendall $\tau = 0.57$) and 0.73 ($P < 0.0001$; Kendall $\tau = 0.58$) when correlating circadian light measurements. There were only minimal differences in accuracy of self-report of light exposure and photopic or “circadian” light measurement between day ($r = 0.77$ and 0.78, respectively) and rotating night shift workers ($r = 0.68$ and 0.69, respectively).

Conclusions: The results of this study provide evidence of the criterion validity of self-reported light exposure using the H-LEA questionnaire.

Impact: This questionnaire is a practical method of assessing light exposure in large-scale epidemiologic studies.

Keywords

Baker FC, Driver HS

Year 2007

Authors Baker FC, Driver HS

Report Name Circadian rhythms, sleep, and the menstrual cycle

Publication Sleep Med

Issue-page numbers 8:613–622 doi:10.1016/j.sleep.2006.09.011. PMID:17383933

URL http://www.sciencedirect.com/science/article/pii/S1389945706006216

Abstract Women with ovulatory menstrual cycles have a circadian rhythm superimposed on the menstrual-associated rhythm; in turn, menstrual events affect the circadian rhythm. In this paper, we review circadian rhythms in temperature, selected hormone profiles, and sleep–wake behavior in healthy women at different phases of the menstrual cycle. The effects on menstrual cycle rhythmicity of disrupted circadian rhythms, for example, with shiftwork and altered circadian rhythms in women with menstrual-related mood disturbances, are discussed. Compared to the follicular phase, in the post-ovulation luteal phase, body temperature is elevated, but the amplitude of the temperature rhythm is reduced. Evidence indicates that the amplitude of other rhythms, such as melatonin and cortisol, may also be blunted in the luteal phase. Subjective sleep quality is lowest around menses, but the timing and composition of sleep remains relatively stable across the menstrual cycle in healthy women, apart from an increase in spindle frequency activity and a minor decrease in rapid eye movement (REM) sleep during the luteal phase. Disruption of circadian rhythms is associated with disturbances in menstrual function. Female shiftworkers compared to non-shiftworkers are more likely to report menstrual irregularity and longer menstrual cycles. There also is accumulating evidence that circadian disruption increases the risk of breast cancer in women, possibly due to altered light exposure and reduced melatonin secretion. Further investigations into the biological consequences of circadian disruption in women will offer insight into some menstrual-associated disorders, including mood changes, as well as reproductive function and possible links with breast cancer.

Keywords Women; Menstrual cycle; Temperature; Melatonin; Shiftwork; Premenstrual syndrome

Balasubramanian D

Year 2000

Authors Balasubramanian D.

Report Name Ultraviolet radiation and cataract

Publication J Ocul Pharmacol Ther

Issue-page numbers Jun;16(3):285-97.

URL http://www.ncbi.nlm.nih.gov/pubmed/10872925

Abstract While solar radiation falling on earth comprises light in the infrared, visible, UVA, UVB, and even UVC ranges, the light incident on, and thus important to the biology of, the eye lens is essentially in the visible and UVA regions. Thus, direct photochemical damage to the lens from UVB radiation is minor, though long-term UVA (and even visible range) irradiation is seen to lead to lens malfunction. Short-term exposure of the lens in vivo to UVA light leads to compromised optical and biochemical properties which are repaired in time, while higher doses affect permanent damage. Such longer wavelength light-mediated changes in the lens occur through photodynamic means, affected by some of the compounds that accumulate in the lens over a period of time, which act as sensitizers. Isolation and chemical identification of over a dozen such compounds has been done, and their photoactive properties have been studied. While several of these are photodynamic and generate reactive oxygen species when UVA light is shone on them, other compounds that accumulate in the lens act as antioxidants.

Keywords

Baldwin WS, Barrett JC **Year** 1998

Authors Baldwin WS, Barrett JC

Report Name Melatonin attenuates hydrogen peroxide toxicity in MCF7 cells only at pharmacological concentrations

Publication Biochem Biophys Res Commun

Issue-page numbers 250:602–605 doi:10.1006/bbrc.1998.9370. PMID:9784392

URL http://www.ingentaconnect.com/content/ap/rc/1998/00000250/00000003/art09370

Abstract Melatonin is proposed to be oncostatic in mammary tissue, and one mechanism by which this hormone may elicit its possible oncostatic effect is as an oxygen radical scavenger Therefore, we examined melatonin's abilities to act as an oxygen radical scavenger at physiological or pharmacological concentrations. Hydrogen peroxide at 400 mgrM killed 97% of treated MCF7 cells within 8 h, and following melatonin at 10-5 and 10-4 M concentrations only 76 and 64% of cells, respectively, were killed by hydrogen peroxide. However, melatonin at lower concentrations (10-7 M) did not protect MCF7 cells. Moreover, pretreatment with melatonin (10-5 or 10-7 M) prior to hydrogen peroxide stress offered no further efficacy, and pretreatment with melatonin followed by the withdrawal of melatonin eliminated its protective effect from hydrogen peroxide toxicity. These findings indicate that melatonin acts directly as an antioxidant and does not stimulate antioxidant defenses in MCF7 cells that protect against hydrogen peroxide. Glutathione levels were examined to substantiate this hypothesis and were not altered by melatonin treatment. In conclusion, melatonin is an excellent oxygen radical scavenger at pharmacological concentrations, but not at physiological concentrations. Thus, loss of melatonin is unlikely to be important in oxidative scavenger mechanisms in human mammary cells.

Keywords

Baldwin WS, Travlos GS, Risinger JI, Barrett JC **Year** 1998

Authors Baldwin WS, Travlos GS, Risinger JI, Barrett JC

Report Name Melatonin does not inhibit estradiolstimulated proliferation in MCF-7 and BG-1 cells.

Publication Carcinogenesis

Issue-page numbers 19:1895–1900 doi:10.1093/carcin/19.11.1895. PMID:9854999

URL http://carcin.oxfordjournals.org/content/19/11/1895.full.pdf

Abstract Melatonin, an indolic pineal hormone, is produced primarily at night in mammals and is important in controlling biological rhythms. Previous research suggested that melatonin can attenuate proliferation in the estrogen-responsive MCF-7 breast cancer cell line. We tested whether these anti-proliferative effects may have physiological consequences upon two estrogen-responsive cell lines, MCF-7 (a breast cancer cell line) and BG-1 (an ovarian adenocarcinoma cell line). Melatonin (10(-9)-10(-5) M) attenuated proliferation of MCF-7 and BG-1 cells by >20% in the absence of estrogen. However, 17beta-estradiol exposure negated the ability of melatonin to inhibit proliferation. To substantiate this finding, cells were estrogen starved followed by multiple treatments with estradiol and melatonin. Melatonin did not inhibit estradiol-stimulated proliferation under this protocol. Estradiol increased MCF-7 and BG-1 cell cycle transition from G1 to S phase, however, melatonin did not inhibit this transition nor did it down-regulate estradiol-induced pS2 mRNA levels measured by northern blotting, further indicating that melatonin was unable to attenuate estradiol-induced proliferation and gene expression. We also examined the effects of melatonin on estradiol-induced proliferation in MCF-7 cell xenografts in athymic nude mice. Melatonin at a dose 28 times greater than 17beta-estradiol did not inhibit estradiol-induced proliferation in vivo. Furthermore, pinealectomy did not increase proliferation. Therefore, we conclude that melatonin does not directly inhibit estradiol-induced proliferation.

Keywords

Authors PHILIP L. BALLARD, JOHN D. BAXTER, STEPHEN J. HIGGINS, GUY G. ROUSSEAU and

Report Name General presence of glucocorticoid receptors in mammalian tissues

Publication Endocrinology

Issue-page numbers 94:998–1002 doi:10.1210/endo-94-4-998. PMID:4362047

URL http://endo.endojournals.org/content/94/4/998

Abstract The adrenal glucocorticoids are almost ubiquitous as physiologic regulators in mammalian tissues. The present experiments show that specific cytoplasmic “receptors” for glucocorticoids are present in most tissues of the juvenile rat and rabbit which respond to these hormones. These findings suggest that most physiologic effects of glucocorticoids are mediated through these receptors. A few tissues such as prostate, uterus, and seminal vesicle lack the receptor and thus may not be direct “targets” for glucocorticoids. Receptor levels in juvenile and fetal rabbit tissues are generally similar. However, with rabbit thymus and rat lung there are marked changes during development, suggesting that in some cases developmental changes in receptor levels may determine hormone responsiveness.

Keywords

Authors Ballard T, Lagorio S, De Angelis G, Verdecchia A

Report Name Cancer incidence and mortality among flight personnel: a meta-analysis

Publication Aviat Space Environ Med

Issue-page numbers 71:216–224. PMID:10716165

URL http://www.ncbi.nlm.nih.gov/pubmed/10716165

Abstract

Increased cancer risk among flight personnel have previously been noted, including breast cancer among flight attendants and acute myeloid leukemia among pilots. Hypothesis: Exposure to cosmic radiation and other physical or chemical agents may pose health risks for flight personnel.
METHODS:

We performed an exhaustive search for published and unpublished cohort studies of flight personnel from 1986-98. We combined relative risks (RR) for selected causes from four mortality and/or incidence studies of pilots and two incidence studies of flight attendants, using standard meta-analytic methods. Heterogeneity among the combined studies was explored and adjustments were made for possible confounding by socioeconomic status (SES), where indicated, using correction factors from published studies.
RESULTS:

SES-adjusted combined RRs were elevated (>1.2) among male pilots for mortality from melanoma 11.97 (95%, CI: 1.02-3.82)] and brain cancer [1.49 (0.89-2.20)], and for cancer incidence of the prostate [1.65 (1.19-2.29)] and the brain [1.74 (0.87-3.30)]. Among female flight attendants, increases were seen for incidence of all cancers [1.29 (0.98-1.70)], melanoma [11.54 (0.83-2.87)], and breast cancer [1.35 (1.00-1.83)].
CONCLUSIONS:

Flight personnel appear to be at increased risk for several types of cancer. Both occupational exposures and well-established non-occupational risk factors may contribute to this increased risk. To better control for confounding factors and to identify exposures potentially amenable to preventive measures, future studies should compare risks within cohorts by flight routes, work history, and exposure to cosmic and UV radiation, electromagnetic fields, and chemical substances.

Keywords

Balsalobre A, Brown SA, Marcacci L et al. **Year** 2000

Authors Aurélio Balsalobre, Steven A. Brown, Lysiane Marcacci, François Tronche, Christoph Kellendonk, Holger M. Reichardt, Günther Schütz and Ueli Schibler

Report Name Resetting of circadian time in peripheral tissues by glucocorticoid signaling.

Publication Science

Issue-page numbers 289:2344–2347 doi:10.1126/science.289.5488.2344. PMID:11009419

URL http://www.sciencemag.org/content/289/5488/2344.short

Abstract In mammals, circadian oscillators reside not only in the suprachiasmatic nucleus of the brain, which harbors the central pacemaker, but also in most peripheral tissues. Here, we show that the glucocorticoid hormone analog dexamethasone induces circadian gene expression in cultured rat-1 fibroblasts and transiently changes the phase of circadian gene expression in liver, kidney, and heart. However, dexamethasone does not affect cyclic gene expression in neurons of the suprachiasmatic nucleus. This enabled us to establish an apparent phase-shift response curve specifically for peripheral clocks in intact animals. In contrast to the central clock, circadian oscillators in peripheral tissues appear to remain responsive to phase resetting throughout the day.

Keywords

Balsalobre A, Damiola F, Schibler **Year** 1998

Authors Balsalobre A, Damiola F, Schibler

Report Name A serum shock induces circadian gene expression in mammalian tissue culture cells.

Publication Cell

Issue-page numbers 93:929–937 doi:10.1016/S0092-8674(00)81199-X. PMID:9635423

URL http://www.cell.com/abstract/S0092-8674%2800%2981199-X

Abstract The treatment of cultured rat-1 fibroblasts or H35 hepatoma cells with high concentrations of serum induces the circadian expression of various genes whose transcription also oscillates in living animals. Oscillating genes include rper1 and rper2(rat homologs of the Drosophila clock gene period), and the genes encoding the transcription factors Rev-Erbα, DBP, and TEF. In rat-1 fibroblasts, up to three consecutive daily oscillations with an average period length of 22.5 hr could be recorded. The temporal sequence of the various mRNA accumulation cycles is the same in cultured cells and in vivo. The serum shock of rat-1 fibroblasts also results in a transient stimulation of c-fos and rper expression and thus mimics light-induced immediate-early gene expression in the suprachiasmatic nucleus.

Keywords

Authors Band PR, Le ND, Fang R et al.

Report Name Cohort study of Air Canada pilots: mortality, cancer incidence, and leukemia risk

Publication Am J Epidemiol

Issue-page numbers 143:137–143. PMID:8546114

URL http://aje.oxfordjournals.org/content/143/2/137.full.pdf

Abstract

Despite the special working environment and exposures of airline pilots, data on risk of death and cancer incidence in this occupational group are limited. The authors investigated a cohort of 2,740 Air Canada pilots who contributed 62,449 person-years of observation. All male pilots employed for at least 1 year on and since January 1,1950, were studied. The cutoff date for outcome information was December 31,1992. Standardized mortality ratio (SMR) and standardized incidence ratio (SIR) were used to compare mortality rates and cancer incidence rates of the cohort with the respective Canadian population rates. Ninety percent confidence intervals of the SMR and SIR were calculated. Statistically significant decreased mortality was observed for all causes (SMR = 0.63, 90% confidence interval (CI) 0.56-0.70), for all cancers (SMR = 0.61, 90% CI 0.48-0.76), and for all noncancer diseases (SMR = 0.53, 90% CI 0.45-0.62). Mortality from aircraft accidents was significantly raised (SMR = 26.57, 90% CI 19.3-35.9). Significantly decreased cancer incidence was observed for all cancers (SIR = 0.71, 90% CI 0.61-0.82), rectal cancer (SIR = 0.42, 90% CI 0.14-0.96), lung cancer (SIR = 0.28, 90% CI 0.16-0.46), and bladder cancer (SIR = 0.36, 90% CI 0.12-0.82). Prostate cancer (SIR = 1.87, 90% CI 1.38-2.49) and acute myeloid leukemia (SIR = 4.72, 90% CI 2.05-9.31) were significantly increased. The preferred relative risk model for radiation-induced nonchronic lymphoid leukemia (Beir V report) was applied to the cohort by using published estimates of in-flight radiation exposures. The estimated relative risk ranged from 1.001 to 1.06 and did not differ significantly from the observed SIR (SIR = 1.88, 90% CI 0.80-3.53). However, the incidence rate of acute myeloid leukemia was significantly increased. Monitoring of in-flight radiation exposure and long-term follow-up of civil aviation crew members is needed to further assess cancer incidence and leukemia risk in this special occupational group.

Keywords aviation; leukemia; mortality; neoplasms; risk

Authors Band PR, Spinelli JJ, Ng VT, Moody J, Gallagher RP.

Report Name Mortality and cancer incidence in a cohort of commercial airline pilots

Publication Aviat Space Environ Med

Issue-page numbers 61:299–302. PMID:2339962

URL http://www.ncbi.nlm.nih.gov/pubmed/2339962

Abstract We undertook a cohort study of all male pilots employed since January 1, 1950, by CP Air, now Canadian Airlines International. A total of 913 eligible pilots--630 active and 283 no longer employed--contributing 18,060 person-years of observation, were identified through company records. As of October 31, 1988, current status was obtained on 891 (97.6%). Standardized mortality ratio (SMR) and standardized incidence ratio (SIR) were used to compare, respectively, the mortality and cancer incidence of the cohort with that of the British Columbia population. Statistical significance of the SMR and SIR by comparison with the Poisson distribution (p less than 0.05 one-sided) and 90% confidence intervals (CI) were calculated. Excess deaths were observed for aircraft accidents (No. = 23; SMR = 21.29; p less than 0.001; CI 14.60, 30.20), brain cancer (No. = 4; SMR = 4.17, p = 0.017; CI 1.40, 9.50) and rectal cancer (No. = 3; SMR = 4.35; p = 0.033; CI 1.20, 11.20). Excess cancer incidence was noted for non-melanoma skin cancer (No. = 26; SIR = 1.59; p = 0.017; CI 1.10, 2.20), brain cancer (No. = 4; SIR = 3.45; p = 0.030; CI 1.20, 7.90) and Hodgkin's Disease (No. = 3; SIR = 4.54; p = 0.030; CI 1.20, 11.70). These findings, suggesting an excess risk for certain cancers in commercial airline pilots, are based on small numbers and need to be confirmed in larger cohort studies.

Keywords

Authors Pamela Barbadoro, Lory Santarelli, Nicola Croce, Massimo Bracci, Daniela Vincitorio, Emilia Prosperol, Andrea Minelli

Report Name Rotating Shift-Work as an Independent Risk Factor for Overweight Italian Workers: A Cross-Sectional Study

Publication PLoS ONE

Issue-page numbers 8(5): e63289. doi:10.1371/journal.pone.0063289

URL http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0063289

Abstract

Background
A job-related factor is attracting a growing interest as a possible determinant of body weight gain in shift-workers.
Objective

The aim of the study was to reinvestigate the issue of overweight between rotating shift workers and daytime workers, taking into consideration possible confounding covariate factors.
Methods

This is a cross-sectional study, conducted by reviewing data from subjects participating in an occupational surveillance program in 2008. Participants answered a self-administered questionnaire to retrieve information about socio-demographic factors and working conditions (job schedule type, job-related physical activity, time in job), subjective health status, health care visits during the previous year, and lifestyle factors (dietary habits, leisure time physical activity, alcohol consumption). Participants underwent a medical examination for measurement of BMI, and acquisition of medical history.
Results

Compared to daytime workers (N = 229), rotating shift workers (N = 110) displayed higher BMI (mean BMI was 27.6±3.9 and 26.7±3.6 for shift workers, and daytime workers, respectively; $p<0.05$). Logistic regression analysis allowed to highlight the role of rotating shift-work as an independent risk factor for increased body weight (OR 1.93, 95%CI 1.01–3.71), being aged between 35 and 54 years was a major determinant of increased BMI (OR 2.39, 95%CI 1.14–5.00). In addition, family history of obesity was the strongest determinant of overweight/obesity (OR 9.79, 95%CI 1.28–74.74). Interestingly, no significant association was found between overweight and other potentially relevant factors, such as diet quality and food choices, alcohol consumption, levels of occupational and leisure-time physical activity.
Conclusions

Present findings seem to support the notion that rotating shift work is an independent risk factor for overweight, regardless of workers' dietary habits and physical activity levels.

Keywords

Barclay JL, Husse J, Bode B, et al. **Year** 2012

Authors Johanna L. Barclay, Jana Husse, Brid Bode, Nadine Naujokat, Judit Meyer-Kovac, Sebastian M. Schmid, Hendrik Lehnert, Henrik Oster

Report Name Circadian Desynchrony Promotes Metabolic Disruption in a Mouse Model of Shiftwork

Publication PLoS ONE

Issue-page numbers 7(5): e37150. doi:10.1371/journal.pone.0037150

URL http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0037150

Abstract

Shiftwork is associated with adverse metabolic pathophysiology, and the rising incidence of shiftwork in modern societies is thought to contribute to the worldwide increase in obesity and metabolic syndrome. The underlying mechanisms are largely unknown, but may involve direct physiological effects of nocturnal light exposure, or indirect consequences of perturbed endogenous circadian clocks. This study employs a two-week paradigm in mice to model the early molecular and physiological effects of shiftwork. Two weeks of timed sleep restriction has moderate effects on diurnal activity patterns, feeding behavior, and clock gene regulation in the circadian pacemaker of the suprachiasmatic nucleus. In contrast, microarray analyses reveal global disruption of diurnal liver transcriptome rhythms, enriched for pathways involved in glucose and lipid metabolism and correlating with first indications of altered metabolism. Although altered food timing itself is not sufficient to provoke these effects, stabilizing peripheral clocks by timed food access can restore molecular rhythms and metabolic function under sleep restriction conditions. This study suggests that peripheral circadian desynchrony marks an early event in the metabolic disruption associated with chronic shiftwork. Thus, strengthening the peripheral circadian system by minimizing food intake during night shifts may counteract the adverse physiological consequences frequently observed in human shift workers.

Keywords

Authors Barghini A, de Medeiros BA.

Report Name Artificial lighting as a vector attractant and cause of disease diffusion.

Publication Environ Health Perspect

Issue-page numbers 2010 Nov;118(11):1503-6.

URL http://www.ncbi.nlm.nih.gov/pubmed/20675268

Abstract

BACKGROUND: Traditionally, epidemiologists have considered electrification to be a positive factor. In fact, electrification and plumbing are typical initiatives that represent the integration of an isolated population into modern society, ensuring the control of pathogens and promoting public health. Nonetheless, electrification is always accompanied by night lighting that attracts insect vectors and changes people's behavior. Although this may lead to new modes of infection and increased transmission of insect-borne diseases, epidemiologists rarely consider the role of night lighting in their surveys.

OBJECTIVE: We reviewed the epidemiological evidence concerning the role of lighting in the spread of vector-borne diseases to encourage other researchers to consider it in future studies.

DISCUSSION:We present three infectious vector-borne diseases-Chagas, leishmaniasis, and malaria-and discuss evidence that suggests that the use of artificial lighting results in behavioral changes among human populations and changes in the prevalence of vector species and in the modes of transmission.

CONCLUSION: Despite a surprising lack of studies, existing evidence supports our hypothesis that artificial lighting leads to a higher risk of infection from vector-borne diseases. We believe that this is related not only to the simple attraction of traditional vectors to light sources but also to changes in the behavior of both humans and insects that result in new modes of disease transmission. Considering the ongoing expansion of night lighting in developing countries, additional research on this subject is urgently needed.

Keywords lighting, disease

Bargiello TA, Jackson FR, Young MW | ***Year*** 1984

Authors Bargiello TA, Jackson FR, Young MW

Report Name Restoration of circadian behavioural rhythms by gene transfer in Drosophila

Publication Nature

Issue-page numbers 312:752–754 doi:10.1038/312752a0. PMID:6440029

URL http://www.nature.com/nature/journal/v312/n5996/abs/312752a0.html

Abstract The per locus of Drosophila melanogaster has a fundamental role in the construction or maintenance of a biological clock. Three classes of per mutations have been identified: per l mutants have circadian behavioural rhythms with a 29-h rather than a 24-h period, per s mutants have short-period rhythms of 19 h, and per 0 mutants have no detectable circadian rhythms1–4. Each of these mutations has a corresponding influence on the 55-s periodicity of male courtship song5. Long-and short-period circadian rhythm phenotypes can also be obtained by altering the dosage of the wild-type gene4: for example, females carrying only one dose of this X-linked gene have circadian rhythms with periodicities about 1 h longer than those carrying two doses. In a previous report6, cloned DNA was used to localize several chromosomal rearrangement breakpoints that alter per locus function. The rearrangements all affected a 7-kilobase (kb) interval that encodes a 4.5-kb poly(A)+ RNA. We report here that when a 7.1-kb fragment from a per + fly, including the sequences encoding the 4.5-kb transcript, is introduced into the genome of a per 0 (arrhythmic) fly by P element-mediated transformation, circadian rhythmicity of behaviour such as eclosion and locomotor activity is restored. The transforming DNA complements per locus deletions and is transcribed, forming a single 4.5-kb poly(A)+ RNA comparableto that produced by wild-type flies.

Keywords

Barnes RG, Deacon SJ, Forbes MJ, Arendt J | ***Year*** 1998

Authors Barnes RG, Deacon SJ, Forbes MJ, Arendt J

Report Name Adaptation of the 6-sulphatoxymelatonin rhythm in shiftworkers on offshore oil installations during a 2-week 12-h night shift

Publication Neurosci Lett

Issue-page numbers 241:9–12 doi:10.1016/S0304-3940(97)00965-8. PMID:95022

URL http://www.sciencedirect.com/science/article/pii/S0304394097009658

Abstract The circadian rhythms of most shiftworkers do not adapt to night shift. We have studied oil workers on a rotating system involving 2 weeks day shift (0600–1800 h) and 2 weeks night shift (1800–0600 h) throughout a day and night shift sequence. Urine samples were collected 3-hourly whilst awake, with an over-sleep collection, for the measurement of 6 sulphatoxymelatonin by radioimmunoassay. In three separate groups results showed adaptation by delay of the 6-sulphatoxymelatonin rhythm in the first week of night shift. The rates of phase shift (mean±SEM) were 1.51±0.16 h/day (n=5), 1.32±0.41 h/day (n=5) and 1.77±0.31 h/day (n=17). Specific environmental and social factors together with the shift schedule on oil rigs may facilitate adaptation to a 12 h night shift within a week.

Keywords Melatonin; 6-Sulphatoxymelatonin; Shiftwork; Circadian rhythm

Barnes RG, Forbes MJ, Arendt J **Year** 1998

Authors Barnes RG, Forbes MJ, Arendt J

Report Name Shift type and season affect adaptation of the 6-sulphatoxymelatonin rhythm in offshore oil rig workers.

Publication Neurosci Lett

Issue-page numbers 252:179–182 doi:10.1016/S0304-3940(98)00585-0. PMID:9739990

URL http://www.sciencedirect.com/science/article/pii/S0304394098005850

Abstract Previously we have shown that the 6-sulphatoxymelatonin rhythm of oil rig workers on a 2-week night shift (1800–0600 h) adapts to the shift via a phase delay. We now report the findings of a study on two offshore drill crews working a 1 week day (1200–0000 h), 1 week night (0000–1200 h) swing shift. Urine samples were collected every 2–3 h throughout the subjective days, with over-sleep collections, for the measurement of 6-sulphatoxymelatonin by radioimmunoassay. One crew (n=11), studied in November, showed no change in their 6-sulphatoxymelatonin rhythm during night shift. The other crew (n=7), studied in March, showed a significant phase advance of the rhythm during night shift. The data indicate that both the type of shift and the season influence the direction and degree of adaptation.

Keywords Melatonin; 6-Sulphatoxymelatonin; Shiftwork; Circadian rhythm

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Barone RM, Abe R, Das Gupta TK **Year** 1972

Authors Barone RM, Abe R, Das Gupta TK

Report Name Pineal ablation in methylcholanthrene-induced fibrosarcoma

Publication Surg Forum

Issue-page numbers 23:115–116. PMID:4671044

URL http://www.ncbi.nlm.nih.gov/pubmed/4671044

Abstract N/A

Keywords

Year 1970

Authors Barone RM, Das Gupta TK

Report Name Role of pinealectomy on Walker 256 carcinoma in rats

Publication J Surg Oncol

Issue-page numbers 2:313–322 doi:10.1002/jso.2930020402. PMID:5520847

URL http://onlinelibrary.wiley.com/doi/10.1002/jso.2930020402/abstract?

Abstract

After years of investigation, today it is generally agreed that mammalian pineal is a functioning organ with endocrine-like properties. Several investigators in the past have shown that pinealectomy possibly alters the growth and spread of tumors in rodents. An experimental system has been devised in this laboratory to study the effects of pinealectomy on the growth and spread of Walker 256 carcinoma in rats. One hundred and ten inbred Holtzman male rats weighing 40–60 g were used. Thirty-nine rats were pinealectomized. Thirty-five rats were subjected to a comparative trauma and bleeding but the pineal was left intact (sham-operated). Thirty-six rats served as controls. Five weeks after operation all the rats were inoculated with 500,000 tumor cells. The rats were observed for 23 days after tumor inoculation. Autopsies were performed on the twenty-fourth day. Results showed the tumor volumes were 149.37 ± 26.46 ml in pinealectomized rats, 104.79 ± 19.97 ml in the sham-operated group, and 103.59 ± 19.61 ml in the control group. This was statistically significant (p = 0.01). Metastatic tumor involvement of the mediastinal lymph nodes occurred in 82% of the pinealectomized rats versus 38% of the controls and 46% of sham-operated animals. Metastatic tumor involvement occurred in 79% of the lungs in pinealectomized rats versus 31% in the sham-operated and 36% in the control animals.

Keywords

Authors Bartness TJ, Song CK, Demas GE

Report Name SCN efferents to peripheral tissues: implications for biological rhythms

Publication J Biol Rhythms

Issue-page numbers 16:196–204. PMID:11407779

URL http://sites.bio.indiana.edu/~demaslab/Sites/Publications_files/Bartness%20J%20Biol%20Rhythm%20SCN%20PRV%20rev%202001.pdf

Abstract

The suprachiasmatic nucleus (SCN) is the principal generator of circadian rhythms and is part of an entrainment system that synchronizes the animal with its environment. Here, the authors review the possible communication of timing information from the SCN to peripheral tissues involved in regulating fundamental physiological functions as revealed using a viral, transneuronal tract tracer, the pseudorabies virus (PRV). The sympathetic nervous system innervation of the pineal gland and the sympathetic outflow from brain to white adipose tissue were the first demonstrations of SCN-peripheral tissue connections. The inclusion of theSCNas part of these and other circuits was the result of lengthened postviral injection times compared with those used previously. Subsequently, theSCNhas been found to be part of the sympathetic outflow fromthe brain to brown adipose tissue, thyroid gland, kidney, bladder, spleen, adrenal medulla, and perhaps the adrenal cortex. The SCN also is involved in the parasympathetic nervous system innervation of the thyroid, liver, pancreas, and submandibular gland. Individual SCN neurons appear connected to more than one autonomic circuit involving both sympathetic and parasympathetic innervation of a single tissue, or sympathetic innervation of two different peripheral tissues. Collectively, the results of these PRV studies require an expansion of the traditional roles of the SCN to include the autonomic innervation of peripheral tissues and perhaps the modulation of neuroendocrine systems traditionally thought to be controlled solely by hypothalamic stimulating/inhibiting factors.

Keywords tract tracing, pseudorabies virus, pineal gland, adipose tissue, thyroid, sympathetic

Bartsch C

Year 2010

Authors Christian Bartsch

Report Name Light-at-night, cancer and aging

Publication Aging (Albany NY)

Issue-page numbers 2010 February; 2(2): 76–77

URL http://www.impactaging.com/papers/v2/n2/pdf/100126.pdf

Abstract Recently, the International Agency for Research on Cancer (IARC) concluded that "shift-work that involves circadian disruption is probably carcinogenic to humans" [1]. This conclusion was based upon limited evidence in humans [2,3] and sufficient evidence in experimental animals [4,5]. The current experimental results of Vinogradova and colleagues from Petrozavodsk and St. Petersburg render further support to this important issue and indicate a number of highly relevant points that will have to be taken into consideration for a better understanding of the mechanisms involved and possible extrapolations to the situation in humans. Their aim was see in which way constant bright light of 750 Lux (LL) may affect survival and tumor development of normal outbred male and female rats of the LIO-strain in comparison to animals kept under a standard photoperiod of LD=12h:12h. LL was applied life-long starting from either 1 or 14 months of age. At one month of age animals are becoming sexually mature whereas at 14 months sexual competence declines. The authors found that dramatic life-shortening effects are observed among female rats, particularly in those where LL-treatment was started at one month of age. They interpret these findings to indicate that constant light probably exerts its detrimental effects on health, tumorigenesis as well as survival via disturbances of the female reproductive cycle [6]. The mechanisms involved can be assumed to include the pineal hormone melatonin as well which as chemical signal of darkness and controlled by the central circadian clock in the N. suprachiasmatici [7] may play a very central part since it is suppressed by LL and participates in the neuroendocrine control of the female reproductive system. In addition, the authors present interesting data that disturbances in the regulation of the anti-oxidative enzymes superoxide-dismutase and catalase due to LL are also involved. These enzymes are known to be controlled by melatonin due to its anti-oxidative action [8]. These fascinating results of the team led by V.N. Anisimov clearly show that for a better understanding of the highly relevant issue of shift-work but also of jet-lag and space-flight and other life-styles connected with circadian disruption [9-12] it will be important to specifically consider developmental aspects. It appears to be very clear that photoperiodic experiences early in life are essential determinants for carcinogenic processes to develop at higher age. An important question to be addressed by future experiments is whether there might be a critical period towards the negative effects of LL in and around early adulthood or whether circadian disturbances have to persist over a longer period of time throughout life to promote cancer. We have to be thankful to the authors that they have started to open our eyes to consider such basic and complex issues and it will have to be seen in which way these findings will be applicable to women who are increasingly afflicted by breast cancer.

Keywords LAN, cancer, aging, circadian clock, melatonin, light at night

Bartsch C, Bartsch H

Year 2011

Authors Christian Bartsch and Hella Bartsch

Report Name Pineal Gland and Cancer—An Epigenetic Approach to the Control of Malignancy: Evaluation of the Role of Melatonin

Publication Madame Curie Bioscience Database [Internet]

Issue-page numbers online

URL http://www.ncbi.nlm.nih.gov/books/NBK6233/

Abstract

The secretion of the pineal hormone melatonin is under control of the hypothalamic suprachiasmatic nuclei, the seat of the central circadian clock, and conveys information concerning time of day as well as season to practically all parts of the body. This means that melatonin is an integral part of the circadian time-keeping system. According to the summarized findings a link exists between the pineal gland and cancer, a mutual and dynamic interaction between the secretion of melatonin and malignant growth. A fresh tumor is “sensed” by the pineal gland via neuroimmunoendocrine changes leading to a stimulation of melatonin secretion which in turn activates endogenous defence processes. At this stage of cancer development melatonin can exert a direct tumor-inhibitory activity. If the tumor increases in size the circulating levels of melatonin are depleted in many types of cancer being accompanied by progressing circadian neuroendocrine as well as vegetative disturbances. Such weakening of the temporal structure of the sub-systems of the host can be viewed as a preparatory step for a successful seeding of metastases. Evidence exists that melatonin is trapped by cancerous tissue which may even possess the feature of ectopic melatonin production from its precursor amino acid tryptophan which in turn limits pineal melatonin production further in the presence of big cancerous masses. Although melatonin does not directly inhibit advanced tumors its substitutional administration appears to be beneficial by overcoming sleep disturbances as well as by fostering the endorphin system leading to a better quality of life. These favourable effects on the central nervous system seem to facilitate a mobilization of endogenous defence mechanisms against the malignant process improving survival. This means that melatonin via indirect systemic mechanisms is able to favourably affect even advanced forms of malignancy. These facts can be viewed as evidence for an involvement of the pineal gland in temporal epigenetic control processes of cancer. On the basis of the present findings it appears to be justified to advocate the development of new strategies for the treatment of solid tumors in which melatonin is combined with conventional therapies. In case of leukemias, however, melatonin should be avoided since it may, due to its stimulatory effects on the haematopoietic system, aggravate this disease. The dynamic changes of circulating melatonin occurring during different phases of malignant disease could be used for diagnostic purposes if intra-individual changes are specifically considered. Evidence exists that other low-molecular weight pineal substances may also play a role possessing a tumor-inhibitory activity even on undifferentiated tumor cells which are refractory to melatonin. Since there are indications that these new pineal substances may be regulated by melatonin the central role of the main pineal hormone in the link between the pineal gland and cancer is thus emphasized.

Keywords

Bartsch C, Bartsch H — *Year* 2006

Authors Bartsch C, Bartsch H

Report Name The anti-tumor activity of pineal melatonin and cancer enhancing life styles in industrialized societies

Publication Cancer Causes Control

Issue-page numbers 17:559–571 doi:10.1007/s10552-005-9011-8. PMID:16596311

URL http://www.springerlink.com/content/535j52785320655n/

Abstract This review discusses the potential role of the anti-tumor activity of pineal melatonin for the aetiology and prevention of cancers related to life-styles in industrialized societies, e.g. frequent long-distance flights as well as chronic night shift work leading to circadian disturbances of neuroendocrine parameters including melatonin. Experimental studies show that melatonin controls not only the growth of well-differentiated cancers, but also possesses anti-carcinogenic properties. Therefore, it is plausible that disturbances of circadian melatonin rhythmicity could be functionally involved in elevated cancer risks among aircrew members and nurses frequently working on night shifts. Due to the suppression of melatonin by light it can be assumed that too much artificial light at night could, at least in part, be responsible for generally increasing rates of e.g. breast cancer in industrialized countries. It is discussed under which conditions a transient substitutional therapy with melatonin could be justified or which forms of living could help to physiologically foster melatonin secretion to optimise control over cancerous growth and development.

Keywords Cancer risk - Experimental cancer - Jet lag - Melatonin - Night shift work

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Bartsch C, Bartsch H, Perschke E — *Year* 2009

Authors Christian Bartsch, Hella Bartsch & Elmar Peschke

Report Name Light, melatonin and cancer: current results and future perspectives

Publication Biological Rhythm Research

Issue-page numbers Volume 40, Issue 1, 2009

URL http://www.tandfonline.com/doi/abs/10.1080/09291010802066983

Abstract N/A

Keywords

Bartsch H, Bartsch C

Year 1981

Authors Hella Bartsch and C. Bartsch

Report Name Effect of melatonin on experimental tumors under different photoperiods and times of administration.

Publication J Neural Transm

Issue-page numbers 52:269–279 doi:10.1007/BF01256752. PMID:7334363

URL http://www.springerlink.com/content/pj6621q560067203/

Abstract The effects of melatonin on experimental tumors so far described in the literature are contradictory. This may partially be due to negligence of the importance of environmental photoperiodic conditions and to the time of day of administration. In order to test whether the effect of melatonin on tumor growth is dependent on the photoperiod and the time of day of administration, the present experiments were carried out. It appears that under long photoperiods melatonin shows opposite effects on fibrosarcoma ascites and Ehrlich solid tumors depending on the time of the day at which the compound was administered. Tumors are stimulated by melatonin injections in the morning and inhibited by late afternoon injections. Experiments under LratioD=12ratio12 and LratioD=8ratio16 do not show such pronounced antagonistic effects. These results support our hypothesis that the effect of melatonin on tumor growth is dependent on the photoperiod and the time of day of administration. Possible mechanisms involved in these effects are discussed.

Keywords

Bartsch H, Bartsch C, Simon WE et al.

Year 1992

Authors Bartsch H, Bartsch C, Simon WE et al.

Report Name Antitumor activity of the pineal gland: effect of unidentified substances versus the effect of melatonin

Publication Oncology

Issue-page numbers 49:27–30 doi:10.1159/000227005. PMID:1542489

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=227005

Abstract There is growing evidence that the pineal gland has antineoplastic properties which, however, can only partially be attributed to its hormone melatonin. While the in vivo tumor-inhibiting activity of melatonin is established, observations on its in vitro effects have been contradictory. The effect of this substance was investigated on six human cancer cell lines and compared to the activity of a partially purified, melatonin-free low molecular weight pineal extract (UM05R). Melatonin showed hardly any effect but UM05R was capable of inhibiting the growth of all the six cell lines tested. It is therefore concluded that a direct inhibiting action on tumor cells is not a general physiological role of melatonin as opposed to UM05R. It will be worthwhile to purify the yet unidentified pineal antitumor activity since it may have a considerable therapeutic potential.

Keywords Human cancer cell lines, Antitumor activity, Melatonin, Pineal extracts

Bartsch H, Buchberger A, Franz H et al. **Year** 2000

Authors Bartsch H, Buchberger A, Franz H, Bartsch C, Maidonis I, Mecke D, Bayer E.

Report Name Effect of melatonin and pineal extracts on human ovarian and mammary tumor cells in a chemosensitivity assay

Publication Life Sci

Issue-page numbers 67:2953–2960 doi:10.1016/S0024-3205(00)00882-1. PMID:11133007

URL http://www.ncbi.nlm.nih.gov/pubmed/11133007

Abstract Pinealectomy enhances tumor growth and metastatic spread in experimental animals. This effect is only in part due to melatonin since melatonin-free pineal extracts containing yet unidentified pineal substances have also shown tumor inhibiting activity. Despite numerous reports suggesting melatonin as a potential anti-cancer agent there have not been sufficient clinical trials to define the actual therapeutic potential of melatonin for the treatment of human cancers. To help fill this gap, we used a chemosensitivity assay designed to test the sensitivity of tumors from individual patients towards chemotherapeutic drugs for assessing the effect of melatonin and pineal extracts on primary human tumor cells. Primary cell cultures from seven ovarian and six mammary tumors were incubated with melatonin, the pineal extract YC05R (containing substances between 500 and 1000 daltons) and chemotherapeutic drugs. The pineal extract YC05R inhibited growth of all tumors in a dose-dependent manner. Physiological concentrations of melatonin (10(-8)-10(-10) M) inhibited the growth of one out of six mammary carcinomas in a dose-dependent manner. Primary cell cultures from three ovarian tumors were affected by melatonin in different ways, i.e., two were inhibited and one was slightly stimulated. There was no correlation between sensitivity towards melatonin and sex steroid receptor status, stage or grade of the tumor. It is concluded that, 1), melatonin may be an inhibitor of human mammary and ovarian carcinoma in individual cases and, 2), the pineal gland contains very active anti-tumor substances inhibiting both, the mammary and ovarian tumors, tested. These substances require chemical and biological identification.

Keywords

Baskett JJ, Cockrem JF, Antunovich TA **Year** 1998

Authors Jonathan J. Basket, John F. Cockrem, Tony A. Antunovich

Report Name Sulphatoxymelatonin excretion in older people: relationship to plasma melatonin and renal function

Publication J Pineal Res

Issue-page numbers 24:58–61 doi:10.1111/j.1600-079X.1998.tb00366.x. PMID:9468119

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1998.tb00366.x/abstract?

Abstract In order to validate measurement of urinary sulphatoxymelatonin as an accurate method of estimating plasma melatonin secretion in older people, we compared 24 h plasma melatonin secretion and sulphatoxymelatonin excretion with renal function in 20 subjects 62–89 years of age. There was a good correlation between plasma and urinary sulphatoxymelatonin over the same 24 h period (R2= 0.797) and no relationship between creatinine clearance and sulphatoxymelatonin excretion (R2= 0.075). The results suggest that sulphatoxymelatonin excretion estimation is a good surrogate measurement of plasma melatonin secretion in older people, at least across the range of creatinine clearance for the subjects in the study, 0.41–1.81 ml/sec.

Keywords melatonin; sulphatoxymelatonin; ageing; renal function

Bass J, Takahashi JS

Year 2010

Authors Joseph Bass and Joseph S. Takahashi

Report Name Circadian Integration of Metabolism and Energetics

Publication Science

Issue-page numbers 3 December 2010: Vol. 330 no. 6009 pp. 1349-1354

URL http://www.sciencemag.org/content/330/6009/1349.abstract

Abstract Circadian clocks align behavioral and biochemical processes with the day/night cycle. Nearly all vertebrate cells possess self-sustained clocks that couple endogenous rhythms with changes in cellular environment. Genetic disruption of clock genes in mice perturbs metabolic functions of specific tissues at distinct phases of the sleep/wake cycle. Circadian desynchrony, a characteristic of shift work and sleep disruption in humans, also leads to metabolic pathologies. Here, we review advances in understanding the interrelationship among circadian disruption, sleep deprivation, obesity, and diabetes and implications for rational therapeutics for these conditions.

Keywords circadian

Baturin DA, Alimova IN, Anisimov VN, et al.

Year 2001

Authors Dmitri A. Baturin,1 Irina N. Alimova,1 Vladimir N. Anisimov,1 Irina G. Popovich,1

Report Name The Effect of Light Regimen and Melatonin on the Development

Publication Neuroendocrinology Letters

Issue-page numbers 2001; 22:441–447

URL http://www.zenbev.com/attachments/nel220601a03_baturin_.pdf

Abstract

OBJECTIVES AND DESIGN: The effect and the mechanism of light regimen and melatonin on the development of mammary tumors in HER2/neu transgenic mice were investigated. Female HER-2/neu mice starting from the age of 2 months were kept under standard light/dark regimen (LD) or constant light illumination (LL) and a part of each group was given melatonin (20 mg/l) during the night time.
RESULTS: The exposure to LL failed to change the incidence of spontaneous mammary adenocarcinoma development, the size of mammary tumors, as well as the incidence and size of lung metastases. However, the number of tumors per mouse was signifi cantly increased in the LL group as compared to the LD group. The number of mice bearing 4 and more tumors was higher in the LL group than in the LD group, whereas the number of mice bearing 1 to 3 tumors was lower in the LL group in comparison with the LD group. Melatonin decreased the incidence and size of mammary adenocarcinomas, and the incidence of lung metastases in the LD group but not in the LL group. The mean number of tumors per mouse was not changed by melatonin treatment in both light regimens. The number of mice bearing 4 and more tumors was reduced by melatonin more signifi cantly in the LL group than in LD group. Melatonin treatment resulted in a 2.5-fold reduction in the expression of HER-2/neu mRNA in mammary tumors from HER-2 /neu transgenic mice.
CONCLUSION: The data demonstrate the infl uence of the LD light regiment and melatonin treatment in the development of spontaneous mammary tumors in HER-2/neu mice suggesting a melatonin-dependent modulation of HER-2/neu gene expression in mammary adenocarcinoma.

Keywords HER-2/neu; transgenic mice; mammary tumors; constant light;

Bauer SE, Wagner SE, Burch J, et al. **Year** 2013

Authors Sarah E Bauer, Sara E Wagner, Jim Burch, Rana Bayakly and John E Vena

Report Name A case-referent study: light at night and breast cancer risk in Georgia

Publication International Journal of Health Geographics

Issue-page numbers 2013, 12:23

URL http://www.ij-healthgeographics.com/content/12/1/23

Abstract

Background
Literature has identified detrimental health effects from the indiscriminate use of artificial nighttime light. We examined the co-distribution of light at night (LAN) and breast cancer (BC) incidence in Georgia, with the goal to contribute to the accumulating evidence that exposure to LAN increases risk of BC.
Methods

Using Georgia Comprehensive Cancer Registry data (2000–2007), we conducted a case-referent study among 34,053 BC cases and 14,458 lung cancer referents. Individuals with lung cancer were used as referents to control for other cancer risk factors that may be associated with elevated LAN, such as air pollution, and since this cancer type was not previously associated with LAN or circadian rhythm disruption. DMSP-OLS Nighttime Light Time Series satellite images (1992–2007) were used to estimate LAN levels; low (0–20 watts per sterradian cm2), medium (21–41 watts per sterradian cm2), high (>41 watts per sterradian cm2). LAN levels were extracted for each year of exposure prior to case/referent diagnosis in ArcGIS.
Results

Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression models controlling for individual-level year of diagnosis, race, age at diagnosis, tumor grade, stage; and population-level determinants including metropolitan statistical area (MSA) status, births per 1,000 women aged 15–50, percentage of female smokers, MSA population mobility, and percentage of population over 16 in the labor force. We found that overall BC incidence was associated with high LAN exposure (OR = 1.12, 95% CI [1.04, 1.20]). When stratified by race, LAN exposure was associated with increased BC risk among whites (OR = 1.13, 95% CI [1.05, 1.22]), but not among blacks (OR = 1.02, 95% CI [0.82, 1.28]).
Conclusions

Our results suggest positive associations between LAN and BC incidence, especially among whites. The consistency of our findings with previous studies suggests that there could be fundamental biological links between exposure to artificial LAN and increased BC incidence, although additional research using exposure metrics at the individual level is required to confirm or refute these findings.

Keywords Light at night (LAN); Artificial LAN; Breast cancer; Circadian disruption

Beattie PE; Dawe RS; Ibbotson SH; Ferguson J **Year** 2003

Authors Paula E. Beattie; Robert S. Dawe; Sally H. Ibbotson; James Ferguson

Report Name Characteristics and prognosis of idiopathic solar urticaria: a cohort of 87 cases

Publication Arch Dermatol

Issue-page numbers 2003;139:1149-1154

URL http://archderm.ama-assn.org/cgi/content/abstract/139/9/1149

Abstract

Background As little has been published on the course of idiopathic solar urticaria (SU) patients cannot receive comprehensive prognostic advice.

Objective To determine the prognosis and photobiological characteristics of idiopathic SU.

Design Historical cohort study, with inception cohort followed up from time of diagnosis. Follow-up for a median of 4 years (range, 3 months to 26 years) after diagnosis.

Setting Tertiary referral center for the investigation of photodermatoses in Scotland.

Patients The study included 87 patients, 61 (70%) of whom were female, with phototest-confirmed idiopathic SU between 1975 and 2000. Sixty patients (69%) were followed up clinically, and 25 patients (29%) were phototested on 2 or more occasions.

Interventions Investigations at time of diagnosis included monochromator phototesting. Further monochromator phototesting was performed in those patients in whom it was clinically indicated (select subgroup), and all patients who could be traced received a follow-up questionnaire.

Main Outcome Measures Characteristics of SU, responsible wave bands, and prognosis for clinical resolution.

Results The prevalence of idiopathic SU in Tayside, Scotland, is estimated to be 3.1 per 100 000. Action spectra were typically broad, with 63% reacting to more than 1 wave band, and the most common provoking wavelengths were the longer UV-A and the shorter visible ones. The majority of subjects were affected perennially (68%), by radiation transmitted through glass (83%) and thin clothing (76%). Coexistent polymorphic light eruption occurred in 20 patients (23%), and another photodermatosis occurred in 6 patients, 3 of whom had chronic actinic dermatitis. In those with SU alone, the mean age at onset was 41 years. The probability of clinical resolution at 5 and 10 years after diagnosis was 0.12 (95% confidence interval, 0.06-0.24) and 0.26 (95% confidence interval, 0.15-0.43), respectively.

Conclusion Idiopathic SU is a chronic disease. The majority of this cohort was still affected after 5 and 10 years.

Keywords

Beatty K

Year 2010

Authors Kelly Beatty

Report Name Night Lights Worsen Smog

Publication Sky and Telescope

Issue-page numbers Dec 2010 online

URL http://www.skyandtelescope.com/news/111959684.html

Abstract Article

Keywords ozone, light at night

Beatty S, Koh H, Phil M, et al.

Year 2000

Authors Beatty S, Koh H, Phil M, Henson D, Boulton M.

Report Name The role of oxidative stress in the pathogenesis of age-related macular degeneration.

Publication Surv Ophthalmol

Issue-page numbers 2000 Sep-Oct;45(2):115-34.

URL http://www.ncbi.nlm.nih.gov/pubmed/11033038?dopt=abstract

Abstract Age-related macular degeneration (AMD) is the leading cause of blind registration in the developed world, and yet its pathogenesis remains poorly understood. Oxidative stress, which refers to cellular damage caused by reactive oxygen intermediates (ROI), has been implicated in many disease processes, especially age-related disorders. ROIs include free radicals, hydrogen peroxide, and singlet oxygen, and they are often the byproducts of oxygen metabolism. The retina is particularly susceptible to oxidative stress because of its high consumption of oxygen, its high proportion of polyunsaturated fatty acids, and its exposure to visible light. In vitro studies have consistently shown that photochemical retinal injury is attributable to oxidative stress and that the antioxidant vitamins A, C, and E protect against this type of injury. Furthermore, there is strong evidence suggesting that lipofuscin is derived, at least in part, from oxidatively damaged photoreceptor outer segments and that it is itself a photoreactive substance. However, the relationships between dietary and serum levels of the antioxidant vitamins and age-related macular disease are less clear, although a protective effect of high plasma concentrations of alpha-tocopherol has been convincingly demonstrated. Macular pigment is also believed to limit retinal oxidative damage by absorbing incoming blue light and/or quenching ROIs. Many putative risk-factors for AMD have been linked to a lack of macular pigment, including female gender, lens density, tobacco use, light iris color, and reduced visual sensitivity. Moreover, the Eye Disease Case-Control Study found that high plasma levels of lutein and zeaxanthin were associated with reduced risk of neovascular AMD. The concept that AMD can be attributed to cumulative oxidative stress is enticing, but remains unproven. With a view to reducing oxidative damage, the effect of nutritional antioxidant supplements on the onset and natural course of age-related macular disease is currently being evaluated.

Keywords

Beckett M, Roden LC

Year 2009

Authors M. Beckett; L.C. Roden

Report Name Mechanisms by which circadian rhythm disruption may lead to cancer

Publication South African Journal of Science

Issue-page numbers vol.105 no.11-12 Pretoria Nov./Dec. 2009

URL http://www.scielo.org.za/scielo.php?pid=S0038-23532009000600011&script=sci_arttext

Abstract

Humans have evolved in a rhythmic environment and display daily (circadian) rhythms in physiology, metabolism and behaviour that are in synchrony with the solar day. Modern lifestyles have compromised the exposure to bright light during the day and dark nights, resulting in the desynchronisation of endogenously generated circadian rhythms from the external environment and loss of coordination between rhythms within the body. This has detrimental effects on physical and mental health, due to the misregulation and uncoupling of important cellular and physiological processes. Long-term shift workers who are exposed to bright light at night experience the greatest disruption of their circadian rhythms. Studies have shown an association between exposure to light at night, circadian rhythm disruption and an increased risk of cancer. Previous reviews have explored the relevance of light and melatonin in cancer, but here we explore the correlation of circadian rhythm disruption and cancer in terms of molecular mechanisms affecting circadian gene expression and melatonin secretion.

Keywords circadian rhythm, carcinogenesis, shift work

Authors Johan Beck-Friis, Jan-Gustaf Ljunggren, Marja Thorén, Dietrich von Rosen, Bengt F. Kjellman, Lennart Wetterberg

Report Name Melatonin, cortisol and ACTH in patients with major depressive disorder and healthy humans with special reference to the outcome of the dexamethasone suppression test.

Publication Psychoneuroendocrinology

Issue-page numbers 10:173–186 doi:10.1016/0306-4530(85)90055-1. PMID:2994141

URL http://www.sciencedirect.com/science/article/pii/0306453085900551

Abstract

The 24 hr profiles of melatonin and cortisol in serum, morning levels of ACTH in plasma, and the dexamethasone suppression test (DST) were investigated in 32 acutely ill patients with a RDC diagnosis of major depressive disorder, 24 patients with a history of longlasting unipolar or bipolar major depressive disorder studied in remission, and 33 healthy subjects. A significant decrease in maximum nocturnal melatonin level (MTmax) was found in the acutely ill depressed patients with abnormal DST compared to both those with normal DSTs and the healthy subjects. The MTmax levels were unaltered when these patients were reinvestigated in remission. A decrease of MTmax was also seen in the group of unipolar and bipolar patients studied in remission. Low nocturnal melatonin is proposed to be a trait marker for major depressive disorder and depressive states with abnormalities in the hypothalamic-pituitary-adrenal (HPA) axis.

A significant decrease of ACTH levels at 0800 hr after dexamethasone administration the preceding evening was found in the healthy subjects, the unipolar-bipolar patients in remission, and the acutely ill depressed patients with normal DSTs, but was not found in the acutely ill depressed patients with abnormal DSTs. These findings support the hypothesis that pituitary ACTH regulation is altered in depressed patients with abnormal DST. Morning plasma ACTH before the administration of dexamethasone did not significantly differ between the acutely ill depressed patients with abnormal DSTs, normal DSTs, the patients with unipolar-bipolar disease in remission, or the healthy subjects. Thus, the abnormalities in the HPA axis in depressed patients are proposed to be due to a hypersecretion of corticotrophin releasing factor (CRF) with a subsequent stimulus-induced pituitary desensitization.

A significant decrease of melatonin after dexamethasone was seen at 0800 hr in the unipolar-bipolar patients in remission as well as in the healthy subjects, at 1600 hr and 2200 hr in the acutely ill depressed patients in remission, but not at 0800 hr in the acutely ill depressed patients in relapse. A significant regression was found between MTmax levels and the degree of non-suppression of cortisol at 0800 hr in the DST in the acutely ill depressed patients both in relapse and in remission. Melatonin thus is proposed to be an inhibiting factor for CRF during depression. A trend to a phase-advance of cortisol nadir and melatonin peak was seen in the acutely ill depressed patients with abnormal DST, possibly indicating an involvement of the suprachiasmatic nuclei in the hypothalamus.

Keywords Melatonin; cortisol; ACTH; dexamethasone suppression; depressive disorder; down-regulation; corticotropin releasing hormone

Beck-Friis J, von Rosen D, Kjellman BF et al. **Year** 1984

Authors Johan Beck-Friis, Dietrich von Rosen, Bengt F. Kjellman, Jan-Gustaf Ljunggren, Lennart Wetterberg

Report Name Melatonin in relation to body measures, sex, age, season and the use of drugs in patients with major affective disorders and healthy subjects.

Publication Psychoneuroendocrinology

Issue-page numbers 9:261–277 doi:10.1016/0306-4530(84)90005-2. PMID:6494381

URL http://www.sciencedirect.com/science/article/pii/0306453084900052

Abstract Serum melatonin levels over a 24 hr period were studied in 30 acutely ill patients with major depressive episode, 24 patients with a history of unipolar or bipolar major affective disorder in remission and 33 healthy subjects. A significant negative correlation (− 0.45) between body height and maximum nocturnal serum melatonin level was found. Maximum serum melatonin levels during the night were lower in both patient groups than in the healthy controls. No difference was found between maximum nocturnal serum melatonin levels in 26 patients investigated when ill and again in remission. We thus propose low nocturnal melatonin to be a trait-dependent marker for major depressive disorder.

A difference in the morning but not night melatonin levels was found between samples taken during the dark, winter season versus samples taken during the bright, spring-summer season. Melatonin levels were not lower in females than in males, when melatonin levels were adjusted for body height. Similar results were found when the nocturnal areas under the curve for melatonin were analyzed.

Keywords Melatonin; circadian rhythm; major affective disorder; healthy subjects; sex; age; body measures; seasons; light; drugs

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Bedrosian TA, Aubrecht TG, Kaugars KE, et al. **Year** 2013

Authors Tracy A. Bedrosian, Taryn G. Aubrecht, Katherine E. Kaugars, Zachary M. Weil, Randy J. Nelson

Report Name Artificial light at night alters delayed-type hypersensitivity reaction in response to acute stress in Siberian hamsters

Publication Brain, Behavior, and Immunity

Issue-page numbers Available online 4 June 2013

URL http://www.sciencedirect.com/science/article/pii/S0889159113001992

Abstract Several physiological and behavioral processes rely on precisely timed light information derived from the natural solar cycle. Using this information, traits have adapted to allow individuals within specific niches to optimize survival and reproduction, but urbanization by humans has significantly altered natural habitats. Nighttime light exposure alters immune function in several species, which could lead to decreased fitness or survival, particularly in the face of an environmental challenge. We exposed male Siberian hamsters (Phodopus sungorus) to five lux of light at night for four weeks, and then administered six hours of acute restraint stress. Delayed-type hypersensitivity (DTH) response was assessed immediately following stress. Acute restraint increased the DTH reaction in dark nights, but exposure to nighttime light prevented this response. Exposure to light at night prolonged the DTH response in non-stressed control hamsters. These results suggest that light pollution may significantly alter physiological responses in Siberian hamsters, particularly in response to a salient environmental challenge such as stress.

Keywords Light pollution; Restraint stress; Immune function; Phodopus sungorus

Bedrosian TA, Fonken LK, Walton JC, et al. **Year** 2011

Authors Bedrosian TA, Fonken LK, Walton JC, Haim A, Nelson RJ.

Report Name Dim light at night provokes depression-like behaviors and reduces CA1 dendritic spine density in female hamsters

Publication Psychoneuroendocrinology

Issue-page numbers 2011 Aug;36(7):1062-9. Epub 2011 Feb 2.

URL http://www.ncbi.nlm.nih.gov/pubmed/21292405

Abstract The prevalence of major depression has increased in recent decades; however, the underlying causes of this phenomenon remain unspecified. One environmental change that has coincided with elevated rates of depression is increased exposure to artificial light at night. Shift workers and others chronically exposed to light at night are at increased risk of mood disorders, suggesting that nighttime illumination may influence brain mechanisms mediating affect. We tested the hypothesis that exposure to dim light at night may impact affective responses and alter morphology of hippocampal neurons. Ovariectomized adult female Siberian hamsters (Phodopus sungorus) were housed for 8 weeks in either a light/dark cycle (LD) or a light/dim light cycle (DM), and then behavior was assayed. DM-hamsters displayed more depression-like responses in the forced swim and the sucrose anhedonia tests compared with LD-hamsters. Conversely, in the elevated plus maze DM-hamsters reduced anxiety-like behaviors. Brains from the same animals were processed using the Golgi-Cox method and hippocampal neurons within CA1, CA3, and the dentate gyrus were analyzed for morphological characteristics. In CA1, DM-hamsters significantly reduced dendritic spine density on both apical and basilar dendrites, an effect which was not mediated by baseline cortisol, as concentrations were equivalent between groups. These results demonstrate dim light at night is sufficient to reduce synaptic spine connections to CA1. Importantly, the present results suggest that night-time low level illumination, comparable to levels that are pervasive in North America and Europe, may contribute to the increasing prevalence of mood disorders.

Keywords light at night, depression

Bedrosian TA, Fonken LK, Walton JC, Nelson RJ **Year** 2011

Authors Tracy A Bedrosian, Laura K Fonken, James C Walton, Randy J Nelson

Report Name Chronic exposure to dim light at night suppresses immune responses in Siberian hamsters.

Publication Biology Letters

Issue-page numbers Volume: 7, Issue: 3, Pages: 468-71

URL http://www.mendeley.com/research/chronic-exposure-dim-light-night-suppresses-immune-responses-siberian-hamsters-1/

Abstract Species have been adapted to specific niches optimizing survival and reproduction; however, urbanization by humans has dramatically altered natural habitats. Artificial light at night (LAN), termed 'light pollution', is an often overlooked, yet increasing disruptor of habitats, which perturbs physiological processes that rely on precise light information. For example, LAN alters the timing of reproduction and activity in some species, which decreases the odds of successful breeding and increases the threat of predation for these individuals, leading to reduced fitness. LAN also suppresses immune function, an important proxy for survival. To investigate the impact of LAN in a species naive to light pollution in its native habitat, immune function was examined in Siberian hamsters derived from wild-caught stock. After four weeks exposure to dim LAN, immune responses to three different challenges were assessed: (i) delayed-type hypersensitivity (DTH), (ii) lipopolysaccharide-induced fever, and (iii) bactericide activity of blood. LAN suppressed DTH response and reduced bactericide activity of blood after lipopolysaccharide treatment, in addition to altering daily patterns of locomotor activity, suggesting that human encroachment on habitats via night-time lighting may inadvertently compromise immune function and ultimately fitness.

Keywords bactericide, delayed type hypersensi, light pollution, lipopolysaccharide, phodopus, tivity

Authors T. A. Bedrosian, A. Galan, C. A. Vaughn, Z. M. Weil, R. J. Nelson

Report Name Light at Night Alters Daily Patterns of Cortisol and Clock Proteins in Female Siberian Hamsters

Publication Journal of Neuroendocrinology

Issue-page numbers Volume 25, Issue 6, pages 590–596, June 2013

URL http://onlinelibrary.wiley.com/doi/10.1111/jne.12036/abstract

Abstract Humans and other organisms have adapted to a 24-h solar cycle in response to life on Earth. The rotation of the planet on its axis and its revolution around the sun cause predictable daily and seasonal patterns in day length. To successfully anticipate and adapt to these patterns in the environment, a variety of biological processes oscillate with a daily rhythm of approximately 24 h in length. These rhythms arise from hierarchally-coupled cellular clocks generated by positive and negative transcription factors of core circadian clock gene expression. From these endogenous cellular clocks, overt rhythms in activity and patterns in hormone secretion and other homeostatic processes emerge. These circadian rhythms in physiology and behaviour can be organised by a variety of cues, although they are most potently entrained by light. In recent history, there has been a major change from naturally-occurring light cycles set by the sun, to artificial and sometimes erratic light cycles determined by the use of electric lighting. Virtually every individual living in an industrialised country experiences light at night (LAN) but, despite its prevalence, the biological effects of such unnatural lighting have not been fully considered. Using female Siberian hamsters (Phodopus sungorus), we investigated the effects of chronic nightly exposure to dim light on daily rhythms in locomotor activity, serum cortisol concentrations and brain expression of circadian clock proteins (i.e. PER1, PER2, BMAL1). Although locomotor activity remained entrained to the light cycle, the diurnal fluctuation of cortisol concentrations was blunted and the expression patterns of clock proteins in the suprachiasmatic nucleus and hippocampus were altered. These results demonstrate that chronic exposure to dim LAN can dramatically affect fundamental cellular function and emergent physiology.

Keywords Phodopus sungorus; PER1; PER2; BMAL1; light pollution

Bedrosian TA, Nelson RJ

Year 2013

Authors T A Bedrosian and R J Nelson

Report Name Influence of the modern light environment on mood

Publication Molecular Psychiatry

Issue-page numbers (2013) 18, 751–757; doi:10.1038/mp.2013.70; published online 28 May 2013

URL http://www.nature.com/mp/journal/v18/n7/full/mp201370a.html

Abstract

Humans and other organisms have adapted to a consistent and predictable 24-h solar cycle, but over the past ~130 years the widespread adoption of electric light has transformed our environment. Instead of aligning behavioral and physiological processes to the natural solar cycle, individuals respond to artificial light cycles created by social and work schedules. Urban light pollution, night shift work, transmeridian travel, televisions and computers have dramatically altered the timing of light used to entrain biological rhythms. In humans and other mammals, light is detected by the retina and intrinsically photosensitive retinal ganglion cells project this information both to the circadian system and limbic brain regions. Therefore, it is possible that exposure to light at night, which has become pervasive, may disrupt both circadian timing and mood. Notably, the rate of major depression has increased in recent decades, in parallel with increasing exposure to light at night. Strong evidence already links circadian disruption to major depression and other mood disorders. Emerging evidence from the past few years suggests that exposure to light at night also negatively influences mood. In this review, we discuss evidence from recent human and rodent studies supporting the novel hypothesis that nighttime exposure to light disrupts circadian organization and contributes to depressed mood.

Keywords circadian; depression; light at night; light pollution

Authors T A Bedrosian, Z M Weil and R J Nelson

Report Name Chronic dim light at night provokes reversible depression-like phenotype: possible role for TNF

Publication Molecular Psychiatry

Issue-page numbers 24 July 2012; doi: 10.1038/mp.2012.96

URL http://www.nature.com/mp/journal/vaop/ncurrent/abs/mp201296a.html

Abstract The prevalence of major depression has increased in recent decades and women are twice as likely as men to develop the disorder. Recent environmental changes almost certainly have a role in this phenomenon, but a complete set of contributors remains unspecified. Exposure to artificial light at night (LAN) has surged in prevalence during the past 50 years, coinciding with rising rates of depression. Chronic exposure to LAN is linked to increased risk of breast cancer, obesity and mood disorders, although the relationship to mood is not well characterized. In this study, we investigated the effects of chronic exposure to 5 lux LAN on depression-like behaviors in female hamsters. Using this model, we also characterized hippocampal brain-derived neurotrophic factor expression and hippocampal dendritic morphology, and investigated the reversibility of these changes 1, 2 or 4 weeks following elimination of LAN. Furthermore, we explored the mechanism of action, focusing on hippocampal proinflammatory cytokines given their dual role in synaptic plasticity and the pathogenesis of depression. Using reverse transcription-quantitative PCR, we identified a reversible increase in hippocampal tumor necrosis factor (TNF), but not interleukin-1β, mRNA expression in hamsters exposed to LAN. Direct intracerebroventricular infusion of a dominant-negative inhibitor of soluble TNF, XPro1595, prevented the development of depression-like behavior under LAN, but had no effect on dendritic spine density in the hippocampus. These results indicate a partial role for TNF in the reversible depression-like phenotype observed under chronic dim LAN. Recent environmental changes, such as LAN exposure, may warrant more attention as possible contributors to rising rates of mood disorders.

Keywords BDNF; cytokine; hamster; hippocampus; light pollution; Phodopus sungorus

Authors Bedrosian, Tracy A.; Weil, Zachary M.; Nelson, Randy J.

Report Name Chronic Citalopram Treatment Ameliorates Depressive Behavior Associated With Light at Night.

Publication Behavioral Neuroscience

Issue-page numbers Aug 13 , 2012, No Pagination Specified. doi: 10.1037/a0029699

URL http://psycnet.apa.org/psycinfo/2012-21305-001/

Abstract

Chronic exposure to light at night (LAN) is a circadian disruptor and may be linked to various health risks, including mood disorders. We recently demonstrated that chronic exposure to dim (5 lux) LAN provokes depressive-like behaviors and reduced hippocampal CA1 dendritic spine density in female hamsters. Whether this model is responsive to selective serotonin reuptake inhibitors remains unspecified. In this study, we exposed hamsters to 5 lux LAN and treated with citalopram to determine effects on depressive-like behavior and CA1 dendritic spine density. Female hamsters were ovariectomized at adulthood and housed in either a standard light–dark cycle (LD) or dim LAN (dLAN). After 4 weeks exposure, treatment with either citalopram or vehicle was administered for 2 weeks while hamsters remained in experimental lighting conditions. Depressive-like behavior was assayed using the forced swim test and brains were processed for Golgi-Cox staining and analyzed for dendritic spine density. Treatment with citalopram rescued behavior in the forced swim test in hamsters housed in dLAN, but had no effect on hamsters housed in LD. Dendritic spine density in CA1 was moderately improved by citalopram treatment, but not fully restored. These results validate our LAN paradigm as a depression model by showing citalopram selectively improves depressive-like behavior in dLAN conditions, but not in LD conditions. These data also suggest standard SSRI therapy may be effective for individuals experiencing depression related to circadian disruption and LAN exposure, such as shift workers.

Keywords

Behar-Cohen F, Martinsons C, Viénot F, et al. **Year** 2011

Authors F. Behar-Cohen, C. Martinsons, F. Viénot, G. Zissis, A. Barlier-Salsi, J.P. Cesarini, O. Enouf, M. Garcia, S. Picaud, D. Attia

Report Name Light-emitting diodes (LED) for domestic lighting: Any risks for the eye?

Publication Progress in Retinal and Eye Research

Issue-page numbers Volume 30, Issue 4, July 2011, Pages 239-257

URL http://www.sciencedirect.com/science/article/pii/S1350946211000267

Abstract Light-emitting diodes (LEDs) are taking an increasing place in the market of domestic lighting because they produce light with low energy consumption. In the EU, by 2016, no traditional incandescent light sources will be available and LEDs may become the major domestic light sources. Due to specific spectral and energetic characteristics of white LEDs as compared to other domestic light sources, some concerns have been raised regarding their safety for human health and particularly potential harmful risks for the eye. To conduct a health risk assessment on systems using LEDs, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), a public body reporting tc the French Ministers for ecology, for health and for employment, has organized a task group. This group consisted physicists, lighting and metrology specialists, retinal biologist and ophthalmologist who have worked together for a year. Part of this work has comprised the evaluation of group risks of different white LEDs commercialized on the French market, according to the standards and found that some of these lights belonged to the group risk 1 or 2.

This paper gives a comprehensive analysis of the potential risks of white LEDs, taking into account pre-clinical knowledge as well as epidemiologic studies and reports the French Agency's recommendations to avoid potential retinal hazards.

Keywords LEDs; Light-toxicity; Blue light; Retina

Behrends J, Prank K, Dogu E, Brabant G **Year** 1998

Authors Behrends J, Prank K, Dogu E, Brabant G

Report Name Central nervous system control of thyrotropin secretion during sleep and wakefulness

Publication Horm Res

Issue-page numbers 49:173–177 doi:10.1159/000023167.PMID:9550121

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=23167

Abstract Thyrotropin (TSH) is a pulsatile secreted hormone with a pronounced circadian rhythmicity and a characteristic nightly surge based on an augmentation of pulsatile release. A number of physiological factors influence TSH secretion via an alteration in the amount of pulsatile released hormone. An increase in somatostatinergic tone during fasting appears to decrease TSH pulse amplitude and sequentially mean TSH serum levels. In contrast, blockade of dopaminergic tone by metoclopramide infusion when circulating TSH levels are low during the afternoon hours increase TSH pulse amplitude to levels comparable to the nightly TSH surge suggesting a physiological dampening of TSH pulse amplitude by dopamine during the daytime.

Keywords Circadian rhythmicity, Pulsatility, Thyrotropin, Dopamine, Somatostatin, Sleep, Review

Bellet MM, Sassone-Corsi P

Year 2010

Authors Marina Maria Bellet and Paolo Sassone-Corsi

Report Name Mammalian circadian clock and metabolism - the epigenetic link

Publication Journal of Cell Science

Issue-page numbers 2010;123(Pt 22):3837-48

URL http://jcs.biologists.org/content/123/22/3837.full.pdf

Abstract Circadian rhythms regulate a wide variety of physiological and metabolic processes. The clock machinery comprises complex transcriptional–translational feedback loops that, through the action of specific transcription factors, modulate the expression of as many as 10% of cellular transcripts. This marked change in gene expression necessarily implicates a global regulation of chromatin remodeling. Indeed, various descriptive studies have indicated that histone modifications occur at promoters of clock-controlled genes (CCGs) in a circadian manner. The finding that CLOCK, a transcription factor crucial for circadian function, has intrinsic histone acetyl transferase (HAT) activity has paved the way to unraveling the molecular mechanisms that govern circadian chromatin remodeling. A search for the histone deacetylase (HDAC) that counterbalances CLOCK activity revealed that SIRT1, a nicotinamide adenin dinucleotide (NAD+)-dependent HDAC, functions in a circadian manner. Importantly, SIRT1 is a regulator of aging, inflammation and metabolism. As many transcripts that oscillate in mammalian peripheral tissues encode proteins that have central roles in metabolic processes, these findings establish a functional and molecular link between energy balance, chromatin remodeling and circadian physiology. Here we review recent studies that support the existence of this link and discuss their implications for understanding mammalian physiology and pathology.

Keywords Chromatin, Epigenetics, Metabolism

Authors Bellipanni G, Bianchi P, Pierpaoli W et al.

Report Name Effects of melatonin in perimenopausal and menopausal women: a randomized and placebo controlled study

Publication Exp Gerontol

Issue-page numbers 36:297–310 doi:10.1016/S0531-5565(00)00217-5. PMID:11226744

URL http://www.sciencedirect.com/science/article/pii/S0531556500002175

Abstract In aging humans, night levels of melatonin (MEL) decline progressively. Also thyroid and gonadal functions decline during aging while gonadotropins (luteotropic hormone (LH) and follicle stimulating hormone (FSH)) steadily increase. A desynchronization of pineal circadian cyclicity as expressed by the progressive decrease of the MEL night peak may be permissively linked to the onset and progression of menopause. We studied the effects of exogenous, evening administration of MEL on the level of hormones which are known to be involved in the genesis and progression of menopause.

Perimenopausal and menopausal women from 42 to 62 years of age with no pathology or medication were selected. MEL was measured in saliva to divide them into low, medium and high-MEL patients. Half of them took 3 mg MEL and half of them Placebo at bedtime (10–12 p.m.) in a fully randomized and double-blind fashion. Three and six months later blood was taken for determination of pituitary (LH, FSH), ovarian, and thyroid hormones I(T3 and T4). All women taking MEL with low basal level of MEL and/or Placebo for three and six months showed a significant increase in levels of thyroid hormones. Before initiation of the study, a negative correlation was found in all women between LH, FSH and basal MEL levels. Within six months of treatment, MEL produced a significant diminution of LH in the younger women (43 to 49 year-old), while no effect was seen in the older women (50–62 years old). A decrement of FSH was observed in MEL-treated women with low basal MEL levels. In addition, most MEL-treated women reported a general improvement of mood and a significant mitigation of depression. MEL decline during aging may thus signal the derangement of pineal and pituitary-controlled ovarian cyclicity and the progressive quenching of fertility in women. These findings seem to show a recovery of pituitary and thyroid functions in MEL-treated women, towards a more juvenile pattern of regulation.

Keywords Pineal gland; Melatonin; Perimenopause; Thyroid function; Gonadotropins; Depression

Beniashvili DS, Benjamin S, Baturin DA, Anisimov VN **Year** 2001

Authors Beniashvili DS, Benjamin S, Baturin DA, Anisimov VN.

Report Name Effect of light/dark regimen on N-nitrosoethylurea-induced transplacental carcinogenesis in rats.

Publication Cancer Lett

Issue-page numbers 2001;163:51-57

URL http://www.ncbi.nlm.nih.gov/pubmed/11163108

Abstract Pregnant females were randomly subdivided into three groups (24 rats per group) and kept at the 12:12 h light/dark regimen (group 1), at the constant light illumination (24 h a day, group 2) or at the continuous darkness (group 3). N-nitrosoethylurea (NEU) has been injected into the tail vein of all rats (80 mg/kg) on the 18-19th day of the pregnancy. After the delivery the lacting dams and their progeny during the lactation period (1 month after delivery) were kept also at the three different light/dark regimens. Then all offspring from each group was kept at the 12:12 h light/dark regimen, males and females separately, and were observed until natural death. The exposure to constant light significantly promoted the transplacental carcinogenesis whereas the exposure to constant darkness inhibited it. The incidence of total tumors, tumors of both a peripheral nervous system and kidney was 2.6; 2.5 and 8.5 times higher, and survival significantly shorter, correspondingly, in rats from the group 2 exposed to the constant light regimen as compared to the group 1 (12:12 h light/dark regimen) ($P<0.05$). On the other hand, the exposure to the continuous darkness during the pregnancy and the lactation period significantly inhibited the transplacental carcinogenesis in the offspring of rats treated with NEU. The incidence of total tumors, tumors of a peripheral nervous system was by 2.4 and 2.7 times less, and survival longer, respectively, in exposed to the darkness rats from the group 3 as compared to the group 1 (12:12 h light/dark regimen) ($P<0.05$). Thus, our data firstly have shown the modifying effect of light-dark regimen on the realization of the transplacental carcinogenesis induced by NEU in rats.

Keywords light, dark

Ben-Jonathan N **Year** 1994

Authors Ben-Jonathan N

Report Name Regulation of prolactin secretion. In: Imura H, Ed

Publication The Pituitary Gland

Issue-page numbers 2nd ed. New York: Raven Press. pp. 261.

URL Book

Abstract N/A

Keywords

Beral V, Robinson N

Year 1981

Authors Beral V, Robinson N.

Report Name The relationship of malignant melanoma, basal and squamous skin cancers to indoor and outdoor work

Publication Br J Cancer

Issue-page numbers 1981 Dec;44(6):886-91.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2010880/pdf/brjcancer00447-0114.pdf

Abstract An analysis of occupational incidence data for malignant melanomas and squamous-and basal-self carcinomas of the skin in England and Wales from 1970 to 1975 is reported. The occupational pattern for melanomas of the trunk and limbs differed markedly from the pattern for melanomas of the head, face and neck. Office work was associated with a large excess of melanomas of the trunk and limbs. In contrast, outdoor work was associated with an excess of melanomas of the head, face and neck; and was also associated with an excess of squamous-and basal-cell carcinomas of the skin. This suggests that prolonged occupational exposure to sunlight is an important cause of squamous-and basal-cell carcinomas and of melanomas of the head, face and neck, but not of melanomas on other parts of the body. The high rate of lesions on the trunk and limbs in office workers may reflect their sunbathing or other recreational habits; but it contrasts clearly with other indoor work, where there is a generally low rate of all forms of skin cancer.

Keywords

Berczi I

Year 1989

Authors Istvan Berczi

Report Name Immunoregulation by neuroendocrine factors

Publication Dev Comp Immunol

Issue-page numbers 13:329–341 doi:10.1016/0145-305X(89)90042-6. PMID:2572464

URL http://www.sciencedirect.com/science/article/pii/0145305X89900426

Abstract The influence of the pituitary gland and of steroid hormones on the lymphoid system was demonstrated experimentally over half a century ago (1–4). Observations indicating the possibility of behavioural modification of immunity were also made at about the same time (5,6). Although these initial observations were followed by numerous investigations, the lack of sufficient basic knowledge of the endocrine and immune systems and serious methodological difficulties led to contradictions from which no definite conclusions could be drawn (7). Thus, the idea of neurohormonal-immune interaction fell gradually into disrepute. The remarkable effect of corticosteroids and their analogues on the immune system was regarded as a pharmacological phenomenon, rather than a physiological mechanism. During the past decade, this area gradually again became one of the forefronts of biomedical investigation and recently a number of volumes have been published on the subject of neurohormonal-immune interactions (8–16). Because of space limitations, only a brief overview of the subject can be given below and the reader is referred to the cited literature for detailed information.

Keywords

Berga SL, Mortola JF, Girton L et al. **Year** 1989

Authors S. L. BERGA, J. F. MORTOLA, L. GIRTON, B. SUH§, G. LAUGHLIN, P. PHAM and S. S. C. YEN|

Report Name Neuroendocrine aberrations in women with functional hypothalamic amenorrhea

Publication J Clin Endocrinol Metab

Issue-page numbers 68:301–308 doi:10.1210/jcem-68-2-301. PMID:2493024

URL http://jcem.endojournals.org/content/68/2/301.short

Abstract

To further elucidate the neuroendocrine regulation of anterior pituitary function in women with functional hypothalamic amenorrhea (FHA), we measured serum LH, FSH, cortisol, GH, PRL, TSH concentrations simultaneously at frequent intervals for 24 h in 10 women with FHA and in 10 normal women in the early follicular phase (NC). Using the same data, we separately analyzed the cortisol-PRL responses to meals in these women. In addition, the pituitary responses to the simultaneous administration of GnRH, CRH, GHRH, and TRH were assessed in 6 FHA and 6 normal women.

The 24-h secretory pattern of each hormone except TSH was altered in the women with FHA. Compared to normal women, the women with FHA had a 53% reduction in LH pulse frequency ($P < 0.0001$) and an increase in the mean LH interpulse interval ($P < 0.01$); LH pulse amplitude was similar. The 24-h integrated LH and FSH concentrations were reduced 30% ($P = 0.01$) and 19% ($P < 0.05$), respectively. The mean cortisol pulse frequency, amplitude, interpulse interval, and duration were similar in the two groups, but integrated 24-h cortisol secretion was 17% higher in the women with FHA ($P < 0.05$). This increase was greatest from 0800–1600 h, but also was present from 2400-0800 h. Cortisol levels were similar in the two groups from 1600–2400 h, resulting in an amplified circadian excursion. In contrast, the 24-h serum PRL levels were markedly lower at all times ($P < 0.0001$), the sleep-associated nocturnal elevation of PRL was proportionately greater ($P < 0.05$), and serum GH levels were increased at night in the women with FHA ($P < 0.05$). Although 24-h serum TSH levels were similar at all times, T3 ($P < 0.05$) and T4 ($P < 0.01$) levels were lower in the FHA women.

The responses of serum cortisol to lunch ($P < 0.01$) and dinner ($P < 0.05$) and those of serum PRL to lunch ($P < 0.05$) and dinner ($P = 0.08$) were blunted in the women with FHA. Pituitary hormone increments in response to the simultaneous iv administration of GnRH, CRH, GHRH, and TRH were similar in the two groups, except for a blunted PRL response to TRH in the women with FHA ($P < 0.05$).

The findings of altered pituitary hormone secretion and impaired hormonal responses to meals together with the preservation of pituitary responsivity to releasing hormones collectively suggest that central neuroregulation of the secretion of multiple pituitary hormones is disturbed in women with FHA. Secretion of reproductive hormones (LH, FSH, and PRL) and TSH, as suggested by the lower serum T4 and T3 values, is suppressed, while that of cortisol and GH is increased.

Keywords

Berga SL, Mortola JF, Yen SS

Year 1988

Authors S.L. Berga, J.F. Mortola and S.S.C. Yen

Report Name Amplification of nocturnal melatonin secretion in women with functional hypothalamic amenorrhea

Publication J Clin Endocrinol Metab

Issue-page numbers 66:242–244 doi:10.1210/jcem-66-1-242. PMID:3335608

URL http://jcem.endojournals.org/content/66/1/242.short

Abstract Plasma melatonin levels were determined by a sensitive RIA at 30 min intervals for 24h in 7 women with functional hypothalamic amenorrhea (HA) and in 7 age and season matched normal cycling women in the early follicular phase (NC). While daytime melatonin concentrations were nondetectable in both groups, the integrated nocturnal levels were 3-fold greater in HA (244 ± 58 (se) vs 74 ± 32 pmol-min/L×103, p<0.005). This melatonin increase in HA was due to an elevated peak amplitude (p<0.01) and extended duration (p<0.05). The latter was mostly due to a significant delay in the offset time of the amplified nocturnal melatonin secretion.

Keywords

Bergman RN

Year 1989

Authors Bergman RN

Report Name Lilly lecture 1989. Toward physiological understanding of glucose tolerance. Minimal-model approach.

Publication Diabetes

Issue-page numbers 38:1512–1527 doi:10.2337/diabetes.38.12.1512. PMID:2684710

URL http://diabetes.diabetesjournals.org/content/38/12/1512.abstract

Abstract Glucose tolerance depends on a complex interaction among insulin secretion from the beta-cells, clearance of the hormone, and the actions of insulin to accelerate glucose disappearance and inhibit endogenous glucose production. An additional factor, less well recognized, is the ability of glucose per se, independent of changes in insulin, to increase glucose uptake and suppress endogenous output (glucose effectiveness). These factors can be measured in the intact organism with physiologically based minimal models of glucose utilization and insulin kinetics. With the glucose minimal model, insulin sensitivity (SI) and glucose effectiveness (SG) are measured by computer analysis of the frequently sampled intravenous glucose tolerance test. The test involves intravenous injection of glucose followed by tolbutamide or insulin and frequent blood sampling. SI varied from a high of 7.6 x 10(-4) min-1.microU-1.ml-1 in young Whites to 2.3 x 10(-4) min-1.microU-1.ml-1 in obese nondiabetic subjects; in all of the nondiabetic subjects, SG was normal. In subjects with non-insulin-dependent diabetes mellitus (NIDDM), not only was SI reduced 90% below normal (0.61 +/- 0.16 x 10(-4) min-1.microU-1.ml-1), but in this group alone, SG was reduced (from 0.026 +/- 0.008 to 0.014 +/- 0.002 min-1); thus, defects in SI and SG are synergistic in causing glucose intolerance in NIDDM. One assumption of the minimal model is that the time delay in insulin action on glucose utilization in vivo is due to sluggish insulin transport across the capillary endothelium. This was tested by comparing insulin concentrations in plasma with those in lymph (representing interstitial fluid) during euglycemic-hyperinsulinemic glucose clamps. Lymph insulin was lower than plasma insulin at basal (12 vs. 18 microU/ml) and at steady state, indicating significant loss of insulin from the interstitial space, presumably due to cellular uptake of the insulin-receptor complex. Additionally, during clamps, lymph insulin changed more slowly than plasma insulin, but the rate of glucose utilization followed a time course identical with that of lymph (r = .96) rather than plasma (r = .71). Thus, lymph insulin, which may be reflective of interstitial fluid, is the signal to which insulin-sensitive tissues are responding. These studies support the concept that, at physiological insulin levels, the time for insulin to cross the capillary endothelium is the process that determines the rate o insulin action in vivo.(ABSTRACT TRUNCATED AT 400 WORDS)

Keywords

Bergmanson J; Sheldon TM

Year 1997

Authors Bergmanson, Jan P.G. OD, PhD, FAAO, FCOptom; Sheldon, Todd M. OD

Report Name Ultraviolet radiation revisited

Publication CLAO Journal

Issue-page numbers 23:196-204.

URL http://journals.lww.com/claojournal/Abstract/1997/07000/Ultraviolet_Radiation_Revisited.10.aspx

Abstract

Purpose and Methods: It is likely that we currently receive a greater lifetime exposure to ultraviolet radiation (UVR) than earlier generations due to increased UVR reaching the earth's surface, our longer life expectancy, and increased activities in UV intense environments. This elevated UVR exposure is likely to lead to a higher incidence of acute and chronic ocular and skin radiation trauma. We reviewed the evidence in the current literature supporting these assertions as well as reports of preventive strategies for blocking UVR.

Results: Hawaii is the most UV-intense location on earth as it has the lowest ozone thickness values ever recorded outside the Antarctic zone. It is anticipated that the overall ozone depletion will continue into the next millennium. Significant evidence suggests a correlation between UVR exposure and conjunctival pterygium, photokeratitis, climatic droplet keratopathy and cataracts. The incidence of skin cancer is also on the rise as a result of the increased amount of UVR reaching the earth secondary to the thinning ozone

Conclusions: There are compelling reasons to counsel our patients on the adverse effects of UVR and to offer them the various options available for UV protection. Sunglasses and UV blocking ophthalmic lenses traditionally have been the most commonly selected forms of UVR protection. The UV blocking hydrogel contact lens, a recent addition to our armamentarium, is a means of blocking UVR.

Keywords

Berler DK, Peyser R

Year 1983

Authors Berler DK, Peyser R.

Report Name Light intensity and visual acuity following cataract surgery

Publication Ophthalmology

Issue-page numbers 1983 Aug;90(8):933-6.

URL http://www.ncbi.nlm.nih.gov/pubmed/6634077

Abstract

The authors analyzed 310 cataract operations that were randomly distributed between two operating rooms, each containing a microscope with different light intensities. The light intensity of one microscope was almost threefold greater than the other. One hundred seventy-seven patients were excluded from this study because of medical or ocular problems that might affect visual acuity. The remaining 133 patients are the subjects of this paper. Seventy-one were operated upon under high intensity light, and 62 were subjected to lower illumination in the operating room. Visual acuity after operation was correlated with type of microscope, age, sex, method of cataract extraction, and use of intraocular lenses. Reduced visual acuity (20/40 or worse) was consistently more common with high intensity light and with increasing age. Further investigation is recommended to establish the cause of this reduced acuity.

Keywords

Berneburg M, Kraemer KH

Year 2007

Authors Berneburg M, Kraemer KH.

Report Name Xeroderma pigmentosum and other DNA repair-deficient photodermatoses

Publication In: Lim HW, Honigsmann H, Hawk JLM, editors. Photodermatology.

Issue-page numbers New York: Informa; 2007. p.240-66.

URL http://informahealthcare.com/doi/abs/10.3109/9781420019964.016

Abstract Xeroderma pigmentosum (XP), Cockayne syndrome (CS), and trichothiodystrophy (TTD) are genodermatoses, characterized by deficiencies in DNA repair, basal transcription, or translesion synthesis. They have defective nucleotide excision repair (NER), a mechanism responsible for the repair of bulky forms of DNA damage such as sunlight induced DNA photoproducts, DNA cross-links, and alkylation damage. With an estimated prevalence on the order of one in a million in Western countries, these diseases are very rare. Consideration of the typical symptoms usually permits making the correct clinical diagnosis. Patients suspected of having one of these diseases can be referred to a center that specializes in their diagnosis and care. In recent years the underlying mechanisms as well as many of the genes involved have been identified. The understanding of mechanisms such as DNA repair, basal transcription, and translesion synthesis has helped to form a mechanistic explanation of symptoms of XP, TTD, and CS. These advances provide important insights into major physiological processes such as aging and carcinogenesis. NER, the central defect in most of these diseases, will be described in more detail.

Keywords Orbital, Oculoplastic, Inflammation, Neurology, Eye, Vision, retina, retinopathy, glaucoma, optic nerve, optical trauma

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Bernhofer EI

Year 2012

Authors Bernhofer, Esther I.

Report Name Light Exposure, Sleep-wake Patterns, Mood, and Pain in Hospitalized Adult Medical Patients

Publication OhioLINK ETD Center

Issue-page numbers Document number: case1341350232

URL http://etd.ohiolink.edu/view.cgi/Bernhofer%20Esther%20I.pdf?case1341350232

Abstract For many patients, the hospital environment may contribute to discomfort by providing a lighting structure that interferes with circadian rhythmicity, sleep, mood, and pain. Using Nightingale's Environmental Theory and the Heitkemper/Shaver Human Response Model, this study described light exposure, sleep-wake patterns, mood, and pain in 40 adult medical inpatients. Over 72 hours, light exposure and sleep-wake patterns were continuously measured with wrist actigraph/light meters, mood was measured using the POMS Brief Form, and pain scores were obtained from participants' medical records. The convenience sample included 23 females and 17 males, mean age 50 years. Light exposure levels were low during the daytime (M = 104.8, SD = 131.13) and nighttime (M = 7.07, SD = 7.00). Sleep time (minutes) was also low during daytime 161.02 (M = 161.02, SD = 81.40) and nighttime (M = 236.35, SD = 72.27). Participants experienced significant pain on a 0-10 scale (M = 5.91, SD = 1.55). POMS total mood disturbance score was also high (M = 19.56, SD = 13.11). Fragmented sleep and low intra-daily stability (IS) scores showed restless sleep and little circadian synchronization with the low levels of hospital lighting (the external zeitgeber). The mood subscale of fatigue significantly predicted pain; light exposure significantly predicted fatigue. This study provides preliminary data, useful in developing and testing future lighting interventions to improve sleep-wake patterns and consequently, mood and pain in hospitalized adults.

Keywords

Bernton E, Bryant H, Holaday J, Dave J

Year 1992

Authors Edward Bernton, Henry Bryant, John Holaday, Jitendra Dave

Report Name Prolactin and prolactin secretagogues reverse immunosuppression in mice treated with cysteamine, glucocorticoids, or cyclosporin-A.

Publication Brain Behav Immun

Issue-page numbers 6:394–408 doi:10.1016/0889-1591(92)90038-P. PMID:1336994

URL http://www.sciencedirect.com/science/article/pii/088915919290038P

Abstract Suppression of prolactin (PRL) secretion with the dopamine agonist, bromocryptine, has been shown in rodents to diminish a variety of immunologic responses, including delayed type hypersensitivity, primary antibody response, T-cell dependent macrophage activation, and ex vivo T- and B-lymphocyte proliferation in response to mitogens. These same responses can be suppressed by endogenous or exogenous glucocorticosteroids and, in large measure, the immunosuppressant peptide cyclosporin A. The sulfhydryl reducing agent cysteamine (2-aminoethanethiol) is known to reduce pituitary and plasma prolactin levels. Treatment of mice with cysteamine at doses which suppressed circulating PRL levels resulted in suppression of ex vivo blastogenic responses of lymphocytes from treated mice. The T-cell-dependent primary IgM response to immunization with sheep red blood cells was also suppressed by cysteamine treatment. Treatment of mice with drugs stimulating the release of endogenous PRL, or with exogenous ovine PRL, was found to antagonize the suppression of lymphocyte proliferative responses to mitogens induced in mice by glucocorticoid or cyclosporin treatment. These data suggest that many drugs in common clinical use could have potential immunomodulatory actions due to suppression or stimulation of pituitary PRL secretion. Furthermore, lactogenic hormones appear to exert counterregulatory actions which may modify glucocorticosteroid actions on immune and other target issues.

Keywords

Bernton EW, Meltzer MS, Holaday JW

Year 1988

Authors Bernton EW, Meltzer MS, Holaday JW

Report Name Suppression of macrophage activation and TIymphocyte function in hypoprolactinemic mice.

Publication Science

Issue-page numbers 239:401–404 doi:10.1126/science.3122324. PMID:3122324

URL http://www.sciencemag.org/content/239/4838/401.short

Abstract The effects of prolactin on lactation and reproductive organs are well known. However, the other possible target organs and physiological consequences of altered levels of circulating prolactin remain poorly understood. In this study, mice were treated with bromocryptine, a dopamine receptor agonist that inhibits pituitary prolactin secretion. Bromocryptine treatment prevented T-cell-dependent induction of macrophage tumoricidal activity after the intraperitoneal injection of Listeria monocytogenes or Mycobacterium bovis. Coincident treatment with ovine prolactin reversed this effect. Of the multiple events leading to macrophage activation in vivo, the production by T-lymphocytes of gamma-interferon was the most impaired in bromocryptine-treated mice. Lymphocyte proliferation after stimulation with mitogens in vitro was also depressed in spleens of bromocryptine-treated mice, and coadministration of prolactin also reversed this effect. Bromocryptine treatment also reduced the number of deaths resulting from inoculation of mice with Listeria; exogenous prolactin significantly reversed this effect. The critical influence of pituitary prolactin release on maintenance of lymphocyte function and on lymphokine-dependent macrophage activation suggests that, in mice, lymphocytes are an important target tissue for circulating prolactin.

Keywords

Berson DM, Dunn FA, Takao M

Year 2002

Authors David M. Berson, Felice A. Dunn and Motoharu Takao

Report Name Phototransduction by Retinal Ganglion Cells That Set the Circadian Clock

Publication Science

Issue-page numbers 2002;295:1070-1073

URL http://www.sciencemag.org/content/295/5557/1070.short

Abstract Light synchronizes mammalian circadian rhythms with environmental time by modulating retinal input to the circadian pacemaker—the suprachiasmatic nucleus (SCN) of the hypothalamus. Such photic entrainment requires neither rods nor cones, the only known retinal photoreceptors. Here, we show that retinal ganglion cells innervating the SCN are intrinsically photosensitive. Unlike other ganglion cells, they depolarized in response to light even when all synaptic input from rods and cones was blocked. The sensitivity, spectral tuning, and slow kinetics of this light response matched those of the photic entrainment mechanism, suggesting that these ganglion cells may be the primary photoreceptors for this system.

Keywords circadian,

Beskonakli E, Palaoglu S, Aksaray S et al.

Year 2001

Authors E. Beskonakli, S. Palaoglu, S. Aksaray, G. Alanoglu, T. Turhan and Y. Taskin

Report Name Effect of pinealectomy on immune parameters in rats with Staphylococcus aureus infection

Publication Neurosurg Rev

Issue-page numbers 24:26–30 doi:10.1007/PL00011962. PMID:11339464

URL http://www.springerlink.com/content/w52nx0v3bnpbqwvj/

Abstract It is generally accepted that the pineal gland is a neuroendocrine organ. Several recent experiments have shown that the pineal gland has functional and anatomical connections, particularly with the immune system, and therefore the gland is now recognized as an important immunoneuroendocrine organ in both man and animals. The present study investigates the effect of pinealectomy on some immune parameters, including hematological alterations, and the response of the brain tissue against infection caused by Staphylococcus aureus. Experiments were performed on two different age groups of rats (neonatal and young). The results showed a significant reduction of the plasma zinc level in the third week following pinealectomy, impairment of the hematological parameters including lymphocyte, erythrocyte, and leucocyte, and the deficiency of the brain response to the infective agent, particularly in pinealectomized neonatal rats. In view of these data and as described previously, the pineal gland has a main regulatory function in immune physiology, but our study indicates that only neonatal immune functions are significantly affected by pinealectomy.

Keywords Immune system - Infection - Pinealectomy - Staphylococcus aureus

Authors Parveen Bhatti, Kara L Cushing-Haugen, Kristine G Wicklund, Jennifer A Doherty, Mary Anne Rossing

Report Name Nightshift work and risk of ovarian cancer

Publication Occup Environ Med

Issue-page numbers doi:10.1136/oemed-2012-101146

URL http://oem.bmj.com/content/early/2013/01/22/oemed-2012-101146.short

Abstract

Objectives Animal evidence suggests that circadian disruption may be associated with ovarian cancer, though very little epidemiological work has been done to assess this potential association. We evaluated the association between self-reported nightshift work, a known circadian disruptor, and ovarian cancer in a population-based case-control study.

Methods The study included 1101 women with invasive epithelial ovarian cancer, 389 women with borderline epithelial ovarian tumours and 1832 controls and was conducted in western Washington state. Shift work data were collected as part of inperson interviews.

Results Working the nightshift was associated with an increased risk of invasive (OR=1.24, 95% CI 1.04 to 1.49) and borderline (OR=1.48, 95% CI 1.15 to 1.90) tumours; however, we observed little evidence that risks increased with increasing cumulative duration of nightshift work, and risks were not elevated in the highest duration category (>7 nightshift work-years). Increased risks were restricted to women who were 50 years of age and older and to serous and mucinous histologies of invasive and borderline tumours. There was suggestive evidence of a decreased risk of ovarian cancer among women reporting a preference for activity during evenings rather than mornings.

Conclusions We found evidence suggesting an association between shift work and ovarian cancer. This observation should be followed up in future studies incorporating detailed assessments of diurnal preference (ie, chronotype) in addition to detailed data on shift schedules.

Keywords

Bhatti P, Mirick DK, Davis S — *Year* 2012

Authors Parveen Bhatti, Dana K. Mirick and Scott Davis

Report Name Racial Differences in the Association Between Night Shift Work and Melatonin Levels Among Women

Publication Am. J. Epidemiol.

Issue-page numbers (2013) doi: 10.1093/aje/kws278 First published online: February 3, 2013

URL http://aje.oxfordjournals.org/content/early/2013/02/03/aje.kws278.abstract

Abstract Reduced suppression of melatonin in response to working the night shift among people of Asian ancestry has been suggested as a possible explanation for the null results observed in a recent analysis of shift work and breast cancer risk in a Chinese cohort. The authors analyzed the impact of Asian versus white race on previously reported differences in urinary 6-sulfatoxymelatonin levels in a 2003–2008 study in Seattle, Washington, of female health-care workers that exclusively worked night or day shifts. A total of 225 white and 51 Asian participants were included in the analysis. Although 6-sulfatoxymelatonin levels were affected by night shift work in both racial groups, Asian night shift workers consistently showed 6-sulfatoxymelatonin levels that were closer to levels in day shift workers than did white night shift workers. Furthermore, differences in 6-sulfatoxymelatonin levels between white and Asian night shift workers relative to day shift workers were statistically significant in every instance ($P < 0.05$). These results suggest that Asians may be better able to maintain a “normal” circadian pattern of melatonin production compared with whites and suggest a biological mechanism by which Asian night shift workers may be at a reduced risk of cancer.

Keywords cancer, melatonin, race, shift work

Billitteri A, Bindoni M — *Year* 1969

Authors Billitteri A, Bindoni M

Report Name [Growth and cell multiplication of Ehrlich’s tumor in the mouse, after removal of the pineal body]

Publication Boll Soc Ital Biol Sper

Issue-page numbers 45:1647–1650. PMID:5400878

URL http://www.ncbi.nlm.nih.gov/pubmed/5400878

Abstract N/A

Keywords

Bilsland D, George SA, Gibbs NK, et al. **Year** 1993

Authors D Bilsland, S A George, N K Gibbs, T Aitchison, B E Johnson, J Ferguson

Report Name A comparison of narrow band phototherapy (TL-01) and photochemotherapy (PUVA) in the management of polymorphic light eruption

Publication The British journal of dermatology

Issue-page numbers Volume: 129, Issue: 6, Pages: 708-712

URL http://www.mendeley.com/research/comparison-narrow-band-phototherapy-tl01-photochemotherapy-puva-management-polymorphic-light-eruption/

Abstract Twenty-five patients suffering from severe polymorphic light eruption (PLE) were randomized to either photochemotherapy (PUVA) or narrow-band phototherapy (TL-01 UVB) treatment in early spring; patients receiving UVB were given placebo tablets to achieve a matching therapy procedure. During the 4 months following treatment, patient exposure to solar UVB was monitored with polysulphone badges. PLE occurrence, severity, and restriction of outdoor activity were recorded, using weekly diary-sheets. Analysis of covariance on this data, using the logarithm of UVB exposure as the explanatory variable, showed no significant differences between the treatments. TL-01 UVB is an effective alternative to PUVA in the management of PLE.

Keywords

Birch-Johansen F, Jensen A, Mortensen L, et al. **Year** 2010

Authors Fatima Birch-Johansen, Allan Jensen, Lone Mortensen, Anne Braae Olesen, Susanne K. Kjær

Report Name Trends in the incidence of nonmelanoma skin cancer in Denmark 1978-2007: Rapid incidence increase among young Danish women

Publication International Journal of Cancer

Issue-page numbers Volume 127, Issue 9, pages 2190–2198, 1 November 2010

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.25411/abstract?

Abstract Nonmelanoma skin cancer (NMSC) is the most common cancer among Caucasian populations worldwide, and incidence rates are increasing. However, NMSC data are not routinely collected by cancer registries, but Denmark has extensive registration of NMSC in two nationwide population-based registries. We assessed incidence trends of NMSC in Denmark from 1978 to 2007. Data for basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) were obtained from the Danish Cancer Registry and the Danish Registry of Pathology. For both genders, age-specific incidence rates and overall incidence rates, age-adjusted according to the World standard population were calculated based on combined data from the two registries. For both genders, a high increase in both BCC and SCC incidence was observed over time. Between 1978 and 2007, the age-adjusted BCC incidence increased from 27.1 to 96.6 cases per 100,000 person-years for women and from 34.2 to 91.2 cases for men. The SCC incidence increased from 4.6 to 12.0 cases per 100,000 person-years for women and from 9.7 to 19.1 cases for men. For both BCC and SCC, women experienced a higher average annual percentage incidence change than men. Furthermore, the average annual percentage change in BCC incidence among persons below 40 years was significantly higher compared to older persons, especially for women. These trends may lead to an alarming NMSC incidence increase over time as population ages and will have major implications for future healthcare services. Our findings underline the need for improved preventive strategies to hamper the increasing NMSC incidence.

Keywords nonmelanoma skin cancer; basal cell carcinoma; squamous cell carcinoma; incidence; Denmark

Biris AS, Boldor D, Palmer J, et al. **Year** 0

Authors Biris, Alexandru S.; Boldor, Dorin; Palmer, Jason; Monroe, William T.; Mahmood, Meena; Dervishi, Enkeleda; Xu, Yang; Li, Zhongrui; Galanzha, Ekaterina I.; Zharov, Vladimir P.

Report Name Nanophotothermolysis of multiple scattered cancer cells with carbon nanotubes guided by time-resolved infrared thermal imaging

Publication Journal of Journal of Biomedical Optics

Issue-page numbers Volume 14, Issue 2, pp. 021007-021007-6 (2009).

URL http://adsabs.harvard.edu/abs/2009JBO....14b1007B

Abstract Nanophotothermolysis with long laser pulses for treatment of scattered cancer cells and their clusters is introduced with the main focus on real-time monitoring of temperature dynamics inside and around individual cancer cells labeled with carbon nanotubes. This technique utilizes advanced time- and spatially-resolved thermal radiometry imaging for the visualization of laser-induced temperature distribution in multiple-point absorbing targets. The capability of this approach was demonstrated for monitoring of thermal effects under long laser exposure (from millisecond to seconds, wavelength 1064 nm, maximum power 1 W) of cervical cancer HeLa cells labeled with carbon nanotubes in vitro. The applications are discussed with a focus on the nanophotothermolysis of small tumors, tumor margins, or micrometastases under the guidance of near-IR and microwave radiometry.

Keywords nanoparticles, nanotechnology, photodynamic therapy, photothermal effects, radiometry, temperature distribution, tumours

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Bittman EL, Dempsey RJ, Karsch FJ **Year** 1983

Authors ERIC L. BITTMAN, ROBERT J. DEMPSEY and FRED J. KARSCH

Report Name Pineal melatonin secretion drives the reproductive response to daylength in the ewe

Publication Endocrinology

Issue-page numbers 113:2276–2283 doi:10.1210/endo-113-6-2276. PMID:6641634

URL http://endo.endojournals.org/content/113/6/2276

Abstract This study was conducted to determine whether the pineal indoleamine melatonin mediates the effects of photoperiod on the capacity of estradiol to inhibit LH secretion in the ewe. Patterns of serum melatonin were characterized in pineal-intact ovariectomized ewes treated with sc Silastic estradiol implants and exposed to 90-day alternations between long and short photoperiods. High fluctuating levels of serum melatonin were found during the night, with the duration of elevated serum levels corresponding to the length of the dark period. Transfer from long to short photoperiods caused a rapid change in the duration of nightly melatonin secretion and reduced the negative feedback potency of estradiol upon LH secretion during the natural anestrous season. In pinealectomized ewes, the nighttime rise of melatonin was absent, and transfer from long to short days failed to reverse the capacity of estradiol to inhibit LH secretion during anestrus. Nightly infusions of melatonin restored patterns of this indoleamine similar to those observed in pineal-intact ewes exposed to the 90-day alternation between long and short days. The melatonin infusions also restored the reproductive response to the inductive photoperiod: in every ewe, the negative feedback effects of estradiol upon LH secretion were diminished after transfer from long to short days. The amplitude and latency of this escape matched those of pinealintact animals. We conclude that the pineal mediates the reproductive response of the ewe to inductive photoperiods through its daily rhythm of melatonin secretion

Keywords

Bjarnason GA, Jordan RC, Sothern RB **Year** 1999

Authors Bjarnason GA, Jordan RC, Sothern RB

Report Name Circadian variation in the expression of cell-cycle proteins in human oral epithelium

Publication Am J Pathol

Issue-page numbers 154:613–622. PMID:10027418

URL http://www.journals.elsevierhealth.com/periodicals/ajpa/article/PIIS0002944010653060/abstract

Abstract At the tissue level, there is experimental and clinical data to suggest a cytokinetic coordination of the cell cycle with a greater proportion of cycling cells entering S-phase and mitosis at specific times of the day. The association of certain cell-cycle proteins with defined events in the cell cycle is well established and may be used to study the timing of cell-cycle phases over 24 hours. In this study oral mucosal biopsies were obtained from six normal human volunteers at 4-hour intervals, six times over 24 hours. Using immunohistochemistry, the number of positive cells expressing the proteins p53, cyclin-E, cyclin-A, cyclin-B1, and Ki-67 was determined for each biopsy and expressed as the number of positive cells per mm of basement membrane. We found a statistically significant circadian variation in the nuclear expression of all of these proteins with the high point of expression for p53 at 10:56 hours, cyclin-E at 14:59 hours, cyclin-A at 16:09 hours, cyclin-B1 at 21:13 hours, and Ki-67 at 02:50 hours. The circadian variation in the nuclear expression of cyclins-E (G1/S phase), -A (G2-phase), and -B1 (M-phase) with a normal physiological progression over time suggests a statistically significant circadian variation in oral epithelial cell proliferation. The finding of a circadian variation in the nuclear expression of p53 protein corresponding to late G1 is novel. This information has clinical implications regarding the timing of chemotherapy and radiotherapy.

Keywords

Bjarnason GA, Jordan RC, Wood PA et al. **Year** 2001

Authors Georg A. Bjarnason, Richard C. K. Jordan, Patricia A. Wood, Qi Li, David W. Lincoln, Robert B. Sothern, William J. M. Hrushesky, and Yaacov Ben-David

Report Name Circadian expression of clock genes in human oral mucosa and skin: association with specific cell-cycle phases

Publication Am J Pathol

Issue-page numbers 158:1793–1801. PMID:11337377

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1891949/

Abstract We studied the relative RNA expression of clock genes throughout one 24-hour period in biopsies obtained from the oral mucosa and skin from eight healthy diurnally active male study participants. We found that the human clock genes hClock, hTim, hPer1, hCry1, and hBmal1 are expressed in oral mucosa and skin, with a circadian profile consistent with that found in the suprachiasmatic nuclei and the peripheral tissues of rodents. hPer1, hCry1, and hBmal1 have a rhythmic expression, peaking early in the morning, in late afternoon, and at night, respectively, whereas hClock and hTim are not rhythmic. This is the first human study to show a circadian profile of expression for all five clock genes as documented in rodents, suggesting their functional importance in man. In concurrent oral mucosa biopsies, thymidylate synthase enzyme activity, a marker for DNA synthesis, had a circadian variation with peak activity in early afternoon, coinciding with the timing of S phase in our previous study on cell-cycle timing in human oral mucosa. The major peak in hPer1 expression occurs at the same time of day as the peak in G1 phase in oral mucosa, suggesting a possible link between the circadian clock and the mammalian cell cycle.

Keywords

Bjorvatn B, Pallesen S

Year 2009

Authors Bjorvatn B, Pallesen S.

Report Name A practical approach to circadian rhythm sleep disorders

Publication Sleep Med Rev

Issue-page numbers Feb;13(1):47-60. Epub 2008 Oct 8.

URL http://www.cmse.ch/pdf/colloque_14_octobre/6_approche%20troubles%20circadiens.pdf

Abstract Circadian rhythm sleep disorders are common in clinical practice. The disorders covered in this review are delayed sleep phase disorder, advanced sleep phase disorder, free-running, irregular sleep-wake rhythm, jet lag disorder and shift work disorder. Bright light treatment and exogenous melatonin administration are considered to be the treatments of choice for these circadian rhythm sleep disorders. Circadian phase needs to be estimated in order to time the treatments appropriately. Inappropriately timed bright light and melatonin will likely worsen the condition. Measurements of core body temperature or endogenous melatonin rhythms will objectively assess circadian phase; however, such measurements are seldom or never used in a busy clinical practice. This review will focus on how to estimate circadian phase based on a careful patient history. Based on such estimations of circadian phase, we will recommend appropriate timing of bright light and/or melatonin in the different circadian rhythm sleep disorders. We hope this practical approach and simple recommendations will stimulate clinicians to treat patients with circadian rhythm sleep disorders.

Keywords Circadian rhythm; disorders; Bright light; Melatonin; Nadir; Sleep regulation

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Blask DE

Year 2008

Authors David E. Blask

Report Name Melatonin, sleep disturbance and cancer risk

Publication Sleep Medicine Reviews

Issue-page numbers Volume 13, Issue 4, August 2009, Pages 257-264

URL http://www.sciencedirect.com/science/article/pii/S1087079208000786

Abstract The pineal hormone melatonin is involved in the circadian regulation and facilitation of sleep, the inhibition of cancer development and growth, and the enhancement of immune function. Individuals, such as night shift workers, who are exposed to light at night on a regular basis experience biological rhythm (i.e., circadian) disruption including circadian phase shifts, nocturnal melatonin suppression, and sleep disturbances. Additionally, these individuals are not only immune suppressed, but they are also at an increased risk of developing a number of different types of cancer. There is a reciprocal interaction and regulation between sleep and the immune system quite independent of melatonin. Sleep disturbances can lead to immune suppression and a shift to the predominance in cancer-stimulatory cytokines. Some studies suggest that a shortened duration of nocturnal sleep is associated with a higher risk of breast cancer development. The relative individual contributions of sleep disturbance, circadian disruption due to light at night exposure, and related impairments of melatonin production and immune function to the initiation and promotion of cancer in high-risk individuals such as night shift workers are unknown. The mutual reinforcement of interacting circadian rhythms of melatonin production, the sleep/wake cycle and immune function may indicate a new role for undisturbed, high quality sleep, and perhaps even more importantly, uninterrupted darkness, as a previously unappreciated endogenous mechanism of cancer prevention.

Keywords Melatonin; Pineal gland; Biological rhythms; Night shift work; Light at night; Circadian disruption; Sleep disturbance; Cancer risk

Blask DE

Year 1993

Authors Blask DE

Report Name Melathonin in oncology. In: Yu HS & Reiter RJ, Ed. elatonin: biosynthesis physiological effects and clinical applications

Publication Boca Raton: CRC press

Issue-page numbers pp. 447–475

URL N/A

Abstract N/A

Keywords

Blask DE

Year 2001

Authors Blask DE

Report Name An overview of the neuroendocrine regulation of experimental tumor growth by melatonin and its analogues and the therapeutic use of melatonin in oncology. In: Bartsch C, Barts

Publication The Pineal Gland and Cancer: Neuroimmunoendocrine

Issue-page numbers pp. 309–342

URL N/A

Abstract N/A

Keywords

Blask DE, Brainard GC, Dauchy RT, et al. ***Year*** 2005

Authors David E. Blask, George C. Brainard, Robert T. Dauchy, John P. Hanifin, Leslie K. Davidson, Jean A. Krause, Leonard A. Sauer, Moises A. Rivera-Bermudez, et al.

Report Name Melatonin-Depleted Blood from Premenopausal Women Exposed to Light at Night Stimulates Growth of Human Breast Cancer Xenografts in Nude Rats

Publication Cancer Research

Issue-page numbers 2005;65:11174-84

URL http://cancerres.aacrjournals.org/content/65/23/11174.abstract

Abstract

The increased breast cancer risk in female night shift workers has been postulated to result from the suppression of pineal melatonin production by exposure to light at night. Exposure of rats bearing rat hepatomas or human breast cancer xenografts to increasing intensities of white fluorescent light during each 12-hour dark phase (0-345 μW/cm2) resulted in a dose-dependent suppression of nocturnal melatonin blood levels and a stimulation of tumor growth and linoleic acid uptake/metabolism to the mitogenic molecule 13-hydroxyoctadecadienoic acid. Venous blood samples were collected from healthy, premenopausal female volunteers during either the daytime, nighttime, or nighttime following 90 minutes of ocular bright, white fluorescent light exposure at 580 μW/cm2 (i.e., 2,800 lx). Compared with tumors perfused with daytime-collected melatonin-deficient blood, human breast cancer xenografts and rat hepatomas perfused in situ, with nocturnal, physiologically melatonin-rich blood collected during the night, exhibited markedly suppressed proliferative activity and linoleic acid uptake/metabolism. Tumors perfused with melatonin-deficient blood collected following ocular exposure to light at night exhibited the daytime pattern of high tumor proliferative activity. These results are the first to show that the tumor growth response to exposure to light during darkness is intensity dependent and that the human nocturnal, circadian melatonin signal not only inhibits human breast cancer growth but that this effect is extinguished by short-term ocular exposure to bright, white light at night. These mechanistic studies are the first to provide a rational biological explanation for the increased breast cancer risk in female night shift workers.

Keywords light at night, melatonin, breast cancer

Authors David E. Blask, Robert T. Dauchy, George C. Brainard, John P. Hanifin

Report Name Circadian Stage-Dependent Inhibition of Human Breast Cancer Metabolism and Growth by the Nocturnal Melatonin Signal: Consequences of Its Disruption by Light at Night in Ra

Publication Integr Cancer Ther

Issue-page numbers December 2009 vol. 8 no. 4 347-353 doi: 10.1177/1534735409352320

URL http://ict.sagepub.com/content/8/4/347.abstract

Abstract The circadian production of melatonin by the pineal gland during the night provides an inhibitory signal to tissue-isolated steroid receptor SR+ and — MCF-7 human breast cancer xenografts in female nude rats. A pivotal mechanism for melatonin's anticancer effects in vivo involves a melatonin receptor-mediated inhibition of linoleic acid (LA) uptake and its metabolism to mitogenically active 13-hydroxyoctadecadienoic acid (13-HODE). Exposure of (SR-) xenograft-bearing rats to increasing intensities of polychromatic white light at night suppresses melatonin while increasing tumor growth rates, DNA content, [3H]thymidine incorporation into DNA, LA uptake, 13-HODE formation cAMP levels and ERK1/2 activation a dose-dependent manner. Similar effects occur in SR- human breast cancer xenografts perfused in situ with melatonin-depleted blood from healthy female subjects after their exposure to a single bright intensity (2800 lux) of polychromatic light at night. Additionally, SR- human breast cancer xenografts exhibit robust circadian rhythms of LA uptake, 13-HODE formation and proliferative activity. Exposure of xenograft-bearing rats to dim light at night results in the complete elimination of these rhythms which culminates in unfettered, high rates of tumor metabolism and growth. The organization of tumor metabolism and growth within circadian time structure by the oncostatic melatonin signal helps create a balance between the cancer and its host that is disrupted by host exposure to light at night. This biological mechanism may partially explain the higher risk of breast and other cancers in women working rotating night shifts and possibly others who also experience prolonged exposure to light at night.

Keywords melatonin, circadian disruption, breast cancer, light at night, tumor metabolism

Blask DE, Dauchy RT, Sauer LA **Year** 2005

Authors Blask DE, Dauchy RT, Sauer LA

Report Name Putting cancer to sleep at night: the neuroendocrine/circadian melatonin signal.

Publication Endocrine

Issue-page numbers 27:179–188 doi:10.1385/ENDO:27:2:179. PMID:16217131

URL http://www.ncbi.nlm.nih.gov/pubmed/16217131

Abstract Physiological and pharmacological blood concentrations of melatonin inhibit tumorigenesis in a variety of in vivo and in vitro experimental models of neoplasia. Evidence indicates that melatonin's anticancer effects are exerted via inhibition of cell proliferation and a stimulation of differentiation and apoptosis. A new mechanism by which physiological and pharmacological blood levels of melatonin inhibit cancer growth in vivois via a melatonin-induced suppression of tumor linoleic acid (LA) uptake and its metabolism to the important mitogenic signaling molecule 13-hydroxyoctadecadienoic acid (13-HODE). Melatonin suppresses cAMP formation and inhibits tumor uptake of LA and its metabolism to 13-HODE via a melatonin receptor-mediated mechanism in both tissue-isolated rat hepatoma 7288 CTC and human breast cancer xenografts. It has been postulated that in industrialized societies, light at night, by suppressing melatonin production, poses a new risk for the development of breast cancer and, perhaps, other cancers as well. In support of this hypothesis, light during darkness suppresses nocturnal melatonin production and stimulates the LA metabolism and growth of rat hepatoma and human breast cancer xenografts. Nocturnal dietary supplementation with melatonin, at levels contained in a melatonin-rich diet, inhibits rat hepatoma growth via the mechanisms described above. The nocturnal melatonin signal organizes tumor metabolism and growth within circadian time structure that can be further reinforced by appropriately timed melatonin supplementation. Dietary melatonin supplementation working in concert with the endogenous melatonin signal has the potential to be a new preventive/therapeutic strategy to optimize the host/cancer balance in favor of host survival and quality of life.

Keywords

Blask DE, Dauchy RT, Sauer LA, et al. **Year** 2003

Authors David E. Blask, Robert T. Dauchy, Leonard A. Sauer, Jean A. Krause and George C. Brainard

Report Name Growth and Fatty Acid Metabolism of Human Breast Cancer (MCF-7) Xenografts in Nude Rats: Impact of Constant Light-Induced Nocturnal Melatonin Suppression

Publication Breast Cancer Research and Treatment

Issue-page numbers Volume 79, Number 3, 313-320, DOI: 10.1023/A:1024030518065

URL http://www.springerlink.com/content/g32223j83h8m7803/

Abstract The nocturnal melatonin (MLT) surge is a relevant oncostatic signal for a variety of experimental malignancies. Population studies support the hypothesis that exposure to light at night may represent a new risk factor for breast cancer possibly through the suppression of pineal MLT production and/or circadian disruption. We tested the ability of constant light exposure to suppress MLT production in female nude rats and stimulate the growth of tissue-isolated MCF-7 human breast cancer xenografts via increased tumor linoleic acid (LA) metabolism. Rats maintained on an alternating light/dark cycle (L:D group) exhibited a robust circadian MLT rhythm that was abolished following constant light exposure. During the exposure of animals bearing tissue-isolated human MCF-7 breast cancer xenografts to constant light, the rate of tumor growth markedly increased relative to the L:D group. Tumor LA uptake and its metabolism to the mitogen 13-hydroxyoctadecadienoic acid (13-HODE) were also substantially higher under constant light conditions. This is the first biological evidence for a potential link between constant light exposure and increased human breast oncogenesis involving MLT suppression and stimulation of tumor LA metabolism.

Keywords circadian disruption - constant light - fatty acids - MCF-7 human breast cancer xenografts - melatonin - pineal gland

Authors Blask DE, Dauchy RT, Sauer LA, Krause JA

Report Name Melatonin uptake and growth prevention in rat hepatoma 7288CTC in response to dietary melatonin: melatonin receptor-mediated inhibition of tumor linoleic acid metabolism to th

Publication Carcinogenesis

Issue-page numbers 25:951–960 doi:10.1093/carcin/bgh090. PMID:14754876

URL http://carcin.oxfordjournals.org/content/25/6/951.full

Abstract

Both physiological and pharmacological levels of the pineal hormone melatonin exhibit substantial anticancer activity in tissue-isolated rat hepatoma 7288CTC via melatonin receptor-mediated blockade of tumor uptake of linoleic acid (LA) and its metabolism to the mitogenic signaling molecule 13-hydroxyoctadecadienoic acid (13-HODE). Melatonin is also present in significant amounts in edible plants and is supplied in nutritional supplements. We confirmed the presence of significant quantities of melatonin in 20 varieties of edible plants. In pinealectomized tumor-free rats, 3 weeks of ingestion of either 5 or 50 microg/day of melatonin contained in a semi-purified diet resulted in a dose-dependent elevation in steady-state plasma melatonin levels within the nocturnal physiological range. In pineal-intact tumor-bearing rats, the daily intake of 5 microg/day of melatonin for 3 weeks resulted in an enhanced amplitude and duration of the nocturnal melatonin levels within physiological circulating limits. The nocturnal melatonin amplitude in rats ingesting 500 ng of melatonin/day remained within the physiological range. A dose-related increase in tumor concentrations of melatonin occurred in animals ingesting melatonin from the diet. Perfusion of tumors in situ with physiological, nocturnal blood levels of melatonin resulted in a mean 31% uptake and retention of the melatonin. Chronic ingestion of 50 ng, 500 ng or 5 microg of melatonin/day supplied in a semi-purified 5% corn oil diet led to a significant dose-dependent reduction in the rates of tumor total fatty acid uptake, LA uptake, 13-HODE production and tumor growth. The co-ingestion of melatonin receptor antagonist S20928 completely blocked the effects and prevented the intra-tumoral accumulation of melatonin. Melatonin receptor-mediated suppression of tumor growth, LA uptake and metabolism, and stimulation of tumor melatonin uptake and retention in response to the dietary intake of phytomelatonin from edible plants or melatonin from nutritional supplements, could play an important role in cancer growth prevention.

Keywords

Authors Blask DE, Hill SM

Report Name Effects of melatonin on cancer: studies on MCF-7 human breast cancer cells in culture.

Publication J Neural Transm

Issue-page numbers Suppl 21:433–449. PMID: 3462341

URL http://www.ncbi.nlm.nih.gov/pubmed/3462341

Abstract There is some evidence to suggest that the pineal gland influences neoplastic growth. Either crude or partially-purified pineal extracts have been used to treat malignant neoplasms in humans. More compelling evidence indicates that the pineal hormone melatonin, in addition to its well known antireproductive effects, may also exert oncostatic effects particularly in animal models of human breast cancer. However, it is not clear whether melatonin inhibits mammary cancer growth via an indirect neuroendocrine mechanism or via an action directly on the cancer cells themselves. Studies are described in which physiological concentrations of melatonin are shown to have marked inhibitory effects directly on MCF-7 human breast cancer cell growth in culture. Supra- or subphysiological levels of melatonin are completely ineffective in retarding breast cancer cell proliferation. Precursors and metabolites of melatonin such as serotonin, N-acetylserotonin and 6-hydroxymelatonin do not inhibit MCF-7 cell growth. Similarly, neither 5-methoxytryptophol nor 5-methoxytryptamine, regarded by some to be putative pineal hormones, exhibit antimitogenic properties. Melatonin completely blocks the estradiol-induced stimulation of MCF-7 cell proliferation. In defined, serum-free medium, melatonin loses its antimitogenic capabilities unless cells are also simultaneously exposed to either estradiol or prolactin. Therefore, the antiproliferative effect of melatonin may be dependent on the presence of serum and a complex interaction with hormones such as estradiol and/or prolactin.

Keywords

Blask DE, Hill SM, Dauchy RT, et al. **Year** 2011

Authors David E. Blask, Steven M. Hill, Robert T. Dauchy, Shulin Xiang, Lin Yuan, Tamika Duplessis, Lulu Mao, Erin Dauchy, Leonard A. Sauer

Report Name Circadian regulation of molecular, dietary, and metabolic signaling mechanisms of human breast cancer growth by the nocturnal melatonin signal and the consequences of its dis

Publication Journal of Pineal Research

Issue-page numbers Volume 51, Issue 3, pages 259-269, October 2011

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2011.00888.x/abstract

Abstract

This review article discusses recent work on the melatonin-mediated circadian regulation and integration of molecular, dietary, and metabolic signaling mechanisms involved in human breast cancer growth and the consequences of circadian disruption by exposure to light at night (LAN). The antiproliferative effects of the circadian melatonin signal are mediated through a major mechanism involving the activation of MT1 melatonin receptors expressed in human breast cancer cell lines and xenografts. In estrogen receptor (ERα+) human breast cancer cells, melatonin suppresses both ERα mRNA expression and estrogen-induced transcriptional activity of the ERα via MT1-induced activation of Gαi2 signaling and reduction of 3′,5′-cyclic adenosine monophosphate (cAMP) levels. Melatonin also regulates the transactivation of additional members of the steroid hormone/nuclear receptor super-family, enzymes involved in estrogen metabolism, expression/activation of telomerase, and the expression of core clock and clock-related genes. The anti-invasive/anti-metastatic actions of melatonin involve the blockade of p38 phosphorylation and the expression of matrix metalloproteinases. Melatonin also inhibits the growth of human breast cancer xenografts via another critical pathway involving MT1-mediated suppression of cAMP leading to blockade of linoleic acid uptake and its metabolism to the mitogenic signaling molecule 13-hydroxyoctadecadienoic acid (13-HODE). Down-regulation of 13-HODE reduces the activation of growth factor pathways supporting cell proliferation and survival. Experimental evidence in rats and humans indicating that LAN-induced circadian disruption of the nocturnal melatonin signal activates human breast cancer growth, metabolism, and signaling provides the strongest mechanistic support, thus far, for population and ecological studies demonstrating elevated breast cancer risk in night shift workers and other individuals increasingly exposed to LAN.

Keywords breast cancer; circadian disruption; diet; melatonin; metabolism; molecular signaling

Blask DE, Pelletier DB, Hill SM et al. **Year** 1991

Authors Blask DE, Pelletier DB, Hill SM et al.

Report Name Pineal melatonin inhibition of tumor promotion in the N-nitroso-N-methylurea model of mammary carcinogenesis: potential involvement of antiestrogenic mechanisms in vivo

Publication J Cancer Res Clin Oncol

Issue-page numbers 117:526–532 doi:10.1007/BF01613283. PMID:1744157

URL http://www.springerlink.com/content/p480307p01332626/

Abstract TheN-methyl-N-nitrosurea (NMU) model of hormone-responsive rat mammary carcinogenesis was used to address the hypothesis that melatonin (Mel), the principle hormone of the pineal gland, inhibits tumorigenesis by acting as an anti-promoting rather than an anti-initiating agent. Daily late-afternoon injections of Mel (500 mgrg/day), restricted to the initiation phase of NMU mammary tumorigenesis, were ineffective in altering tumor growth over a 20-week period. When Mel treatment was delayed for 4 weeks after NMU and then continued through the remainder of the promotion phase, only tumor number was significantly lower than in controls. However, when Mel injections encompassed the entire promotion phase, both tumor incidence and number were significantly lower than in the controls. Although elimination of the endogenous Mel signal via pinealectomy promoted tumor growth, the effect was not statistically significant. Serum levels of estradiol and tumor estrogen receptor content were unaltered by either Mel or pinealectomy. While Mel treatment failed to affect circulating prolactin levels, pinealectomy caused a two-fold increase in serum prolactin. The estradiol-stimulated recrudescence of tumors following ovariectomy was completely blocked by either 20, 100 or 500 mgrg Mel/day or tamoxifen (20 mgrg/day). Thus, Mel appears to be an antipromoting hormone that may antagonize the tumor-promoting actions of estradiol in this model of mammary tumorigenesis.

Keywords Pineal - Melatonin - Breast cancer - Hormones - N-Nitroso-N-methylurea

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Blask DE, Sauer LA, Dauchy R, et al. **Year** 1999

Authors Blask DE, Sauer LA, Dauchy R, Holowachuk EW, Ruhoff MS.

Report Name New actions of melatonin on tumor metabolism and growth

Publication Biol Signals Recept

Issue-page numbers Jan-Apr;8(1-2):49-55

URL http://www.ncbi.nlm.nih.gov/pubmed/10085462

Abstract Melatonin is an important inhibitor of cancer growth promotion while the essential polyunsaturated fatty acid, linoleic acid is an important promoter of cancer progression. Following its rapid uptake by tumor tissue, linoleic acid is oxidized via a lipoxygenase to the growth-signaling molecule, 13-hydroxyoctadecadienoic acid (13-HODE) which stimulates epidermal growth factor (EGF)-dependent mitogenesis. The uptake of plasma linoleic acid and its metabolism to 13-HODE by rat hepatoma 7288CTC, which expresses both fatty acid transport protein and melatonin receptors, is inhibited by melatonin in a circadian-dependent manner. This inhibitory effect of melatonin is reversible with either pertussis toxin, forskolin or cAMP. While melatonin inhibits tumor linoleic acid uptake, metabolism and growth, pinealectomy or constant light exposure stimulates these processes. Thus, melatonin and linoleic acid represent two important environmental signals that interact in a unique manner to regulate tumor progression and ultimately the host-cancer balance.

Keywords

Authors Blask DE, Sauer LA, Dauchy RT

Report Name Melatonin as a chronobiotic/anticancer agent: cellular, biochemical, and molecular mechanisms of action and their implications for circadian-based cancer therapy

Publication Curr Top Med Chem

Issue-page numbers 2:113–132 doi:10.2174/1568026023394407. PMID:11899096

URL http://www.ncbi.nlm.nih.gov/pubmed/11899096

Abstract Melatonin, as a new member of an expanding group of regulatory factors that control cell proliferation and loss, is the only known chronobiotic, hormonal regulator of neoplastic cell growth. At physiological circulating concentrations, this indoleamine is cytostatic and inhibits cancer cell proliferation in vitro via specific cell cycle effects. At pharmacological concentrations, melatonin exhibits cytotoxic activity in cancer cells. At both physiological and pharmacological concentrations, melatonin acts as a differentiating agent in some cancer cells and lowers their invasive and metastatic status through alterations in adhesion molecules and maintenance of gap junctional intercellular communication. In other cancer cell types, melatonin, either alone or in combination with other agents, induces apoptotic cell death. Biochemical and molecular mechanisms of melatonin's oncostatic action may include regulation of estrogen receptor expression and transactivation, calcium/calmodulin activity, protein kinase C activity, cytoskeletal architecture and function, intracellular redox status, melatonin receptor-mediated signal transduction cascades, and fatty acid transport and metabolism. A major mechanism mediating melatonin's circadian stage-dependent tumor growth inhibitory action is the suppression of epidermal growth factor receptor (EGFR)/mitogen-activated protein kinase (MAPK) activity. This occurs via melatonin receptor-mediated blockade of tumor linoleic acid uptake and its conversion to 13-hydroxyoctadecadienoic acid (13-HODE) which normally activates EGFR/MAPK mitogenic signaling. This represents a potentially unifying model for the chronobiological inhibitory regulation of cancer growth by melatonin in the maintenance of the host/cancer balance. It also provides the first biological explanation of melatonin-induced enhancement of the efficacy and reduced toxicity of chemo- and radiotherapy in cancer patients.

Keywords

Blask DE, Sauer LA, Dauchy RT, et al. ***Year*** 1999

Authors David E. Blask, Leonard A. Sauer, Robert T. Dauchy, Eugene W. Holowachuk, Mary S. Ruhoff, and Heather S. Kopff

Report Name Melatonin Inhibition of Cancer Growth in Vivo Involves Suppression of Tumor Fatty Acid Metabolism via Melatonin Receptor-mediated Signal Transduction Events

Publication Cancer Research

Issue-page numbers 1999;59:4693-4701

URL http://cancerres.aacrjournals.org/content/59/18/4693.abstract

Abstract

The growth of rat hepatoma 7288CTC in vivo is stimulated by the uptake of linoleic acid (LA) and its metabolism to 13-hydroxyoctadecadienoic acid (13-HODE), an important mitogenic signaling molecule within this tumor. Conversely, the growth of a variety of experimental cancers in vivo is inhibited by either physiological or pharmacological levels of the pineal gland hormone melatonin, although the mechanism(s) are unknown. We tested the hypothesis that the mechanism of melatonin's anticancer action in vivo involves the inhibition of tumor LA uptake and metabolism to 13-HODE in hepatoma 7288CTC. Tumor uptake of LA and release of 13-HODE, measured in tissue-isolated rat hepatoma 7288CTC at 4-h intervals over a 24-h period, were highest during the light phase and lowest during the mid-dark phase, when plasma melatonin levels were lowest and highest, respectively. Pinealectomy eliminated this rhythm of tumor LA uptake and 13-HODE production, indicating that it was driven by the circadian melatonin rhythm. Perfusion of tissue-isolated tumors in situ with melatonin (1 nm) rapidly and reversibly inhibited the uptake of plasma fatty acids (FAs), including LA, and its metabolism to 13-HODE. These inhibitory effects of melatonin on tumor FA uptake and 13-HODE release were completely reversed by perfusion of tumors in situ with melatonin receptor antagonist S-20928, pertussis toxin, forskolin, or 8-bromo-cAMP. Perfusion of tumors in situ with melatonin also decreased tumor [3H]thymidine incorporation and DNA content; these effects on DNA synthesis were also prevented by the coperfusion of tumors with melatonin and S-20928, pertussis toxin, forskolin, 8-Br-cAMP, or 13-HODE. Pinealectomy stimulated tumor growth, LA uptake and metabolism to 13-HODE, and FA storage in hepatoma 7288CTC, whereas melatonin administration (200 μg/day) was inhibitory in vivo. Northern blot analysis revealed that, compared with normal liver tissue, hepatoma 7288CTC overexpressed mRNA transcripts for a plasma membrane-associated FA transport protein (FATP). FATP mRNA expression was unaffected by the treatment of tumor-bearing rats with daily afternoon melatonin injections or exposure to constant light. These results support a novel mechanism of tumor growth inhibition by melatonin involving a melatonin receptor-mediated suppression of cAMP levels, resulting in diminished tumor FA transport, possibly via decreased FATP function. The inhibition of these signal transduction events by melatonin culminates in the suppression of LA uptake, LA metabolism to the mitogenic signaling molecule 13-HODE, and cancer growth.

Keywords melatonin

Blask DE, Wilson ST, Zalatan F

Year 1997

Authors David E. Blask, Sean T. Wilson, and Fred Zalatan

Report Name Physiological melatonin inhibition of human breast cancer cell growth in vitro: evidence for a glutathione-mediated pathway

Publication Cancer Res

Issue-page numbers 57:1909–1914.PMID:9157984

URL http://cancerres.aacrjournals.org/content/57/10/1909

Abstract

Melatonin, the chief hormone secreted by the pineal gland, has been previously shown to inhibit human breast cancer cell growth at the physiological concentration of 1 nm in vitro. In this study, using the estrogen receptor (ER)-positive human breast tumor cell line MCF-7, we have shown that 10 μm l-buthionine-[S,R]-sulfoximine (L-BSO), an inhibitor of γ-glutamylcysteine synthetase (the rate-limiting enzyme in glutathione synthesis), blocks the oncostatic action of 1 nm melatonin over a 5-day incubation, indicating that glutathione is required for melatonin action. The result was repeated with ZR75-1 cells, suggesting that the glutathione requirement is a general phenomenon among ER+ breast cancer cells. Addition of exogenous glutathione (1 μm) to L-BSO-treated groups restored the melatonin response in both cell lines. Further demonstration of the importance of glutathione was shown using the ER- breast tumor cell line HS578T, which is normally unresponsive to melatonin. Growth in this cell line was inhibited in the presence of 1 μm ethacrynic acid (an inhibitor of glutathione S-transferase) plus 1 nm melatonin, and this effect was blocked with 10 μm L-BSO. We also observed a steady decrease of intracellular glutathione in MCF-7 cells over a 5-day incubation, suggesting that these cells metabolize glutathione differently than do normal cells.

Keywords

Authors Blettner M, Zeeb H, Auvinen A et al.

Report Name Mortality from cancer and other causes among male airline cockpit crew in Europe

Publication Int J Cancer

Issue-page numbers 106:946–952.doi:10.1002/ijc.11328 PMID:12918075

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.11328/pdf

Abstract Airline pilots and flight engineers are exposed to ionizing radiation of cosmic origin and other occupational and lifestyle factors that may influence their health status and mortality. In a cohort study in 9 European countries we studied the mortality of this occupational group. Cockpit crew cohorts were identified and followed-up in Denmark, Finland, Germany, Great Britain, Greece, Iceland, Italy, Norway and
Sweden, including a total of 28,000 persons. Observed and expected deaths for the period 1960–97 were compared based on national mortality rates. The influence of period and duration of employment was analyzed in stratified and Poisson regression analyses. The study comprised 547,564 person-years at risk, and 2,244 deaths were recorded in male cockpit crew (standardized mortality ratio [SMR] 0.64,
95% confidence interval [CI] 0.61–0.67). Overall cancer mortality was decreased (SMR 0.68; 95% CI 0.63–0.74). We found an increased mortality from malignant melanoma (SMR 1.78, 95% CI 1.15–2.67) and a reduced mortality from lung cancer (SMR 0.53, 95% CI 0.44–0.62). No consistent association between employment period or duration and cancer mortality was observed. A low cardiovascular mortality and an increased mortality caused by aviation accidents were noted. Our study shows that cockpit crew have
a low overall mortality. The results are consistent with previous reports of an increased risk of malignant melanoma in airline pilots. Occupational risk factors apart from aircraft accidents seem to be of limited influence with regard to the mortality of cockpit crew in Europe.

Keywords

Authors Maria Blettner, Hajo Zeeb, Ingo Langner, Gaël P. Hammer and Thomas Schafft

Report Name Mortality from cancer and other causes among airline cabin attendants in Germany, 1960–1997

Publication Am J Epidemiol

Issue-page numbers 156:556–565.doi:10.1093/aje/kwf083 PMID:12226003

URL http://aje.oxfordjournals.org/content/156/6/556.short

Abstract

Airline cabin attendants are exposed to several potential occupational hazards, including cosmic radiation. Little is known about the mortality pattern and cancer risk of these persons. The authors conducted a historical cohort study among cabin attendants who had been employed by two German airlines in 1953 or later. Mortality follow-up was completed through December 31, 1997. The authors computed standardized mortality ratios (SMRs) for specific causes of death using German population rates. The effect of duration of employment was evaluated with Poisson regression. The cohort included 16,014 women and 4,537 men (approximately 250,000 person-years of follow-up). Among women, the total number of deaths (n = 141) was lower than expected (SMR = 0.79, 95% confidence interval (CI): 0.67, 0.94). The SMR for all cancers (n = 44) was 0.79 (95% CI: 0.54, 1.17), and the SMR for breast cancer (n = 19) was 1.28 (95% CI: 0.72, 2.20). The SMR did not increase with duration of employment. Among men, 170 deaths were observed (SMR = 1.10, 95% CI: 0.94, 1.28). The SMR for all cancers (n = 21) was 0.71 (95% CI: 0.41, 1.18). The authors found a high number of deaths from acquired immunodeficiency syndrome (SMR = 40; 95% CI: 28.9, 55.8) and from aircraft accidents among the men. In this cohort, ionizing radiation probably contributed less to the small excess in breast cancer mortality than reproductive risk factors. Occupational causes seem not to contribute strongly to the mortality of airline cabin attendants.

Keywords

Bobu C, Sandu C, Laurent V, et al. **Year** 2013

Authors Corina Bobu, Cristina Sandu, Virginie Laurent, Marie-Paule Felder-Schmittbuhl, David Hicks

Report Name Prolonged light exposure induces widespread phase shifting in the circadian clock and visual pigment gene expression of the Arvicanthis ansorgei retina

Publication Molecular Vision

Issue-page numbers 2013; 19:1060-1073 <http://www.molvis.org/molvis/v19/1060>

URL http://scholar.google.com/scholar_url?hl=en&q=http://www.molvis.org/molvis/v19/1060/mv-v19-1060.pdf&sa=X&scisig=AAGBfm0SXZWO519V8K4Xuuq_dii_lj_rPg&oi=scholaralr

Abstract

Purpose: Prolonged periods of constant lighting are known to perturb circadian clock function at the molecular, physiological, and behavioral levels. However, the effects of ambient lighting regimes on clock gene expression and clock outputs in retinal photoreceptors—rods, cones and intrinsically photosensitive retinal ganglion cells—are only poorly understood.
Methods: Cone-rich diurnal rodents (Muridae: Arvicanthis ansorgei) were maintained under and entrained to a 12 h:12 h light-dark cycle (LD; light: ~300 lux). Three groups were then examined: control (continued maintenance on LD); animals exposed to a 36 h dark period before sampling over an additional 24 h period of darkness (DD); and animals exposed to a 36 h light period before sampling over an additional 24 h period of light (~300 lux, LL). Animals were killed every 3 or 4 h over 24 h, their retinas dissected, and RNA extracted. Oligonucleotide primers were designed for the Arvicanthis clock genes Per1, Per2, Cry1, Cry2, and Bmal1, and for transcripts specific for rods (rhodopsin), cones (short- and mid-wavelength sensitive cone opsin, cone arrestin, arylalkylamine N-acetyltransferase) and intrinsically photosensitive retinal ganglion cells (melanopsin). Gene expression was analyzed by real-time PCR.
Results: In LD, expression of all genes except cone arrestin was rhythmic and coordinated, with acrophases of most genes at or shortly following the time of lights on (defined as zeitgeber time 0). Arylalkylamine N-acetyltransferase showed maximal expression at zeitgeber time 20. In DD conditions the respective profiles showed similar phase profiles, but were mostly attenuated in amplitude, or in the case of melanopsin, did not retain rhythmic expression. In LL, however, the expression profiles of all clock genes and most putative output genes were greatly altered, with either abolition of daily variation (mid-wavelength cone opsin) or peak expression shifted by 4–10 h.
Conclusions: These data are the first to provide detailed measures of retinal clock gene and putative clock output gene expression in a diurnal mammal, and show the highly disruptive effects of inappropriate (nocturnal) lighting on circadian and photoreceptor gene regulation.

Keywords

Boettner EA, Wolter JR

Year 1962

Authors EDWARD A. BOETTNER and J. REIMER WOLTER

Report Name Transmission of the ocular media

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers December 1962 vol. 1 no. 6 776-783

URL http://www.iovs.org/content/1/6/776

Abstract The spectral transmittance of idtraviolet, visible, and near infrared light through the ocularmedia of humans has been measured. Using freshly enucleated eyes, the transmittances of each component part (cornea, aqueous humor, lens, vitreous humor) were determined for the wavelength range from 0.22 to 2.8 μ. To date, 9 eyes have been measured, from persons ranging in age from 4 weeks to 75 years. Two types of measurements were made, the first to measure the total light transmitted (direct and scattered) a each wavelength, and the second to measure the per cent transmittanceof that light passing directly through the various media tuithout absorption or scattering. The results show that: (a) The transmission of idtraviolet radiation decreases with the age of the eye. (b) The transmission of infrared radiation appears to be independent of the age. (c) The maximum total transmittance of the whole eye, which is about 84 per cent, is obtained in the region from 650 to 850 mμ

Keywords

Boeve BF, Molano JR, Ferman TJ, et al.

Year 2011

Authors Bradley F Boeve, Jennifer R Molano, Tanis J Ferman, Glenn E Smith, Siong-Chi Lin, et al.

Report Name Effects of an advanced sleep schedule and morning short wavelength light exposure on circadian phase in young adults with late sleep schedules.

Publication Sleep Medicine

Issue-page numbers Volume: 12, Issue: 7, Publisher: Elsevier B.V., Pages: 445-453

URL http://www.mendeley.com/research/validation-mayo-sleep-questionnaire-screen-rem-sleep-behavior-disorder-aging-dementia-cohort/

Abstract We examined the effects of an advanced sleep/wake schedule and morning short wavelength (blue) light in 25 adults (mean ageSD=21.83 years; 13 women) with late sleep schedules and subclinical features of delayed sleep phase disorder (DSPD).

Keywords

Bøggild H, Knutsson A

Year 1999

Authors Bøggild H, Knutsson A

Report Name Shift work, risk factors and cardiovascular disease

Publication Scand J Work Environ Health

Issue-page numbers 25:85–99. PMID:10360463

URL http://www.ncbi.nlm.nih.gov/pubmed/10360463

Abstract The literature on shift work, morbidity and mortality from cardiovascular disease, and changes in traditional risk factors is reviewed. Seventeen studies have dealt with shift work and cardiovascular disease risk. On balance, shift workers were found to have a 40% increase in risk. Causal mechanisms of this risk via known cardiovascular risk factors, in relation to circadian rhythms, disturbed sociotemporal patterns, social support, stress, behavior (smoking, diet, alcohol, exercise), and biochemical changes (cholesterol, triglycerides, etc) are discussed. The risk is probably multifactorial, but the literature has focused on the behavior of shift workers and has neglected other possible causal connections. In most studies methodological problems are present; these problems are related to selection bias, exposure classification, outcome classification, and the appropriateness of comparison groups. Suggestions for the direction of future research on this topic are proposed.

Keywords

Boivin DB, Boudreau P, James FO, Ng Ying Kin NMK

Year 2012

Authors Diane B. Boivin, Philippe Boudreau, Francine O. James, and N. M. K. Ng Ying Kin

Report Name Photic Resetting in Night-Shift Work: Impact on Nurses' Sleep

Publication Chronobiology International

Issue-page numbers June 2012, Vol. 29, No. 5 , Pages 619-628 (doi:10.3109/07420528.2012.675257)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2012.675257

Abstract The objective of this study was to quantify daytime sleep in night-shift workers with and without an intervention designed to recover the normal relationship between the endogenous circadian pacemaker and the sleep/wake cycle. Workers of the treatment group received intermittent exposure to full-spectrum bright light during night shifts and wore dark goggles during the morning commute home. All workers maintained stable 8-h daytime sleep/darkness schedules. The authors found that workers of the treatment group had daytime sleep episodes that lasted 7.1 ± .1 h (mean ± SEM) versus 6.6 ± .2 h for workers in the control group (p = .04). The increase in total sleep time co-occurred with a larger proportion of the melatonin secretory episode during daytime sleep in workers of the treatment group. The results of this study showed reestablishment of a phase angle that is comparable to that observed on a day-oriented schedule favors longer daytime sleep episodes in night-shift workers.

Keywords Bright light, Melatonin, Night-Shift, Phase shift adjustment, Shiftwork, Sleep

Boivin DB, Duffy JF, Kronauer RE, Czeisler CA

Year 1996

Authors Diane B. Boivin, Jeanne F. Duffy, Richard E. Kronauer & Charles A. Czeisler

Report Name Dose-response relationships for resetting of human circadian clock by light

Publication Nature

Issue-page numbers 379:540–542 doi:10.1038/379540a0. PMID:8596632

URL http://www.nature.com/nature/journal/v379/n6565/abs/379540a0.html

Abstract SINCE the first report in unicells1, studies across diverse species have demonstrated that light is a powerful synchronizer which resets, in an intensity-dependent manner, endogenous circadian pacemakers1–5. Although it is recognized that bright light (~7,000 to 13,000 lux) is an effective circadian synchronizer in humans6–10, it is widely believed that the human circadian pacemaker is insensitive to ordinary indoor illumination (~50–3001ux)11. It has been proposed that the relationship between the resetting effect of light and its intensity follows a compressive nonlinear function12, such that exposure to lower illuminances still exerts a robust effect13. We therefore undertook a series of experiments which support this hypothesis and report here that light of even relatively low intensity (~180 lux) significantly phase-shifts the human circadian pacemaker. Our results clearly demonstrate that humans are much more sensitive to light than initially suspected and support the conclusion that they are not qualitatively different from other mammals in their mechanism of circadian entrainment

Keywords

Boivin DB, James FO

Year 2005

Authors Diane B. BOIVIN and Francine O. JAMES

Report Name Light Treatment and Circadian Adaptation to Shift Work

Publication Industrial Health

Issue-page numbers 2005, 43, 34–48

URL http://www.jniosh.go.jp/en/indu_hel/pdf/43-1-6.pdf

Abstract Work at unconventional hours can have both long and short term consequences. Shift workers are often required to perform their duties at times that are not favoured by the body's endogenous clock, or circadian pacemaker. A typical night shift worker, for example, may report reductions in alertness and performance during shifts, or significant difficulty attaining sleep of recuperative value in the day, all the while being more likely to develop health complications. The study of circadian physiology has significantly contributed to our current ability to aid the shift worker deal with atypical schedules. We discuss the usefulness of light treatment as a countermeasure for maladaptation to atypical work schedules.

Keywords Shift work, Circadian, Bright light, Night shift work

Bojkowski CJ, Aldhous ME, English J et al. **Year** 1987

Authors C J Bojkowski, M E Aldhous, J English, C Franey, A L Poulton, D J Skene, J Arendt

Report Name Suppression of nocturnal plasma melatonin and 6-sulphatoxymelatonin by bright and dim light in man

Publication Horm Metab Res

Issue-page numbers 19:437–440 doi:10.1055/s-2007-1011846. PMID:3692439

URL http://www.mendeley.com/research/suppression-of-nocturnal-plasma-melatonin-and-6sulphatoxymelatonin-by-bright-and-dim-light-in-man/

Abstract Previous studies have shown that bright light (2500 lux) suppresses nocturnal secretion of melatonin, while dim light (500 lux) has little or no effect. We have studied the effect of varying intensities of light on 5 normal male volunteers (age 18-28). The experiment was divided into 3 parts which took place at weekly intervals. Subjects remained under artificial light (fluorescent strip 150-250 lux) between 2000 h-2300 h, they then retired to bed in darkness. On each occasion, between 0030 h and 0100 h, the subjects were required to get up and were treated with light of different intensities; (a) less than 1 lux, (b) 300 lux and (c) 2500 lux respectively. Subjects returned to bed in darkness until 0700 h. Blood was sampled hourly from 2000 h-1000 h with additional samples at 2330 h, 0015 h, 0030 h, 0045 h, 0115 h and 0130 h. Plasma melatonin and 6-sulphatoxymelatonin (aMT6s), the major melatonin metabolite, were measured by radioimmunoassay. Dim (300 lux) and bright (2500 lux) light, both significantly suppressed melatonin levels compared to less than 1 lux (P less than 0.05 and P less than 0.01 respectively) at the following time points 0100 h, 0115 h and 0130 h. One subject did not show suppression with 300 lux. There was also a significant suppression of aMT6s levels, compared to less than 1 lux, after both 300 lux and 2500 lux at 0115 h (P less than 0.05, P less than 0.01), 0130 h (P less than 0.01, P less than 0.01) and 0200 h (P less than 0.01, P less than 0.001) respectively.

Keywords

Bojkowski CJ, Arendt J **Year** 1988

Authors Christopher J. Bojkowski and Josephine Arendt

Report Name Annual changes in 6-sulphatoxymelatonin excretion in man

Publication Acta Endocrinol (Copenh)

Issue-page numbers 117:470–476. PMID:3389039

URL http://www.eje.org/content/117/4/470.abstract

Abstract Abstract: A recently developed RIA for 6-sulphatoxymelatonin, the major urinary metabolite of melatonin, has been used to investigate the annual change in melatonin secretion in humans. Twenty plasma samples were taken from 18 volunteers throughout a 24-h period and simultaneous 6-hourly urine samples were also collected. Plasma melatonin and urinary 6-sulphatoxymelatonin were measured by RIA. 6-Sulphatoxymelatonin assayed in the urine samples was shown to be a good index of the rhythmic characteristics of the plasma melatonin secretion. To study annual changes in excretion four sequential 6-hourly urine samples were collected at monthly intervals from 16 normal volunteers for 13 months. Cosinor curves were fitted to the 6-sulphatoxymelatonin excretion data and the 24-h rhythm was described by the cosinor parameters: amplitude, mesor and acrophase. Significant differences in the acrophase were found during the year. The summer acrophase was phase advanced relative to the winter acrophase by about 1.5 h while intermediate phase positions were observed in spring/autumn. The 24-h excretion of urinary 6-sulphatoxymelatonin was remarkably consistent and there was no annual rhythm. In contrast, the daytime 6-sulphatoxymelatonin excretion between 12.00–18.00 h showed a statistically significant seasonal rhythm, with peaks in December/January and in July.

Keywords

Bojkowski CJ, Arendt J, Shih MC, Markey SP | ***Year*** 1987

Authors Bojkowski CJ, Arendt J, Shih MC, Markey SP

Report Name Melatonin secretion in humans assessed by measuring its metabolite, 6-sulfatoxymelatonin

Publication Clin Chem

Issue-page numbers 33:1343–1348. PMID:3608151

URL http://www.clinchem.org/cgi/content/abstract/33/8/1343

Abstract Comparing a direct radioimmunoassay for 6-sulfatoxymelatonin (aMT6s) with an established gas chromatographic/mass spectrometric method for 6- hydroxymelatonin, we found a good correlation r = 0.94 (P less than 0.001, n = 100). aMT6s was stable, both in urine and plasma samples, without preservative, for at least two years at -20 degrees C and for five days at room temperature. Urinary excretion of aMT6s showed considerable inter-individual differences; however, the aMT6s excretion of any one individual was consistent over a four-day period, as assessed by continuous collection from 18 normal volunteers. Total 24-h urinary excretion of aMT6s was significantly correlated with the area under the curve of the respective profiles for plasma melatonin (r = 0.75, P = 0.0002) and plasma aMT6s (r = 0.70, P = 0.0005) for 22 healthy volunteers. At 24:00 h and 03:00 h, sampling plasma at 30-s intervals provided no evidence for episodic secretion (in short pulses) of either melatonin or aMT6s.

Keywords

Bok D | ***Year*** 1990

Authors Dean Bok

Report Name Processing and transport of retinoids by the retinal pigment epithelium

Publication Eye

Issue-page numbers 4, 326–332; doi: 10.1038/eye.1990.44

URL http://www.nature.com/eye/journal/v4/n2/abs/eye199044a.html

Abstract Recent developments regarding our understanding of retinoid processing and transport during the visual cycle and related events are reviewed. Retinoids are bound and protected by a cohort of retinoid binding proteins, each of which is unique. The production of retinol (Vitamin A) derivatives is accomplished by a group of membrane-bound enzymes, some of which appear to be coupled in their actions.

Keywords

Authors Bonde JP, Hansen J, Kolstad HA, Mikkelsen S, Olsen JH, Blask DE, Härmä M, Kjuus H, de Koning HJ, Olsen J, Møller M, Schernhammer ES, Stevens RG, Akerstedt T.

Report Name Work at night and breast cancer – report on evidence-based options for preventive actions

Publication Scand J Work Environ Health

Issue-page numbers online first. doi:10.5271/sjweh.3282

URL http://www.ncbi.nlm.nih.gov/pubmed/22349009

Abstract

In 2007, the International Agency for Research on Cancer classified shift work involving circadian disruption as probably carcinogenic to humans (group 2A), primarily based on experimental and epidemiologic evidence for breast cancer. In order to examine options for evidence-based preventive actions, 16 researchers in basic, epidemiological and applied sciences convened at a workshop in Copenhagen 26–27 October 2011. This paper summarizes the evidence from epidemiological and experimental studies and presents possible recommendations for prevention of the effects of night work on breast cancer.
Among those studies that quantified duration of shift work, there were statistically significant elevations in risk only after about 20 years working night shift. It is unclear from these studies whether or not there is a modest but real elevated risk for shorter durations. Hence, restriction of the total number of years working night shift could be one future preventive recommendation for shift workers. The diurnal secretion of melatonin by the pineal gland with peak in secretory activity during the night is a good biochemical marker of the circadian rhythm. Disruption of the diurnal melatonin secretion pattern can be diminished by restricting the number of consecutive night shifts. Reddish light and reduced light intensity during work at night could potentially help diminish the inhibitory activity of light with strong intensity on the melatonin secretion, but further mechanistic insight is needed before definite recommendations can be made. Earlier or more intensive mammography screening among female night shift worker is not recommended because the harm–benefit ratio in this age group may not be beneficial. Preventive effects of melatonin supplementation on breast cancer risk have not been clearly documented, but may be a promising avenue if a lack of side effects can be shown even after long-term ingestion. Women with previous or current breast cancer should be advised not to work night shifts because of strong experimental evidence demonstrating accelerated tumor growth by suppression of melatonin secretion.
Work during the night is widespread worldwide. To provide additional evidence-based recommendations on prevention of diseases related to night shift work, large studies on the impact of various shift schedules and type of light on circadian rhythms need to be conducted in real work environments.

Keywords circadian rhythm; melatonin; occupational disease; night work; prevention; shift work

Borisenkov MF

Year 2011

Authors Mikhail F. Borisenkov

Report Name Latitude of Residence and Position in Time Zone are Predictors of Cancer Incidence, Cancer Mortality, and Life Expectancy at Birth

Publication Chronobiology International

Issue-page numbers 28:2, 155-162

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2010.541312

Abstract According to the hypothesis of circadian disruption, external factors that disturb the function of the circadian system can raise the risk of malignant neoplasm and reduce life span. Recent work has shown that the functionality of the circadian system is dependent not only on latitude of residence but also on the region's position in the time zone. The purpose of the present research was to examine the influence of latitude and time zone on cancer incidence, cancer mortality, and life expectancy at birth. A stepwise multiple regression analysis was carried out on residents of 59 regions of the European part of the Russian Federation (EPRF) using age-standardized parameters (per 100,000) of cancer incidence (CI), cancer mortality (CM), and life expectancy at birth (LE, yrs) as dependent variables. The geographical coordinates (latitude and position in the time zone) of the regions were used as independent variables, controlling for the level of economic development in the regions. The same analysis was carried out for LE in 31 regions in China. Latitude was the strongest predictor of LE in the EPRF population; it explained 48% and 45% of the variability in LE of women and men, respectively. Position within the time zone accounted for an additional 4% and 3% variability of LE in women and men, respectively. The highest values for LE were observed in the southeast of the EPRF. In China, latitude was not a predictor of LE, whereas position in the time zone explained 15% and 18% of the LE variability in women and men, respectively. The highest values of LE were observed in the eastern regions of China. Both latitude and position within the time zone were predictors for CI and CM of the EPRF population. Latitude was the best predictor of stomach CI and CM; this predictor explained 46% and 50% of the variability, respectively. Position within the time zone was the best predictor of female breast CM; it explained 15% of the variability. In most cases, CI and CM increased with increasing latitude of residence, from the eastern to the western border of the time zone, and with increasing level of economic development within the region. The dependence of CI, CM, and LE on the geographical coordinates of residence is in agreement with the hypothesis of circadian disruption.

Keywords Cancer incidence, Cancer mortality, Cancer Predictor, Latitude of residence, Life expectancy at birth, Position in time zone

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Borjigin J, Zhang LS, Calinescu A

Year 2012

Authors Jimo Borjigin, L. Samantha Zhang, Anda-Alexandra Calinescu

Report Name Circadian regulation of pineal gland rhythmicity

Publication Molecular and Cellular Endocrinology

Issue-page numbers Volume 349, Issue 1, 5 February 2012, Pages 13-19

URL http://www.sciencedirect.com/science/article/pii/S0303720711003856

Abstract The pineal gland is a neuroendocrine organ of the brain. Its main task is to synthesize and secrete melatonin, a nocturnal hormone with diverse physiological functions. This review will focus on the central and pineal mechanisms in generation of mammalian pineal rhythmicity including melatonin production. In particular, this review covers the following topics: (1) local control of serotonin and melatonin rhythms; (2) neurotransmitters involved in central control of melatonin; (3) plasticity of the neural circuit controlling melatonin production; (4) role of clock genes in melatonin formation; (5) phase control of pineal rhythmicity; (6) impact of light at night on pineal rhythms; and (7) physiological function of the pineal rhythmicity.

Keywords Pineal gland; Melatonin; Circadian rhythms

Born J, Muth S, Fehm HL **Year** 1988

Authors Born J, Muth S, Fehm HL

Report Name The significance of sleep onset and slow wave sleep for nocturnal release of growth hormone (GH) and cortisol

Publication Psychoneuroendocrinology

Issue-page numbers 13:233–243 doi:10.1016/0306-4530(88)90021-2. PMID:3406323

URL http://www.ncbi.nlm.nih.gov/pubmed/3406323

Abstract The present experiments were designed to compare the influences of delayed sleep onset and temporary slow wave sleep (SWS) deprivation on nocturnal GH and cortisol release in humans. Polysomnographic recordings and blood samples were obtained from 10 male subjects each participating on three experimental nights. On all nights the subjects went to bed at 2300 h and were wakened at 0700 h. On the baseline night, the lights were turned off at 2300 h, enabling the subject to fall asleep. To delay sleep onset, on the second night, the subjects were kept awake until 0200 h. On the third night, the subjects were deprived of SWS between 2300 h and 0200 h. SWS deprivation was accomplished by sounding a tone as soon as it appeared the subject was going into stage 3 sleep. The order of experimental conditions was randomized. On the baseline nights, the occurrence of SWS was closely associated with the occurrence of GH secretory bursts, and plasma cortisol concentrations were low at that time. Delaying sleep onset after 0200 h substantially delayed the GH secretory bursts, which again coincided with the initial periods of SWS. Deprivation of SWS between 2300 h and 0200 h did not significantly reduce the time spent in SWS, because it recovered after the deprivation was discontinued. On these nights, the GH secretory peaks were not significantly changed in amplitude. However, they were dissociated from SWS, because they occurred mostly subsequent to sleep onset rather than during the main epochs of SWS occurring after 0200 h. Nocturnal cortisol release was distinctly delayed with delayed sleep onset, whereas temporary SWS suppression had no significant effect. Thus, the timing of both nocturnal GH and cortisol secretion seems more dependent on sleep onset than on SWS.

Keywords

Bottino CJ, Rifas-Shiman SL, Kleinman KP, et al. **Year** 2012

Authors Clement J. Bottino, Sheryl L. Rifas-Shiman, Ken P. Kleinman, Emily Oken, Susan Redline, Diane Gold, Joel Schwartz, Steven J. Melly, Petros Koutrakis, Matthew W. Gillman, E

Report Name The association of urbanicity with infant sleep duration

Publication Health & Place

Issue-page numbers Volume 18, Issue 5, September 2012, Pages 1000–1005

URL http://www.sciencedirect.com/science/article/pii/S1353829212001141

Abstract Short sleep duration is associated with multiple adverse child outcomes. We examined associations of the built environment with infant sleep duration among 1226 participants in a pre-birth cohort. From residential addresses, we used a geographic information system to determine urbanicity, population density, and closeness to major roadways. The main outcome was mother's report of her infant's average daily sleep duration at 1 year of age. We ranked urbanicity and population density as quintiles, categorized distance to major roads into 8 categories, and used linear regression adjusted for socio-demographic characteristics, smoking during pregnancy, gestational age, fetal growth, and television viewing at 1 year. In this sample, mean (SD) sleep duration at age 1 year was 12.8 (1.6) h/day. In multivariable adjusted analyses, children living in the highest quintile of urbanicity slept −19.2 min/day (95% CI:−37.0, −1.50) less than those living in the lowest quintile. Neither population density nor closeness to major roadways was associated with infant sleep duration after multivariable adjustment. Our findings suggest that living in more urban environments may be associated with reduced infant sleep.

Keywords

Boulton M, Docchio F, Dayhaw-Barker P, et al. **Year** 0

Authors Mike Boulton, Franco Docchio, Pierrette Dayhaw-Barker, Roberta Ramponi, Rinaldo Cubeddu

Report Name Age related changes in the morphology, absorption and fluorescence of melanosomes and lipofuscin granules of the retinal pigment epithelium

Publication Vision Research

Issue-page numbers Volume 30, Issue 9, 1990, Pages 1291-1303

URL http://www.sciencedirect.com/science/article/pii/0042698990900034

Abstract The morphological and spectral characteristics of purified populations of melanosomes and lipofuscin granules from the human retinal pigment epithelium (RPE) were studied with respect to donor age. All melanosome and lipofuscin fractions exhibited the typical ultrastructural appearance associated with these granules. Absorption profiles of both melanin and lipofuscin granules demonstrated an increased optical density of the granules with increasing age. The former was associated with an overall increase of melanin within the granules. Melanosomes were weakly fluorescent; emission in the blue decreased with increasing age while emission in the red increased. The fluorescent intensity of lipofuscin granules increased with age.

These results provide support for the concept that melanogenesis is occurring within the human RPE throughout life and that pigment granules within the RPE undergo age-related modifications during life.

Keywords Melanin; Lipofuscin; Morphology; Absorption; Fluorescence; Melanogenesis

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Boulton M, Rozanowska M, Rózanowski B **Year** 2001

Authors M Boulton, Rozanowska M, B Rózanowski

Report Name Retinal photodamage

Publication Journal of Photochemistry and Photobiology B Biology

Issue-page numbers Volume: 64, Issue: 2-3, Pages: 144-161

URL http://www.mendeley.com/research/retinal-photodamage-1/

Abstract The retina represents a paradox, in that, while light and oxygen are essential for vision, these conditions also favour the formation of reactive oxygen species leading to photochemical damage to the retina. Such light damage seems to be multi-factorial and is dependent on the photoreactivity of a variety of chromophores (e.g., vitamin A metabolites, lipofuscin, melanin, flavins, porphyrins, carotenoids) endogenous to the retina. The aim of this article is to provide a detailed review of our current understanding of the photochemistry and photobiology of these chromophores and to consider how they may contribute to retinal ageing and pathology.

Keywords

Boyce P, Barriball E

Year 2010

Authors Boyce P, Barriball E.

Report Name Circadian rhythms and depression

Publication Australian Family Physician

Issue-page numbers Vol. 39, No. 5, May 2010 307-310

URL http://www.racgp.org.au/afp/201005/201005boyce.pdf

Abstract

Background
Depression is a common disorder in primary care. Disruptions to the circadian rhythms associated with depression have received little attention yet offer new and exciting approaches to treatment.
Objective
This article discusses circadian rhythms and the disruption to them associated with depression, and reviews nonpharmaceutical and pharmaceutical interventions to shift circadian rhythms.
Discussion
Features of depression suggestive of a disturbance to circadian rhythms include early morning waking, diurnal mood changes, changes in sleep architecture, changes in timing of the temperature nadir, and peak cortisol levels. Interpersonal social rhythm therapy involves learning to manage interpersonal relationships more effectively and stabilisation of social cues, such as including sleep and wake times, meal times, and timing of social contact. Bright light therapy is used to treat seasonal affective disorders. Agomelatine is an antidepressant that works in a novel way by targeting melatonergic receptors.

Keywords circadian rhythm, depression

Boyton RM, Clark JJ

Year 1962

Authors Boyton, R. M. and J. J. Clark

Report Name Sources for Entropic Scatter in the Human Eye

Publication J. Opt. Soc. Am.

Issue-page numbers 54 (1962) p. 1326

URL N/A

Abstract N/A

Keywords glare

Brabant G, Prank K, Ranft U et al. ***Year*** 1990

Authors G. BRABANT, K. PRANK, U. RANFT, Th. SCHUERMEYER, T. O. F. WAGNER, H. HAUSER, B. KUMMER, H. FEISTNER, R. D. HESCH and A. VON ZUR MÜHLEN

Report Name Physiological regulation of circadian and pulsatile thyrotropin secretion in normal man and woman

Publication J Clin Endocrinol Metab

Issue-page numbers 70:403–409 doi:10.1210/jcem-70-2-403. PMID:2105332

URL http://jcem.endojournals.org/content/70/2/403.short

Abstract The circadian and pulsatile TSH secretion profiles were investigated in 5 females at the time of menstruation and 21 healthy males by sampling blood every 10 min for 24 h. Computer-assisted analysis, i.e. the Cluster and Desade programs, revealed means of 9.9 ± 1.7 (Cluster) and 11.4 ± 3.9 (Desade) pulses/24 h. More than 50% of the TSH pulses were detected between 2000–0400 h. Male and female subjects showed no significant difference in the basal mean and pulsatile secretion of TSH or in the TSH response to TRH (200 μg). Repetition of the TSH secretion analysis in 4 healthy subjects after 1, 2, and 6 months (2 subjects) revealed a significantly better crosscorrelation within than between individuals ($P < 0.0001$).

We modulated the circadian TSH secretion pattern by acute sleep withdrawal or prolonged sleep after a night of sleep withdrawal in six healthy male volunteers. Sleep withdrawal augmented the nightly TSH secretion (mean serum TSH, 2.1 ± 1.3 mU/L; mean TSH in sleep, 1.3 ± 0.5 mU/L; $P < 0.05$), whereas sleep after sleep withdrawal almost completely suppressed the circadian variation (mean TSH, 1.1 ± 0.7 mU/L; $P < 0.01$). This modulation is due to a significant decrease in pulse amplitude, but not to an alteration in the frequency or temporal distribution of TSH pulses.

Keywords

Bracci M, Copertaro A, Manzella N, et al. ***Year*** 2013

Authors Bracci M, Copertaro A, Manzella N, Staffolani S, Strafella E, Nocchi L, Barbaresi M, Copertaro B, Rapisarda V, Valentino M, Santarelli L.

Report Name Influence of night-shift and napping at work on urinary melatonin, 17-ß-estradiol and clock gene expression in pre-menopausal nurses.

Publication J Biol Regul Homeost Agents.

Issue-page numbers 2013 Jan-Mar;27(1):267-74.

URL http://www.ncbi.nlm.nih.gov/pubmed/23489707

Abstract Night-workers experience disruption of the sleep-wake cycle and light at night which may increase breast cancer risk by suppressing the nocturnal melatonin surge, resulting in higher levels of circulating estrogens. Night-work may also deregulate peripheral clock genes which have been found to be altered in breast cancer. This study investigated urinary 6-sulfatoxymelatonin (aMT6s), serum 17-beta-estradiol levels in premenopausal shift nurses at the end of the night-shift compared to a control group of daytime nurses. Peripheral clock gene expression in lymphocytes were also investigated. All participants were sampled in the follicular phase of the menstrual cycle. The effect of nurses ability to take a short nap during the night-shift was also explored. The shift-work group had significantly lower aMT6s levels than daytime nurses independently of a nap. Night-shift napping significantly influences 17-beta-estradiol levels resulting in higher outcomes in nurses who do not take a nap compared to napping group and daytime workers. Peripheral clock genes expression investigated was not significantly different among the groups. Our findings suggest that shift nurses experience changes in aMT6s levels after a night-shift. Napping habits influence 17-beta-estradiol levels at the end of a night-shift. These findings might be related to the increased cancer risk reported in night-shift workers and suggest that a short nap during night-shifts may exert a positive effect.

Keywords

Brainard GC

Year 2000

Authors Brainard, G.C.

Report Name Light Effects on Melatonin

Publication Proc. of Int. Symp. on Low frequency EMF, Visible Light, Melatonin and Cancer

Issue-page numbers May 4-5, 2000, University of Cologne, Germany

URL http://www.uni-koeln.de/symposium2000/contrib/index.html

Abstract

t has been hypothesized that increased risk of breast cancer in industrialized countries is partially due to increased exposure to electromagnetic fields and light at night which reduces melatonin production.(1) To assess this hypothesis, it is fundamentally important to understand how the human eye transduces light stimuli for melatonin regulation. In both animals and humans, more light is required to activate the circadian and neuroendocrine systems than to stimulate the visual system. Specifically, it is often thought that bright light of at least 2500 lux is needed to phase shift the rhythm or acutely suppress melatonin secretion from the human pineal gland. When exposure of the human eye is carefully controlled, however, illuminances as low as 5 - 17 lux of monochromatic green light or 100 lux of broadband white light can produce significant suppression of melatonin in normal human volunteers.(2) To understand how these lower illuminances can regulate pineal melatonin secretion, it is necessary to examine the ocular physiology that mediates this photic effect. In humans, factors which can significantly alter the amount and spectral quality of light reaching the retina include: 1) gaze behavior relative to a light source, 2) the age of the ocular lens, and 3) pupillary dilation. Once a light stimulus reaches the retina, physiology within the retina and within the circadian system determines the capacity of the stimulus to alter melatonin synthesis. This physiology includes: 1) the sensitivity of the operative photopigments and photoreceptors, 2) location of these photoreceptors within the retina, 3) the ability of the circadian system to integrate photic stimuli spatially and temporally and 4) the state of photoreceptor adaptation. Given the increasing exposure of citizens to light during the night in industrialized countries it is useful from both a scientific as well as a clinical perspective to elucidate the specific photosensory physiology in the eye which mediates melatonin regulation. This work was supported by the following grants: NIH RO1NS36590; FDA #785346, NASA #NAGW 1196, and the Philadelphia Chapter of the Illuminating Engineering Society.

Keywords

Brainard GC, Hanifin JP

Year 2005

Authors George C. Brainard, John P. Hanifin

Report Name Photons, Clocks, and Consciousness

Publication J Biol Rhythms

Issue-page numbers August 2005 vol. 20 no. 4 314-325

URL http://jbr.sagepub.com/content/20/4/314.abstract

Abstract Light profoundly impacts human consciousness through the stimulation of the visual system and powerfully regulates the human circadian system, which, in turn, has a broad regulatory impact on virtually all tissues in the body. For more than 25 years, the techniques of action spectroscopy have yielded insights into the wavelength sensitivity of circadian input in humans and other mammalian species. The seminal discovery of melanopsin, the photopigmentin intrinsically photosensitive retinal ganglion cells, has provided a significant turning point for understanding human circadian phototransduction. Action spectra in humans show that the peak wavelength sensitivity for this newly discovered sensory system is within the blue portion of the spectrum. This is fundamentally different from the three-cone photopic visual system, as well as the individual rod and cone photoreceptor peaks. Studies on rodents, nonhuman primates, and humans indicate that despite having a different wavelength fingerprint, these classic visual photoreceptors still provide an element of input to the circadian system. These findings open the door to innovations in light therapy for circadian and affective disorders, as well as possible architectural light applications.

Keywords action spectra, circadian, melanopsin, melatonin, neuroendocrine, photopigment, photoreception, pineal gland

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Brainard GC, Hanifin JP, Greeson JM, et al.

Year 2001

Authors George C. Brainard, John P. Hanifin, Jeffrey M. Greeson, Brenda Byrne, Gena Glickman, Edward Gerner, nd

Report Name Action Spectrum for Melatonin Regulation in Humans: Evidence for a Novel Circadian Photoreceptor

Publication Journal of Neuroscience

Issue-page numbers 15 August 2001, 21(16): 6405-6412

URL http://www.jneurosci.org/content/21/16/6405.short

Abstract The photopigment in the human eye that transduces light for circadian and neuroendocrine regulation, is unknown. The aim of this study was to establish an action spectrum for light-induced melatonin suppression that could help elucidate the ocular photoreceptor system for regulating the human pineal gland. Subjects (37 females, 35 males, mean age of 24.5 ± 0.3 years) were healthy and had normal color vision. Full-field, monochromatic light exposures took place between 2:00 and 3:30 A.M. while subjects' pupils were dilated. Blood samples collected before and after light exposures were quantified for melatonin. Each subject was tested with at least seven different irradiances of one wavelength with a minimum of 1 week between each nighttime exposure. Nighttime melatonin suppression tests (n = 627) were completed with wavelengths from 420 to 600 nm. The data were fit to eight univariant, sigmoidal fluence–response curves (R 2 = 0.81–0.95). The action spectrum constructed from these data fit an opsin template (R 2 = 0.91), which identifies 446–477 nm as the most potent wavelength region providing circadian input for regulating melatonin secretion. The results suggest that, in humans, a single photopigment may be primarily responsible for melatonin suppression, and its peak absorbance appears to be distinct from that of rod and cone cell photopigments for vision. The data also suggest that this new photopigment is retinaldehyde based. These findings suggest that there is a novel opsin photopigment in the human eye that mediates circadian photoreception.

Keywords melatonin, action spectrum, circadian, wavelength, light, pineal gland, neuroendocrine, photoreception, photopigment, human

Brainard GC, Hanifin JP, Rollag MD, et al. **Year** 2001

Authors George C. Brainard, John P. Hanifin, Mark D. Rollag, Jeffrey Greeson, Brenda Byrne, Gena Glickman, Edward Gerner and Britt Sanford

Report Name Human Melatonin Regulation Is Not Mediated by the Three Cone Photopic Visual System

Publication Journal of Clinical Endocrinology and Metabolism

Issue-page numbers 86(1):433-436, 2001

URL http://jcem.endojournals.org/content/86/1/433.abstract

Abstract The aim of this study was to test if the three cone photopic visual system is the primary ocular photoreceptor input for human circadian regulation by determining the effects of different wavelengths on light-induced melatonin suppression. Healthy subjects with stable sleeping patterns (wake-up time 7:30 AM ± 12 min) and normal color vision were exposed at night to full-field 505 nm or 555 nm monochromatic stimuli or darkness for 90 min. Plasma collected before and after exposures was quantified for melatonin. Subjects exposed to 10 irradiances at 505 nm showed no significant differences across mean pre-exposure melatonin values (F=0.505). A sigmoidal fluence-response curve fitted to the melatonin suppression data (R2=0.97) indicated that 9.34 × 1012 photons/cm2/sec induced a half-saturation response (ED50) while 6.84 × 1013 photons/cm2/sec induced a saturation melatonin suppression response. Further, a dose of 4.19 × 1013 photon/cm2/sec at 505 nm was significantly stronger (P < 0.01) than an equal photon dose at 555 nm for melatonin suppression. These data demonstrate that the cone system that mediates human photopic vision is not the primary photoreceptor system to tranduce light stimuli for melatonin regulation.

Keywords melatonin

Brainard GC, Kavet R, Kheifets LI **Year** 1999

Authors Brainard GC, Kavet R, Kheifets LI.

Report Name The relationship between electromagnetic field and light exposures to melatonin and breast cancer risk: a review of the relevant literature

Publication J Pineal Res

Issue-page numbers Mar;26(2):65-100.

URL http://www.ncbi.nlm.nih.gov/pubmed/10100735Worldwide, breast cancer is the most common malignancy accounting for 20-32% of all female cancers. This review summarizes t

Abstract

Keywords

Brainard GC, Lewy AJ, Menaker M, et al. **Year** 1988

Authors George C. Brainard, Alfred J. Lewy, Michael Menaker, Richard H. Fredrickson, L. Stephen Miller, Richard G. Weleber, Vincent Cassone, David Hudson

Report Name Dose-response relationship between light irradiance and the suppression of plasma melatonin in human volunteers

Publication Brain Research

Issue-page numbers Volume 454, Issues 1-2, 28 June 1988, Pages 212-218

URL http://www.sciencedirect.com/science/article/pii/0006899388908207

Abstract This study tested the capacity of different irradiances of monochromatic light to reduce plasma melatonin in normal humans. Six healthy male volunteers, 24–34 years old, were exposed to 0.01, 0.3, 1.6,5, or 13 μW/cm2 of 509 nm monochromatic light for 1 h during the night on separate occasions. Light irradiance depressed plasma melatonin in a dose-response pattern. The data indicate that the mean threshold irradiance for suppressing melatonin is between 1.6 and 5μW/cm2. Individual variations in threshold responses to monochromatic light were observed among the volunteers.

Keywords Melatonin; Light; Pineal; Wavelength; Circadian

Brainard GC, Rollag MD, Hanifin JP **Year** 1997

Authors George C. Brainard, Mark D. Rollag, John P. Hanifin

Report Name Photic Regulation of Melatonin in Humans: Ocular and Neural Signal Transduction

Publication Journal of Biological Rhythms

Issue-page numbers December 1997 vol. 12 no. 6 537-546

URL http://jbr.sagepub.com/content/12/6/537.abstract

Abstract Light is a potent stimulus for regulating the pineal gland's production of melatonin and the broader circadian system in humans. It initially was thought that only very bright photic stimuli (≥ 2500 lux) could suppress nocturnal melatonin secretion and induce other circadian responses. It is now known that markedly lower illuminances (≤ 200 lux) can acutely suppress melatonin or entrain and phase shift melatonin rhythms when exposure conditions are optimized. The elements for physical/biological stimulus processing that regulate photic influences on melatonin secretion include the physics of the light source, gaze behavior relative to the light source, and the transduction of light energy through the pupil and ocular media. Elements for sensory/neural signal processing become involved as photons are absorbed by retinal photopigments and neural signals are generated in the retinohypothalamic tract. Aspects of this physiology include the ability of the circadian system to integrate photic stimuli spatially and temporally as well as the wavelength sensitivity of the operative photoreceptors. Acute, light-induced suppression of melatonin is proving to be a powerful tool for clarifying how these elements of ocular and neural physiology influence the interaction between light and the secretion of melatonin from the human pineal gland.

Keywords pineal gland, melatonin suppression, light, eye, lens, pupil, photoreceptor

Brainard GC, Sliney D, Hanifin JP, et al. **Year** 2008

Authors Brainard GC, Sliney D, Hanifin JP, Glickman G, Byrne B, Greeson JM, et al.

Report Name Sensitivity of the human circadian system to short-wavelength (420-nm) light

Publication J Biol Rhythms

Issue-page numbers October 2008 vol. 23 no. 5 379-386

URL http://jbr.sagepub.com/content/23/5/379.abstract

Abstract The circadian and neurobehavioral effects of light are primarily mediated by a retinal ganglion cell photoreceptor in the mammalian eye containing the photopigment melanopsin. Nine action spectrum studies using rodents, monkeys, and humans for these responses indicate peak sensitivities in the blue region of the visible spectrum ranging from 459 to 484 nm, with some disagreement in short-wavelength sensitivity of the spectrum. The aim of this work was to quantify the sensitivity of human volunteers to monochromatic 420-nm light for plasma melatonin suppression. Adult female (n = 14) and male (n = 12) subjects participated in 2 studies, each employing a within-subjects design. In a fluence-response study, subjects (n = 8) were tested with 8 light irradiances at 420 nm ranging over a 4-log unit photon density range of 1010 to 1014 photons/cm 2/sec and 1 dark exposure control night. In the other study, subjects (n = 18) completed an experiment comparing melatonin suppression with equal photon doses (1.21 × 1013 photons/cm2/sec) of 420 nm and 460 nm monochromatic light and a dark exposure control night. The first study demonstrated a clear fluence-response relationship between 420-nm light and melatonin suppression ($p < 0.001$) with a half-saturation constant of 2.74 × 1011 photons/cm2/sec. The second study showed that 460-nm light is significantly stronger than 420-nm light for suppressing melatonin ($p < 0.04$). Together, the results clarify the visible short-wavelength sensitivity of the human melatonin suppression action spectrum. This basic physiological finding may be useful for optimizing lighting for therapeutic and other applications.

Keywords melatonin, action spectrum, circadian, wavelength, light, pineal gland, neuroendocrine, photoreception

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Bray MS, Young ME **Year** 2012

Authors Molly S. Bray and Martin E. Young

Report Name Chronobiological Effects on Obesity

Publication Current Obesity Reports

Issue-page numbers DOI: 10.1007/s13679-011-0005-4

URL http://www.springerlink.com/content/r1rj956235606p51/

Abstract The development of obesity is the consequence of a multitude of complex interactions between both genetic and environmental factors. It has been suggested that the dramatic increase in the prevalence of obesity over the past 30 years has been the result of environmental changes that have enabled the full realization of genetic susceptibility present in the population. Among the many environmental alterations that have occurred in our recent history is the ever-increasing dyssynchrony between natural cycles of light/dark and altered patterns of sleep/wake and eating behavior associated with our “24-hour” lifestyle. An extensive research literature has established clear links between increased risk for obesity and both sleep deprivation and shift work, and our understanding of the consequences of such dyssynchrony at the molecular level is beginning to emerge. Studies linking alterations in cellular circadian clocks to metabolic dysfunction point to the increasing importance of chronobiology in obesity etiology.

Keywords Obesity – Circadian – Molecular clock – Rhythm – Transcription – Sleep – Shift work – Gene – Chronobiological effects

Brismar K, Werner S, Thorén M, Wetterberg L **Year** 1985

Authors Brismar K, Werner S, Thorén M, Wetterberg L

Report Name Metyrapone: an agent for melatonin as well as ACTH and cortisol secretion.

Publication J Endocrinol Invest

Issue-page numbers 8:91–95. PMID:2993405

URL

Abstract N/A

Keywords

Broadway J, Arendt J, Folkard S **Year** 1987

Authors Broadway J, Arendt J, Folkard S

Report Name Bright light phase shifts the human melatonin rhythm during the Antarctic winter

Publication Neurosci Lett

Issue-page numbers 79:185–189 doi :10.1016/0304-3940(87)90694-X.PMID:3670728

URL http://www.sciencedirect.com/science/article/pii/030439408790694X

Abstract In most species daily and seasonal changes in the light-dark cycle are the most important synchronisers (zeitgebers) of daily and seasonal rhythms. In humans only bright light (2500 lux) appears to be an effective circadian zeitgeber. Seasonal effects of light on human physiology have not been investigated. We have exploited the low intensity illumination of the Antarctic winter to investigate the effects of bright-or dim-light treatment for an hour in the morning and in the evening (a 'skeleton' 12.5-h day) for 6 weeks on the plasma melatonin rhythm, together with mood and a number of behavioural variables. In parallel seasonal changes in melatonin were observed. Melatonin is known to convey daylength information in photoperiodic seasonal breeders through characteristics of its night-time secretion profile. Bright-, but not dim-, light treatment in winter induced a marked phase advance of the melatonin rhythm, similar to that found in the summer, without marked effect on the other variables. Thus at least one human seasonal change appears to be light-dependent.

Keywords Melatonin; Light; Circadian rhythm; Man

Brown DL, Feskanich D, Sánchez BN, et al. **Year** 2009

Authors Devin L. Brown, Diane Feskanich, Brisa N. Sánchez, Kathryn M. Rexrode, Eva S. Schernhammer, and Lynda D. Lisabeth

Report Name Rotating Night Shift Work and the Risk of Ischemic Stroke

Publication Am J Epidemiol

Issue-page numbers 2009 June 1; 169(11): 1370–1377.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2727250/

Abstract

Rotating night shift work disrupts circadian rhythms and is associated with coronary heart disease. The relation between rotating night shift work and ischemic stroke is unclear. The Nurses' Health Study, an ongoing cohort study of registered female nurses, assessed in 1988 the total number of years the nurses had worked rotating night shifts. The majority (69%) of stroke outcomes from 1988 to 2004 were confirmed by physician chart review. The authors used Cox proportional hazards models to assess the relation between years of rotating night shift work and ischemic stroke, adjusting for multiple vascular risk factors. Of 80,108 subjects available for analysis, 60% reported at least 1 year of rotating night shift work. There were 1,660 ischemic strokes. Rotating night shift work was associated with a 4% increased risk of ischemic stroke for every 5 years (hazard ratio = 1.04, 95% confidence interval: 1.01, 1.07; Ptrend = 0.01). This increase in risk was similar when limited to the 1,152 confirmed ischemic strokes (hazard ratio = 1.03, 95% confidence interval: 0.99, 1.07; Ptrend = 0.10) and may be confined to women with a history of 15 or more years of rotating shift work. Women appear to have a modestly increased risk of stroke after extended periods of rotating night shift work.

Keywords risk factors, sleep disorders, circadian rhythm, stroke

Brown LR

Year 2009

Authors Brown LR.

Report Name Plan B 4.0: Mobilizing to Save Civilization

Publication WW Norton & Co

Issue-page numbers book

URL http://www.earth-policy.org/devcart/index.php?target=products&product_id=29788

Abstract

Food, the weak link that brought down earlier civilizations, is the sector most affected by climate change. And it could bring our own civilization down if we stay with business as usual.

We are entering a new food era, one marked by higher food prices, growing numbers of hungry people, and an intensifying competition for land and water that has now crossed national boundaries as food-importing countries buy or lease vast tracts of land in other countries.

Unlike earlier world grain price hikes that were event-driven—a drought in the Soviet Union or a monsoon failure in India—and were typically remedied by the next harvest, this recent rise is trend-driven. Among the trends responsible are expanding population, falling water tables, rising temperatures, melting glaciers, and using grain to produce fuel for cars.

The historic grain price climb in the last few years underlines the gravity of the situation. From mid-2006 to mid-2008 world prices of wheat, rice, corn, and soybeans roughly tripled, reaching historic highs. It took the worst economic meltdown since the Great Depression to lower grain prices.

We are in a race between political tipping points and natural tipping points. Can we cut carbon emissions fast enough to save the Greenland ice sheet and avoid the resulting rise in sea level? Can we close coal-fired power plants fast enough to save the glaciers in the Himalayas and on the Tibetan Plateau, the glaciers whose ice melt sustains the major rivers and irrigation systems of Asia during the dry season? Can we stabilize population by reducing fertility before nature takes over and halts population growth by raising mortality?

Can we win this race? We think we can …. That is what Plan B 4.0 is about.

Keywords

Brown NJ

Year 2011

Authors Nellie J. Brown

Report Name Shift Work and Working Long Hours: Risks and Risk Reducation

Publication New York Water Environment Assocation, Inc.

Issue-page numbers 2011 Winter; 23-28

URL http://nywea.org/clearwaters/11-4-winter/6.pdf

Abstract

Keywords circadian disruption

Brown R, Pang G, Husband AJ, King MG

Year 1989

Authors Brown R, Pang G, Husband AJ, King MG

Report Name Suppression of immunity to influenza virus infection in the respiratory tract following sleep disturbance

Publication Reg Immunol

Issue-page numbers 2:321–325. PMID:2562046

URL http://www.ncbi.nlm.nih.gov/pubmed/2562046

Abstract The extent to which sleep deprivation interferes with immunity in the respiratory tract to influenza virus has been assessed in mice. Mice were orally immunized with influenza virus on two occasions separated by a one week interval and challenged intranasally one week later. Some animals were deprived of sleep for a 7 h period immediately following challenge. Three days after challenge, virus clearance and virus specific antibody were determined in lungs of sleep deprived and normally sleeping mice and the results compared with unimmunized mice subjected to the same protocol. Whereas immunized, normal sleep mice achieved total virus clearance, sleep deprivation in immunized mice completely abrogated this effect such that sleep deprived animals behaved as though they had never been immunized. There was no difference in viral clearance in unimmunized mice whether sleep deprived or not, indicating that sleep deprivation did not itself have a direct effect on viral replication. The data reported here support the concept that sleep is a behavioral state which is essential for optimal immune function in the presence of a respiratory tract pathogen.

Keywords

Brown R, Price RJ, King MG, Husband AJ **Year** 1989

Authors Brown R, Price RJ, King MG, Husband AJ

Report Name Interleukin-1 beta and muramyl dipeptide can prevent decreased antibody response associated with sleep deprivation

Publication Brain Behav Immun

Issue-page numbers 3:320–330 doi:10.1016/0889-1591(89)90031-7. PMID:2575411

URL http://www.ncbi.nlm.nih.gov/pubmed/2575411

Abstract A single, brief (8 h) period of sleep deprivation (DEP) was found to suppress secondary antibody response to sheep red blood cells in rats. This decrease could be totally prevented if either interleukin-1 beta (IL-1) or muramyl dipeptide (MDP) was administered at the beginning of the DEP vigil. Twenty-five units of IL-1 or 250 micrograms/kg MDP was found to be immunosuppressive in sleeping rats but, paradoxically, the combination of such doses with DEP alleviated this effect. Increased colonic temperatures associated with antigen and/or adjuvant administration were not related to the differences in antibody levels between sleeping and DEP animals. Activation of hypothalamic dopamine in IL-1-treated rats following DEP suggests that this monoamine transmitter system may participate in the observed protective activity of IL-1. The present findings extend the immune adjuvant effects of both IL-1 and MDP to protection of the host against behaviorally induced immunosuppression.

Keywords

Brown TM, Tsujimura S, Allen AE, et al. **Year** 2012

Authors Timothy M. Brown, Sei-ichi Tsujimura, Annette E. Allen, Jonathan Wynne, Robert Bedford, Graham Vickery, Anthony Vugler, Robert J. Lucas

Report Name Melanopsin-Based Brightness Discrimination in Mice and Humans

Publication Current Biology

Issue-page numbers Volume 22, Issue 12, 19 June 2012, Pages 1134–1141

URL http://www.sciencedirect.com/science/article/pii/S0960982212004599

Abstract Photoreception in the mammalian retina is not restricted to rods and cones but extends to a small number of intrinsically photoreceptive retinal ganglion cells (ipRGCs), expressing the photopigment melanopsin [[1], [2], [3] and [4]]. ipRGCs are known to support various accessory visual functions including circadian photoentrainment and pupillary reflexes. However, despite anatomical and physiological evidence that they contribute to the thalamocortical visual projection [[5], [6] and [7]], no aspect of visual discrimination has been shown to rely upon ipRGCs. Based on their currently known roles, we hypothesized that ipRGCs may contribute to distinguishing brightness. This percept is related to an object's luminance—a photometric measure of light intensity relevant for cone photoreceptors. However, the perceived brightness of different sources is not always predicted by their respective luminance [[8], [9], [10], [11] and [12]]. Here, we used parallel behavioral and electrophysiological experiments to first show that melanopsin contributes to brightness discrimination in both retinally degenerate and fully sighted mice. We continued to use comparable paradigms in psychophysical experiments to provide evidence for a similar role in healthy human subjects. These data represent the first direct evidence that an aspect of visual discrimination in normally sighted subjects can be supported by inner retinal photoreceptors.

Keywords

Brun J, Claustrat B, David M — *Year* 1987

Authors Brun J, Claustrat B, David M

Report Name Urinary melatonin, LH, oestradiol, progesterone excretion during the menstrual cycle or in women taking oral contraceptives

Publication Acta Endocrinol (Copenh)

Issue-page numbers 116:145–149. PMID:3661054

URL http://www.mendeley.com/research/urinary-melatonin-lh-oestradiol-progesterone-excretion-during-the-menstrual-cycle-or-in-women-taking-oral-contraceptives/

Abstract Nocturnal urinary excretion of melatonin, LH, progesterone and oestradiol was measured by radioimmunoassay in nine normal women during a complete cycle. In addition, these hormonal excretions were studied in two women taking an oral contraceptive. A high within-subject coefficient of variation was observed for melatonin excretion in the two groups. In the nine normal cycling women, melatonin excretion was not decreased at the time of ovulation, but was significantly increased during the luteal phase compared with that of the follicular phase (P less than 0.01). These data are consistent with a positive relationship between melatonin and progesterone during the luteal phase. In the two women under an oral contraceptive, melatonin excretion was found within the same range as for the other nine. The results are discussed in terms of pineal investigation in human.

Keywords

Brunwin AD, Cox GL, Stewart JL — *Year* 1928

Authors A.D. Brunwin M.D., G. Lissant Cox M.D., J. Logan Stewart M.B

Report Name Artificial light treatment at tuberculosis dispensaries in the administrative county of Lancaster

Publication Tubercle

Issue-page numbers Volume 10, Issue 1, October 1928, Pages 1-12

URL http://www.sciencedirect.com/science/article/pii/S0041387928800274

Abstract N/A

Keywords

Bruze M, Forsgren A, Ljunggren B

Year 1985

Authors Bruze M, Forsgren A, Ljunggren B.

Report Name Antinuclear antibodies in mice induced by long wave ultraviolet radiation (UVA)

Publication Acta Derm Venereol

Issue-page numbers 1985;65(1):25-30.

URL http://www.ncbi.nlm.nih.gov/pubmed/2578702

Abstract PUVA therapy has been reported to induce antinuclear antibodies (ANA). The generation of ANA following ultraviolet irradiation was studied experimentally in albino mice. When treated with long wave ultraviolet radiation (UVA) from blacklight fluorescent tubes a significant number of animals developed positive ANA titres, whereas no change was noted in groups, treated with PUVA, 8-methoxypsoralen only or medium wave ultraviolet irradiation (UVB) respectively. The tendency for UVA-irradiated mice to develop ANA was stronger when higher ANA titres were compared. UVA induces ANA in mice, and PUVA-induced ANA may be due to the UVA component of this therapy.

Keywords

Bryant PA, Trinder J, Curtis N

Year 2004

Authors Penelope A. Bryant, John Trinder & Nigel Curtis

Report Name Sick and tired: Does sleep have a vital role in the immune system?

Publication Nat Rev Immunol

Issue-page numbers 4:457–467 doi:10.1038/nri1369. PMID:15173834

URL http://www.nature.com/nri/journal/v4/n6/abs/nri1369.html

Abstract It is a common belief that we are more susceptible to infections when deprived of sleep. Consistent with this, there is increasing evidence that sleep deprivation has detrimental effects on the immune response, indicating that sleep should be considered a vital part of the immune system and that there is a reciprocal relationship between sleep and immunity. This relationship is important because, over recent decades, there has been a documented decrease in the mean duration and quality of sleep in the population. The concept that lack of sleep might be compromising immunity in the population has far-reaching public-health implications for both individuals and society.

Keywords

Brzezinski A

Year 1997

Authors Brzezinski A.

Report Name Melatonin in humans

Publication N Engl J Med

Issue-page numbers 1997 Jan 16;336(3):186-95.

URL http://www.ncbi.nlm.nih.gov/pubmed/8988899

Abstract N/A

Keywords N/A

Brzezinski A, Fibich T, Cohen M et al.

Year 1992

Authors Brzezinski A, Fibich T, Cohen M et al.

Report Name Effects of melatonin on progesterone production by human granulosa lutein cells in culture.

Publication Fertil Steril

Issue-page numbers 58:526–529. PMID:1521647

URL http://www.ncbi.nlm.nih.gov/pubmed/1521647

Abstract OBJECTIVE:

To test the hypothesis that melatonin modulates steroid synthesis in the human ovary.
DESIGN:

Granulosa lutein cells obtained from in vitro fertilization cycles were cultured in medium containing melatonin and human chorionic gonadotropin (hCG).
RESULTS:

Progesterone (P) secretion by granulosa lutein cells increased progressively in both basal and hCG-stimulated conditions, up to 96 hours in culture, plateaued at 144 and decreased thereafter. Melatonin (10(-7), 10(-9), 10(-11) M) had no effect on basal P or 17 beta-estradiol production. The addition of melatonin to the hCG-treated granulosa lutein cells significantly (P less than 0.05) potentiated the stimulatory effect of hCG on P production. The effect was most prominent after 144 and 196 hours of incubation.
CONCLUSION:

This observation suggests a role for melatonin in the intraovarian control of P production in the human ovary.

Keywords

Brzezinski A, Lynch HJ, Seibel MM et al. **Year** 1988

Authors Brzezinski A, Lynch HJ, Seibel MM et al.

Report Name The circadian rhythm of plasma melatonin during the normal menstrual cycle and in amenorrheic women.

Publication J Clin Endocrinol Metab

Issue-page numbers 66:891–895 doi:10.1210/jcem-66-5-891. PMID:3129448

URL http://www.hopkinsguides.com/hopkins/ub/citation/3129448/The_circadian_rhythm_of_plasma_melatonin_during_the_normal_menstrual_cycle_and_in_amenorrheic_women_

Abstract Plasma melatonin, PRL, and LH levels were measured in samples collected every 2 h for 24 h from 14 normally cycling women during the early follicular, periovulatory, and luteal phases of their menstrual cycles. Plasma melatonin levels also were measured in samples collected at the same interval from 7 patients with hypothalamic amenorrhea. A distinct daily rhythm in plasma melatonin was evident in all subjects, with peaks occurring around 0300 h. Each woman's rhythm was remarkably consistent throughout the menstrual cycle (in terms of the phase, amplitude, and total melatonin secreted). Plasma PRL levels also exhibited daily rhythms which did not change during the menstrual cycle; the nocturnal peak plasma PRL level tended to occur 1-2 h after that for melatonin. Among the amenorrheic women, both daytime and nighttime melatonin levels were significantly higher (P less than 0.005) than in the normal women. Their plasma PRL levels were similar to those in the normal women. We conclude that, as for PRL, the circadian rhythm of melatonin secretion does not change significantly during the normal menstrual cycle. The elevated plasma melatonin levels in women with hypothalamic amenorrhea suggest that the hormone may be involved in the neuroendocrine pathology underlying this disorder.

Keywords

Brzezinski A, Vangel MG, Wurtman RJ et al. **Year** 2005

Authors Amnon Brzezinski, Mark G. Vangel, Richard J. Wurtman, Gillian Norrie, Irina Zhdanova, Abraham Ben-Shushan, Ian Ford

Report Name Effects of exogenous melatonin on sleep: a meta-analysis

Publication Sleep Med Rev

Issue-page numbers 9:41–50 doi:10.1016/j.smrv.2004.06.004. PMID:15649737

URL http://www.smrv-journal.com/article/S1087-0792%2804%2900060-7/abstract

Abstract Exogenous melatonin reportedly induces drowsiness and sleep, and may ameliorate sleep disturbances, including the nocturnal awakenings associated with old age. However, existing studies on the soporific efficacy of melatonin have been highly heterogeneous in regard to inclusion and exclusion criteria, measures to evaluate insomnia, doses of the medication, and routes of administration. We reviewed and analyzed (by meta-analysis) available information on effects of exogenous melatonin on sleep. A MEDLINE search (1980 to December 2003) provided English-language articles, supplemented by personal files maintained by the authors. The analysis used information derived from 17 different studies (involving 284 subjects) that satisfied inclusion criteria. Sleep onset latency, total sleep duration, and sleep efficiency were selected as the outcome measures. The study effect size was taken to be the difference between the response on placebo and the mean response on melatonin for each outcome measured. Melatonin treatment significantly reduced sleep onset latency by 4.0 min (95% CI 2.5, 5.4); increased sleep efficiency by 2.2% (95% CI 0.2, 4.2), and increased total sleep duration by 12.8 min (95% CI 2.9, 22.8). Since 15 of the 17 studies enrolled healthy subjects or people with no relevant medical condition other than insomnia, the analysis was also done including only these 15 studies. The sleep onset results were changed to 3.9 min (95% CI (2.5, 5.4)); sleep efficiency increased to 3.1% (95% CI (0.7, 5.5)); sleep duration increased to 13.7 min (95% CI (3.1, 24.3)).

Keywords

Buijs RM, Kalsbeek A **Year** 2001

Authors Buijs RM, Kalsbeek A

Report Name Hypothalamic integration of central and peripheral clocks

Publication Nat Rev Neurosci

Issue-page numbers 2:521–526 doi:10.1038/35081582. PMID:11433377

URL http://www.nature.com/nrn/journal/v2/n7/abs/nrn0701_521a.html

Abstract During sleep, our biological clock prepares us for the forthcoming period of activity by controlling the release of hormones and the activity of the autonomic nervous system. Here, we review the history of the study of circadian rhythms and highlight recent observations indicating that the same mechanisms that govern our central clock might be at work in the cells of peripheral organs. Peripheral clocks are proposed to synchronize the activity of the organ, enhancing the functional message of the central clock. We speculate that peripheral visceral information is then fed back to the same brain areas that are directly controlled by the central clock. Both clock mechanisms are proposed to have a complementary function in the organization of behaviour and hormone secretion.

Keywords

Buijs RM, Wortel J, Van Heerikhuize JJ et al. **Year** 1999

Authors Buijs RM, Wortel J, Van Heerikhuize JJ et al.

Report Name Anatomical and functional demonstration of a multisynaptic suprachiasmatic nucleus adrenal (cortex) pathway.

Publication Eur J Neurosci

Issue-page numbers 11:1535–1544 doi:10.1046/j.1460-9568.1999.00575.x. PMID:10215906

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1460-9568.1999.00575.x/abstract?

Abstract In view of mounting evidence that the suprachiasmatic nucleus (SCN) is directly involved in the setting of sensitivity of the adrenal cortex to ACTH, the present study investigated possible anatomical and functional connections between SCN and adrenal. Transneuronal virus tracing from the adrenal revealed first order labelling in neurons in the intermedio-lateral column of the spinal cord that were shown to receive an input from oxytocin fibres and subsequently second-order labelling in neurons of the autonomic division of the paraventricular nucleus. The latter neurons were shown to receive an input from vasopressin or vasoactive intestinal peptide (VIP) containing SCN efferents. The true character of this SCN input to second-order neurons was also demonstrated by the fact that third-order labelling was present within the SCN, vasopressin or VIP neurons. The functional presence of the SCN–adrenal connection was demonstrated by a light-induced fast decrease in plasma corticosterone that could not be attributed to a decrease in ACTH. Using intact and SCN-lesioned animals, the immediate decrease in plasma corticosterone was only observed in intact animals and only at the beginning of the dark period. This fast decrease of corticosterone was accompanied by constant basal levels of blood adrenaline and noradrenaline, and is proposed to be due to a direct inhibition of the neuronal output to the adrenal cortex by light-mediated activation of SCN neurons. As a consequence, it is proposed that the SCN utilizes neuronal pathways to spread its time of the day message, not only to the pineal, but also to other organs, including the adrenal, utilizing the autonomic nervous system.

Keywords circadian rhythm; corticosterone; melatonin; noradrenaline; paraventricular nucleus; sympathetic; parasympathetic

Authors Buja A, Mastrangelo G, Perissinotto E et al.

Report Name Cancer incidence among female flight attendants: a meta-analysis of published data

Publication J Womens Health (Larchmt)

Issue-page numbers 98–105.doi:10.1089/jwh.2006.15.98 PMID:16417424

URL http://www.biostat.jhsph.edu/~fdominic/papers/Buja.pdf

Abstract Background: Flight attendants are exposed to cosmic ionizing radiation and other potential cancer risk factors, but only recently have epidemiological studies been performed to assess the risk of cancer among these workers. The aim of the present work was to evaluate the incidence of various types of cancer among female cabin attendants by combining cancer incidence estimates reported in published studies.
Methods: All follow-up studies reporting standardized incidence ratio (SIR) for cancer among female flight attendants were obtained from online databases and analyzed. A metaanalysis was performed by applying Bayesian hierarchical models, which take into account studies that reported SIR ¬ 0 and natural heterogeneity of study-specific SIRs.
Results: A total of seven published studies reporting SIR for several cancer types were extracted. Meta-analysis showed a significant excess of melanoma (meta-SIR 2.15, 95% posterior interval [PI] 1.56-2.88) and breast carcinoma (meta-SIR 1.40; PI 1.19-1.65) and a slight but not significant excess of cancer incidence across types (meta-SIR 1.11, PI 0.98-1.25).
Conclusions: Although further studies are necessary to clarify the exact role of occupational exposure, all airlines should, as some companies do, estimate radiation dose, organize the schedules of crew members in order to reduce further exposure in highly exposed flight attendants, inform crew members about health risks, and give special protection to pregnant women.

Keywords

Bukalev AV, Vinogradova IA, Zabezhinskii MA, et al. ***Year*** 2012

Authors A. V. Bukalev, I. A. Vinogradova, M. A. Zabezhinskii, A. V. Semenchenko, V. N. Anisimov

Report Name Light pollution increases in the morbidity and mortality rates from different causes in male rats

Publication Uspekhi Gerontologii

Issue-page numbers 2012, Vol. 25, No. 1, pp. 49–56.

URL http://link.springer.com/article/10.1134%2FS2079057012040042?LI=true

Abstract This paper investigates the effects of different light regimes (constant light, LL; constant darkness, DD; standard light regime, LD; 12 h light/12 h darkness, natural light of northwest Russia, NL) on the dynamics of lifetime morbidity, spontaneous carcinogenesis, and the incidence of certain types of nontumorous pathologies that were identified during autopsy of male rats. As well, it was found that keeping the animals from the age of 25 days under conditions of LL and NL led to an increased frequency of infectious diseases, significantly more rapid development of spontaneous tumors, and expansion of the range and frequency of non-neoplastic diseases as compared with animals that were under standard light conditions (LD). Light deprivation (DD) contributed to a significant reduction of the incidence of neoplasm, non-neoplastic, and infectious diseases as compared with rats that were kept under standard lighting.

Keywords

Bunger MK, Wilsbacher LD, Moran SM et al. ***Year*** 2000

Authors Maureen K. Bunger, Lisa D. Wilsbacher, Susan M. Moran, Cynthia Clendenin, Laurel A. Radcliffe, John B. Hogenesch, M.Celeste Simon, Joseph S. Takahashi and Christopher A

Report Name Mop3 is an essential component of the master circadian pacemaker in mammals

Publication Cell

Issue-page numbers 103:1009–1017 doi:10.1016/S0092-8674(00)00205-1. PMID:11163178

URL http://www.cell.com/abstract/S0092-8674%2800%2900205-1

Abstract Circadian oscillations in mammalian physiology and behavior are regulated by an endogenous biological clock. Here we show that loss of the PAS protein MOP3 (also known as BMAL1) in mice results in immediate and complete loss of circadian rhythmicity in constant darkness. Additionally, locomotor activity in light–dark (LD) cycles is impaired and activity levels are reduced in Mop3−/− mice. Analysis of Period gene expression in the suprachiasmatic nucleus (SCN) indicates that these behavioral phenotypes arise from loss of circadian function at the molecular level. These results provide genetic evidence that MOP3 is the bona fide heterodimeric partner of mCLOCK. Furthermore, these data demonstrate that MOP3 is a nonredundant and essential component of the circadian pacemaker in mammals.

Keywords

Authors Burch JB, Yost MG, Johnson W, Allen E

Report Name Melatonin, sleep, and shift work adaptation

Publication J Occup Environ Med

Issue-page numbers 47:893–901 doi:10.1097/01.jom.0000177336.21147.9f. PMID:16155474

URL http://journals.lww.com/joem/Abstract/2005/09000/Melatonin,_Sleep,_and_Shift_Work_Adaptation.4.aspx

Abstract

Background: Night work is associated with disrupted circadian rhythms, fatigue, accidents, and chronic disease. Melatonin secretion helps regulate sleep and circadian rhythms.

Objective: Melatonin, sleep disturbances, and symptoms (sleep, fatigue, mental) were compared among workers on permanent day, swing, and night shifts.

Methods: Urinary 6-hydroxymelatonin sulfate (6-OHMS) was measured in postwork and postsleep samples. Disrupted circadian melatonin production was evaluated using the sleep:work 6-OHMS ratio. Wrist actigraphy characterized light exposures and sleep characteristics.

Results: Night workers had altered melatonin, disrupted sleep, and elevated symptom prevalence. Subjects grouped by their sleep:work 6-OHMS ratio rather than shift had even greater symptom prevalence. Risks for two or more symptoms were 3.5 to 8 times greater among workers with sleep:work ratios ≤1 compared to those with ratios >1.

Conclusions: This ratio may help identify workers at increased risk for accidents or injuries.

Keywords

Burgess HJ, Eastman CI

Year 2005

Authors HELEN J . BURGESS and CHARMANE I . EASTMAN

Report Name The dim light melatonin onset following fixed and free sleep schedules

Publication J. Sleep Res.

Issue-page numbers 14, 229-237

URL http://www.sciencesleep.org/ziliao/The%20dim%20light%20melatonin%20onset%20following%20fixed%20and%20free%20sleep%20schedules.pdf

Abstract

The time at which the dim light melatonin onset (DLMO) occurs can be used to ensure the correct timing of light and/or melatonin administration in order to produce desired circadian phase shifts. Sometimes however, measuring the DLMO is not feasible. Here we determined if the DLMO was best estimated from fixed sleep times (based on habitual sleep times) or free (ad libitum) sleep times. Young healthy sleepers on fixed (n ¼ 60) or free (n ¼ 60) sleep schedules slept at home for 6 days. Sleep times were recorded with sleep logs verified with wrist actigraphy. Half-hourly saliva samples were then collected during a dim light phase assessment and were later assayed to determine the DLMO. We found that the DLMO was more highly correlated with sleep times in the free sleepers than in the fixed sleepers (DLMO versus wake time, r ¼ 0.70 and r ¼ 0.44, both P < 0.05). The regression equation between wake time and the DLMO in the free sleepers predicted the DLMO in an independent sample of free sleepers (n ¼ 23) to within 1.5 h of the actual DLMO in 96% of cases. These results indicate that the DLMO can be readily estimated in people whose sleep times are minimally affected by work, class and family commitments. Further work is necessary to determine if the DLMO can be accurately estimated in people with greater work and family responsibilities that affect their sleep times, perhaps by using weekend wake times, and if this method will apply to the elderly and patients with circadian rhythm disorders.

Keywords bedtime, circadian rhythms, dim light melatonin onset, melatonin, sleep,

Burgess HJ, Savic N, Sletten T, et al. **Year** 2003

Authors Helen J Burgess, Natasha Savic, Tracey Sletten, Gregory Roach, Saul S. Gilbert Drew Dawson

Report Name The Relationship Between the Dim Light Melatonin Onset and Sleep on a Regular Schedule in Young Health Adults

Publication

Issue-page numbers

URL http://www.unisanet.unisa.edu.au/staff/matthewthomas/GREG/burgess%28onset%2903.pdf

Abstract The endogenous melatonin onset in dim light (DLMO) is a mark of circadian phase that can be used to appropriately time the administration of bright light or exogenous melatonin in order to elicit a desired phase shift.…

Keywords

Burgess HJ, Sharkey KM, Eastman CI **Year** 2002

Authors Burgess HJ, Sharkey KM, Eastman CI

Report Name Bright light, dark and melatonin can promote circadian adaptation in night shift workers.

Publication Sleep Med Rev

Issue-page numbers 6:407–420. PMID:12531129

URL http://www.sciencedirect.com/science/article/pii/S1087079201902151

Abstract The circadian rhythms of shift workers do not usually phase shift to adapt to working at night and sleeping during the day. This misalignment results in a multitude of negative symptoms including poor performance and reduced alertness during night work and poor daytime sleep at home. After an introduction to circadian principles, we discuss the efficacy of appropriately timed bright light exposure (natural and artificial) and exogenous melatonin administration for producing circadian adaptation to night work. Interventions that generate alternative 24 h light/dark patterns that facilitate appropriate circadian phase shifting are discussed. Such interventions include minimizing night workers' exposure to the external light/dark cycle, and the use of intermittent and moving patterns of bright light at work. The efficacy of melatonin in phase shifting circadian rhythms in the field is also addressed and compared to that of bright light. We present sleep/light exposure schedules that could produce circadian adaptation in permanent night workers. We conclude this review by discussing the impact of individual differences on possible circadian interventions and issues associated with the use of bright light interventions in the field.

Keywords chronobiotic, phase, rhythm, sleep

Burns T, Breathnach S, Cox N, Griffiths C

Year 2004

Authors Burns T, Breathnach S, Cox N, Griffiths C

Report Name Metabolic and nutritional disorders: The individual porphyrias

Publication In: Rook's Textbook of Dermatology. 7th ed. Blackwell Science

Issue-page numbers 2004. p57.12-8.

URL http://onlinelibrary.wiley.com/doi/10.1002/9780470750520.ch57/summary

Abstract N/A

Keywords

Cagnacci A

Year 1997

Authors Angelo Cagnacci

Report Name Influences of Melatonin on Human Orcadian Rhythms

Publication Chronobiology International

Issue-page numbers 14:2, 205-220

URL http://informahealthcare.com/doi/abs/10.3109/07420529709001156

Abstract Administration of melatonin is useful in the treatment of desynchro-nized conditions. The mechanisms through which melatonin exerts its effect are not completely clear. Melatonin exerts direct effects on several biological functions, such as the regulation of body temperature, but there is no proof that these actions are important in the indirect regulation of main pacemaker activity. By contrast, it is very likely that melatonin exerts direct effects on circadian clocks, and that depending on the time of its administration/presence, it antagonizes or promotes the phase-shifting effects exerted by light. It is possible that melatonin regulates its own secretion and that its prolonged or shortened secretion in die period of the night-day transition is responsible for the lengthening or shortening, respectively, of the nocturnal melatonin rise. This possibility that needs to be confirmed by extensive studies may represent a physiological mechanism through which photoperiodic information is more rapidly and efficiently transformed by melatonin in a circadian signal to all the body.

Keywords Phase shifts, SCN, Light, Seasonality, Body temperature

Authors Cagnacci A, Elliott JA, Yen SS

Report Name Melatonin: a major regulator of the circadian rhythm of core temperature in humans

Publication J Clin Endocrinol Metab

Issue-page numbers 75:447–452 doi:10.1210/jc.75.2.447. PMID:1639946

URL http://jcem.endojournals.org/content/75/2/447.short

Abstract The circadian rhythm of core body temperature (BTc), with maxima during the day and minima at night, is normally coupled with the sleep-wake cycle. Pineal melatonin secretion occurs contemporaneously during the nighttime hours and is mediated by the activation of beta-adrenergic receptors during darkness. The hypothesis that nocturnal melatonin secretion may be involved in the regulation of the human circadian BTc rhythm was examined. The temporal relationship between melatonin and the circadian BTc rhythm was characterized in 12 young women, normally entrained to the light-dark cycle. Melatonin levels were manipulated through the administration of exogenous melatonin (2.5 mg, orally) during the daytime (n = 6) or suppression of endogenous nocturnal melatonin secretion by the beta-adrenergic antagonist atenolol (100 mg; n = 6) in double blind placebo-controlled experiments conducted during 2 consecutive days. Serum melatonin levels and BTc were monitored at 20- and 10-min intervals, respectively. In a nightshift worker the temporal relationship between the circadian rhythm of melatonin and BTc was investigated before and after entrainment to a reversed wake-sleep cycle. Our data show that in normally entrained subjects, the time course and amplitude of nocturnal melatonin secretion were temporally coupled with the decline of BTc (r = 0.97; P less than 0.00001). The same occurred in the nightshift worker, both during the dissociation and after entrainment to the reversed sleep-wake cycle. Compared with placebo, administration of melatonin significantly reduced daytime BTc (P less than 0.01), and the suppression of melatonin (by atenolol) attenuated the nocturnal decline of BTc (P less than 0.01). Cosinor analysis showed that the amplitude of the circadian BTc rhythm was reduced by about 40% in response to both daytime melatonin administration (P less than 0.05) and nocturnal melatonin suppression (P less than 0.02). In conclusion, circadian rhythms of melatonin and BTc are inversely coupled. The demonstrated hypothermic properties of melatonin are accountable for the generation of at least 40% of the amplitude of the circadian BTc rhythm. Manipulation of melatonin levels might be clinically useful to resynchronize the BTc rhythm under conditions of BTc rhythm desynchronization.

Keywords

Cagnacci A, Paoletti AM, Soldani R et al. **Year** 1995

Authors Cagnacci A, Paoletti AM, Soldani R et al.

Report Name Melatonin enhances the luteinizing hormone and follicle-stimulating hormone responses to gonadotropin-releasing hormone in the follicular, but not in the luteal, menstrual phase

Publication J Clin Endocrinol Metab

Issue-page numbers 80:1095–1099 doi:10.1210/jc.80.4.1095. PMID:7714075

URL http://www.ncbi.nlm.nih.gov/pubmed/7714075

Abstract Exogenous melatonin enhances LH pulse amplitude and mean LH levels in women during the follicular, but not the luteal, menstrual phase. In this study we investigated whether an increased pituitary response to GnRH is involved in the stimulatory effect of melatonin. Eight normal cycling women were studied on 2 consecutive days during the follicular stage (days 4-6), and eight were studied during the luteal phase (days 19-21) of the menstrual cycle. On 2 consecutive days, each women received, randomly and in a double blind fashion, placebo or 3 mg melatonin (1 mg at 0800, 1000, and 1200 h), whereas the pituitary LH and FSH responses to GnRH were tested by the iv administration of three submaximal doses of GnRH (1 microgram at 0900 h, 5 micrograms at 1100 h, and 10 micrograms at 1300 h). In the follicular phase, melatonin administration enhanced the LH and FSH responses to all three GnRH stimuli, whereas in the luteal phase, melatonin administration was ineffective. The present data indicate that an enhancing effect of melatonin on the LH and FSH responses to submaximal GnRH stimuli is evident in the follicular, but not the luteal, phase of the menstrual cycle and infer an endocrine window for the effect of melatonin on gonadotropin secretion.

Keywords

Cagnacci A, Soldani R, Yen SS **Year** 1995

Authors Angelo Cagnacci, Renza Soldani and Samuel SC Yen

Report Name Melatonin enhances cortisol levels in aged but not young women

Publication Eur J Endocrinol

Issue-page numbers 133:691–695 doi:10.1530/eje.0.1330691. PMID:8548054

URL http://www.eje-online.org/content/133/6/691.abstract

Abstract In spite of animal data showing an effect of melatonin in the regulation of the hypothalamus–pituitary–adrenal (HPA) axis, no effect of melatonin on cortisol has been evidenced in young men. Gender and aging are believed to influence the regulation of the HPA axis, and may thus modulate the melatonin effect on cortisol. In this study we investigated whether an effect of melatonin on cortisol can be observed in women of different age. Six young women in early follicular phase (22–32 years; EFW) and eight aged women in postmenopause (54–62 years; PMW) were studied. At 08.00 h on two consecutive days each woman received, randomly and in double-blind fashion, a pill of placebo or melatonin (100 mg). Serum levels of melatonin and cortisol were evaluated at 20-min intervals for 48 h. In comparison to EFW, PMW showed an earlier onset of nocturnal melatonin ($p < 0.05$) and cortisol rise ($p < 0.01$) and higher cortisol levels at lunch ($p < 0.05$) and early evening ($p < 0.01$). Melatonin administration did not modify serum cortisol levels in EFW but elicited a marked increase of daytime cortisol levels in PMW ($p < 0.02$). The present data reveal that in aged PMW the cortisol levels are enhanced at selected circadian times and are stimulated by melatonin.

Keywords

Year 2007

Authors Christian Cajochen

Report Name Alerting effects of light

Publication Sleep Medicine Reviews

Issue-page numbers (2007) 11, 453–464

URL http://www.chronobiology.ch/publications/2007_06.pdf

Abstract Summary Light exerts powerful non-visual effects on a wide range of biological functions and behavior. In humans, light is intuitively linked with an alert or wakeful state. Compared to the effects of light on human circadian rhythms, little attention has been paid to its acute alerting action. Here I summarize studies from the past two decades, which have defined and quantified the dose (illuminance levels), exposure duration, timing and wavelength of light needed to evoke alerting responses in humans, as well as their temporal relationship to light-induced changes in endocrinological and electrophysiological sequelae of alertness. Furthermore, neuroanatomical and neurophysiological findings from animal studies elucidating a potential role of light in the regulation of sleep/wake states are discussed. A brief outlook of promising clinical and non-clinical applications of lights' alerting properties will be given, and its involvement in the design of more effective lighting at home and in the workplace will be considered.

Keywords Non-image forming, visual system;, Circadian system; Performance; Shift work; Monochromatic light; Sleepiness; Melatonin; Thermoregulation

Cajochen C, Frey S, Anders D, et al. **Year** 2011

Authors Christian Cajochen, Sylvia Frey, Doreen Anders, Jakub Späti, Matthias Bues, Achim Pross, Ralph Mager, Anna Wirz-Justice, and Oliver Stefani

Report Name Evening exposure to a light-emitting diodes (LED)-backlit computer screen affects circadian physiology and cognitive performance

Publication Journal of Applied Physiology

Issue-page numbers May 2011 vol. 110 no. 5 1432-1438

URL http://jap.physiology.org/content/110/5/1432.abstract

Abstract Many people spend an increasing amount of time in front of computer screens equipped with light-emitting diodes (LED) with a short wavelength (blue range). Thus we investigated the repercussions on melatonin (a marker of the circadian clock), alertness, and cognitive performance levels in 13 young male volunteers under controlled laboratory conditions in a balanced crossover design. A 5-h evening exposure to a white LED-backlit screen with more than twice as much 464 nm light emission {irradiance of 0,241 Watt/(steradian × m2) [W/(sr × m2)], 2.1 × 1013 photons/(cm2 × s), in the wavelength range of 454 and 474 nm} than a white non-LED-backlit screen [irradiance of 0,099 W/(sr × m2), 0.7 × 1013 photons/(cm2 × s), in the wavelength range of 454 and 474 nm] elicited a significant suppression of the evening rise in endogenous melatonin and subjective as well as objective sleepiness, as indexed by a reduced incidence of slow eye movements and EEG low-frequency activity (1–7 Hz) in frontal brain regions. Concomitantly, sustained attention, as determined by the GO/NOGO task; working memory/attention, as assessed by “explicit timing”; and declarative memory performance in a word-learning paradigm were significantly enhanced in the LED-backlit screen compared with the non-LED condition. Screen quality and visual comfort were rated the same in both screen conditions, whereas the non-LED screen tended to be considered brighter. Our data indicate that the spectral profile of light emitted by computer screens impacts on circadian physiology, alertness, and cognitive performance levels. The challenge will be to design a computer screen with a spectral profile that can be individually programmed to add timed, essential light information to the circadian system in humans.

Keywords

Cajochen C, Jud C, Münch M, et al. **Year** 2006

Authors Christian Cajochen, Corinne Jud, Mirjam Münch, Szymon Kobialka, Anna Wirz-Justice, Urs Albrecht

Report Name Evening exposure to blue light stimulates the expression of the clock gene PER2 in humans

Publication European Journal of Neuroscience

Issue-page numbers Volume 23, Issue 4, pages 1082–1086, February 2006

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1460-9568.2006.04613.x/full

Abstract We developed a non-invasive method to measure and quantify human circadian PER2 gene expression in oral mucosa samples and show that this gene oscillates in a circadian (= about a day) fashion. We also have the first evidence that induction of human PER2 expression is stimulated by exposing subjects to 2 h of light in the evening. This increase in PER2 expression was statistically significant in comparison to a non-light control condition only after light at 460 nm (blue) but not after light exposure at 550 nm (green). Our results indicate that the non-image-forming visual system is involved in human circadian gene expression. The demonstration of a functional circadian machinery in human buccal samples and its response to light opens the door for investigation of human circadian rhythms at the gene level and their associated disorders.

Keywords

Cajochen C, Münch M, Kobialka S, et al. **Year** 2005

Authors Christian Cajochen, Mirjam Münch, Szymon Kobialka, Kurt Kräuchi, Roland Steiner, Peter Oelhafen, Selim Orgül and Anna Wirz-Justice

Report Name High Sensitivity of Human Melatonin, Alertness, Thermoregulation, and Heart Rate to Short Wavelength Light

Publication Journal of Clinical Endocrinology & Metabolism

Issue-page numbers March 1, 2005 vol. 90 no. 3 1311-1316

URL http://jcem.endojournals.org/content/90/3/1311.full

Abstract Light can elicit acute physiological and alerting responses in humans, the magnitude of which depends on the timing, intensity, and duration of light exposure. Here, we report that the alerting response of light as well as its effects on thermoregulation and heart rate are also wavelength dependent. Exposure to 2 h of monochromatic light at 460 nm in the late evening induced a significantly greater melatonin suppression than occurred with 550-nm monochromatic light, concomitant with a significantly greater alerting response and increased core body temperature and heart rate (~2.8 × 1013 photons/cm2/sec for each light treatment). Light diminished the distal-proximal skin temperature gradient, a measure of the degree of vasoconstriction, independent of wavelength. Nonclassical ocular photoreceptors with peak sensitivity around 460 nm have been found to regulate circadian rhythm function as measured by melatonin suppression and phase shifting. Our findings—that the sensitivity of the human alerting response to light and its thermoregulatory sequelae are blue-shifted relative to the three-cone visual photopic system—indicate an additional role for these novel photoreceptors in modifying human alertness, thermophysiology, and heart rate.

Keywords

Cajochen C, Zeitzer JM, Czeisler CA, Dijk D-J **Year** 2000

Authors Cajochen C, Zeitzer JM, Czeisler CA, Dijk D-J

Report Name Dose-response relationship for light intensity and ocular and electroencephalographic correlates of human alertness

Publication Behav Brain Res

Issue-page numbers 115:75–83 doi:10.1016/S0166-4328(00)00236-9. PMID:10996410

URL http://www.chronobiology.ch/publications/2000_12.pdf

Abstract Light can elicit both circadian and acute physiological responses in humans. In a dose response protocol men and women were exposed to illuminances ranging from 3 to 9100 lux for 6.5 h during the early biological night after they had been exposed to B3 lux for several hours. Light exerted an acute alerting response as assessed by a reduction in the incidence of slow-eye movements, a reduction of EEG activity in the theta–alpha frequencies (power density in the 5–9 Hz range) as well as a reduction in self-reported sleepiness. This alerting response was positively correlated with the degree of melatonin suppression by light. In accordance with the dose response function for circadian resetting and melatonin suppression, the responses of all three indices of alertness to variations in illuminance were consistent with a logistic dose response curve. Half of the maximum alerting response to bright light of 9100 lux was obtained with room light of ┐100 lux. This sensitivity to light indicates that variations in illuminance within the range of typical, ambient, room light (90–180 lux) can have a significant impact on subjective alertness and its electrophysiologic concomitants in humans during the early biological night.

Keywords

Calandra T, Bernhagen J, Metz CN et al. **Year** 1995

Authors Thierry Calandra, Jürgen Bernhagen, Christine N. Metz, Lori A. Spiegel, Michael Bacher, Thomas Donnelly, Anthony Cerami & Richard Bucala

Report Name MIF as a glucocorticoid-induced modulator of cytokine production.

Publication Nature

Issue-page numbers 377:68–71 doi:10.1038/377068a0. PMID:7659164

URL http://www.nature.com/nature/journal/v377/n6544/abs/377068a0.html

Abstract GLUCOCORTICOID hormones are important for vital functions and act to modulate inflammatory and immune responses1,2. Yet, in contrast to other hormonal systems, no endogenous mediators have been identified that can directly counter-regulate their potent anti-inflammatory and immunosuppressive properties. Recent investigations of the protein macrophage migration inhibitory factor (MIF), which was discovered originally to be a T-lymphocyte-derived factor3,4, have established it to be a pro-inflammatory pituitary and macrophage cytokine and a critical mediator of septic shock5–7. Here we report the unexpected finding that low con-centrations of glucocorticoids induce rather than inhibit MIF production from macrophages. MIF then acts to override gluco-corticoid-mediated inhibition of cytokine secretion by lipopoly-saccharide (LPS)-stimulated monocytes and to overcome glucocorticoid protection against lethal endotoxaemia. These observations identify a unique counter-regulatory system that functions to control inflammatory and immune responses.

Keywords

Cappuccio FP, Miller MA, Lockley SW **Year** 2010

Authors Francesco P. Cappuccio, Michelle A. Miller and Steven W. Lockley

Report Name Sleep, Health and Society: From Aetiology to Public Health

Publication Oxford, UK: Oxford University Press

Issue-page numbers 2010

URL http://www.us.oup.com/us/catalog/general/subject/Medicine/EpidemiologyBiostatistics/?view=usa&ci=9780199566594

Abstract Sleep disturbances and sleep deprivation are common in modern society. Increasingly populations have been subjected to a steady constant decline in the number of hours devoted to sleep, due to changes in a variety of environmental and social conditions. Through the application of epidemiological methods of investigation sleep deprivation has been shown to be associated with a variety of chronic conditions and health outcomes, detectable across the entire lifespan, from childhood to adulthood to older age.

Sleep medicine is rapidly being recognised as a growing area of clinical medicine, affecting wide-ranging specialists including respiratory physicians, neurologists, cardiologists and psychiatrists. However, it also has huge implications in the fields of epidemiology, public health, and preventive medicine.

This book summarises for the first time the epidemiological evidence linking sleep deprivation and disruption to several chronic conditions, and explores the public health implications with the view to developing preventive strategies. It will appeal to both preventive medicine specialists, sleep researchers, and clinicians involved in the various specialities that impact upon this growing field.

Keywords

Cardinali DP, Lynch HJ, Wurtman RJ

Year 1972

Authors DANIEL P. CARDINALI, HARRY J. LYNCH and RICHARD J. WURTMAN

Report Name Binding of melatonin to human and rat plasma proteins.

Publication Endocrinology

Issue-page numbers 91:1213–1218 doi:10.1210/endo-91-5-1213. PMID:4538504

URL http://endo.endojournals.org/content/91/5/1213

Abstract H-Melatonin was not metabolized when incubated with rat venous blood in vitro and 72-82% of the added radioactivity was recovered in the plasma fractions. The binding of 3H-melatonin to rat and human plasma proteins was studied by equilibrium dialysis; there were no significant differences between the binding capacities of human and rat plasma, and the proportions bound (77.8 ± 4.3% and 60.7 ± 4.8% at 4 and 37 C, respectively) were independent of melatonin concentration up to 1.5 HIM, indicating a highcapacity binder protein. The in vitro binding of melatonin to plasma proteins was not modified by the presence of other indole derivatives. Equilibrium dialysis of 3H-melatonin with purified plasma protein fractions and electrophoresis of plasma preincubated with melatonin revealed that albumin was the only melatonin-binding protein detectable in plasma. No significant association was observed between melatonin and macromolecules in fresh cerebrospinal fluid (CSF) from goats unless the protein concentration of the CSF was increased by ultrafiltration. Neither the addition of 4% albumin solutions nor of whole plasma modified the melanin aggregation caused by melatonin in melanophores of Rana pipiens larvae, in vivo or in vitro.

Keywords

Caroleo MC, Nisticò G, Doria G

Year 1992

Authors Caroleo MC, Nisticò G, Doria G

Report Name Effect of melatonin on the immune system

Publication Pharmacol Res

Issue-page numbers 26 Suppl 2;34–37 doi:10.1016/1043-6618(92)90587-2. PMID:1409318

URL http://www.ncbi.nlm.nih.gov/pubmed/1409318

Abstract N/A

Keywords

Carpentier S, Knaus M, Suh M

Year 2009

Authors Carpentier S, Knaus M, Suh M.

Report Name Associations between lutein, zeaxanthin, and age-related macular degeneration: an overview

Publication Crit Rev Food Sci Nutr

Issue-page numbers 2009 Apr;49(4):313-26.

URL http://www.ncbi.nlm.nih.gov/pubmed/19234943

Abstract Age-related macular degeneration, the leading cause of blindness in the elderly, is a degenerative condition of the macula characterized by death or dysfunction of the photoreceptors. With the aging population growing, the incidence of age-related macular degeneration is expected to increase. This raises concern about the future of visual dysfunction related falls and the resulting injuries in the elderly population. Lutein and zeaxanthin are macular pigments that may play a role in reducing the development and progression of age-related macular degeneration. Evidence is accumulating on the consumption of lutein and zeaxanthin (in whole food or supplemental form), the resulting concentrations in the serum, and tissue distribution throughout the body, particularly in the retina. Lutein and zeaxanthin intake increases serum concentrations which in turn increases macular pigment density. Existing literature focuses on factors affecting macular pigment density, functions of lutein and zeaxanthin as blue-light filters and antioxidants, and risk factors associated with age-related macular degeneration. Few studies have focused on the impact of dietary lutein and zeaxanthin on retinal function and the potential to preserve vision and prevent further degeneration. This presents an opportunity for further research to determine an effective dose that delays the progression of age-related macular degeneration.

Keywords

Carrillo-Vico A, Calvo JR, Abreu P et al.

Year 2004

Authors ANTONIO CARRILLO-VICO, JUAN R. CALVO, PEDRO ABREU, PATRICIA J. LARDONE, SOFÍA GARCÍA-MAURIÑO, RUSSEL J. REITER and JUAN M. GUERRERO

Report Name Evidence of melatonin synthesis by human lymphocytes and its physiological significance: possible role as intracrine, autocrine, and/or paracrine substance.

Publication FASEB J

Issue-page numbers 18:537–539. PMID: 14715696

URL http://www.fasebj.org/content/18/3/537.full

Abstract It has been historically assumed that the pineal gland is the major source of melatonin in vertebrates. Melatonin plays a central role in fine tuning circadian rhythms in vertebrate physiology. Additionally, melatonin shows a remarkable functional versatility exhibiting antioxidant, oncostatic, anti-aging, and immunomodulatory properties. Its biosynthesis from tryptophan involves four well-defined intracellular steps catalyzed by tryptophan hydroxylase (TPH), aromatic amino acid decarboxylase (AADC), serotonin-N-acetyltransferase (NAT), and hydroxyndole-O-methyltransferase (HIOMT). This paper shows that both resting and stimulated human lymphocytes have the necessary machinery to synthesize melatonin as well as synthesize and release large amounts of melatonin. Moreover, melatonin released to the culture medium is synthesized in the cells since blocking the enzymes required for its biosynthesis produced a significant reduction in melatonin release. This inhibition caused decrease in IL-2 production, which was restored by adding exogenous melatonin. These findings indicate that human lymphoid cells are an important physiological source of melatonin which could be involved in the regulation of the human immune system.

Keywords

Carrillo-Vico A, Guerrero JM, Lardone PJ, Reiter RJ

Year 2005

Authors Carrillo-Vico A, Guerrero JM, Lardone PJ, Reiter RJ

Report Name A review of the multiple actions of melatonin on the immune system

Publication Endocrine

Issue-page numbers 27:189–200 doi:10.1385/ENDO:27:2:189. PMID:16217132

URL http://www.springerlink.com/content/wn23478464343308/

Abstract This review summarizes the numerous observations published in recent years which have shown that one of the most significant of melatonin's pleiotropic effects is the regulation of the immune system. The overview summarizes the immune effects of pinealectomy and the association between rhythmic melatonin production and adjustments in the immune system as markers of melatonin's immunomodulatory actions. The effects of both in vivo and in vitro melatonin administration on non-specific, humoral, and cellular immune responses as well as on cellular proliferation and immune mediator production are presented. One of the main features that distinguishes melatonin from the classical hormones is its synthesis by a number of nonendocrine extrapineal organs, including the immune system. Herein, we summarize the presence of immune system-synthesized melatonin, its direct immunomodulatory effects on cytokine production, and its masking effects on exogenous melatonin action. The mechanisms of action of melatonin in the immune system are also discussed, focusing attention on the presence of membrane and nuclear receptors and the characterization of several physiological roles mediated by some receptor analogs in immune cells. The review focuses on melatonin's actions in several immune pathologies including infection, inflammation, and autoimmunity together with the relation between melatonin, immunity, and cancer.

Keywords Melatonin - immune system - pineal gland - neuroimmunomodulation - extrapineal melatonin - melatonin receptors - immune pathologies

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Carroll EC, Hospes M, Valladares C, et al.

Year 2011

Authors Elizabeth C. Carroll, Marijke Hospes, Carmen Valladares, Klaas J. Hellingwerf and Delmar S. Larsen

Report Name Is the photoactive yellow protein a UV-B/blue light photoreceptor?

Publication Photochem. Photobiol. Sci.

Issue-page numbers 2011, 10, 464-468 DOI: 10.1039/C0PP00274G

URL http://pubs.rsc.org/en/Content/ArticleLanding/2011/PP/c0pp00274g

Abstract UV light below 300 nm is shown to generate the first photocycle intermediate in the blue light photoreceptor Photoactive Yellow Protein. Fluorescence and ultrafast transient absorption measurements indicate two excitation pathways: UV-B absorption by the chromophore and Fluorescence Resonant Energy Transfer (FRET) from tryptophan and tyrosine residues.

Keywords

Authors Carter DS, Hall VD, Tamarkin L, Goldman BD

Report Name Pineal is required for testicular maintenance in the turkish hamster (mesocricetus brandti)

Publication Endocrinology

Issue-page numbers 111:863–871 doi:10.1210/endo-111-3-863. PMID:6809448

URL http://www.ncbi.nlm.nih.gov/pubmed/6809448

Abstract

The effect of pinealectomy on reproductive function was examined in the Turkish hamster, Mesocricetus brandti. Pinealectomy resulted in testicular regression in this species. This result was unexpected since pinealectomy prevents short day-induced regression of the gonads in the closely related Syrian hamster, Mesocricetus auratus. Decentralization of the superior cervical ganglia and exposure to continuous illumination also caused testicular regression in the Turkish hamster. These manipulations are believed to block pineal melatonin synthesis. In each case (i.e. pinealectomy, decentralization of the superior cervical ganglia, exposure to continuous illumination), the testes regressed after approximately 3--9 weeks and underwent recrudescence after approximately 16--28 weeks. This cycle of testicular regression and recrudescence was similar to that observed in Turkish hamsters exposed to a short day photoperiod. In further experiments, the effects of exogenous melatonin were studied in Turkish and Syrian hamsters. The results of these studies suggest that, in Turkish hamsters, pineal melatonin may be involved in both the maintenance of testis function during exposure to a long day photoperiod and also in the suppression of reproductive function in short days. This is in contrast to the Syrian hamster, in which melatonin appears to be important only for inhibition of gonadal function in short days.

Keywords

Caruso CC

Year 2013

Authors Claire C. Caruso

Report Name Negative Impacts of Shiftwork and Long Work Hours

Publication Rehabilitation Nursing

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1002/rnj.107/abstract;jsessionid=659FE5D7232F11D420B36F6DC9A5A4BC.d04t01?deniedAccessCustomisedMessage=&userIsAuthenticat

Abstract

Purpose
Healthcare organizations often have to provide patient care around the clock. Shift work (any shift outside of 7 a.m. to 6 p.m) and long work hours increase the risk for short sleep duration and sleep disturbances. Thirty-two percent of healthcare workers report they do not get enough sleep. The purpose of the article is to give an overview of the wide range of risks to nurses, patients, and employers that are linked to shift work, long work hours, and poor sleep from other sources.
Findings

Shift work and long work hours increase the risk for reduced performance on the job, obesity, injuries, and a wide range of chronic diseases. In addition, fatigue-related errors could harm patients. Fatigued nurses also endanger others during their commute to and from work.
Conclusion and Clinical Relevance

The key strategy to reduce these risks is making sleep a priority in the employer's systems for organizing work and in the nurse's personal life.

Keywords Shift work; occupational diseases; occupational injury; occupational exposure; work schedule tolerance; circadian rhythms; job stress

Castroviejo DA

Year 2006

Authors Dr. Darío Acuña Castroviejo

Report Name SCIENTIFIC REPORT ON THE EFFECTS OF ELECTROMAGNETIC FIELDS ON THE HUMAN ENDOCRINE SYSTEM AND ASSOCIATED PATHOLOGIES

Publication DEPARTMENT OF PHYSIOLOGY, FACULTY OF MEDICINE

Issue-page numbers

URL http://pranan.com/images/informew_english.pdf

Abstract

Human body health is maintained thanks to the perfect functioning of several regulatory systems, being the endocrine the one with a perfect control to maintain communication between the nervous and immune systems. Thus we speak of neuro-inmuno-endocrine system, responsible for the functional balance, that is, the body homeostasis, working in close communication. This intercommunication is possible because the cells of the three systems share specific receptors and other mediators. In turn, this relationship between the systems explains a series of events which explain that situations such as depression, emotional stress or anxiety, are accompanied by increased susceptibility to infections, cancer or autoimmune disease, which means poorer health and shorter longevity. By contrast, pleasant situations and optimistic vital status helps to overcome illness, and in general to have better health. Moreover, it has been confirmed that alterations of the immune system, as may happen in an infectious process, modify negatively the functionality of nervous and endocrine systems, and vice versa. In all these cases, health disorders are accompanied by a significant increase in oxidative stress and imbalance in redox state of the cell. Therefore, any impact on one of the system regulators affects the rest, which is of great importance in medicine, when seeking the causes of certain diseases.

Keywords

Catalano PM, Tyzbir ED, Wolfe RR et al. **Year** 1993

Authors P. M. Catalano, E. D. Tyzbir, R. R. Wolfe, J. Calles, N. M. Roman, S. B. Amini, and E. A. Sims

Report Name Carbohydrate metabolism during pregnancy in control subjects and women with gestational diabetes.

Publication Am J Physiol

Issue-page numbers 264:E60–E67. PMID:8430789

URL http://ajpendo.physiology.org/content/264/1/E60.short

Abstract

The purpose of this study was to characterize carbohydrate metabolism associated with the development of gestational diabetes. Six control (Ctl) and ten women with gestational diabetes mellitus (GDM) were evaluated using an intravenous glucose tolerance test and hyperinsulinemic-euglycemic clamp with [6,6-2H2]glucose prior to conception (P) and at 12-14 (E), and 34-36 wk of gestation (L). There was an increase (P = 0.0001) in first-phase insulin response in Ctl (P 174 +/- 133, E 388 +/- 120, and L 587 +/- 303 microU/ml) and GDM (P 197 +/- 94, E 267 +/- 77, and L 376 +/- 162 microU/ml) but a significant (P = 0.02) lag in change in GDM with advancing gestation. Basal endogenous glucose production increased during gestation [Ctl: P 2.74 +/- 0.23, E 2.62 +/- 0.38, and L 3.14 +/- 0.36; GDM: P 2.68 +/- 0.51, E 2.78 +/- 0.45, and L 2.98 +/- 0.48 mg.kg fat-free mass (FFM)-1 x min-1; P = 0.02], but there was resistance to suppression by insulin infusion (P = 0.03) in late gestation (GDM: 0.61 +/- 0.44 vs. Ctl: 0.16 +/- 0.17 mg.kg FFM-1 x min-1). Insulin sensitivity decreased during gestation (Ctl: P 10.78 +/- 2.78, E 8.34 +/- 2.36, and L 4.75 +/- 1.22; GDM: P 7.49 +/- 2.13, E 7.40 +/- 1.45, and L 4.21 +/- 1.01 mg.kg FFM-1 x min-1; P = 0.0001) and was primarily decreased (P = 0.04) in GDM compared with Ctl from P through E. These findings closely resemble those of non-insulin-dependent, predominantly insulin-resistant diabetes, which is often a sequel of GDM.

Keywords

Catena-Dell'Osso M, Marazziti D, Rotella F, Bellantuono C **Year** 2012

Authors Catena-Dell'Osso, Mario; Marazziti, Donatella; Rotella, Francesco; Bellantuono, Cesario

Report Name Emerging Targets for the Pharmacological Treatment of Depression: Focus on Melatonergic System

Publication Current Medicinal Chemistry

Issue-page numbers Volume 19, Number 3, January 2012 , pp. 428-437(10)

URL http://www.ingentaconnect.com/content/ben/cmc/2012/00000019/00000003/art00008

Abstract Depression is a disabling condition which adversely affects a person's family, social and work life, and that is associated with a heavy burden to society. Although the available antidepressants have shown their effectiveness and have greatly improved the prognosis of the disorder, the current management of depression is far from being satisfactory. In the last years, besides the classical research involving serotonin, norepineprine and dopamine, non-monoaminergic mechanisms have been explored in the attempt to discover new antidepressants. One such innovative approach focused on melatonergic system, as melatonin is involved in synchronizing circadian rhythms, which are known to be altered in depression. This narrative review aims to provide a comprehensive overview of different aspects of the melatonergic system, including biochemical and anatomical characteristics, impact on the sleep/wake system, and implications for the treatment of depression. In particular, the observation that melatonin may promote sleep and synchronize the internal clock led to development of high-affinity agonists for melatonin receptors (MT). Agomelatine, a naphthalene bioisostere of melatonin, which combines a potent MT1 and MT2 agonism with 5-HT2C receptor antagonism, has been found to be effective in the treatment of depressive and anxiety symptoms associated with major depression, with rapid and beneficial effects on the regulation of sleep continuity and quality. If substantiated by further evidence, the observation that melatonergic system dysfunctions contribute to the development of depression, as well as that the antidepressant action of agomelatine is linked to its binding properties to MT1/MT2 receptors, might open new avenues for the discovery of antidepressive agents.

Keywords Agomelatine; antidepressants; arylalkylamine; N-acetyltransferase; depression; melatonin;

Cermakian N, Boivin DB **Year** 2009

Authors N Cermakian, D B Boivin

Report Name The regulation of central and peripheral circadian clocks in humans

Publication Obesity reviews

Issue-page numbers Volume: 10 Suppl 2, Issue: s2 Circadian Biology and Sleep in Obesity and Metabolism, Publisher: Blackwell Publishing Ltd, Pages: 25-36

URL http://www.mendeley.com/research/the-regulation-of-central-and-peripheral-circadian-clocks-in-humans/

Abstract Many circadian rhythms are controlled by the central clock of the suprachiasmatic nucleus of the hypothalamus, as well as clocks located in other brain regions and most peripheral tissues. These central and peripheral clocks are based on clock genes and their protein products. In recent years, the expression of clock genes has started to be investigated in human samples, primarily white blood cells, but also skin, oral mucosa, colon cells, adipose tissue as well as post-mortem brain tissue. The expression of clock genes in those peripheral tissues offers a way to monitor human peripheral clocks and to compare their function and regulation with those of the central clock, which is followed by markers such as melatonin, cortisol and core body temperature. We have recently used such an approach to compare central and peripheral rhythms in subjects under different lighting conditions. In particular, we have monitored the entrainment of the clock of blood cells in subjects undergoing a simulated night shift protocol with bright light treatment, known to efficiently reset the central clock. This line of research will be helpful for learning more about the human circadian system and to find ways to alleviate health problems of shift workers, and other populations experiencing altered circadian rhythms.

Keywords

Challet E, Pévet P — *Year* 2003

Authors Etienne Challet and Paul Pévet

Report Name Interactions between photic and nonphotic stimuli to synchronize the master circadian clock in mammals

Publication Front Biosci

Issue-page numbers 8:s246–s257 doi:10.2741/1039. PMID:12700025

URL http://www.bioscience.org/u37153137/gaDTRQo7632rgysaGWQYT64356/2003/v8/s/1039/1039.pdf

Abstract The master circadian clock is located in the suprachiasmatic nuclei (SCN) in mammals. The most
powerful synchronizer of the SCN clock is the daily variation in light intensity. Several other nonphotic cues are well known to be able to shift or synchronize the circadian clock in the absence of photic cues. Some results obtained at systems, cellular and molecular levels provide evidence in contrast to the view that nonphotic signals reset the SCN clock independently of the mechanisms of photic synchronization. Rather, the SCN appear to integrate a wide range of information from the environment to finetune photic synchronization. The neuronal mechanisms underlying this integration are far from being understood.
Nevertheless, in real-life situations, multiple interactions between photic and nonphotic cues could be of importance for the daily phase adjustment of the circadian clock and its control of the 24-h temporal organization of the whole organism.

Keywords

Chamorro E, Bonnin-Arias C, Pérez-Carrasco MJ, et al. — *Year* 2012

Authors Eva Chamorro, Cristina Bonnin-Arias, María Jesús Pérez-Carrasco, Javier Muñoz de Luna, Daniel Vázquez,

Report Name Effects of Light-emitting Diode Radiations on Human Retinal Pigment Epithelial Cells In Vitro

Publication Photochemistry and Photobiology

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2012.01237.x/abstract

Abstract Human visual system is exposed to high levels of natural and artificial lights of different spectra and intensities along lifetime. Light-emitting diodes (LEDs) are the basic lighting components in screens of PCs, phones and TV sets; hence it is so important to know the implications of LED radiations on the human visual system. The aim of this study was to investigate the effect of LEDs radiations on human retinal pigment epithelial cells (HRPEpiC). They were exposed to three light–darkness (12 h/12 h) cycles, using blue-468 nm, green-525 nm, red-616 nm and white light. Cellular viability of HRPEpiC was evaluated by labeling all nuclei with DAPI; Production of reactive oxygen species (ROS) was determined by H2DCFDA staining; mitochondrial membrane potential was quantified by TMRM staining; DNA damage was determined by H2AX histone activation, and apoptosis was evaluated by caspases-3,-7 activation. It is shown that LED radiations decrease 75–99% cellular viability, and increase 66–89% cellular apoptosis. They also increase ROS production and DNA damage. Fluorescence intensity of apoptosis was 3.7% in nonirradiated cells and 88.8%, 86.1%, 83.9% and 65.5% in cells exposed to white, blue, green or red light, respectively. This study indicates three light–darkness (12 h/12 h) cycles of exposure to LED lighting affect in vitro HRPEpiC

Keywords

Chang A, Scheer FA, Czeisler CA **Year** 2011

Authors Anne-Marie Chang, Frank A. J. L. Scheer and Charles A. Czeisler

Report Name The human circadian system adapts to prior photic history

Publication The Journal of Physiology

Issue-page numbers March 1, 2011, 589, 1095-1102.

URL http://jp.physoc.org/content/589/5/1095.short

Abstract

Light is the most potent stimulus for synchronizing the endogenous circadian timing system to the 24 h day. The timing, intensity, duration, pattern and wavelength of light are known to modulate photic resetting of the circadian system and acute suppression of melatonin secretion. The effect of prior photic history on these processes, however, is not well understood. Although previous studies have shown that light history affects the suppression of melatonin in response to a subsequent light exposure, here we show for the first time that a very dim light history, as opposed to a typical indoor room illuminance, amplifies the phase-shifting response to a subsequent sub-saturating light stimulus by 60–70%. This greater efficacy provides evidence for dynamic adaptive changes in the sensitivity of circadian ocular photoreception. This plasticity has important implications for the optimization of light therapy for the treatment of circadian rhythm sleep disorders.

Keywords circadian, melatonin, light at night

Authors Chellappa SL, Steiner R, Blattner P, Oelhafen P, Götz T, Christian Cajochen

Report Name Non-visual effects of light on melatonin, alertness and cognitive performance: can blue-enriched light keep us alert?

Publication PLoS ONE

Issue-page numbers 6(1): e16429. doi:10.1371/journal.pone.0016429

URL http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0016429

Abstract

Background

Light exposure can cascade numerous effects on the human circadian process via the non-imaging forming system, whose spectral relevance is highest in the short-wavelength range. Here we investigated if commercially available compact fluorescent lamps with different colour temperatures can impact on alertness and cognitive performance.
Methods

Sixteen healthy young men were studied in a balanced cross-over design with light exposure of 3 different light settings (compact fluorescent lamps with light of 40 lux at 6500K and at 2500K and incandescent lamps of 40 lux at 3000K) during 2 h in the evening.
Results

Exposure to light at 6500K induced greater melatonin suppression, together with enhanced subjective alertness, well-being and visual comfort. With respect to cognitive performance, light at 6500K led to significantly faster reaction times in tasks associated with sustained attention (Psychomotor Vigilance and GO/NOGO Task), but not in tasks associated with executive function (Paced Visual Serial Addition Task). This cognitive improvement was strongly related with attenuated salivary melatonin levels, particularly for the light condition at 6500K.
Conclusions

Our findings suggest that the sensitivity of the human alerting and cognitive response to polychromatic light at levels as low as 40 lux, is blue-shifted relative to the three-cone visual photopic system. Thus, the selection of commercially available compact fluorescent lights with different colour temperatures significantly impacts on circadian physiology and cognitive performance at home and in the workplace.

Keywords

Chellappa SL, Steiner R, Oelhafen P, et al. **Year** 2013

Authors Sarah L. Chellappa, Roland Steiner, Peter Oelhafen, Dieter Lang, Thomas Götz, Julia Krebs, Christian Cajochen

Report Name Acute exposure to evening blue-enriched light impacts on human sleep

Publication Journal of Sleep Research

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1111/jsr.12050/abstract?deniedAccessCustomisedMessage=&userIsAuthenticated=false

Abstract

Light in the short wavelength range (blue light: 446–483 nm) elicits direct effects on human melatonin secretion, alertness and cognitive performance via non-image-forming photoreceptors. However, the impact of blue-enriched polychromatic light on human sleep architecture and sleep electroencephalographic activity remains fairly unknown. In this study we investigated sleep structure and sleep electroencephalographic characteristics of 30 healthy young participants (16 men, 14 women; age range 20–31 years) following 2 h of evening light exposure to polychromatic light at 6500 K, 2500 K and 3000 K. Sleep structure across the first three non-rapid eye movement non-rapid eye movement – rapid eye movement sleep cycles did not differ significantly with respect to the light conditions. All-night non-rapid eye movement sleep electroencephalographic power density indicated that exposure to light at 6500 K resulted in a tendency for less frontal non-rapid eye movement electroencephalographic power density, compared to light at 2500 K and 3000 K. The dynamics of non-rapid eye movement electroencephalographic slow wave activity (2.0–4.0 Hz), a functional index of homeostatic sleep pressure, were such that slow wave activity was reduced significantly during the first sleep cycle after light at 6500 K compared to light at 2500 K and 3000 K, particularly in the frontal derivation. Our data suggest that exposure to blue-enriched polychromatic light at relatively low room light levels impacts upon homeostatic sleep regulation, as indexed by reduction in frontal slow wave activity during the first non-rapid eye movement episode.

Keywords non-image-forming system; non-rapid eye movement sleep; polychromatic blue light; sleep electroencephalographic power density; slow wave activity

Chellappa SL, Viola AU, Schmidt C, Bachmann V, et al. ***Year*** 0

Authors Sarah L. Chellappa, Antoine U. Viola, Christina Schmidt, Valérie Bachmann, Virginie Gabel, Micheline Maire, Carolin F. Reichert, Amandine Valomon, Thomas Götz, Hans-Peter

Report Name Human Melatonin and Alerting Response to Blue-Enriched Light Depend on a Polymorphism in the Clock Gene PER3

Publication The Journal of Clinical Endocrinology & Metabolism

Issue-page numbers Published online before print December 21, 2011, doi: 10.1210/jc.2011-2391

URL http://jcem.endojournals.org/content/early/2011/12/19/jc.2011-2391.abstract

Abstract

Context: Light exposure, particularly at the short-wavelength range, triggers several nonvisual responses in humans. However, the extent to which the melatonin-suppressing and alerting effect of light differs among individuals remains unknown.

Objective: Here we investigated whether blue-enriched polychromatic light impacts differentially on melatonin and subjective and objective alertness in healthy participants genotyped for the PERIOD3 (PER3) variable-number, tandem-repeat polymorphism.

Design, Setting, and Participants: Eighteen healthy young men homozygous for the PER3 polymorphism (PER35/5and PER34/4) underwent a balanced crossover design during the winter season, with light exposure to compact fluorescent lamps of 40 lux at 6500 K and at 2500 K during 2 h in the evening.

Results: In comparison to light at 2500 K, blue-enriched light at 6500 K induced a significant suppression of the evening rise in endogenous melatonin levels in PER35/5 individuals but not in PER34/4. Likewise, PER35/5 individuals exhibited a more pronounced alerting response to light at 6500 K than PER34/4 volunteers. Waking electroencephalographic activity in the theta range (5–7 Hz), a putative correlate of sleepiness, was drastically attenuated during light exposure at 6500 K in PER35/5 individuals as compared with PER34/4.

Conclusions: We provide first evidence that humans homozygous for the PER3 5/5 allele are particularly sensitive to blue-enriched light, as indexed by the suppression of endogenous melatonin and waking theta activity. Light sensitivity in humans may be modulated by a clock gene polymorphism implicated in the sleep-wake regulation.

Keywords

Chen E

Year 1993

Authors Enping Chen

Report Name INHIBITION OF CYTOCHROME OXIDASE AND BLUE - LIGHT DAMAGE IN RAT RETINA

Publication Acta Ophthalmologica

Issue-page numbers Volume 71, Issue S208, pages 1g–22g, March 1993

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1755-3768.1993.tb08724.x/abstract?

Abstract

The activity of cytochrome oxidase, outer nuclear layer thickness and edema were quantitatively evaluated in the blue-light-exposed rat retina. Dark-adapted or cyclic-light-reared rats were exposed to blue light with a retinal dose of 380 kJ/m2. Immediately, one, two, and three day(s) after exposure, the retinas of six rats from each adaptation group were examined. There was no difference between the dark-adapted and cyclic-light-reared rats. Immediately after light exposure, cytochrome oxidase activity decreased. The activity in the inner segments remained low at day one, while severe edema was observed in the inner and outer segments. The outer nuclear layer thickness decreased one to three days after exposure. The blue-light exposure inhibited cytochrome oxidase activity and caused retinal injury. Similarity of the injury process in the dark-adapted and cyclic-light-reared retinas suggests that rhodopsin was not involved. The inhibition of cytochrome oxidase could be a cause of retinal damage.

Keywords

Chen E, Söderberg PG, Lindström B

Year 1993

Authors Enping Chen, Per G. Söderberg, Bo Lindström

Report Name Cytochrome oxidase activity in rat retina after exposure to 404 nm blue light

Publication Acta Ophthalmologica

Issue-page numbers Volume 71, Issue S208, pages 825f–831f, March 1993

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1755-3768.1993.tb08723.x/abstract

Abstract

Cytochrome oxidase (CYO), a key enzyme in the respiratory chain, was observed as an indicator of retinal metabolism after an in vivo blue light exposure.

Thirty Sprague—Dawley rats were exposed to optic radiation of 404 nm with a retinal dose of 110kJ/m2. Immediately after exposure, the CYO activity in the pigment epithelium, in the outer and inner segments of photoreceptors, and in the outer plexiform layer of the exposed retina, was reduced to one—third—to—half of the control level. However, there was an increase in CYO activity in the exposed retina one day after exposure. One week after exposure, the CYO activity in the inner segment and the outer plexiform layer was higher, while the activity in the other two layers was lower, than that at one day, although still higher than in the control. Two weeks after exposure, the CYO activity in the four retinal layers returned to the level of the control retina, as did the activity four weeks after. After exposure, no ophthalmoscopically visible retinal change and no light-microscopically evident morphological alterations were found. There was no retinal edema or loss of photoreceptor cells.

The observed alteration in CYO activity after blue light exposure may represent an inhibition of retinal metabolism. The inhibition was reversible. If this compensation mechanism is overwhelmed, retinal damage may occur.

Keywords

Chen E, Söderberg PG, Qian W

Year 1992

Authors Chen E, Söderberg PG, Qian W.

Report Name Inhibition of cytochrome oxidase by blue light (404 nm). A factor that causes retinal injury?

Publication Invest Ophthalmol Vis Sci

Issue-page numbers 1992a; 33:919.

URL

Abstract N/A

Keywords

Chen J, Simon MI, Matthes MT, et al.

Year 1999

Authors Jeannie Chen, Melvin I. Simon, Michael T. Matthes, Douglas Yasumura and Matthew M. LaVail

Report Name Increased susceptibility to light damage in an arrestin knockout mouse model of Oguchi disease (stationary night blindness).

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers November 1999 vol. 40 no. 12 2978-2982

URL http://www.iovs.org/content/40/12/2978

Abstract

purpose. To determine whether constitutive signal flow arising from defective rhodopsin shut-off causes photoreceptor cell death in arrestin knockout mice.

methods. The retinas of cyclic-light–reared, pigmented arrestin knockout mice and wild-type littermate control mice were examined histologically for photoreceptor cell loss from 100 days to 1 year of age. In separate experiments, to determine whether constant light would accelerate the degeneration in arrestin knockout mice, these animals and wild-type control mice were exposed for 1, 2, or 3 weeks to fluorescent light at an intensity of 115 to 150 fc. The degree of photoreceptor cell loss was quantified histologically by obtaining a mean outer nuclear layer thickness for each animal.

results. In arrestin knockout mice maintained in cyclic light, photoreceptor loss was evident at 100 days of age, and it became progressively more severe, with less than 50% of photoreceptors surviving at 1 year of age. The photoreceptor degeneration appeared to be caused by light, because when these mice were reared in the dark, the retinal structure was indistinguishable from normal. When exposed to constant light, the retinas of wild-type pigmented mice showed no light-induced damage, regardless of exposure duration. By contrast, the retinas of arrestin knockout mice showed rapid degeneration in constant light, with a loss of 30% of photoreceptors after 1 week of exposure and greater than 60% after 3 weeks of exposure.

conclusions. The results indicate that constitutive signal flow due to arrestin knockout leads to photoreceptor degeneration. Excessive light accelerates the cell death process in pigmented arrestin knockout mice. Human patients with naturally occurring mutations that lead to nonfunctional arrestin and rhodopsin kinase have Oguchi disease, a form of stationary night blindness. The present findings suggest that such patients may be at greater risk of the damaging effects of light than those with other forms of retinal degeneration, and they provide an impetus to restrict excessive light exposure as a protective measure in patients with constitutive signal flow in phototransduction.

Keywords

Authors Mei Chen, Elizabeth Muckersie, John V Forrester and Heping Xu

Report Name Immune activation in Retinal Aging: A Gene Expression Study

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers June 9, 2010 iovs.09-5103

URL http://www.iovs.org/content/early/2010/06/10/iovs.09-5103

Abstract

PURPOSE: To investigate changes in gene expression during retinal aging.

METHODS: Total RNA was extracted from the neuroretina of young (3-month) and old (20-month) mice and processed for microarray analysis using Agilent Whole Mouse Genome Oligo Microarrays 4×44K. Differentially expressed genes were assessed by the empirical Bayes shrinkage moderated t-statistics method. Statistical significance was based on dual criteria of fold-change >2 and $p < 0.01$ using this method. Differential expression in eleven selected genes was further verified by qPCR. Functional pathways involved in retinal aging were analysed by the DAVID-2008 software using differentially expressed gene lists. The identified pathways were further confirmed by immunohistochemistry.

RESULTS: With age, 298 genes were up-regulated and 137 genes were down-regulated in the retina. Functional annotation showed that genes linked to immune responses (Ir-genes) and to tissue stress/injury responses (TS/I-genes) were most likely to be modified by age. Ir-genes affected included genes regulating leukocyte activation, chemotaxis, endocytosis, complement activation, phagocytosis and myeloid cell differentiation, most of which were up-regulated and only a few down-regulated. Increased microglial and complement activation in the aging retina was further confirmed by immunohistochemistry. The most strongly up-regulated gene was the calcitonin receptor (Calcr, >40 times).

CONCLUSIONS: The results suggest that retinal aging is accompanied by activation of gene sets involving in local inflammatory responses. A modified form of low-grade chronic inflammation (para-inflammation) characterizes these aging changes. The marked up-regulation of the Calcr in aging mice most likely reflects this chronic inflammatory/stress response since calcitonin is a known systemic biomarker of inflammation/sepsis.

Keywords immunoregulation, gene expression, retinal degeneration, immunocytochemistry, aging, microarray

Chen ST, Choo KB, Hou MF et al. **Year** 2005

Authors Shou-Tung Chen, Kong-Bung Choo, Ming-Feng Hou, Kun-Tu Yeh, Shou-Jen Kuo and Jan-Gowth Chang

Report Name Deregulated expression of the PER1, PER2 and PER3 genes in breast cancers.

Publication Carcinogenesis

Issue-page numbers 26:1241–1246 doi:10.1093/carcin/bgi075. PMID:15790588

URL http://carcin.oxfordjournals.org/content/26/7/1241.short

Abstract Disruption of circadian rhythm may be a risk factor in the development of breast cancer, but molecular changes in circadian rhythm controlled genes in breast cancer cells are still unexplored. We used immunohistochemical staining, methylation specific PCR and direct sequencing methods to analyze molecular changes in three most important genes, namely PER1, PER2 and PER3, in circadian rhythm in 55 cases of breast cancer of Taiwanese women. Our results reveal disturbances in the expression of the three period (PER) genes in most (>95%) of the breast cancerous cells in comparison with the nearby non-cancerous cells. The PER gene deregulation is not caused by genetic mutations but most probably by methylation of the PER1 or PER2 promoter. Methylation of the PER gene promoters has a strong correlation with c-erbB2 expression (P = 0.017). Since the circadian clock controls expression of cell-cycle related genes, we suggest that disturbances in PER gene expression may result in disruption of the control of the normal circadian clock, thus benefiting the survival of cancer cells and promoting carcinogenesis. Differential expression of circadian genes in non-cancerous and cancerous cells may provide a molecular basis for chronotherapy of breast cancer.

Keywords

Cheng HY, Papp JW, Varlamova O et al. **Year** 2007

Authors Hai-Ying M Cheng; Joseph W Papp; Olga Varlamova; Heather Dziema; Brandon Russell; John P Curfman; Takanobu Nakazawa; Kimiko Shimizu; Hitoshi Okamura; Soren Impe

Report Name microRNA modulation of circadian-clock period and entrainment

Publication Neuron

Issue-page numbers 54:813–829 doi:10.1016/j.neuron.2007.05.017. PMID:17553428

URL http://www.biomedsearch.com/nih/microRNA-modulation-circadian-clock-period/17553428.html

Abstract microRNAs (miRNAs) are a class of small, noncoding RNAs that regulate the stability or translation of mRNA transcripts. Although recent work has implicated miRNAs in development and in disease, the expression and function of miRNAs in the adult mammalian nervous system have not been extensively characterized. Here, we examine the role of two brain-specific miRNAs, miR-219 and miR-132, in modulating the circadian clock located in the suprachiasmatic nucleus. miR-219 is a target of the CLOCK and BMAL1 complex, exhibits robust circadian rhythms of expression, and the in vivo knockdown of miR-219 lengthens the circadian period. miR-132 is induced by photic entrainment cues via a MAPK/CREB-dependent mechanism, modulates clock-gene expression, and attenuates the entraining effects of light. Collectively, these data reveal miRNAs as clock- and light-regulated genes and provide a mechanistic examination of their roles as effectors of pacemaker activity and entrainment.

Keywords

Cheng MY, Bullock CM, Li C et al. **Year** 2002

Authors Michelle Y. Cheng, Clayton M. Bullock, Chuanyu Li, Alex G. Lee, Jason C. Bermak, James Belluzzi, David R. Weaver, Frances M. Leslie & Qun-Yong Zhou

Report Name Prokineticin 2 transmits the behavioural circadian rhythm of the suprachiasmatic nucleus.

Publication Nature

Issue-page numbers 417:405–410 doi:10.1038/417405a. PMID:12024206

URL http://www.nature.com/nature/journal/v417/n6887/abs/417405a.html

Abstract The suprachiasmatic nucleus (SCN) controls the circadian rhythm of physiological and behavioural processes in mammals. Here we show that prokineticin 2 (PK2), a cysteine-rich secreted protein, functions as an output molecule from the SCN circadian clock. PK2 messenger RNA is rhythmically expressed in the SCN, and the phase of PK2 rhythm is responsive to light entrainment. Molecular and genetic studies have revealed that PK2 is a gene that is controlled by a circadian clock (clock-controlled). Receptor for PK2 (PKR2) is abundantly expressed in major target nuclei of the SCN output pathway. Inhibition of nocturnal locomotor activity in rats by intracerebroventricular delivery of recombinant PK2 during subjective night, when the endogenous PK2 mRNA level is low, further supports the hypothesis that PK2 is an output molecule that transmits behavioural circadian rhythm. The high expression of PKR2 mRNA within the SCN and the positive feedback of PK2 on its own transcription through activation of PKR2 suggest that PK2 may also function locally within the SCN to synchronize output.

Keywords

Chepesiuk R **Year** 2009

Authors Ron Chepesiuk

Report Name Missing the Dark: Health Effects of Light Pollution

Publication Environ Health Perspect

Issue-page numbers 117:A20-A27

URL http://dx.doi.org/10.1289/ehp.117-a20

Abstract Article

Keywords circadian rhythm, light at night

Authors Chew EY, Sperduto RD, Milton RC, Clemons TE, Gensler GR, Bressler SB, Klein R, Klein BE, Ferris FL 3rd.

Report Name Risk of advanced age-related macular degeneration after cataract surgery in the Age-Related Eye Disease Study: AREDS report 25

Publication Ophthalmology

Issue-page numbers 2009 Feb;116(2):297-303. Epub 2008 Dec 16.

URL http://www.ncbi.nlm.nih.gov/pubmed/19091420

Abstract

PURPOSE:

To assess the risk of advanced age-related macular degeneration (AMD) developing after cataract surgery.
DESIGN:

Cohort study.
PARTICIPANTS:

Four thousand five hundred seventy-seven participants (8050 eyes) from a multicenter, controlled, randomized clinical trial, the Age-Related Eye Disease Study (AREDS).
METHODS:

Development of advanced AMD, either neovascular (NV) AMD or geographic atrophy (GA), was evaluated with annual fundus photographs, and history of cataract surgery was assessed every 6 months. Cox proportional hazard models with time-dependent covariates were conducted for NV AMD and GA separately.
MAIN OUTCOME MEASURES:

Neovascular AMD, GA, and central GA (CGA; involving the center of the macula).
RESULTS:

The Cox proportional hazards model of right eyes showed nonsignificant hazard ratios of 1.20 (95% confidence interval [CI], 0.82-1.75) for NV AMD, 0.80 (95% CI, 0.61-1.06) for GA, and 0.87 (95% CI, 0.64-1.18) for CGA. Similar results were obtained for left eyes: 1.07 (95% CI, 0.72-1.58) for NV AMD, 0.94 (95% CI, 0.71-1.25) for GA, and 0.86 (95% CI, 0.63-1.19) for CGA. For participants with advanced AMD in 1 eye (AREDS category 4), the hazard ratios for fellow eyes were 1.08 (95% CI, 0.65-1.72) for NV AMD and 0.98 (95% CI, 0.64-1.49) for CGA.
CONCLUSIONS:
The AREDS results showed no clear effect of cataract surgery on the risk of progression to advanced AMD.

Keywords

Chin-Chance C, Polonsky KS, Schoeller DA

Year 2000

Authors Catherine Chin-Chance, Kenneth S. Polonsky and Dale A. Schoeller

Report Name Twenty-four-hour leptin levels respond to cumulative short-term energy imbalance and predict subsequent intake

Publication J Clin Endocrinol Metab

Issue-page numbers 85:2685–2691 doi:10.1210/jc.85.8.2685. PMID:10946866

URL http://jcem.endojournals.org/content/85/8/2685.short

Abstract Leptin plays a vital role in the regulation of energy balance in rodent models of obesity. However, less information is available about its homeostatic role in humans. The aim of this study was to determine whether leptin serves as an indicator of short-term energy balance by measuring acute effects of small manipulations in energy intake on leptin levels in normal individuals. The 12-day study was composed of four consecutive dietary-treatment periods of 3 days each. Baseline (BASE) [100% total energy expenditure (TEE)] feeding, followed by random crossover periods of overfeeding (130% TEE) or underfeeding (70% TEE) separated by a eucaloric (100% TEE) washout (WASH) period. The study participants were six healthy, nonobese subjects. Leptin levels serially measured throughout the study period allowed a daily profile for each treatment period to be constructed and a 24-h average to be calculated; ad libitum intake during breakfast“ buffet” following each treatment period was also measured. Average changes in mesor leptin levels during WASH, which were sensitive to energy balance effected during the prior period, were observed. After underfeeding, leptin levels during WASH were 88 ± 16% of those during BASE compared with 135 ± 22% following overfeeding (P = 0.03). Leptin levels did not return to BASE during WASH when intake returned to 100% TEE, but instead were restored (104 ± 21% and 106 ± 16%; not significant) only after subjects crossed-over to complementary dietary treatment that restored cumulative energy balance. Changes in ad libitum intake from BASE correlated with changes in leptin levels (r2 = 0.40; P = 0.01). Leptin levels are acutely responsive to modest changes in energy balance. Because leptin levels returned to BASE only after completion of a complementary feeding period and restoration of cumulative energy balance, leptin levels reflect short-term cumulative energy balance. Leptin seems to maintain cumulative energy balance by modulating energy intake.

Keywords

Cho K

Year 2001

Authors Kwangwook Cho

Report Name Chronic ‘jet lag’ produces temporal lobe atrophy and spatial cognitive deficits

Publication Nat Neurosci

Issue-page numbers 4:567–568 doi:10.1038/88384. PMID:11369936

URL http://www.nature.com/neuro/journal/v4/n6/full/nn0601_567.html

Abstract Time-zone travelers encounter a pattern of light and darkness, and their endogenous circadian rhythms adapt to the new external time cue until both timing systems synchronize1, but the long-term repeated disturbance of synchronization between the two timing systems impairs physiological and psychological health and induces stress2. Salivary cortisol levels in cabin crew after repeated exposure to jet lag were significantly higher than after short distance flights3, and the higher cortisol levels were associated with cognitive deficits that were dependent on non-semantic stimuli3. The present study demonstrates that significant prolonged cortisol elevations produce reduced temporal lobe volume and deficits in spatial learning and memory; these cognitive deficits became apparent after five years of exposure to high cortisol levels.

Keywords

Cho K, Ennaceur A, Cole JC, Suh CK

Year 2000

Authors Kwangwook Cho, A. Ennaceur, Jon C. Cole, and Chang Kook Suh

Report Name Chronic jet lag produces cognitive deficits

Publication J Neurosci

Issue-page numbers 20:RC66. PMID:10704520

URL http://www.jneurosci.org/content/20/6/RC66.short

Abstract

Traveling across time zones causes disruption to the normal circadian rhythms and social schedules because of travelers' shift in time. As the endogenous circadian timing system adapts slowly to new time cues, the phase relationship between biological rhythms and external time cues are out of synchronization for a period of time. This disturbance of circadian rhythms has been shown to impair physical and psychological health (Winget et al., 1984). To test the effects of repeated jet lag on mental abilities, airline cabin crew were compared with ground crew. Salivary cortisol was used as a physiological marker for circadian disruption. The cabin crew group, who had a history of repeated jet lag, had significantly higher salivary cortisol levels in an average working day. In addition, this elevated level of cortisol was only seen in the same subjects when the cabin crew were on transmeridian flights but not domestic flights. Cabin crew also exhibited cognitive deficits, possibly in working memory, that became apparent after several years of chronic disruption of circadian rhythms.

Keywords jet lag; cortisol; stress; human subject; cognition; memory

Choi NW, Howe GR, Miller AB et al. **Year** 1978

Authors N. W. CHOI, G. R. HOWE, A. B. MILLER, V. MATTHEWS, R. W. MORGAN, L. MUNAN, J. D. BURCH,

Report Name An epidemiologic study of breast cancer

Publication Am J Epidemiol

Issue-page numbers 107:510–521. PMID:665665

URL http://aje.oxfordjournals.org/content/107/6/510.short

Abstract A case-control study has been conducted In four areas of Canada In which 400 cases of breast cancer matched by age and marital status with neighborhood controls were administered medical and dietary questionnaires. The study is suggestive of an Increased risk of breast cancer In post-menopausal women with younger age at menarche and an Increased risk with delay of age at natural menopause. No protective effect of early age at first pregnancy was demonstrated in either pre- or post-menopausal women. An Increased frequency of pregnancies of four months duration or less was found In cases compared to controls and a greater frequency In pre-menopausal cases compared to controls of a history of irregular menstrual periods. In premenopausal women no association has been found between Increased height and weight as risk factors for breast cancer. For post-menopausal women, however, a weak association with Increased height has been found, while a strong association with Increased weight both at the time of menopause and the 12 months preceding diagnosis has been confirmed.

Keywords breast neoplasms, cancer, epidemiology

CIE **Year** 2004

Authors Commission Internationale de l'Eclairage.

Report Name Ocular Lighting Effects on Human Physiology and Behaviour, Commission Internationale de l'Eclairage, Technical Report #158

Publication Commission Internationale de l'Eclairage

Issue-page numbers Report #158, Vienna, 1-54, 2004

URL http://div6.cie.co.at/?i_ca_id=611&pubid=185

Abstract The nonvisual biological and behavioural effects of light in animals and humans are mediated by specific neuroanatomical pathways. Controlled empirical studies have shown that light can be used to treat some clinical disorders and may have broader, nonclinical applications for problems of shift work and jet lag. Studies are testing how lighting may be incorporated into architectural designs that are optimal for vision as well as physiological and behavioural stimulation.

The Report is written in English, with a short summary in French and German. It consists of 59 pages with 9 figures.
Errata 2009: http://www.cie.co.at/div6/cie_158-2004%20erratum.pdf

Keywords

CIE/IEC

Year 2006

Authors CIE/IEC

Report Name Photobiological safety of lamps and lamp systems

Publication CEI/IEC 62471/2006

Issue-page numbers International Standard

URL http://www.techstreet.com/standards/cie/s_009_e_2002_iec_62471_2006?product_id=1519485

Abstract

Lamps were developed and produced in large quantities and became commonplace in an era when industry-wide safety standards were not the norm. The evaluation and control of optical radiation hazards from lamps and lamp systems is a far more complicated subject than similar tasks for a single-wavelength laser system.

The required radiometric measurements are quite involved, for they do not deal with the simple optics of a point source, but rather with an extended source that may or may not be altered by diffusers or projection optics. Also the wavelength distribution of the lamp may be altered by ancillary optical elements, diffusers, lenses, and the like, as well as variations in operating conditions.

To evaluate a broad-band optical source, such as an arc lamp, an incandescent lamp, a fluorescent lamp, an array of lamps or a lamp system, it is first necessary to determine the spectral distribution of optical radiation emitted from the source at the point or points of nearest human access. This accessible emission spectral distribution of interest for a lighting system may differ from that actually being emitted by the lamp alone due to the filtration by any optical elements (e.g., projection optics) in the light path. Secondly, the size, or projected size, of the source must be characterized in the retinal hazard spectral region.

Thirdly, it may be necessary to determine the variation of irradiance and effective radiance with distance. The performance of the necessary measurements is normally not an easy task without sophisticated instruments. Thus it was decided to include reference measurement techniques for lamps and lamp systems in this standard. The measurement techniques along with the described risk group classification scheme will provide common ground for both lamp manufacturers and users to define the specific photobiological hazards of any given lamp and/or lamp system.

Finally, there are well known optical radiation hazards associated with some lamps and lamp systems. The purpose of this standard is to provide a standardized technique for evaluation of potential radiation hazards that may be associated with various lamps and lamp systems.

Keywords

Authors A H Cincotta, T L Knisely, R J Landry, W R Miers, P J Gutierrez, P Esperanza, A H Meier

Report Name The immunoregulatory effects of prolactin in mice are time of day dependent

Publication Endocrinology

Issue-page numbers 136:2163–2171 doi:10.1210/en.136.5.2163. PMID:7720666

URL http://www.mendeley.com/research/immunoregulatory-effects-prolactin-mice-time-day-dependent/

Abstract

The effects of timed administration of PRL on immune activities were investigated in male BALB/c mice. Ten daily injections of PRL (1 mg/kg) were made 0/24, 4, 8, 12, 16, or 20 h after light onset (HALO). On day 11, spleen cells were harvested between 1-3 HALO and cocultured with gamma-irradiated C57BL/6 spleen cells for 5 days, and proliferative responses to alloantigen were assayed (mixed lymphocyte reaction). When given in vivo at 4-12 HALO, PRL strongly stimulated proliferation by more than 2-fold, whereas PRL injections when given at 24 HALO substantially inhibited proliferation and had no effect when given at 16-20 HALO. When endogenous PRL secretion was stimulated for 7 days with injections of domperidone or 5-hydroxytryptophan, the splenocyte response increased by 48% and 64%, respectively, when injections were given at 9-10 HALO, but did not increase when they were given at 23-0 HALO. Inhibition of endogenous PRL secretion for 7 days with bromocriptine (2.5 mg/kg.day) inhibited splenocyte responsiveness by 40% when injected at 9 HALO, but had no effect when administered at 0 HALO. Furthermore, such bromocriptine treatment inhibited T- and B-cell mitogenic responses to Concanavalin-A (by 48%) and lipopolysaccharide (38%) when administered at 10, but not 0, HALO. In a manner similar to mixed lymphocyte reaction responses, daily PRL injections for 10 days at 11 HALO stimulated (40%) the in vivo delayed-type hypersensitivity response to antigen (azobenzenearsonate), whereas injections at 0 HALO were nonstimulatory. Bromocriptine treatment (1.5 mg/kg.day) suppressed the delayed-type hypersensitivity response (43% less than the control value) when administered at 10-12 HALO, but had no effect when administered at light onset. Timed PRL injections for 28 days in adult mice increased (42%) the total thymic cell number when administered at 11 HALO, but had no effect when injected at 0 HALO. Together, these results show that immunocyte responsiveness to PRL is time of day dependent. Thus, these findings support an essential and heretofore unrecognized circadian role in PRL regulation of immunity.

Keywords

Cini G, Neri B, Pacini A et al. **Year** 2005

Authors Cini G, Neri B, Pacini A et al.

Report Name Antiproliferative activity of melatonin by transcriptional inhibition of cyclin D1 expression: a molecular basis for melatonin-induced oncostatic effects.

Publication J Pineal Res

Issue-page numbers 39:12–20 doi:10.1111/j.1600-079X.2004.00206.x. PMID:15978052

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2004.00206.x/full

Abstract Melatonin is endowed with a growth inhibitory effect in MCF-7 breast cancer cells whose mechanism has been related to an antiestrogenic activity exerted by inhibition of binding of the estradiol–estrogen receptor complex to its DNA responsive element. Looking for downstream gene determinants of this effect, we performed a transcriptome profiling by high-density microarrays of estrogen-treated MCF-7 cells exposed or not to melatonin. We found that cyclin D1 was one of the main downregulated genes by melatonin. Validation experiments clearly confirm that in MCF-7 cells the estrogen-induced growth inhibitory activity of melatonin is consistently associated with inhibition of estrogen-elicited cyclin D1 induction. This effect is almost purely transcriptional. Reporter gene assays indicate that the same portion of the cyclin D1 promoter which confers estrogen sensitivity, encompassing a potential cAMP responsive element binding site, is repressed by melatonin. Transcriptional downregulation of cyclin D1 is the key molecular event for melatonin's antiproliferative activity, as this activity can be completely and selectively rescued by transient cyclin D1 overexpression. Finally, we provide indirect evidence that the effect of melatonin on the cyclin D1 promoter is mediated by the c-jun and ATF-2 proteins, known to bind the minimal estrogen-sensitive cyclin D1 promoter element. These findings establish for the first time a molecular link between melatonin and its effects on the cell cycle, providing at the same time a rationale for its use in adjuvant chemotherapy

Keywords 17-β-estradiol; cAMP responsive element; cell cycle; cyclin D1; MCF-7 cells; melatonin

Cinzano P, Falchi F, Elvidge CD **Year** 2001

Authors Cinzano, P., Falchi, F., Elvidge C.D.

Report Name The first world atlas of the artificial night sky brightness.

Publication Monthly Notices of Royal Astronomical Society

Issue-page numbers 2001;328:689-707 doi: 10.1046/j.1365-8711.2001.04882.x.

URL http://www.lightpollution.it/cinzano/download/0108052.pdf

Abstract We present the first World Atlas of the zenith artificial night sky brightness at sea level. Based on radiance calibrated high resolution DMSP satellite data and on accurate modelling of light propagation in the atmosphere, it provides a nearly global picture of how mankind is proceeding to envelope itself in a luminous fog. Comparing the Atlas with the U.S. Department of Energy (DOE) population density database we determined the fraction of population who are living under a sky of given brightness. About two thirds of the World population and 99% of the population in US (excluding Alaska and Hawaii) and EU live in areas where the night sky is above the threshold set for polluted status. Assuming average eye functionality, about one fifth of the World population, more than two thirds of the US population and more than one half of the EU population have already lost naked eye visibility of the Milky Way. Finally, about one tenth of the World population, more than 40% of the US population and one sixth of the EU population no longer view the heavens with the eye adapted to night vision because the sky brightnes

Keywords

Year 2005

Authors Cizza G, Skarulis M, Mignot E

Report Name A link between short sleep and obesity: building the evidence for causation

Publication Sleep

Issue-page numbers 28:1217–1220. PMID:16295203

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=26232

Abstract

IN THIS ISSUE OF SLEEP, GANGWISCH AND COLLEAGUES1 REPORT THAT INADEQUATE SLEEP IS A RISK FACTOR FOR OBESITY. IN A NEW ANALYSIS OF data obtained from the National Health and Nutrition Examination Survey (NHANES) I, a large probability sample of the civilian noninstitutionalized population of the United States, the authors observed that subjects between the ages of 32 and 49 years (n=3682) who reported sleeping less than 7 hours at the time of entry into the study had a higher average body mass index (BMI) and were more likely to be obese (BMI >30) than subjects who reported sleeping 7 hours. This statistical relationship was not observed in older subjects (n=5906, 50-86 years old), an observation the authors suggested may be due to decreased survival of older obese subjects and other factors including changing sleep requirements with increasing age.

Keywords

Clark CD, Denton ML, Thomas RJ

Year 2011

Authors Clifton D. Clark III, Michael L. Denton, and Robert J. Thomas

Report Name Mathematical model that describes the transition from thermal to photochemical damage in retinal pigment epithelial cell culture

Publication Journal of Biomedical Optics

Issue-page numbers v. 16, no 2, Feb 2011

URL http://www.dtic.mil/cgi-bin/GetTRDoc?AD=ADA537270&Location=U2&doc=GetTRDoc.pdf

Abstract We propose a rate process model for describing photochemical damage to retinal cells by short wavelength laser exposures. The rate equation for photochemical damage contains a positive rate that is temperature independent,and a negative (quenching) rate that is temperature dependent. Using the traditional Arrhenius integral to describe thermal damage, we derive damage threshold doses for both thermal and photochemical mechanisms, and show that the model accounts for the sharp transition from thermal to photochemical damage thresholds that have recently been observed in an in-vitro retinal model.

Keywords

Claudio L

Year 2009

Authors Luz Claudio

Report Name Switch On the Night: Policies for Smarter Lighting

Publication Environ Health Perspect

Issue-page numbers 117:A28-A31

URL http://dx.doi.org/10.1289/ehp.117-a28

Abstract Article

Keywords Night, circadian rhythm, dark

Authors Clausen OP, Iversen OH, Thorud E

Report Name Circadian variation in the susceptibility of mouse epidermis to tumour induction by methylnitrosourea

Publication Virchows Arch B Cell Pathol Incl Mol Pathol

Issue-page numbers 45:325–329 doi:10.1007/BF02889874. PMID:6146223

URL http://www.mendeley.com/research/circadian-variation-in-the-susceptibility-of-mouse-epidermis-to-tumour-induction-by-methylnitrosourea/

Abstract

To study possible circadian differences in the sensitivity of hairless mouse epidermis to a small dose of a short-acting alkylating carcinogen, groups of animals were painted once with 0.2 mg methylnitrosourea (MNU) at 08.00, 12.00, 20.00 and 24.00 h. Other animals were painted three times at weekly intervals at 08.00 and at 20.00 h, respectively. Significantly higher tumour yields were found in animals painted at 20.00 h (when the cell cycle progression and DNA synthesis rate are lowest, and when relatively large numbers of late G1 cells may accumulate) than at any other time point investigated. Hence a circadian variation in sensitivity to MNU in mouse epidermis is confirmed. This may be due to the variations in flux of cells through the S phase. The formation of DNA/carcinogen adducts may be facilitated at times of low flux with many cells in late G1, and fixation of these errors in DNA may take place by the subsequent increased flux through S, before repair is possible.

Keywords

Year 2005

Authors Claustrat B, Brun J, Chazot G

Report Name The basic physiology and pathophysiology of melatonin

Publication Sleep Med Rev

Issue-page numbers 9:11–24 doi:10.1016/j.smrv.2004.08.001. PMID:15649735

URL http://www.chiroonline.net/_fileCabinet/melatonin_medicalreview.pdf

Abstract Summary Melatonin is a methoxyindole synthesized and secreted principally by the pineal gland at night under normal environmental conditions. The endogenous rhythm of secretion is generated by the suprachiasmatic nuclei and entrained to the light/dark cycle. Light is able to either suppress or synchronize melatonin production according to the light schedule. The nycthohemeral rhythm of this hormone can be determined by repeated measurement of plasma or saliva melatonin or urine sulfatoxymelatonin, the main hepatic metabolite.
The primary physiological function of melatonin, whose secretion adjusts to night length, is to convey information concerning the daily cycle of light and darkness to body physiology. This information is used for the organisation of functions, which respond to changes in the photoperiod such as the seasonal rhythms. Seasonal rhythmicity of physiological functions in humans related to possible alteration of the melatonin message remains, however, of limited evidence in temperate areas in field conditions. Also, the daily melatonin secretion, which is a very robust biochemical signal of night, can be used for the organisation of circadian rhythms. Although functions of this hormone in humans are mainly based on correlative observations, there is some evidence that melatonin stabilises and strengthens coupling of circadian rhythms, especially of core temperature and sleep-wake rhythms.
The circadian organisation of other physiological functions could depend on the melatonin signal, for instance immune, antioxidative defences, hemostasis and glucose regulation.
Since the regulating system of melatonin secretion is complex, following central and autonomic pathways, there are many pathophysiological situations where the melatonin secretion can be disturbed. The resulting alteration could increase predisposition to disease, add to the severity of symptoms or modify the course and outcome of the disorder.

Keywords Melatonin; Human; Circadian rhythms; Physiology; Pathophysiology

Cohen M, Lippman M, Chabner B

Year 1978

Authors Michael Cohen, Marc Lippman, Bruce Chabner

Report Name Role of pineal gland in aetiology and treatment of breast cancer

Publication Lancet

Issue-page numbers 312:814–816 doi:10.1016/S0140-6736(78)92591-6. PMID:81365

URL http://www.sciencedirect.com/science/article/pii/S0140673678925916

Abstract The hypothesis that diminished function of the pineal gland may promote the development of breast cancer in human beings is suggested by the relation between breast cancer and prolonged œstrogen excess, and by the observation that the pineal secretion, melatonin, inhibits ovarian œstrogen production, pituitary gonadotrophin production, and sexual development and maturation. The hypothesis is supported by the following points. (1) Pineal calcification is commonest in countries with high rates of breast cancer and lowest in areas with a low incidence; the incidences of pineal calcification and of breast cancer are moderate among the black population in the United States. (2) Chlorpromazine raises serum-melatonin; there are reports that psychiatric patients taking chlorpromazine have a lower incidence of breast cancer. (3) Although information is lacking on breast cancer, the pineal and melatonin may influence tumour induction and growth in experimental animals. (4) The demonstration of a melatonin receptor in human ovary suggests a direct influence of this hormone on the ovarian function, and possibly œstrogen production. (5) Impaired pineal secretion is believed to be an important factor triggering puberty (early menarche is a risk factor for breast cancer).

Keywords

Cohen M, Lippman M, Chabner B.

Year 1978

Authors Michael Cohen, Marc Lippman, Bruce Chabner

Report Name Lancet

Publication Pineal gland and breast cancer

Issue-page numbers 2:1381–2. doi: 10.1016/S0140-6736(78)92018-4

URL http://www.sciencedirect.com/science/article/pii/S0140673678920184

Abstract N/A

Keywords

Cole RJ, Kripke DF, Wisbey J, et al. **Year** 1995

Authors Roger J. Cole, Daniel F. Kripke, Joyce Wisbey, William J. Mason, William Gruen, Peter J. Hauri, Silvia Juarez

Report Name Seasonal Variation in Human Illumination Exposure at Two Different Latitudes

Publication J Biol Rhythms

Issue-page numbers December 1995 vol. 10 no. 4 324-334

URL http://jbr.sagepub.com/content/10/4/324.abstract

Abstract The authors measured ambient illumination exposure in healthy volun teers in San Diego, California (latitude 32° 43' N, n = 30), and Rochester, Minne sota (latitude 44° 1'N, n = 24), during each of the four quarters of the year, which were centered on the solstices and equinoxes. Subjects wore photosensors on their wrists and lapels (or foreheads while in bed) 24 h per day for an average of 5-6 days per quarter. The maximum of the two illumination readings was stored each minute. Annual average time spent per day in outdoor illumination (≥ 1000 lux) was significantly higher in San Diego than it was in Rochester ($p < .04$). Daily durations of illumination at or exceeding thresholds of 1,10,100,1000, and 10,000 lux were highly seasonal in the sample as a whole ($p < .01$ at 1 lux, $p < .0001$ at other thresholds). Seasonal variation in outdoor illumination was far more pronounced in Rochester than it was in San Diego (interaction $p < .001$) but remained significant in San Diego ($p \leq .03$). Seasonal variation in indoor illumi nation was generally similar in the two cities. The median Rochester subject experienced illumination ≥ 1000 lux for 2 h 23 min per day during summer and 23 min per day during winter. The corresponding times in San Diego were 2 h 10 min and 1 h 20 min. Neither age nor gender predicted illumination duration at any level. Both season and geographic location strongly influenced human illumination exposure, and behavior (choice of indoor vs. outdoor environment) was the most important mediating factor.

Keywords illumination, light, exposure, season, latitude, human

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Colombo LL, Chen GJ, Lopez MC, Watson RR **Year** 1992

Authors Colombo LL, Chen GJ, Lopez MC, Watson RR

Report Name Melatonin induced increase in gamma-interferon production by murine splenocytes

Publication Immunol Lett

Issue-page numbers 33:123–126 doi:10.1016/0165-2478(92)90035-M. PMID:1446916

URL http://www.mendeley.com/research/melatonin-induced-increase-gammainterferon-production-murine-splenocytes/

Abstract Previously, we demonstrated that production of gamma-interferon (gamma-IFN) by the mouse splenocytes isolated at night was higher than from those isolated in the morning. In this paper we show that melatonin increased gamma-IFN production by murine splenocytes. Moreover, this stimulating effect was significantly higher (10 times) in the cells isolated at night than in those isolated in the morning (2 times).

Keywords

Comas M, Beersma DGM, Spoelstra K, Daan S **Year** 2007

Authors M. Comas, D.G.M. Beersma, K. Spoelstra, S. Daan

Report Name Circadian Response Reduction in Light and Response Restoration in Darkness: A “Skeleton” Light Pulse PRC Study in Mice (Mus musculus)

Publication J Biol Rhythms

Issue-page numbers October 2007 vol. 22 no. 5 432-444

URL http://jbr.sagepub.com/content/22/5/432.abstract

Abstract

Entrainment may involve responses to dawn, to dusk, and to the light in between these transitions. Previous studies showed that the circadian system responds to only 2 light pulses, one at the beginning and one at the end of the day, in a similar way as to a full photoperiod, as long as the photoperiod is less than approximately 1/2 τ. The authors used a double 1-h light pulse protocol with different intervals of darkness in between (1, 2, 4, 7, 10, and 16 h) to study the phase responses of mice. The phase response curves obtained were compared to full light pulse PRCs of corresponding durations. Up to 6 hours, phase responses induced by double light pulses are virtually the same as by a corresponding full light pulse. The authors made a simple phase-only model to estimate the response reduction due to light exposure and response restoration due to dark exposure of the system. In this model, they assumed a 100% contribution of the first 1-h light pulse and fitted the reduction factor for the second light pulse to yield the best fit to the observations. The results suggest that after 1 h of light followed by less than 4 h of darkness, there is a considerable reduction in response to the second light pulse. Full response restoration requires more than 10 h of darkness. To investigate the influence of the duration of light on the response saturation, the authors performed a second series of experiments where the duration of the 2 light pulses was varied from 4 to 60 min each with a fixed duration of the stimulus (4 h). The response to 2 light pulses saturates when they are between 30 and 60 min long. In conclusion, double pulses replace single full light pulses of a corresponding duration of up to 6 h due to a response reduction during light, combined with response restoration during darkness. By the combined response reduction and response restoration, mice can maintain stable entrainment to the external LD cycle without being continuously exposed to it.

Keywords circadian clock, phase resetting, phase response curve, Mus musculus

Authors Committee on Breast Cancer and the Environment: The Scientific

Report Name Breast Cancer and the Environment

Publication The National Academies

Issue-page numbers THE NATIONAL ACADEMIES PRESS

URL https://download.nap.edu/catalog.php?record_id=13263

Abstract

Shift Work
According to IARC (2010a), the average prevalence of shift work involving night work in the United States is 14.8 percent (16.7% in men and 12.4% in women). It is most common among those in health care, transportation, communication, leisure and hospitality, and the service, mining, and industrial manufacturing sectors. It is more common in younger workers, decreasing to a prevalence of about 10 percent after age 55 (IARC, 2010a).
It has been proposed that shift work is a risk factor in breast cancer etiology. This phenomenon has been studied through epidemiologic, animal and in vitro studies, and was reviewed extensively by IARC in 2010. In the past decade, eight major epidemiologic studies have examined the relation between shift work and risk for breast cancer among female workers, although these studies had vastly differing definitions of shift work (IARC, 2010a). Among the two prospective cohort studies (Schernhammer et al., 2001; Schernhammer and Hankinson, 2005), one nationwide census-based cohort study (Schwartzbaum et al., 2007), three nested case–control studies (Tynes et al., 1996; Hansen, 2001; Lie et al., 2006), and two case–control studies (Davis et al., 2001; O'Leary et al., 2006), the majority studied postmenopausal women (IARC, 2010b). A notable limitation of the data from these studies is the lack of racial diversity, with only one study including a small subset of Latina and African American women (O'Leary et al., 2006). Despite differences in study methodologies, meta-analyses and systematic reviews of the literature consistently note an increase in relative risk of breast cancer associated with shift work (Megdal et al., 2005; Hansen, 2006; Kolstad, 2008; IARC, 2010b). Megdal et al. (2005) reported an aggregate RR estimate based on 13 combined studies of 1.48 (95% CI, 1.36–1.61).
Animal and in vitro studies on shift work-induced breast cancer are more difficult to design and conduct. Because "shift work" itself cannot be imposed on animals, experimental studies have used models of alteration of light and dark environments, which affect circadian pacemaker function. The exposure to light during the night, and the altered sleep cycle that ensues, has been proposed as the mechanism for shift work-induced breast cancer (Straif et al., 2007).
Numerous animal studies have evaluated the effect of varying light cycles on mammary tumorigenesis in animal models. In CBA mice, continuous light exposure increased the incidence of different spontaneous tumors from a variety of tissues in females, and also reduced overall life span (Anisimov et al., 2004). However, the numbers for mammary adenocarcinomas were very small (one spontaneous adenocarcinoma in light/dark exposed mice, and two adenocarcinomas in the light/light exposed group, with 50 animals in each group (Anisimov et al., 2004). Anderson

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et al. (2000a) demonstrated in rats that constant light exposure followed by exposure to a chemical carcinogen such as DMBA results in an increased incidence of mammary tumors when compared to an alternating light/dark cycle. Cos et al. (2006) examined the effects of constant light or different patterns of "light at night" on established DMBA-induced mammary carcinomas in female Sprague Dawley rats. They found that female rats exposed to light at night,

especially those under a constant dim light during the darkness phase, showed (1) significantly higher rates of tumor growth as well as lower survival than controls (typical 12-hour light–dark cycle), (2) elevated serum estradiol concentration, and (3) decreased nocturnal excretion of 6-sulfatoxymelatonin, but no differences between nocturnal and diurnal levels. They concluded from this that circadian and endocrine disruption induced by light pollution could induce the growth of mammary tumors. The role of stress induced from the constant light exposure cannot be ruled out. It could be a fundamental part of the mechanism of action, and stress would also be relevant to humans with constant disruption of light at night/circadian rhythm. Other studies have shown that light exposure at night increases the growth of different kinds of transplantable tumors in rats (Dauchy et al., 1997, 1999; Blask et al., 2002).
Melatonin is hypothesized to play an important role in shift work-induced breast cancer; this hormone transmits informational cues of environmental light and darkness from the eye to the hypothalamus, to all tissues of the body, helping to set an organism's biological clock. Importantly, "melatonin has anti-proliferative effects on human cancer cells cultured in vitro" (IARC, 2010a, p. 663). According to the melatonin hypothesis, light exposure at night results in a reduction in the circulating levels of melatonin, which removes its check on estrogen, allowing for rising levels of estrogen to promote cell proliferation and increase the risk for malignant transformation (Graham et al., 2001). As an antiestrogen, melatonin down-regulates ERα transcription and alters its functional activity (Molis et al., 1994; Rato et al., 1999; del Río et al., 2004; Cini et al., 2005). Despite numerous in vitro studies on the oncostatic effects of melatonin, there is insufficient evidence regarding the use of melatonin supplements to determine their impact on risk of breast cancer, making this a potential subject area for future studies.
IARC (2010a) concluded that "shift work that involves circadian disruption is probably carcinogenic to humans" (Straif et al., 2007, p. 1065; IARC, 2010a, p. 764). To understand the role of "light at night" in breast cancer etiology, further studies are needed on its influence on women who do not perform shift work, but who are exposed to light at night in their homes.

Keywords

Conlon M, Lightfoot N, Kreiger N

Year 2007

Authors Conlon M, Lightfoot N, Kreiger N

Report Name Rotating shift work and risk of prostate cancer

Publication Epidemiology

Issue-page numbers 18:182–183.doi:10.1097/01.ede.0000249519.33978.31 PMID:17179764

URL http://journals.lww.com/epidem/Fulltext/2007/01000/Rotating_Shift_Work_and_Risk_of_Prostate_Cancer.27.aspx

Abstract Letter to Editor

Keywords

Cook MR, Graham C, Kavet R et al. **Year** 2000

Authors Cook MR, Graham C, Kavet R et al.

Report Name Morning urinary assessment of nocturnal melatonin secretion in older women

Publication J Pineal Res

Issue-page numbers 28:41–47 doi:10.1034/j.1600-079x.2000.280106.x. PMID:10626600

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079x.2000.280106.x/abstract?

Abstract We evaluated the feasibility of using morning urine samples in epidemiological studies aimed at clarifying the relationship between nocturnal melatonin levels and breast cancer risk. Initially, a laboratory-based study of 29 women (40–70 yr old) was performed to examine the correlation between plasma melatonin levels in hourly nocturnal blood samples and both melatonin and its major enzymatic metabolite, 6-hydroxymelatonin-sulfate (6-OHMS) in morning urine samples. In a companion field study, morning urine samples were collected from 203 healthy women to assess similarities and differences in laboratory versus field measures. Taken together, our results indicate: 1) levels of melatonin and of creatinine-corrected 6-OHMS in the first morning void urine are strongly correlated with total nocturnal plasma melatonin output (P<0.001) and also with peak nocturnal melatonin values (P<0.001); 2) similar ranges for 6-OHMS were found in the laboratory and the field; and 3) neither menopausal status nor hormonal replacement therapy altered 6-OHMS values in morning void urine. The inclusion of morning urine samples in epidemiological studies of cancer could allow cost-effective, widespread testing of the role played by melatonin in human health and disease.

Keywords age; breast cancer; melatonin; 6-OHMS; 6-sulfatoxymelatonin

Coomans CP, van den Berg SAA, Houben T, et al. **Year** 2013

Authors Claudia P. Coomans, Sjoerd A. A. van den Berg, Thijs Houben, Jan-Bert van Klinken, Rosa van den Berg, Amanda C. M. Pronk, Louis M. Havekes, Johannes A. Romijn†, Ko Wi

Report Name Detrimental effects of constant light exposure and high-fat diet on circadian energy metabolism and insulin sensitivity

Publication

Issue-page numbers Published online before print January 9, 2013, doi: 10.1096/fj.12-210898 fj.12-210898

URL http://www.fasebj.org/content/early/2013/01/09/fj.12-210898.short

Abstract Circadian rhythm disturbances are observed in, e.g., aging and neurodegenerative diseases and are associated with an increased incidence of obesity and diabetes. We subjected male C57Bl/6J mice to constant light [12-h light-light (LL) cycle] to examine the effects of a disturbed circadian rhythm on energy metabolism and insulin sensitivity. In vivo electrophysiological recordings in the central pacemaker of the suprachiasmatic nuclei (SCN) revealed an immediate reduction in rhythm amplitude, stabilizing at 44% of normal amplitude values after 4 d LL. Food intake was increased (+26%) and energy expenditure decreased (−13%), and we observed immediate body weight gain (d 4: +2.4%, d 14: +5.0%). Mixed model analysis revealed that weight gain developed more rapidly in response to LL as compared to high fat. After 4 wk in LL, the circadian pattern in feeding and energy expenditure was completely lost, despite continuing low-amplitude rhythms in the SCN and in behavior, whereas weight gain had stabilized. Hyperinsulinemic-euglycemic clamp analysis revealed complete abolishment of normal circadian variation in insulin sensitivity in LL. In conclusion, a reduction in amplitude of the SCN, to values previously observed in aged mice, is sufficient to induce a complete loss of circadian rhythms in energy metabolism and insulin sensitivity.—Coomans, C. P., van den Berg, S. A. A., Houben, T., van Klinken, J.-B., van den Berg, R., Pronk, A. C. M., Havekes, L. M., Romijn, J. A., van Dijk, K. W., Biermasz, N. R., Meijer, J. H. Detrimental effects of constant light exposure and high-fat diet on circadian energy metabolism and insulin sensitivity.

Keywords

Coon SL, McCune SK, Sugden D, Klein DC **Year** 1997

Authors Steven L. Coon, Susan K. McCune, David Sugden, David C. Klein

Report Name Regulation of Pineal α1B-Adrenergic Receptor mRNA: Day/Night Rhythm and β-Adrenergic Receptor/Cyclic AMP Control

Publication Molecular Pharmacology

Issue-page numbers April 1, 1997 vol. 51 no. 4 551-557

URL http://molpharm.aspetjournals.org/content/51/4/551.short

Abstract Mammalian pineal function is regulated by norepinephrine acting through α1B- and β1-adrenergic receptors (ARs). Noradrenergic stimulation of α1B-ARs potentiates the β1-AR-driven increase in cAMP, serotoninN-acetyltransferase, and melatonin production. In the present study, we describe a 3-fold daily rhythm in mRNA-encoding α1B-ARs in the pineal gland, with a peak at midnight. Pharmacological studies indicate that this increase in α1B-AR mRNA is due to activation of β-ARs. Second messenger studies indicate tha α1B-AR mRNA is increased by agents that increase cAMP, including dibutyryl cAMP, cholera toxin, forskolin, or vasoactive intestinal peptide. These observations indicate that α1B-AR mRNA can be physiologically regulated by a β-AR-dependent enhancement of cAMP. It also was observed that in vivo and in vitrochanges in α1B-AR mRNA are not accompanied by similar changes in α1B-AR binding, indicating that turnover of α1B-AR protein is significantly slower than that of α1B-AR mRNA and that post-transcriptional mechanisms play an important role in regulating α1B-AR binding.

Keywords

Cooper DA, Duckett M, Petts V, Penny R **Year** 1979

Authors Cooper DA, Duckett M, Petts V, Penny R

Report Name Corticosteroid enhancement of immunoglobulin synthesis by pokeweed mitogen-stimulated human lymphocytes.

Publication Clin Exp Immunol

Issue-page numbers 37:145–151. PMID:487651

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1537658/

Abstract The effects of the addition in vitro of corticosteroid on pokeweed mitogen (PWM) induced Ig synthesis by human peripheral blood lymphocytes were studied. IgG in supernatants produced under standardized culture conditions was measured by double antibody radioimmunoassay. The addition of 10(-6)M prednisolone caused a remarkable enhancement of PWM-stimulated IgG synthesis beginning at day 4 of culture and increasing at a faster rate than that in cultures with PWM alone. 10(-6)M prednisolone resulted in a geometric mean enhancement of 5.6-fold of PWM-stimulated IgG synthesis in all twenty-five normal controls studied. This enhancement occurred up to 3 days after the addition of PWM. 10(-6)M and 10(-5)M prednisolone resulted in significantly greater enhancement of PWM-stimulated IgG synthesis than 10(-7)M prednisolone. Hydrocortisone, prednisolone, methylprednisolone, betamethasone and dexamethasone at 10(-6)M were all equally effective in the enhancement of PWM-induced IgG synthesis.

Keywords

Authors Georges Copinschi, Elif Akseki, Rodrigo Moreno-Reyes, Rachel Leproult, Mireille L'Hermite-Baleriaux, Anne Caufriez, Francoise Vertongen and Eve Van Cauter

Report Name Effects of bedtime administration of zolpidem on circadian and sleep-related hormonal profiles in normal women.

Publication Sleep

Issue-page numbers 18:417–424. PMID:7481412

URL http://journalsleep.org/ViewAbstract.aspx?pid=24563

Abstract

Short-acting benzodiazepine hypnotics may phase-shift circadian rhythms and improve adaptation of sleep patterns to abrupt time shifts, depending on the timing of administration. The aim of the present study was to determine whether bedtime administration of zolpidem, a non- benzodiazepine hypnotic, causes alterations in circadian rhythmicity or in the normal interactions between sleep and hormones. Eight normal women (aged 21-33 years) each participated in a baseline study and a study with zolpidem administration. On each occasion, blood samples were obtained at 20-minute intervals for 25 hours, starting at 1000 hours. Zolpidem (10 mg) was given orally at 2245 hours. Zolpidem administration was associated with an increase in stages III + IV sleep. Cortisol, melatonin, thyrotropin and growth hormone profiles were similar in both experimental conditions. In contrast, though remaining in the normal range, the nocturnal elevation of prolactin was enhanced two-fold in all subjects after zolpidem during early sleep, and prolactin levels were still 50% higher than baseline in late sleep. Morning levels were similar in both studies. In conclusion, bedtime administration of 10 mg zolpidem, a standard clinical dosage, systematically induces a transient moderate hyperprolactinemia, but does not alter other sleep-related hormonal secretions or endocrine markers of circadian rhythmicity.

Keywords

Authors Copinschi G, Van Onderbergen A, L'Hermite-Balériaux M, Szyper M, Caufriez A, Bosson D, L'Hermite M, Robyn C, Turek FW, Van Cauter E.

Report Name Effects of the short-acting benzodiazepine triazolam, taken at bedtime, on circadian and sleep-related hormonal profiles in normal men

Publication Sleep

Issue-page numbers 13:232–244. PMID:2356395

URL http://www.ncbi.nlm.nih.gov/pubmed/2356395

Abstract

Studies in rodents have shown that triazolam, a commonly used hypnotic, may shift circadian rhythms, with the direction and magnitude of the phase-shifts being dependent on the time of drug administration. To determine whether benzodiazepine, taken at standard bedtime, modifies the amount and/or temporal organization of hormonal secretion, six normal men were studied during basal conditions and on the first and third days of treatment with 0.5 mg triazolam. In each study, sleep was polygraphically monitored and plasma cortisol, growth hormone (GH), melatonin, and prolactin (PRL) (i.e., hormones influenced by circadian rhythmicity and/or sleep) were measured at 20-min intervals for 24 h. The sleep latency and the number and duration of awakenings were reduced during triazolam treatment as compared to baseline conditions. The only alteration of sleep architecture was a partial suppression of stages III + IV (SW) in late sleep. Triazolam did not affect the mean cortisol and melatonin levels or the total amount of GH secreted over the 24-h span. The circadian timings of the onsets of cortisol and melatonin secretions were essentially unaltered. The nocturnal rise of melatonin was prolonged by 45 to 60 minutes. Sleep-associated GH release was not modified by triazolam. Sleep-associated PRL secretion persisted, but in half of the nights studied was enhanced almost threefold. This effect of the drug on nocturnal PRL secretion was not specific to either the first or the third night of treatment, nor was it specific to certain subjects. Irrespective of the magnitude of the nocturnal elevation, morning PRL levels were slightly but consistently higher after triazolam treatment than under basal conditions. Normal PRL levels resumed around noon. In conclusion, administration of 0.5 mg triazolam at normal bedtime (2230) for three consecutive days may induce a transient hyperprolactinemia, but does not abolish sleep-related hormone secretion and does not affect the timing of endocrine events controlled by the circadian clock. These findings are consistent with studies in hamsters where treatment with triazolam in the early subjective night was also without effect on the rodent circadian clock.

Keywords

Authors Dolores Corbalán-Tutau, Juan Antonio Madrid, Francisco Nicolás, Marta Garaulet

Report Name Daily profile in two circadian markers “melatonin and cortisol” and associations with metabolic syndrome components

Publication Physiology & Behavior

Issue-page numbers Available online 13 June 2012

URL http://www.sciencedirect.com/science/article/pii/S0031938412002296

Abstract

bjetive

The aim of the present work was to investigate associations in circadian markers, melatonin (MT) and cortisol, with metabolic syndrome (MetS) parameters, and with leptin, adiponectin and ghrelin plasma values.
Methods

The study was conducted in 70 women (mean age: 41 ± 10 years) that were classified without MetS (n = 30) and with MetS (n = 40). Blood collection, plasma separation and processing, and biochemical analyses for plasma lipids were performed. For measuring salivary melatonin, participants collected two samples. The first simple was obtained before lunch (at 14:00 p.m.) and the second sample was taken at night (3:00 a.m.). On a random working day, participants delivered repeated salivary cortisol samples. The first sample was obtained in the morning (09:00 a.m.), then before lunch at (14:00 p.m.), and finally just before bedtime (23:00 p.m.).
Results

Significant differences were found between the MT measurements taken at night in women without and with MetS. With respect to cortisol, significant differences were found in the different times cortisol levels toward a more flattened pattern among MetS women. Both parameters were positive correlated between them. Of note MT and cortisol night/morning ratios were associated with MetS score and metabolic syndrome components.
Conclusion

The findings indicate that diminished daily amplitude in MT and cortisol circadian patterns was associated with metabolic disturbances in blood pressure, glucose and plasma lipids regulation, ghrelin and adipocyte-secreted hormones such as leptin and adiponectin.

Keywords Melatonin; Cortisol; Metabolic syndrome; Adiponectin; Leptin; Ghrelin

Corbalán-Tutau MD, Madrid JA, Ordovás JM, et al. **Year** 2011

Authors M. D. Corbalán-Tutau, J. A. Madrid, J. M. Ordovás, C. E. Smith, F. Nicolás and M. Garaulet

Report Name Differences in Daily Rhythms of Wrist Temperature Between Obese and Normal-Weight Women: Associations With Metabolic Syndrome Features

Publication Chronobiology International

Issue-page numbers 28:5, 425-433

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.574766

Abstract The circadian rhythm of core body temperature is associated with widespread physiological effects. However, studies with other more practical temperature measures, such as wrist (WT) and proximal temperatures, are still scarce. The aim of this study was to investigate whether obesity is associated with differences in mean WT values or in its daily rhythmicity patterns. Daily patterns of cortisol, melatonin, and different metabolic syndrome (MetS) features were also analyzed in an attempt to clarify the potential association between chronodisruption and MetS. The study was conducted on 20 normal-weight women (age: 38 ± 11 yrs and BMI: 22 ± 2.6 kg/m2) and 50 obese women (age: 42 ± 10 yrs and BMI: 33.5 ± 3.2 kg/m2) (mean ± SEM). Skin temperature was measured over a 3-day period every 10 min with the “Thermochron iButton.” Rhythmic parameters were obtained using an integrated package for time-series analysis, “Circadianware.” Obese women displayed significantly lower mean WT (34.1°C ± 0.3°C) with a more flattened 24-h pattern, a lower-quality rhythm, and a higher intraday variability (IV). Particularly interesting were the marked differences between obese and normal-weight women in the secondary WT peak in the postprandial period (second-harmonic power [P2]), considered as a marker of chronodisruption and of metabolic alterations. WT rhythmicity characteristics were related to MetS features, obesity-related proteins, and circadian markers, such as melatonin. In summary, obese women displayed a lower-quality WT daily rhythm with a more flattened pattern (particularly in the postprandial period) and increased IV, which suggests a greater fragmentation of the rest/activity rhythm compared to normal-weight women. These 24-h changes were associated with higher MetS risk.

Keywords Abdominal obesity, Circadian, Core temperature circadian rhythm, Cortisol, Melatonin, Metabolic Syndrome, Obesity, Skin temperature

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Coroneo MT, Müller-Stolzenburg NW, Ho A **Year** 1991

Authors Coroneo MT, Müller-Stolzenburg NW, Ho A.

Report Name Peripheral light focusing by the anterior eye and the ophthalmohelioses

Publication Ophthalmic Surg

Issue-page numbers 1991 Dec;22(12):705-11.

URL http://www.ncbi.nlm.nih.gov/pubmed/1787933

Abstract Peripheral focusing of light by the anterior eye may provide a unifying concept to explain the location and etiology of sun-related eye conditions (ophthalmohelioses). Using a bovine eye model, along with computer-assisted ray-tracing techniques to model limbal focusing, we demonstrated a correlation between the locations of the foci of scattered incident light (resulting in a 20-fold concentration of light at the limbus) and the usual locations of pterygium and cortical cataract. These findings suggest the need for improved ocular protective devices, particularly ones that provide lateral protection of the eye against the increased ultraviolet insolation resulting from thinning of the ozone layer.

Keywords

Authors Samuel Cos, Rosario Fernández

Report Name Melatonin effects on intercellular junctional communication in MCF-7 human breast cancer cells.

Publication J Pineal Res

Issue-page numbers 29:166–171 doi:10.1034/j.1600-079X.2000.290306.x. PMID:11034114

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079X.2000.290306.x/abstract?

Abstract

Melatonin exerts a direct antiproliferative effect on estrogen-responsive MCF-7 cells in culture. Recently, the importance of the anti-invasive actions of melatonin as a part of the oncostatic action of this indolamine has been reported. Gap junctional intercellular communication is known to be involved in controlling cell proliferation and differentiation, and a decrease in intercellular junctional communication has been described in highly invasive mammary cancer cells. Because melatonin at physiological doses (1 nM) shifts MCF-7 cells to a lower invasive status, we postulate that melatonin could modulate the levels of gap junctional intercellular communication in these tumor cells. To test our hypothesis, we studied gap junctional intercellular communication in MCF-7 human breast cancer cells previously (7–8 days) treated, or not, with melatonin (10 μM or 1 nM). Using the scrape-loading assay dye-transfer technique to introduce 0.05% Lucifer yellow into cells, we measured the ability of the tumor cells to transfer dye to adjacent cells. Rhodamine dextran (0.05%) was used as a control dye to verify that dye-transfer occurs through intercellular junctions. The presence of melatonin (10 μM or 1 nM) in the culture medium significantly increased ($P<0.01$) the transfer of the dye to adjacent cells through gap junctions. This increase was greater at 10 μM melatonin, and averaged scan profiles of cells treated with melatonin 10 μM showed a statistically significant increase ($P<0.01$) in the integrated optical density values, and a broadening of the densitometric scan. These findings suggest that melatonin could exert its antitumor action, at least in part, by increasing regulatory signals that are passed between adjacent epithelial cells through intercellular junctions.

Keywords breast cancer; gap junctions; intercellular communication; MCF-7 cells; melatonin; pineal gland

Authors Cos S, Fernández R, Güézmes A, Sánchez-Barceló EJ

Report Name Influence of melatonin on invasive and metastatic properties of MCF-7 human breast cancer cells

Publication Cancer Res

Issue-page numbers 58:4383–4390. PMID:9766668

URL http://cancerres.aacrjournals.org/content/58/19/4383

Abstract

Melatonin, the principal pineal gland hormone, exerts a direct antiproliferative effect on estrogen-responsive MCF-7 cells in culture. The purpose of the current study was to investigate the effects of melatonin on the invasion capacity of MCF-7 cells.

In vitro, melatonin at physiological doses (1 nm) reduced ($P < 0.001$) the invasiveness of tumoral cells measured in Falcon invasion chambers. Subphysiological (0.1 pm) and pharmacological concentrations (10 μm) of melatonin failed to inhibit cell invasion. Melatonin was also able to block 17β-estradiol-induced invasion ($P < 0.001$). Pretreatment of MCF-7 cells with 1 nm melatonin increased the response of tumoral cells to the anti-invasive effects of this indolamine. To explore possible mechanisms by which melatonin reduces invasiveness, we measured the attachment of MCF-7 cells to a basement membrane, the chemotactic response of the cells, and their type IV collagenolytic activity. The presence of melatonin (1 nm) in the culture medium significantly reduced the ability of MCF-7 cells to attach to the basement membrane; this effect was enhanced by pretreating the cells with the same indolamine ($P < 0.001$). Melatonin also counteracts the stimulatory effects of 17β-estradiol on cell adhesion ($P < 0.001$). The chemotactic response of MCF-7 cells also decreased in the presence of 1 nm melatonin, and this melatonin-induced reduction of cell migration was more effective on cells that were previously incubated for 5 days with melatonin than it was on nonpretreated cells ($P < 0.001$). The simultaneous addition of 17β-estradiol and melatonin resulted in a significantly lower chemotactic response than that of 17β-estradiol-treated cells ($P < 0.001$). However, type IV collagenolytic activity was not influenced by melatonin. Our results demonstrate that melatonin reduces the invasiveness of MCF-7 cells, causing a decrease in cell attachment and cell motility, probably by interacting with the estrogen-mediated mechanisms of MCF-7 cell invasiveness. In addition, we also studied the influence of melatonin on the expression of two cell surface adhesion molecules (E-cadherin and β1 integrin) and an intermediate filament protein (vimentin), the expression of which has been correlated with the relative invasive capacity of human breast cancer cells. The culture of tumor cells in the presence of melatonin (1 nm) increased the membrane staining for E-cadherin and β1 integrin as well as the number of E-cadherin and β1 integrin immunoreactive cells ($P < 0.01$). Neither control MCF-7 cells nor those treated with melatonin stained for vimentin.

Preliminary in vivo experiments carried out on ovariectomized athymic nude mice implanted with 17β-estradiol pellets and inoculated with 5 × 106 MCF-7 cells in the inguinal mammary fat pad suggest that melatonin could decrease the tumorigenicity of these tumor cells. However, these results need further confirmation.

Taken together, our results suggest that melatonin shifts MCF-7 human breast cancer cells to a lower invasive status by increasing the β1 integrin subunit and E-cadherin expression and promoting the differentiation of tumor cells. Finally, our study points out the existence of the anti-invasive actions of melatonin as a part of the oncostatic action of melatonin.

Keywords

Authors Cos S, González A, Güezmes A et al.

Report Name Melatonin inhibits the growth of DMBA-induced mammary tumors by decreasing the local biosynthesis of estrogens through the modulation of aromatase activity

Publication Int J Cancer

Issue-page numbers 118:274–278 doi:10.1002/ijc.21401. PMID:16080194

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.21401/pdf

Abstract Melatonin inhibits the growth of breast cancer cells by interacting with estrogen-responsive pathways, thus behaving as an antiestrogenic hormone. Recently, we described that melatonin reduces aromatase expression and activity in MCF-7 human breast cancer cells, thus modulating the local estrogen biosynthesis. To investigate the in vivo aromatase-inhibitory properties of melatonin in our current study, this indoleamine was administered to rats bearing DMBA-induced mammary tumors, ovariectomized (ovx) and treated with testosterone. In these castrated animals, the growth of the estrogen-sensitive mammary tumors depends on the local aromatization of testosterone to estrogens. Ovariectomy significantly reduced the size of the tumors while the administration of testosterone to ovx animals stimulated tumor growth, an effect that was suppressed by administration of melatonin or the aromatase inhibitor aminoglutethimide. Uterine weight of ovx rats, which depends on the local synthesis of estrogens, was increased by testosterone, except in those animals that were also treated with melatonin or aminoglutethimide. The growth-stimulatory effects of testosterone on the uterus and tumors depend exclusively on locally formed estrogens, since no changes in serum estradiol were appreciated in testosterone-treated rats. Tumors from animals treated with melatonin had lower microsomal aromatase activity than tumors of animals from other groups, and incubation with melatonin decreased the aromatase activity of microsomal fractions of tumors. Animals treated with melatonin had the same survival probability as the castrated animals and significantly higher survival probability than the uncastrated. We conclude that melatonin could exert its antitumoral effects on hormone-dependent mammary tumors by inhibiting the aromatase activity of the tumoral tissue.

Keywords

Cos S, Martínez-Campa C, Mediavilla MD, Sánchez-Barceló EJ **Year** 2005

Authors Cos S, Martínez-Campa C, Mediavilla MD, Sánchez-Barceló EJ

Report Name Melatonin modulates aromatase activity in MCF-7 human breast cancer cells.

Publication J Pineal Res

Issue-page numbers 38:136–142 doi:10.1111/j.1600-079X.2004.00186.x. PMID:15683469

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2004.00186.x/abstract

Abstract Most of the current knowledge about the mechanisms by which melatonin inhibits the growth of breast cancer cells point to an interaction of melatonin with estrogen-responsive pathways, thus behaving as an antiestrogenic hormone. However, a possible effect of melatonin on the local synthesis of estrogens had not been examined. The objective of this work was to study whether melatonin may modify the aromatase activity in MCF-7 breast cancer cells thus modulating the local estrogen biosynthesis. In MCF-7 cells cultured with testosterone in estradiol-free media, melatonin (1 nm) counteracts the testosterone-induced cell proliferation dependent on the local biosynthesis of estrogens from testosterone by the aromatase activity of the cells. We found that melatonin reduces the aromatase activity (measured by the tritiated water release assay) of MCF-7 cells both a basal conditions and when aromatase activity was stimulated by cAMP or cortisol. The greatest inhibition of the aromatase activity was obtained with 1 nm melatonin, the same concentration that gives the highest antiproliferative and anti-invasive effects of MCF-7 cells. Finally, by RT-PCR, we found that melatonin downregulates aromatase expression at the transcriptional level in the MCF-7 cells. We conclude that melatonin, at physiological concentrations, decreases aromatase activity and expression in MCF-7 cells. This aromatase inhibitory effect of melatonin, together with its already known antiestrogenic properties interacting with the estrogen-receptor, makes this indoleamine an interesting tool to be considered in the prevention and treatment of hormone-dependent mammary neoplasias.

Keywords aromatase; breast cancer; MCF-7 cells; melatonin; pineal

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Cos S, Mediavilla D, Martı´nez-Campa C, et al. **Year** 2006

Authors Samuel Cos, Dolores Mediavilla, Carlos Martı´nez-Campa, Alicia Gonza´lez, Carolina Alonso-Gonza´lez, Emilio J. Sa´nchez-Barcelo´*

Report Name Exposure to light-at-night increases the growth of DMBA-induced mammary adenocarcinomas in rats

Publication Cancer Letters

Issue-page numbers 235 (2006) 266-271

URL http://www.unican.es/NR/rdonlyres/14A82410-77A0-44C2-9FFF-6B65FFD1C912/0/18ExposuretolightatnightincreasesthegrowthofDMBA.pdf

Abstract In order to assess whether light exposure at night influences the growth of mammary tumors, as well as the role of melatonin in this process, female rats bearing DMBA-induced mammary adenocarcinomas were exposed to different lighting environments. Animals exposed to light-at-night, especially those under a constant dim light during the darkness phase, showed: (a) significantly higher rates of tumor growth as well as lower survival than controls, (b) higher concentration of serum estradiol, and (c) lower nocturnal excretion of 6-sulfatoxymelatonin, without there being differences between nocturnal and diurnal levels. These results suggest that circadian and endocrine disruption induced by light pollution, could induce the growth of mammary tumors.

Keywords light at night, tumor growth

Cos S, Mediavilla MD, Fernández R et al. **Year** 2002

Authors Samuel Cos, Maria Dolores Mediavilla, Rosario Fernández, Domingo González-Lamuño, Emilio J. Sánchez-Barceló

Report Name Does melatonin induce apoptosis in MCF-7 human breast cancer cells in vitro?

Publication J Pineal Res

Issue-page numbers 32:90–96 doi:10.1034/j.1600-079x.2002.1821.x.PMID:12071473

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079x.2002.1821.x/abstract?

Abstract Melatonin inhibits proliferation of the estrogen-responsive MCF-7 human breast cancer cells. The objective of this work was to assess whether melatonin not only regulates MCF-7 cell proliferation but also induces apoptosis. In this experiment we used 1,25-dihydroxycholecalciferol (D3) as a positive control because it inhibits MCF-7 cell proliferation and induces apoptosis. MCF-7 cells were cultured with either 1 nM melatonin, 100 nM D3 or its diluent to determine their effects on cell proliferation, cell viability, cell-cycle phase distribution, population of apoptotic cells, and expression of p53, p21WAF1, bcl-2, bcl-XL and bax proteins. After 24 or 48 hr of incubation, both melatonin and D3-treatment significantly decreased the number of viable cells in relation to the controls, although no differences in cell viability were observed between the treatments. The incidence of apoptosis, measured as the population of cells falling in the sub-G1 region of the DNA histogram, or by the TUNEL reaction, was similar in melatonin-treated and control cells whereas, as expected, apoptosis was higher among cells treated with D3 than in controls. The expression of p53 and p21WAF1 proteins significantly increased after 24 or 48 hr of incubation with either melatonin or D3. No significant changes in bcl-2, bcl-XL and bax mRNAs were detected after treatment with melatonin whereas in D3-treated cells, a significant drop in bcl-XL was observed. These data support the hypothesis that melatonin reduces MCF-7 cell proliferation by modulating cell-cycle length through the control of the p53–p21 pathway, but without clearly inducing apoptosis.

Keywords

Cos S, Sánchez-Barceló EJ **Year** 1995

Authors Cos S, Sánchez-Barceló EJ

Report Name Melatonin inhibition of MCF-7 human breast-cancer cells growth: influence of cell proliferation rate.

Publication Cancer Lett

Issue-page numbers 93:207–212 doi:10.1016/0304-3835(95)03811-A. PMID:7621430

URL http://www.sciencedirect.com/science/article/pii/030438359503811A

Abstract We have studied whether the cell proliferation rate modifies the inhibitory actions of melatonin on MCF-7 cell growth. The proliferative rate of cells was altered by plating them at different densities (5 × 104 to 100 × 104 cells/dish) in media with low charcoal-stripped serum concentrations. In this way, population doubling time ranged from 33 h (for density = 100 × 104 cells/dish) to 75 h (for density = 5 × 104 cells/dish). Melatonin (10−9M) only inhibited fast proliferating MCF-7 cells, increasing their cell doubling time, and did not significantly modify the length of doubling time in the cultures with low proliferation rate, in which doubling time was already long. These data clearly show that there is a direct relation between proliferative rate of cells and melatonin inhibitory actions on MCF-7 cells.

Keywords Melatonin; Pineal gland; MCF-7 cell; Cell growth; Breast cancer

Costa G

Year 2010

Authors Costa G.

Report Name [Shift work and breast cancer]

Publication G Ital Med Lav Ergon

Issue-page numbers Oct-Dec;32(4):454-7

URL http://www.ncbi.nlm.nih.gov/pubmed/21086703

Abstract The International Agency on Research on Cancer (IARC) has recently classified "shiftwork that involves circadian disruption" as "probably carcinogenic to humans" (Group 2A) on the basis of "limited evidence in humans for the carcinogenicity of shift-work that involves nightwork", and "sufficient evidence in experimental animals for the carcinogenicity of light during the daily dark period (biological night)". The epidemiologic evidence of a relationship between shift and night work and breast cancer in women is based upon nine studies, six of which suggest a moderately increased risk to develop breast cancer after prolonged exposure to shift and night work. The aim of this paper is to summarize the possible physio-pathological mechanisms (internal disruption of biological circadian rhythms and clock genes, melatonin suppression through light by night, sleep deprivation) and the problems connected with a proper risk assessment of the risk for breast cancer risk in women shift workers.

Keywords

Costa G

Year 1996

Authors Costa G

Report Name The impact of shift and night work on health

Publication Appl Ergon

Issue-page numbers 27:9–16 doi:10.1016/0003-6870(95)00047-X. PMID:15676307

URL http://www.ncbi.nlm.nih.gov/pubmed/15676307

Abstract Shift work, in particular night work, can have a negative impact on health and well-being of workers as it can cause: (a) disturbances of the normal circadian rhythms of the psychophysiological functions, beginning with the sleep/wake cycle; (b) interferences with work performance and efficiency over the 24 hour span, with consequent errors and accidents; (c) difficulties in maintaining the usual relationships both at family and social level, with consequent negative influences on marital relations, care of children and social contacts; (d) deterioration of health that can be manifested in disturbances of sleeping and eating habits and, in the long run, in more severe disorders that deal prevalently with the gastrointestinal (colitis, gastroduodenitis and peptic ulcer), neuro-psychic (chronic fatigue, anxiety, depression) and, probably, cardiovascular (hypertension, ischemic heart diseases) functions. Besides, shift and night work may have more specific adverse effects on women's health both in relation to their particular hormonal and reproductive function, and their family roles. It has been estimated that about 20% of all workers have to leave shift work in a very short time because of serious disturbances; those remaining in shift work show different levels of (mal)adaptation and (in)tolerance, that can become more or less manifest in different times, and with different intensity. In fact, the effects of such stress condition can vary widely among the shift workers in relation to many 'intervening variables' concerning both individual factors (e.g. age, personality traits, physiological characteristics), as well as working situations (e.g. work loads, shift schedules) and social conditions (e.g. number and age of children, housing, commuting).

Keywords

Costa G

Year 2003

Authors Giovanni Costa

Report Name Factors influencing health of workers and tolerance to shift work

Publication Theor Issues Ergon Sci

Issue-page numbers 4:263–288 doi:10.1080/14639220210158880

URL http://www.tandfonline.com/doi/abs/10.1080/14639220210158880

Abstract Shift and night work are a well recognized risk factors for health and well-being, but the outcomes are not always in agreement and sometimes contradictory, due to both different working and living conditions of the groups examined, and to different approaches and methods used. Moreover, variations in historical and epidemiological relevance of the disorders, health perception and surveillance, as well as combined effects with other individual and social risk factors make the problem multifaceted and difficult to interpret properly. Consequently, also tolerance to shift and night work is a complex phenomenon, related to several aspects pertaining to different domains, dealing with personal characteristics and coping strategies, family and social conditions, working situations and, particularly, working hours organization. The result of their interactions depends not only on the specific load of each factor, but also on their temporal occurrence and duration in the worker's life. Thus, it is necessary to clarify as much as possible the interactions among individual aspects, social conditions and work organization, for an effective promotion of shift workers' health and well-being. The aim of the paper is to review the main factors that can intervene on such aspects trying to present 'lights and shadows' on this context.

Keywords

Costa G, Akerstedt T, Nachreiner F et al. **Year** 2004

Authors Giovanni Costa, Torbjorn Åkerstedt, Friedhelm Nachreiner, Federica Baltieri, José Carvalhais, Simon Folkard, Monique Frings Dresen, Charles Gadbois, Johannes Gartner, et al

Report Name Flexible working hours, health, and well-being in Europe: some considerations from a SALTSA project

Publication Chronobiol Int

Issue-page numbers 21:831–844 doi:10.1081/CBI-200035935. PMID:15646231

URL http://informahealthcare.com/doi/abs/10.1081/CBI-200035935?journalCode=cbi

Abstract The project brought together researchers from 9 EU-Countries and resulted in a number of actions, in particular the following: (a) There is an urgent need of defining the concept of flexible working hours, since it has been used in many different and even counterintuitive ways; the most obvious distinction is where the influence over the working hours lies, that is between the “company-based flexibility” and the “individual-oriented flexibility”; (b) The review of the Legislation in force in the 15 European countries shows that the regulation of working times is quite extensive and covers (Council Directive 93/104/EC) almost all the various arrangements of working hours (i.e., part-time, overtime, shift, and night work), but fails to provide for flexibility; (c) According to the data of the Third EU Survey on Working Conditions, longer and “irregular” working hours are in general linked to lower levels of health and well-being; moreover, low (individual) flexibility and high variability of working hours (i.e., company-based flexibility) were consistently associated with poor health and well-being, while low variability combined with high autonomy showed positive effects; (d) Six substudies from different countries demonstrated that flexible working hours vary according to country, economic sector, social status, and gender; overtime is the most frequent form of company-based flexibility but has negative effects on stress, sleep, and social and mental health; individual flexibility alleviates the negative effects of the company-based flexibility on subjective health, safety, and social well-being; (e) The literature review was able to list more than 1,000 references, but it was striking that most of these documents were mainly argumentative with very little empirical data. Thus, one may conclude that there is a large-scale intervention ongoing in our society with almost completely unknown and uncontrolled effects. Consequently, there is a strong need for systematic research and well-controlled actions in order to examine in detail what flexible working hours are considered, what and where are their positive effects, in particular, as concerns autonomy, and what regulation seem most reasonable.

Keywords Flexible working hours, Health, Well-being, Shift work, Work flexibility

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Costa G, Ghirlanda G, Minors DS, Waterhouse JM **Year** 1993

Authors G Costa, G Ghirlanda, D S Minors, J M Waterhouse

Report Name Effect of bright light on tolerance to night work

Publication Scandinavian journal of work environment health (1993)

Issue-page numbers

URL http://www.mendeley.com/research/effect-bright-light-tolerance-night-work/

Abstract Fifteen young (mean age 23.4 years) female nurses engaged in a resuscitation unit and working on a fast rotating shift schedule comprising two consecutive night shifts were exposed to short periods (4 x 20 min) of bright light (2350 lx) during their night duty to test a possible positive effect on their tolerance to night work. Two nights with normal lighting (20-380 lx) and two nights with bright light were compared. The following positive effects of bright light upon psychophysical conditions and performance efficiency were noted: in particular, signs of better physical fitness; less tiredness and sleepiness; a more balanced sleep pattern; and higher performance efficiency (letter cancellation test). This result could not be attributed to shifts of the internal clock although the exact cause remains to be determined. In fact, hormonal excretion and body temperature did not show any effect from bright light. In addition melatonin excretion was not suppressed appreciably by the bright light used.

Keywords

Costa G, Haus E, Stevens R

Year 2010

Authors Costa G, Haus E, Stevens R.

Report Name Shift work and cancer - considerations on rationale, mechanisms, and epidemiology

Publication Scand J Work Environ Health

Issue-page numbers 2010 Mar;36(2):163-79. Epub 2010 Feb 2.

URL http://www.ncbi.nlm.nih.gov/pubmed/20126969

Abstract This paper summarizes the rationale for, possible mechanisms of, and problems related to risk assessment of the association between shift work and cancer. The mechanisms by which circadian disruption may favor the induction and/or promotion of malignant tumors are complex and multifactorial. The multilevel endocrine changes caused by circadian disruption with melatonin suppression through light at night (LAN) lead to the oncogenic targeting of the endocrine-responsive breast in women and possibly the prostate in men. Repeated phase shifting with internal desynchronization may lead to defects in the regulation of the circadian cell cycle, thus favoring uncontrolled growth. Sleep deprivation leads to the suppression of immune surveillance that may permit the establishment and/or growth of malignant clones. The epidemiological studies published so far, although dealing with large cohorts and controlling for several personal confounders, have defined the exposure to shift and/or night work rather loosely and consequently do not allow for the proper assessment of the risk connected with circadian disruption.

Keywords

Costa G, Lievore F, Casaletti G et al.

Year 1989

Authors Costa G, Lievore F, Casaletti G et al.

Report Name Circadian characteristics influencing interindividual differences in tolerance and adjustment to shiftwork

Publication Ergonomics

Issue-page numbers 32:373–385 doi:10.1080/00140138908966104. PMID:2753014

URL http://www.ncbi.nlm.nih.gov/pubmed/2753014

Abstract The study was carried out to evaluate whether shiftworkers showing different long-term tolerance to shiftwork differ in their circadian adjustments and/or in some behavioural characteristics. Three groups of eight workers, engaged on three shifts in a graphic plant and matched for age and work experience, were selected according to the presence or not of complaints related to shiftwork: (1) no complaints; (2) nervous complaints (anxiety/depression, severe sleep disturbances); (3) digestive disorders (gastroduodenitis, peptic ulcer). They answered questionnaires on family conditions, health status, rigidity of sleeping habits, ability to overcome drowsiness, morningness, manifest anxiety. They also recorded several physiological parameters (oral temperature, grip strength, peak expiratory flow rate, pulse rate, sleep hours) during day and night-shifts. The data obtained indicate that the characteristics of flexibility of sleeping habits, ability to overcome drowsiness, and lower manifest anxiety, are associated with better tolerance to shiftwork. These characteristics do not seem to influence the adjustment of the circadian rhythm of oral temperature passing from day to night-shifts and vice versa. Conversely, morningness appeared to be unrelated to long-term tolerance, but did influence circadian adjustments and sleep behaviour. Among the groups, the subjects with digestive disorders showed a greater phase shift and a reduction of the amplitude on night-work, suggesting a possible relationship also between the short-term circadian adjustment and the long-term tolerance to shiftwork, as pointed out by other authors.

Keywords

Authors Ana Coto-Montes, Jose Antonio Boga, Sergio Rosales-Corral, Lorena Fuentes-Broto, Dun-Xian Tan, Russel J. Reiter

Report Name Role of melatonin in the regulation of autophagy and mitophagy: A review

Publication Molecular and Cellular Endocrinology

Issue-page numbers Volume 361, Issues 1–2, 25 September 2012, Pages 12–23

URL http://www.sciencedirect.com/science/article/pii/S0303720712002626

Abstract Oxidative stress plays an essential role in triggering many cellular processes including programmed cell death. Proving a relationship between apoptosis and reactive oxygen species has been the goal of numerous studies. Accumulating data point to an essential role for oxidative stress in the activation of autophagy. The term autophagy encompasses several processes including not only survival or death mechanisms, but also pexophagy, mitophagy, ER-phagy or ribophagy, depending of which organelles are targeted for specific autophagic degradation. However, whether the outcome of autophagy is survival or death and whether the initiating conditions are starvation, pathogens or death receptors, reactive oxygen species are invariably involved. The role of antioxidants in the regulation of these processes, however, has been sparingly investigated. Among the known antioxidants, melatonin has high efficacy and, in both experimental and clinical situations, its protective actions against oxidative stress are well documented. Beneficial effects against mitochondrial dysfunction have also been described for melatonin; thus, this indoleamine seems to be linked to mitophagy. The present review focuses on data and the most recent advances related to the role of melatonin in health and disease, on autophagy activation in general, and on mitophagy in particular.

Keywords

Cournot M, Ruidavets JB, Marquié JC et al. **Year** 2004

Authors Maxime Cournota, Jean-Bernard Ruidavetsa, Jean-Claude Marquiéb, Yolande Esquirolc, Bruno Baracatb, Jean Ferrièeres

Report Name Environmental factors associated with body mass index in a population of Southern France.

Publication Eur J Cardiovasc Prev Rehabil

Issue-page numbers 11:291–297. PMID:15292762 doi:10.1097/01.hjr.0000129738.22970.62

URL http://cpr.sagepub.com/content/11/4/291.abstract

Abstract Study objective Environmental-factor changes may largely be accountable for the dramatic increase of obesity prevalence in industrialized countries. This study investigated the relationships between body mass index (BMI) and various socioeconomic, clinical, behavioural and reproductive factors in a population from Southern France.

Methods Using a cross-sectional study, a sample of 3127 current and former salaried workers (1658 men and 1469 women) completed a questionnaire on personal and medical histories, and had a clinical examination including height and weight measurements. Age-adjusted and multiple linear regression analyses were performed.

Results The overall prevalence of obesity (BMI ≤ 30kg/m2) was 9.8% and was higher in men than in women (11.1 versus 8.3%). Multivariate analyses showed that in both sexes, low educational level, television watching, low physical activity and ex-smoking habits, were independently associated with a higher BMI. Furthermore, in women, we found independent and positive associations between BMI and the number of naps per week, short sleep duration, daily alcohol consumption, the number of pregnancies, early age at menarche or the non-use of oral contraceptives.

Conclusions Our results reveal the complexity that exists between BMI and environmental factors and stress the need to analyse and to handle these factors simultaneously.

Keywords body fatness, sleeping time, television watching, nap, age at menarche

Cowan CL **Year** 1992

Authors C. L. Cowan, Jr

Report Name Light hazards in the operating room

Publication J Natl Med Assoc

Issue-page numbers 1992 May; 84(5): 425–429.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2637703/

Abstract The use of high-intensity illumination devices is routine for many ophthalmic diagnostic and therapeutic procedures. However, the exposure of patients to high-level photic energy may be damaging even in the absence of visible abnormalities. Devices such as the operating microscope, indirect ophthalmoscope, and endoilluminator are capable of irradiances sufficient to cause retinal damage and should be used with a degree of restraint that reflects a recognition of their potential for phototoxicity.

Keywords

Cox GL

Year 1929

Authors G. Lissant Cox

Report Name Artificial light treatment at tuberculosis dispensaries for non- pulmonary tuberculosis

Publication British Journal of Tuberculosis

Issue-page numbers Volume 23, Issue 1, January 1929, Pages 1-6

URL http://www.sciencedirect.com/science/article/pii/S0366085029800014

Abstract

Keywords

Cox GL

Year 1934

Authors G. Lissant Cox

Report Name Artificial light treatment at tuberculosis dispensaries

Publication British Journal of Tuberculosis

Issue-page numbers

URL http://www.sciencedirect.com/science/article/pii/S0366085034800361

Abstract N/A

Keywords

	Cox GL	***Year***	1930
Authors	G. Lissant Cox		
Report Name	RESULTS OF ARTIFICIAL LIGHT TREATMENT FOR TUBERCULOSIS.		
Publication	The Lancet		
Issue-page numbers	Volume 216, Issue 5582, 23 August 1930, Pages 422-425		
URL	http://www.sciencedirect.com/science/article/pii/S014067360109287X		
Abstract			
Keywords			

	Cripps DJ, Rankin J	***Year***	1973
Authors	Cripps DJ, Rankin J.		
Report Name	Action spectra of lupus erythematosus and experimental immunofluorescence		
Publication	Arch Dermatol		
Issue-page numbers	1973 Apr;107(4):563-7.		
URL	http://www.ncbi.nlm.nih.gov/pubmed/4572568		
Abstract	N/A		
Keywords			

Authors Cruickshanks KJ, Klein R, Klein BE, Nondahl DM.

Report Name Sunlight and the 5-year incidence of early agerelated maculopathy: the beaver dam eye study

Publication Arch Ophthalmol

Issue-page numbers 2001 Feb;119(2):246-50.

URL http://www.ncbi.nlm.nih.gov/pubmed/11176987

Abstract

OBJECTIVE:

To investigate the relation of sunlight exposure and indicators of sun sensitivity with the 5-year incidence of early age-related maculopathy (ARM).
DESIGN:

Longitudinal, population-based study. Participants (aged 43-86 years at baseline) in the Beaver Dam Eye Study were reexamined from 1993 to 1995, 5 years after the baseline examination. Questionnaire data about sunlight exposure and sun sensitivity were obtained at baseline. Additional information about earlier life patterns of exposure was ascertained at follow-up. Stereoscopic color fundus photographs were graded to determine the presence of ARM at the 5-year follow-up in eyes free from signs of early ARM at the baseline examination.
RESULTS:

Leisure time spent outdoors while persons were teenagers (aged 13-19 years) and in their 30s (aged 30-39 years) was significantly associated with the risk of early ARM (odds ratio, 2.09; 95% confidence interval, 1.19-3.65). There was a slight, but nonsignificant, protective effect associated with use of hats and sunglasses while persons were teenagers and in their 30s (odds ratio, 0.72; 95% confidence interval, 0.50-1.03). People with red or blond hair were slightly more likely to develop early ARM than people with darker hair (odds ratio, 1.33; 95% confidence interval, 0.97-1.83). There were no associations between estimated ambient UV-B exposure or markers of sun sensitivity and the incidence of early ARM.
CONCLUSION:

Exposure to sunlight may be associated with the development of early ARM.

Keywords

Cullen AP

Year 2002

Authors Anthony P. Cullen

Report Name Photokeratitis and other phototoxic effects on the cornea and conjunctiva

Publication International Journal of Toxicology

Issue-page numbers November 2002 vol. 21 no. 6 455-464

URL http://ijt.sagepub.com/content/21/6/455

Abstract Except when sleeping, the cornea and interpalpebral conjunctiva are exposed to the ambient environment, both natural and man-made. Levels of solar ultraviolet irradiance reaching the eye may exceed the damage threshold under a number of circumstances. The consequences of overexposure may be acute after a latent period, sequelae to an acute exposure, or long-term chronic effects. Previously derived action spectra for photokeratitis and photoconjunctivitis due to incoherent ultraviolet are presented. These reveal interspecies similarities for the levels of radiant energy reaching each tissue. The initial in vivo (clinical) signs of photokeratitis are due to lost or damaged epithelial cells with other signs produced by this primary response. The conjunctival signs include injection and chemosis. Chronic exposure to solar ultraviolet is a factor in climatic droplet keratopathy and pterygium. Phototoxic compounds or their by-products potentially can reach the cornea from the air, via the tears or aqueous humor, or from the limbal capillaries. However, the human cornea appears to be much less susceptible to the influence of phototoxic agents than the skin.

Keywords Action Spectrum, Conjunctiva, Cornea, Droplet Keratopathy, Photoconjunctivitis, Photokeratitis, Phototoxicity, Pterygium, Ultraviolet Radiation

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Curie T, Franken P

Year 2012

Authors Thomas Curie and Paul Franken

Report Name Circadian Clock Genes and the Regulation of Sleep

Publication Sleep Loss and Obesity

Issue-page numbers 2012, 1-12, DOI: 10.1007/978-1-4614-3492-4_1

URL http://www.springerlink.com/content/h56199763164wr56/

Abstract Sleep and waking are controlled by opposing interactions between circadian and homeostatic processes. A circadian process generated by the suprachiasmatic nucleus determines when sleep should occur, while a homeostatic process keeps track of time spent awake and asleep and signals sleep need or sleep propensity. Recent evidence indicates that these two processes employ many of the same set of genes. Herein, we review the basic concepts of the circadian and homeostatic regulation of sleep, and then outline the molecular components of circadian clock. We then discuss the evidence demonstrating a role of clock genes in sleep homeostasis in flies, mice, and humans. We conclude by suggesting that clock genes might be crucial for integrating homeostatic need, not only that of sleep but also of food intake and energy metabolism.

Keywords

Currier NL, Sun LZ-Y, Miller SC **Year** 2000

Authors Currier NL, Sun LZ-Y, Miller SC

Report Name Exogenous melatonin: quantitative enhancement in vivo of cells mediating non-specific immunity.

Publication J Neuroimmunol

Issue-page numbers 104:101–108 doi:10.1016/S0165-5728(99)00271-4. PMID:10713348

URL http://www.jni-journal.com/article/S0165-5728%2899%2900271-4/abstract

Abstract Melatonin (MLT), a biogenic indoleamine and neuromodulator produced by the pineal gland, is known to activate T helper cells by means of direct binding to melatonin receptors on both Th1 and Th2 cells. The present in vivo study aimed to investigate the effect of exogenously administered MLT on the hemopoietic and immune cell populations of the bone marrow and spleen in healthy, young adult male mice at two distinct MLT exposure intervals. The neurohormone, administered daily through the diet (7–14 days), was homogenized into finely ground chow. Control mice received ground chow without MLT. The results revealed cell lineage-specific, quantitative, MLT exposure-time-dependent changes in both the bone marrow and spleen. NK cells and monocytes (both components of the non-specific immune system functioning as the first line of defense against neoplasia and virus infected cells) were significantly increased in the bone marrow by both 7 and 14 days of dietary melatonin. The quantitative increment in these two cell populations, in the organ of their production, i.e. the bone marrow, indicates that new cell proliferation/production may have been stimulated by MLT. In the spleen, as in the bone marrow, NK cell levels remained significantly elevated at both 7 and 14 days after melatonin exposure. However, the number of monocytes in the spleen did not maintain, at day 14 of MLT exposure, the high levels observed after 7 days of MLT, in spite of their sustained, high numbers at 14 days in the bone marrow. This suggests that the progeny of the apparently increased monocyte production in the bone marrow (elevated absolute numbers therein), had localized in anatomical sites (other than the spleen) also common to these cells. Thus, the selective, positive influences of in vivo administered, exogenous melatonin on cells mediating non-specific immunity suggests a plausible mechanism for numerous claims that it is responsible for tumor amelioration in patients.

Keywords Hemopoiesis, Melatonin, Monocytes, NK cells

Cutando A, LÓpez-Valverde A, Arias-Santiago S, et al. **Year** 2012

Authors ANTONIO CUTANDO, ANTONIO LÓPEZ-VALVERDE, SALVADOR ARIAS-SANTIAGO, JOAQUIN DE VICENTE and RAFAEL GÓMEZ DE DIEGO

Report Name Role of Melatonin in Cancer Treatment

Publication Anticancer Research

Issue-page numbers July 2012 vol. 32 no. 7 2747-2753

URL http://ar.iiarjournals.org/content/32/7/2747.abstract

Abstract Melatonin has revealed itself to be a pleiotropic and multitasking molecule. The mechanisms that control its synthesis and the biological clock processes that modulate the circadian production of melatonin in the pineal gland have been well-characterized. A feature that characterizes melatonin is the variety of mechanisms it employs to modulate the physiology and molecular biology of cells. Research has implicated the pineal gland and melatonin in the processes of both aging and age-related diseases. The decline in the production of melatonin with age is thought to contribute to immunosenescence and potential development of neoplastic diseases. Melatonin has been shown to inhibit growth of different tumors under both in vitro and in vivo conditions. There is evidence that the administration of melatonin alone or in combination with interleukin-2 in conjunction with chemoradiotherapy and/or supportive care in cancer patients with advanced solid tumors, has been associated with improved outcomes of tumor regression and survival. Moreover, chemotherapy has been shown to be better tolerated in patients treated with melatonin.

Keywords Melatonin, melatonin receptors, immune mechanisms, cancer

Czeisler CA, Allan JS, Strogatz SH, et al. **Year** 1986

Authors CA Czeisler, JS Allan, SH Strogatz, JM Ronda, R Sanchez, CD Rios, WO Freitag, GS Richardson and RE Kronauer

Report Name Bright light resets the human circadian pacemaker independent of the timing of the sleep-wake cycle

Publication Science

Issue-page numbers 8 August 1986: Vol. 233 no. 4764 pp. 667-671

URL http://www.sciencemag.org/content/233/4764/667.abstract

Abstract Human circadian rhythms were once thought to be insensitive to light, with synchronization to the 24-hour day accomplished either through social contacts or the sleep-wake schedule. Yet the demonstration of an intensity-dependent neuroendocrine response to bright light has led to renewed consideration of light as a possible synchronizer of the human circadian pacemaker. In a laboratory study, the output of the circadian pacemaker of an elderly woman was monitored before and after exposure to 4 hours of bright light for seven consecutive evenings, and before and after a control study in ordinary room light while her sleep-wake schedule and social contacts remained unchanged. The exposure to bright light in the evening induced a 6-hour delay shift of her circadian pacemaker, as indicated by recordings of body temperature and cortisol secretion. The unexpected magnitude, rapidity, and stability of the shift challenge existing concepts regarding circadian phase-resetting capacity in man and suggest that exposure to bright light can indeed reset the human circadian pacemaker, which controls daily variations in physiologic, behavioral, and cognitive function.

Keywords circadian, light at night

Czeisler CA, Gooley JJ **Year** 2007

Authors Czeisler CA, Gooley JJ.

Report Name Sleep and circadian rhythms in humans.

Publication Cold Spring Harb Symp Quant Biol

Issue-page numbers 2007;72:579-97.

URL http://www.ncbi.nlm.nih.gov/pubmed/18419318

Abstract During the past 50 years, converging evidence reveals that the fundamental properties of the human circadian system are shared in common with those of other organisms. Concurrent data from multiple physiological rhythms in humans revealed that under some conditions, rhythms oscillated at different periods within the same individuals and led to the conclusion 30 years ago that the human circadian system was composed of multiple oscillators organized hierarchically; this inference has recently been confirmed using molecular techniques in species ranging from unicellular marine organisms to mammals. Although humans were once thought to be insensitive to the resetting effects of light, light is now recognized as the principal circadian synchronizer in humans, capable of eliciting weak (Type 1) or strong (Type 0) resetting, depending on stimulus strength and timing. Realization that circadian photoreception could be maintained in the absence of sight was first recognized in blind humans, as was the property of adaptation of the sensitivity of circadian photoreception to prior light history. In sighted humans, the intrinsic circadian period is very tightly distributed around approximately 24.2 hours and exhibits aftereffects of prior entrainment. Phase angle of entrainment is dependent on circadian period, at least in young adults. Circadian pacemakers in humans drive daily variations in many physiologic and behavioral variables, including circadian rhythms in alertness and sleep propensity. Under entrained conditions, these rhythms interact with homeostatic regulation of the sleep/wake cycle to determine the ability to sustain vigilance during the day and to sleep at night. Quantitative understanding of the fundamental properties of the multioscillator circadian system in humans and their interaction with sleep/wake homeostasis has many applications to health and disease, including the development of treatments for circadian rhythm and sleep disorders.

Keywords

Authors Charles A. Czeisler, Michael P. Johnson, Jeanne F. Duffy, Emery N. Brown, Joseph M. Ronda, and Richard E. Kronauer

Report Name Exposure to bright light and darkness to treat physiologic maladaptation to night work

Publication N Engl J Med

Issue-page numbers 1990; 322:1253–9

URL http://www.nejm.org/doi/full/10.1056/NEJM199005033221801

Abstract

Working at night results in a misalignment between the sleep–wake cycle and the output of the hypothalamic pacemaker that regulates the circadian rhythms of certain physiologic and behavioral variables. We evaluated whether such physiologic maladaptation to nighttime work could be prevented effectively by a treatment regimen of exposure to bright light during the night and darkness during the day. We assessed the functioning of the circadian pacemaker in five control and five treatment studies in order to assess the extent of adaptation in eight normal young men to a week of night work.

In the control studies, on the sixth consecutive night of sedentary work in ordinary light (approximately 150 lux), the mean (±SEM) nadir of the endogenous temperature cycle continued to occur during the night (at 03:31 ±0:56 hours), indicating a lack of circadian adaptation to the nighttime work schedule. In contrast, the subjects in the treatment studies were exposed to bright light (7000 to 12,000 lux) at night and to nearly complete darkness during the day, and the temperature nadir shifted after four days of treatment to a significantly later, midafternoon hour (14:53±0:32; $P<0.0001$), indicating a successful circadian adaptation to daytime sleep and nighttime work. There were concomitant shifts in the 24-hour patterns of plasma cortisol concentration, urinary excretion rate, subjective assessment of alertness, and cognitive performance in the treatment studies. These shifts resulted in a significant improvement in both alertness and cognitive performance in the treatment group during the night-shift hours.

We conclude that maladaptation of the human circadian system to night work, with its associated decline in alertness, performance, and quality of daytime sleep, can be treated effectively with scheduled exposure to bright light at night and darkness during the day.

Keywords

Czeisler CA, Klerman EB

Year 1999

Authors Czeisler CA, Klerman EB

Report Name Circadian and sleep-dependent regulation of hormone release in humans.

Publication Recent Prog Horm Res

Issue-page numbers 54:97–130, discussion 130–132. PMID:10548874

URL http://www.ncbi.nlm.nih.gov/pubmed/10548874

Abstract Daily oscillations characterize the release of nearly every hormone. The circadian pacemaker, located in the suprachiasmatic nucleus of the hypothalamus, generates circadian, approximately 24-hour rhythms in many physiologic functions. However, the observed hormonal oscillations do not simply reflect the output of this internal clock. Instead, daily hormonal profiles are the product of a complex interaction between the output of the circadian pacemaker, periodic changes in behavior, light exposure, neuroendocrine feedback mechanisms, gender, age, and the timing of sleep and wakefulness. The interaction of these factors can affect hormonal secretory pulse frequency and amplitude, with each endocrine system differentially affected by these factors. This chapter examines recent advances in understanding the effects on endocrine rhythms of a number of these factors. Sleep exerts a profound effect on endocrine secretion. Sleep is a dynamic process that is characterized by periodic changes in electrophysiologic activity. These electrophysiologic changes, which are used to mark the state and depth of sleep, are associated with periodic, short-term variations in hormonal levels. The secretion of hormones such as renin and human growth hormone are strongly influenced by sleep or wake state, while melatonin and cortisol levels are relatively unaffected by sleep or wake state. In addition, sleep is associated with changes in posture, behavior, and light exposure, each of which is known to affect endocrine secretion. Furthermore, the tight concordance of habitual sleep and wake times with certain circadian phases has made it difficult to distinguish sleep and circadian effects on these hormones. Specific protocols, designed to extract circadian and sleep information semi-independently, have been developed and have yielded important insights into the effects of these regulatory processes. These results may help to account for changes in endocrine rhythms observed in circadian rhythm sleep disorders, including the dyssomnia of shift work and visual impairment. Yet to be fully investigated are the interactions of these factors with age and gender. Characterization of the factors governing hormone secretion is critical to understanding the temporal regulation of endocrine systems and presents many exciting areas for future research.

Keywords

Czeisler CA, Wright KP Jr

Year 1999

Authors Czeisler CA, Wright KP Jr

Report Name Influence of light on circadian rhythmicity in humans

Publication Neurobiology of Sleep and Circadian Rhythms

Issue-page numbers Marcel Decker, Inc: New York.

URL N/A

Abstract N/A

Keywords

Dacey DM, Liao J, Peterson BB, et al. **Year** 2005

Authors Dennis M. Dacey, Hsi-Wen Liao, Beth B. Peterson, Farrel R. Robinson, Vivianne C. Smith, Joel Pokorny, King-Wai Yau & Paul D. Gamlin

Report Name Melanopsin-expressing ganglion cells in primate retina signal colour and irradiance and project to the LGN

Publication Nature

Issue-page numbers 433, 749-754 (17 February 2005)

URL http://www.nature.com/nature/journal/v433/n7027/abs/nature03387.html?lang=en

Abstract

Human vision starts with the activation of rod photoreceptors in dim light and short (S)-, medium (M)-, and long (L)- wavelength-sensitive cone photoreceptors in daylight. Recently a parallel, non-rod, non-cone photoreceptive pathway, arising from a population of retinal ganglion cells, was discovered in nocturnal rodents1. These ganglion cells express the putative photopigment melanopsin and by signalling gross changes in light intensity serve the subconscious, 'non-image-forming' functions of circadian photoentrainment and pupil constriction1, 2, 3, 4, 5, 6, 7. Here we show an anatomically distinct population of 'giant', melanopsin-expressing ganglion cells in the primate retina that, in addition to being intrinsically photosensitive, are strongly activated by rods and cones, and display a rare, S-Off, (L + M)-On type of colour-opponent receptive field. The intrinsic, rod and (L + M) cone-derived light responses combine in these giant cells to signal irradiance over the full dynamic range of human vision. In accordance with cone-based colour opponency, the giant cells project to the lateral geniculate nucleus, the thalamic relay to primary visual cortex. Thus, in the diurnal trichromatic primate, 'non-image-forming' and conventional 'image-forming' retinal pathways are merged, and the melanopsin-based signal might contribute to conscious visual perception.

Keywords

Authors Dallman MF, Strack AM, Akana SF et al.

Report Name Feast and famine: critical role of glucocorticoids with insulin in daily energy flow.

Publication Front Neuroendocrinol

Issue-page numbers 14:303–347 doi:10.1006/frne.1993.1010. PMID:8258378

URL http://www.sciencedirect.com/science/article/pii/S0091302283710101

Abstract The hypothesis proposed in this review is that normal diurnal rhythms in the hypothalamic-pituitary-adrenal (HPA) axis are highly regulated by activity in medial hypothalamic nuclei to effect an interaction between corticosteroids and insulin such that optimal metabolism results in response to changes in the fed or fasted state of the animal. There are marked diurnal rhythms in function of the HPA axis under both basal and stress conditions. The HPA axis controls corticosteroid output from the adrenal and, in turn, forward elements of this axis are inhibited by feedback from circulating plasma corticosteroid levels. Basal activity in the HPA axis of mammals fed ad lib peaks about 2 h before the peak of the diurnal feeding rhythm, and is controlled by input from the suprachiasmatic nuclei. The rhythm in stress responsiveness is lowest at the time of the basal peak and highest at the time of the basal trough in the HPA axis activity. There are also diurnal rhythms in corticosteroid feedback sensitivity of basal and stress-induced ACTH secretion which peak at the time of the basal trough. These rhythms are all overridden when feeding, and thus insulin secretion, is disrupted. Corticosteroids interact with insulin on food intake and body composition, and curticosteroids also increase insulin secretion. Corticosteroids stimulate feeding at low doses but inhibit it at high doses; however, it is the high levels of insulin, induced by high levels of corticosteroids, that may inhibit feeding. The effects of corticosteroids on liver, fat, and muscle cell metabolism, with emphasis on their interactions with insulin, are briefly reviewed. Corticosteroids both synergize with and antagonize the effects of insulin. The effects of stress hormones, and their interactions with insulin on lipid and protein metabolism, followed by some of the metabolic effects of injury stress, with or without nutritional support, are evaluated. In the presence of elevated insulin stimulated by glucocorticoids and nutrition, stress causes less severe catabolic effects. In the central nervous system, regulation of function in the HPA axis is clearly affected by the activity of medial hypothalamic nuclei that also alter feeding, metabolism, and obesity in rats. Lesions of the arcuate (ARC) and ventromedial (VMN) paraventricular (PVN) nuclei result in obesity and hyperactivity in the HPA axis. Moreover, adrenalectomy inhibits or prevents development of the lesion-induced obesity. There are interactions among these nuclei; one mode of communication is via inputs of neuropeptide Y (NPY) cells in the ARC to the VMN, dorsomedial nuclei, and PVN. We suggest that these NPY-ergic pathways, the activity of which is increased by fasting, and reduced by feeding, insulin, and lack of glucocorticoids, may mediate the fasting-induced override of diurnal rhythms in the HPA axis. Supporting data are drawn from studies of diabetic rats and rodents with genetic obesities. We conclude that (a) There are marked interactions between glucocorticoids and insulin on most aspects of metabolism; (b) The NPY-ergic pathway from arcuate to paraventricular nuclei probably mediates fasting-induced alterations in hunger and the HPA axis activity; (c) modulation of NPY-ergic activity in the arcuate is mediated by glucocorticoids through stimulation of insulin secretion; insulin, in turn, inhibits NPY-ergic activity in the arcuate; (d) the interaction between corticosteroids and insulin serves as a peripheral hormonal feedback loop that regulates this NPY-ergic feeding-fasting system.

Keywords Neuropeptide Y—HPA axis—Rhythms—Metabolism—Arcuate—Ventromedial—Paraventricular—Suprachiasmatic Nuclei

Dardente H, Wyse CA, Birnie MJ, et al. **Year** 0

Authors Hugues Dardente, Cathy A. Wyse, Mike J. Birnie, Sandrine M. Dupré, Andrew S.I. Loudon, Gerald A. Lincoln, David G. Hazlerigg

Report Name A Molecular Switch for Photoperiod Responsiveness in Mammals

Publication Current Biology

Issue-page numbers Volume 20, Issue 24, 21 December 2010, Pages 2193-2198

URL http://www.sciencedirect.com/science/article/pii/S0960982210013655

Abstract Seasonal synchronization based on day length (photoperiod) allows organisms to anticipate environmental change. Photoperiodic decoding relies on circadian clocks, but the underlying molecular pathways have remained elusive [1]. In mammals and birds, photoperiodic responses depend crucially on expression of thyrotrophin β subunit RNA (TSHβ) in the pars tuberalis (PT) of the pituitary gland [[2] , [3] and [4]]. Now, using our well-characterized Soay sheep model [2], we describe a molecular switch governing TSHβ transcription through the circadian clock. Central to this is a conserved D element in the TSHβ promoter, controlled by the circadian transcription factor thyrotroph embryonic factor (Tef). In the PT, long-day exposure rapidly induces expression of the coactivator eyes absent 3 (Eya3), which synergizes with Tef to maximize TSHβ transcription. The pineal hormone melatonin, secreted nocturnally, sets the phase of rhythmic Eya3 expression in the PT to peak 12 hr after nightfall. Additionally, nocturnal melatonin levels directly suppress Eya3 expression. Together, these effects form a switch triggering a strong morning peak of Eya3 expression under long days. Species variability in the TSHβ D element influences sensitivity to TEF, reflecting species variability in photoperiodic responsiveness. Our findings define a molecular pathway linking the circadian clock to the evolution of seasonal timing in mammals.

Keywords

Das Gupta TK **Year** 1968

Authors Das Gupta TK

Report Name Influence of the pineal gland on the growth and spread of malignant tumors

Publication Surg Forum

Issue-page numbers 19:83–84. PMID:5752735

URL http://www.ncbi.nlm.nih.gov/pubmed/5752735

Abstract N/A

Keywords

Das Gupta TK, Terz J

Year 1967

Authors Taposh K. Das Gupta, and Jose Terz

Report Name Influence of pineal gland on the growth and spread of melanoma in the hamster

Publication Cancer Res

Issue-page numbers 27:1306–1311. PMID:4952523

URL http://cancerres.aacrjournals.org/content/27/7/1306

Abstract Pigmented malignant melanoma (M Mel No. 1) was transplanted into the subcutaneous tissue of the dorsum of control, sham-operated, and pinealectomized Syrian hamsters of both sexes and weighing between 80 and 110 gm. Animals from each group were sacrificed at regular intervals and autopsied. The pinealectomized group of hamsters had significantly larger primary tumors and more extensive metastases than the control or sham-operated animals at every phase of the study.

It is felt that these findings are possible indications of a relationship between the pineal gland and growth and spread of pigmented melanomata in hamsters.

Keywords

Dauchy EM, Dauchy RT, Davidson LK et al.

Year 2006

Authors Dauchy EM, Dauchy RT, Davidson LK et al.

Report Name Human cancer xenograft perfusion in situ in rats: a new perfusion system that minimizes delivery time and maintains normal tissue physiology and responsiveness to growth-inhil

Publication J Am Assoc Lab Anim Sci

Issue-page numbers 45:38–44. PMID:16642969

URL http://www.biomedsearch.com/nih/Human-cancer-xenograft-perfusion-in/16642969.html

Abstract We developed an artificial lung and catheter system for perfusing tissue-isolated tumors in situ that dramatically minimizes perfusate delivery time. Our investigations demonstrated that the circadian neurohormone melatonin (MLT), eicosapentaenoic acid (EPA), and conjugated linoleic acid (CLA) inhibit growth and metabolism in several rodent and human tumors. These anticancer agents function in a receptor-mediated manner to suppress tumor uptake of linoleic acid (LA), the principal tumor growth-promoting fatty acid, and its conversion to the mitogenic agent 13-hydroxyoctadecadienoic acid (13-HODE). Using this perfusion system and MCF-7 human breast xenografts, we examined the efficacy and timing of perfusate delivery to tumors. Tumors were perfused with rat donor blood to establish baseline LA uptake values; after 36 min of perfusion, we supplemented the perfusate with MLT, EPA, or CLA and collected arteriovenous whole-blood samples over 5-min intervals for a total perfusion period of 70 min. Arterial blood pH, pO2, and pCO2 (mean+/-33.7+/-1.9, and 59.8+/-1.9 mm Hg, respectively; none of these values varied during the perfusions. Tumor LA uptake and 13-HODE production were 1.06+/-0.28 microg/min/g and 1.38+/-0.02 ng/min/g, respectively, and were completely suppressed within 5 min after delivery of anticancer agents to the tissue. This new system provides rapid perfusate delivery for use with both normal and neoplastic tissues while maintaining normal physiologic tissue parameters.

Keywords

Dauchy RT, Blask DE, Sauer LA, et al. **Year** 1999

Authors Robert T Dauchy, David E Blask, Leonard A Sauer, George C Brainard, Jean A Krause

Report Name Dim light during darkness stimulates tumor progression by enhancing tumor fatty acid uptake and metabolism

Publication Cancer Letters

Issue-page numbers Volume 144, Issue 2 , Pages 131-136, 1 October 1999

URL http://www.cancerletters.info/article/S0304-3835%2899%2900207-4/abstract

Abstract Tumor linoleic acid uptake and metabolism, and growth are suppressed by melatonin, the synthesis of which is inhibited by light. Linoleic acid, via its mitogenic metabolite 13-hydroxyoctadecadienoic acid (13-HODE) is an important growth stimulant of rat hepatoma 7288CTC. Here we compared the effects of an alternating light:dark cycle (12L:12D), dim light (0.25 lux) present during the dark phase of a diurnal light cycle, and constant light on growth and fatty acid metabolism in hepatoma 7288CTC. Our results show that dim light suppressed melatonin release by the pineal gland, increased tumor linoleic acid uptake and 13-HODE production, and promoted tumor growth as effectively as did constant light.

Keywords Hepatoma, Light, Melatonin, Pineal, Linoleic acid

Dauchy RT, Dauchy EM, Davidson LK et al. **Year** 2007

Authors Dauchy RT, Dauchy EM, Davidson LK et al.

Report Name Inhibition of fatty acid transport and proliferative activity in tissue-isolated human squamous cell cancer xenografts perfused in situ with melatonin or eicosapentaenoic or conjuga

Publication Comp Med

Issue-page numbers 57:377–382. PMID:17803052

URL http://www.mendeley.com/research/inhibition-fatty-acid-transport-proliferative-activity-tissueisolated-human-squamous-cell-cancer-xenografts-perfused-situ-melatonin-eicosapent

Abstract Melatonin and eicosapentaenoic and 10t,12c-conjugated linoleic acids suppress the growth-stimulating effects of linoleic acid (LA) and its metabolism to the mitogenic agent 13-(S)-hydroxyoctadecadienoic acid (13-(S)-HODE) in established rodent tumors and human cancer xenografts. Here we compared the effects of these 3 inhibitory agents on growth and LA uptake and metabolism in human FaDu squamous cell carcinoma xenografts perfused in situ in male nude rats. Results demonstrated that these agents caused rapid inhibition of LA uptake, tumor cAMP content, 13-(S)-HODE formation, extracellular signal-regulated kinase p44/ p42 (ERK 1/2) activity, mitogen-activated protein kinase kinase (MEK) activity, and 3Hthymidine incorporation into tumor DNA. Melatonin's inhibitory effects were reversible with either the melatonin receptor antagonist S20928, pertussis toxin, forskolin, or 8-bromoadenosine-cAMP, suggesting that its growth-inhibitory effect occurs in vivo via a receptor-mediated, pertussis-toxin-sensitive pathway.

Keywords

Dauchy RT, Dauchy EM, Tirrell RP, et al. **Year** 2010

Authors Robert T Dauchy, Erin M Dauchy, Robert P Tirrell, Cody R Hill, Leslie K Davidson, Michael W Greene, Paul C Tirrell, Jinghai Wu, Leonard A Sauer, David E Blask

Report Name Dark-Phase Light Contamination Disrupts Circadian Rhythms in Plasma Measures of Endocrine Physiology and Metabolism in Rats

Publication Comp Med.

Issue-page numbers October; 60(5): 348–356.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2958202/

Abstract Dark-phase light contamination can significantly disrupt chronobiologic rhythms, thereby potentially altering the endocrine physiology and metabolism of experimental animals and influencing the outcome of scientific investigations. We sought to determine whether exposure to low-level light contamination during the dark phase influenced the normally entrained circadian rhythms of various substances in plasma. Male Sprague–Dawley rats (n = 6 per group) were housed in photobiologic light-exposure chambers configured to create 1) a 12:12-h light:dark cycle without dark-phase light contamination (control condition; 123 μW/cm2, lights on at 0600), 2) experimental exposure to a low level of light during the 12-h dark phase (with 0.02, 0.05, 0.06, or 0.08 μW/cm2 light at night), or 3) constant bright light (123 μW/cm2). Dietary and water intakes were recorded daily. After 2 wk, rats underwent 6 low-volume blood draws at 4-h intervals (beginning at 0400) during both the light and dark phases. Circadian rhythms in dietary and water intake and levels of plasma total fatty acids and lipid fractions remained entrained during exposure to either control conditions or low-intensity light during the dark phase. However, these patterns were disrupted in rats exposed to constant bright light. Circadian patterns of plasma melatonin, glucose, lactic acid, and corticosterone were maintained in all rats except those exposed to constant bright light or the highest level of light during the dark phase. Therefore even minimal light contamination during the dark phase can disrupt normal circadian rhythms of endocrine metabolism and physiology and may alter the outcome of scientific investigations.

Keywords FFA, free fatty acid; SCN, suprachiasmatic nuclei; TFA, total fatty acid

Dauchy RT, Dupepe, LM, Ooms TG, et al. **Year** 2011

Authors Dauchy, Robert T; Dupepe, Lynell M.; Ooms, Tara G.; Dauchy, Erin M.; Hill, Cody R.; Mao, Lulu; Belancio, Victoria P.; Slakey, Lauren M.; Hill, Steven M.; Blask, David E.

Report Name Eliminating Animal Facility Light-at-Night Contamination and Its Effect on Circadian Regulation of Rodent Physiology, Tumor Growth, and Metabolism: A Challenge in the Reloca

Publication Journal of the American Association for Laboratory Animal Science

Issue-page numbers Volume 50, Number 3, May 2011 , pp. 326-336(11)

URL http://www.ingentaconnect.com/content/aalas/jaalas/2011/00000050/00000003/art00005

Abstract Appropriate laboratory animal facility lighting and lighting protocols are essential for maintaining the health and wellbeing of laboratory animals and ensuring the credible outcome of scientific investigations. Our recent experience in relocating to a new laboratory facility illustrates the importance of these considerations. Previous studies in our laboratory demonstrated that animal room contamination with light-at-night (LAN) of as little as 0.2 lx at rodent eye level during an otherwise normal dark-phase disrupted host circadian rhythms and stimulated the metabolism and proliferation of human cancer xenografts in rats. Here we examined how simple improvements in facility design at our new location completely eliminated dark-phase LAN contamination and restored normal circadian rhythms in nontumor-bearing rats and normal tumor metabolism and growth in host rats bearing tissue-isolated MCF7(SR−) human breast tumor xenografts or 7288CTC rodent hepatomas. Reducing LAN contamination in the animal quarters from 24.5 ± 2.5 lx to nondetectable levels (complete darkness) restored normal circadian regulation of rodent arterial blood melatonin, glucose, total fatty and linoleic acid concentrations, tumor uptake of O2, glucose, total fatty acid and CO2 production and tumor levels of cAMP, triglycerides, free fatty acids, phospholipids, and cholesterol esters, as well as extracellular-signal-regulated kinase, mitogen-activated protein kinase, serine-threonine protein kinase, glycogen synthase kinase 3β, γ-histone 2AX, and proliferating cell nuclear antigen.

Keywords

Dauchy RT, Sauer LA, Blask De, Vaughan GM **Year** 1997

Authors Robert T. Dauchy, Leonard A. Sauer, David E. Blask, and George M. Vaughan

Report Name Light Contamination During the Dark Phase in "Photoperiodically Controlled" Animal Rooms:

Publication Laboratory Animal Science

Issue-page numbers Vol 47, No 5 October 1997 511-518

URL http://www.ncbi.nlm.nih.gov/pubmed/9355094

Abstract

Enhanced neoplastic growth and metabolism have been reported in animals maintained in a constant light (24L:0D) environment. Results from this laboratory indicate that tumor growth is directly dependent upon increased ambient blood concentrations of arachidonic and linoleic acids, particularly linoleic acid. Tumor linoleic acid utilization and production if its putative mitogenic metabolite, 13-hydroxyoctadecadienoic acid (13-HODE), are suppressed by the circadian neurohormone melatonin, the production of which is itself regulated by light in all mammals. This study was performed to determine whether minimal light contamination (0.2 lux) in an animal room during an otherwise normal dark phase may disrupt normal circadian production of melatonin and affect tumor growth and metabolism. Animals of groups I (12L:12D), II (12L:12-h light-contaminated dark phase), and III (24L:0D) had plasma total fatty acid (TFA), linoleic acid (LA), and melatonin concentrations measured prior to tumor implantation; groups I and II had daily cycles in plasma TFA and LA values, whereas group III had constant values throughout the day. The integrated mean TFA and LA values for the entire day were similar in all groups. Although group-I animals had a normal nocturnal surge of melatonin (127.0 pg/ml) at 2400 h, the nocturnal amplitude was suppressed in group-II animals (16.0 pg/ml); circadian variation in melatonin concentration was not seen in group-III animals (7.4 pg/ml). At 12 weeks of age, rats had the Morris hepatoma 7288CTC implanted as “tissue-isolated” tumors grown subcutaneously. Latency to onset of palpable tumor mass for groups I, II, and III was 11, 9, and 5 days respectively. Tumor growth rates were 0.72 ± 0.09, 1.30 ± 0.15, and 1.48 ± 0.17 g/d (mean ± SD, n = 6/group) in groups I, II, and III respectively. Arteriovenous difference measurements for TFA and LA across the tumors were 4.22 ± 0.89 and 0.83 ± 0.18 (group I), 8.26 ± 0.66 and 1.64 ± 0.13 (group II), and 7.10 ± 0.78 and 1.50 ± 0.16 (group III) /min/g, and groups II and III were significantly different from group I ($P < 0.05$). Tumor TFA and LA contents were 14.3 ± 1.7 and 1.8 ± 0.3 (group I), 52.9 ± 5.5 and 7.9 ± 0.8 (group II), and 106.0 ± 12.0 and 18.5 ± 2.4 (group III) g/g and were significantly different from each other ($P < 0.001$). Production of 13-HODE by the hepatomas in groups I, II, and III was 35.5 ± 6.3, 109.6 ± 10.6, and 196.2 ± 34.9 ng/min/g respectively, values which also were significantly different among groups ($P < 0.001$). The results indicate that minimal light contamination of only 0.2 lux during an otherwise normal dark phase inhibits host melatonin secretion and increases the rate of tumor growth and lipid uptake and metabolism. These data suggest that great care must be taken to prevent “light-leaks” in animal rooms during the dark phase of a diurnal cycle because such contamination may adversely affect the outcome of tumor growth investigations.

Keywords

Davidson AJ, Castanon-Cervantes O, Leise TL, et al. ***Year*** 2009

Authors Davidson AJ, Castanon-Cervantes O, Leise TL, Molyneux PC, Harrington ME.

Report Name Visualizing jet lag in the mouse suprachiasmatic nucleus and peripheral circadian timing system

Publication Eur J Neurosci

Issue-page numbers Jan;29(1):171-80. Epub 2008 Nov 21.

URL http://www.mendeley.com/research/visualizing-jet-lag-in-the-mouse-suprachiasmatic-nucleus-and-peripheral-circadian-timing-system-3/

Abstract Circadian rhythms regulate most physiological processes. Adjustments to circadian time, called phase shifts, are necessary following international travel and on a more frequent basis for individuals who work non-traditional schedules such as rotating shifts. As the disruption that results from frequent phase shifts is deleterious to both animals and humans, we sought to better understand the kinetics of resynchronization of the mouse circadian system to one of the most disruptive phase shifts, a 6-h phase advance. Mice bearing a luciferase reporter gene for mPer2 were subjected to a 6-h advance of the light cycle and molecular rhythms in suprachiasmatic nuclei (SCN), thymus, spleen, lung and esophagus were measured periodically for 2 weeks following the shift. For the SCN, the master pacemaker in the brain, we employed high-resolution imaging of the brain slice to describe the resynchronization of rhythms in single SCN neurons during adjustment to the new light cycle. We observed significant differences in shifting kinetics among mice, among organs such as the spleen and lung, and importantly among neurons in the SCN. The phase distribution among all Period2-expressing SCN neurons widened on the day following a shift of the light cycle, which was partially due to cells in the ventral SCN exhibiting a larger initial phase shift than cells in the dorsal SCN. There was no clear delineation of ventral and dorsal regions, however, as the SCN appear to have a population of fast-shifting cells whose anatomical distribution is organized in a ventral-dorsal gradient. Full resynchronization of the SCN and peripheral timing system, as measured by a circadian reporter gene, did not occur until after 8 days in the advanced light cycle.

Keywords

Davidson JR, Moldofsky H, Lue FA ***Year*** 1991

Authors Davidson JR, Moldofsky H, Lue FA

Report Name Growth hormone and cortisol secretion in relation to sleep and wakefulness

Publication J Psychiatry Neurosci

Issue-page numbers 16:96–102. PMID:1911740

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1188300/

Abstract The study investigated secretory patterns of growth hormone (GH) and cortisol in relation to sleep and wakefulness. Plasma hormone levels were monitored in 10 young men during baseline waking and sleeping, during 40 hours of wakefulness, and during sleep following deprivation. The normal nocturnal GH surge disappeared with sleep deprivation, and was intensified following sleep deprivation. Mean GH levels were higher during slow wave sleep (SWS) compared with other sleep stages. During sleep after deprivation, GH secretion was prolonged, and second GH peaks occurred in three subjects which were not associated with SWS. Average 24-hour cortisol levels were not altered by sleep deprivation or sleep following deprivation, but the nocturnal cortisol rise occurred approximately one hour earlier with sleep deprivation and one hour later with resumed sleep, compared to baseline. This effect on the timing of the rise is consistent with an initial inhibitory influence of sleep on cortisol secretion. The results demonstrate that: the nocturnal growth hormone surge is largely sleep-dependent; temporal associations between GH and SWS are not reliable after sleep deprivation; although the cortisol rhythm is not sleep-dependent, the timing of the cortisol rise may be influenced by sudden changes in the sleep-wake schedule.

Keywords

Davies NP, Morland AB

Year 2004

Authors Nigel P Davies and Antony B Morland

Report Name Macular pigments: their characteristics and putative role

Publication Prog Retin Eye Res

Issue-page numbers 23(5):533-59 (2004) PMID 15302350

URL http://pubget.com/paper/15302350

Abstract The macular pigments (MP) absorb light in the blue-green region of the visible spectrum and comprise two carotenoids, lutein and zeaxanthin. In humans the concentration of MP varies widely across the normal population. There are two (not mutually exclusive) proposed roles for MP: to improve visual function and to act as an antioxidant and protect the macula from damage by oxidative stress. In this article we review the origin, spectral characteristics and ocular distribution of MP and also discuss the effect MP has on central visual function and the techniques available for measurement of MP optical density in vivo. Finally, we review the evidence for both proposed physiological roles of MP. Considering the first of these, we conclude that although MP might improve visual function in theory, to date there is no firm evidence that higher levels of MP are correlated with enhanced measures of visual performance. There is a growing body of evidence that has highlighted associations between macular disease and low levels of MP, most particularly with age-related macular degeneration (AMD) and with risk factors for AMD. However, all findings to date are associative only and there is no direct evidence for high MP levels conferring a protective effect. Increased dietary intake of MP gives rise to increased levels of serum and retinal MP. This, taken together with the associative evidence of low MP levels in disease, indicates that a potential, and perhaps serendipitous, therapeutic strategy for macular disease exists. We conclude, however, that the potential protective properties of MP will only be fully evaluated by undertaking longitudinal studies that follow initially healthy participants through to the development of macular disease.

Keywords

Davis FC

Year 1997

Authors Davis FC

Report Name Melatonin: role in development

Publication J Biol Rhythms

Issue-page numbers 12:498–508 doi:10.1177/074873049701200603. PMID:9406023

URL http://jbr.sagepub.com/content/12/6/498.abstract

Abstract Melatonin is the mammalian fetus's window to periodicity of the outside world. Through melatonin, the fetus "knows" what time of year it is and, in all likelihood, also knows the time of day. The best known function of melatonin during development is to communicate information about photoperiod and thereby adaptively regulate reproductive development. A second likely function of melatonin during development, which may be related to but more widespread than the first, is to entrain the developing circadian pacemaker. Prenatal maternal entrainment occurs in all of the eutherian mammals in which it has been examined, and in Syrian hamsters exogenous melatonin during development causes entrainment. The broader distribution and greater abundance of melatonin receptors during development, relative to mature animals, suggests that developmental effects of melatonin are greater and more diverse. The human fetal suprachiasmatic nucleus expresses melatonin binding sites and is therefore likely to be affected by both endogenous and exogenous melatonin with consequences for the prenatal and postnatal expression and entrainment of circadian rhythms. Caution is warranted, not only concerning the use of exogenous melatonin during pregnancy and lactation but also concerning behavior that might disrupt the mother's endogenous melatonin rhythm.

Keywords melatonin, SCN, fetus, puberty, entrainment, development, photoperiod

Davis S, Kaune WT, Mirick DK et al. **Year** 2001

Authors Scott Davis, William T. Kaune, Dana K. Mirick, Chu Chen and Richard G. Stevens

Report Name Residential magnetic fields, light-at-night, and nocturnal urinary 6-sulfatoxymelatonin concentration in women

Publication Am J Epidemiol

Issue-page numbers 154:591–600 doi:10.1093/aje/154.7.591. PMID:11581092

URL http://aje.oxfordjournals.org/content/154/7/591.short

Abstract Exposure to 60-Hz magnetic fields may increase breast cancer risk by suppressing the normal nocturnal rise in melatonin. This 1994–1996 Washington State study investigated whether such exposure was associated with lower nocturnal urinary concentration of 6-sulfatoxymelatonin in 203 women aged 20–74 years with no history of breast cancer. Each woman was interviewed and provided data on the following for a 72-hour period at two different seasons of the year: 1) magnetic field and ambient light measured every 30 seconds in her bedroom, 2) personal magnetic field measured at 30-second intervals, and 3) complete nighttime urine samples on three consecutive nights. Lower nocturnal urinary 6-sulfatoxymelatonin level was associated with more hours of daylight, older age, higher body mass index, current alcohol consumption, and current use of medications classified as beta blockers, calcium channel blockers, or psychotropics. After adjustment for these factors, higher bedroom magnetic field level was associated with significantly lower urinary concentration of 6-sulfatoxymelatonin during the same night, primarily in women who used these medications and during times of the year with the fewest hours of darkness. These results suggest that exposure to nighttime residential 60-Hz magnetic fields can depress the normal nocturnal rise in melatonin.

Keywords breast neoplasms, carcinogens, environmental, circadian rhythm, electricity, electromagnetic fields, melatonin

Davis S, Mirick DK, Chen C, Stanczyk FZ **Year** 2012

Authors Scott Davis, Dana K. Mirick, Chu Chen, and Frank Z. Stanczyk

Report Name Night Shift Work and Hormone Levels in Women

Publication Cancer Epidemiology, Biomarkers & Prevention

Issue-page numbers Published OnlineFirst February 7, 2012; doi: 10.1158/1055-9965.EPI-11-1128

URL http://cebp.aacrjournals.org/content/early/2012/02/04/1055-9965.EPI-11-1128.abstract

Abstract Background: Nightshift work may disrupt the normal nocturnal rise in melatonin, resulting in increased breast cancer risk, possibly through increased reproductive hormone levels. We investigated whether nightshift work is associated with decreased levels of urinary 6-sulfatoxymelatonin, the primary metabolite of melatonin, and increased urinary reproductive hormone levels. Methods:Participants were 172 nightshift and 151 dayshift-working nurses, aged 20-49, with regular menstrual cycles. Urine samples were collected throughout work and sleep periods and assayed for 6-sulfatoxymelatonin, LH, FSH, and E1C. Results:6-sulfatoxymelatonin levels were 62% lower and FSH and LH were 62% and 58% higher, respectively, in nightshift-working women during daytime sleep compared to dayshift-working women during nighttime sleep ($p \leq 0.0001$). Nighttime sleep on off nights was associated with 42% lower 6-sulfatoxymelatonin levels among the nightshift workers, relative to the dayshift workers ($p<0.0001$); no significant differences in LH or FSH were observed. 6-sulfatoxymelatonin levels during night work were approximately 69% lower and FSH and LH were 35% and 38% higher, compared to dayshift workers during nighttime sleep. No differences in E1C levels between night and day shift workers were observed. Within nightshift workers, 6-sulfatoxymelatonin levels were lower and reproductive hormone levels were higher during daytime sleep and nighttime work, relative to nighttime sleep ($p<0.05$). Conclusions:These results indicate nightshift workers have substantially reduced 6-sulfatoxymelatonin levels during night work and daytime sleep, and that levels remain low even when a nightshift worker sleeps at night. Impact:Shift work could be an important risk factor for many other cancers in addition to breast cancer.

Keywords

Davis S, Mirick DK, Stevens RG

Year 2001

Authors Scott Davis, Dana K. Mirick and Richard G. Stevens

Report Name Night Shift Work, Light at Night, and Risk of Breast Cancer

Publication J Natl Cancer Inst

Issue-page numbers 93 (20): 1557-1562.

URL http://jnci.oxfordjournals.org/content/93/20/1557.full

Abstract

Background: Exposure to light at night may increase the risk of breast cancer by suppressing the normal nocturnal production of melatonin by the pineal gland, which, in turn, could increase the release of estrogen by the ovaries. This study investigated whether such exposure is associated with an increased risk of breast cancer in women. Methods: Case patients (n = 813), aged 20–74 years, were diagnosed from November 1992 through March 1995; control subjects (n = 793) were identified by random-digit dialing and were frequency matched according to 5-year age groups. An in-person interview was used to gather information on sleep habits and bedroom lighting environment in the 10 years before diagnosis and lifetime occupational history. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by use of conditional logistic regression, with adjustment for other potential risk factors. Results: Breast cancer risk was increased among subjects who frequently did not sleep during the period of the night when melatonin levels are typically at their highest (OR = 1.14 for each night per week; 95% CI = 1.01 to 1.28). Risk did not increase with interrupted sleep accompanied by turning on a light. There was an indication of increased risk among subjects with the brightest bedrooms. Graveyard shiftwork was associated with increased breast cancer risk (OR = 1.6; 95% CI = 1.0 to 2.5), with a trend of increased risk with increasing years and with more hours per week of graveyard shiftwork (P = .02, Wald chi-squared test). Conclusion: The results of this study provide evidence that indicators of exposure to light at night may be associated with the risk of developing breast cancer.

It has been proposed that exposure to light at night and power frequency (50–60 Hz) magnetic fields may increase the risk of breast cancer by suppressing the normal nocturnal production of melatonin by the pineal gland, which, in turn, could increase the release of estrogen by the ovaries (1,,2). Studies of breast cancer and measures of magnetic field exposure have led to conflicting results [reviewed in (3)]. To date, no study has investigated the relationship between the risk of breast cancer and exposure to light at night as estimated from characteristics of sleep habits or bedroom environment. Shiftwork has also been proposed to increase the risk of breast cancer (1), and four studies (4–,7) investigating this have all reported increased risk among women who work during the night.

The purpose of this study was to investigate whether the risk of breast cancer is associated with exposure to light at night as characterized by sleep habits, bedroom lighting environment, and shiftwork in the 10 years before diagnosis and/or residential exposure to power frequency magnetic fields. Results regarding magnetic field exposure are described elsewhere (8). This report presents the primary findings regarding indicators of light at night exposure.

Keywords shift work, light at night, breast cancer

Dawe RS

Year 2009

Authors Robert S. Dawe

Report Name Prevalences of chronic photodermatoses in Scotland

Publication Photodermatology, Photoimmunology & Photomedicine

Issue-page numbers Volume 25, Issue 1, pages 59–60, February 2009

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0781.2009.00394.x/abstract

Abstract N/A

Keywords

Dawe RS, Ferguson J

Year 2003

Authors Robert S. Dawe, James Ferguson

Report Name Diagnosis and treatment of chronic actinic dermatitis

Publication Dermatologic Therapy

Issue-page numbers Volume 16, Issue 1, pages 45–51, March 2003

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1529-8019.2003.01607.x/full

Abstract Chronic actinic dermatitis, synonymous with the photosensitivity dermatitis and actinic reticuloid syndrome, presents as a dermatitis and/or a pseudolymphomatous eruption. Abnormal photosensitivity to ultraviolet (UV) and often visible radiation is a feature. Many patients also have multiple contact allergens. Histopathologic features vary, with a spectrum from mild dermatitis to pseudolymphomatous (reticuloid) features. The essential tests to make the diagnosis and to guide advice on avoidance of the responsible wavelengths and any contact allergens are phototesting and patch testing. Chronic actinic dermatitis can be regarded as a disorder of increased susceptibility, for reasons that remain uncertain, to develop delayed-type allergic responses to both endogenous photoallergens and exogenous allergens. Treatment consists of detailed advice on sunlight and allergen avoidance (guided by the results of investigations), topical corticosteroids, and emollients. When these measures are insufficient alone, systemic immunosuppressives may be considered: systemic prednisolone for acute exacerbations or azathioprine if systemic treatment is required for more than a few weeks.

Keywords chronic actinic dermatitis; diagnosis; photosensitivity dermatitis and actinic reticuloid syndrome

Dawson D, Lack L, Morris M | ***Year*** 1993

Authors Dawson D, Lack L, Morris M

Report Name Phase resetting of the human circadian pacemaker with use of a single pulse of bright light.

Publication Chronobiol Int

Issue-page numbers 10:94–102 doi:10.3109/07420529309059697. PMID:8500194

URL http://www.ncbi.nlm.nih.gov/pubmed/8500194

Abstract Examined the phase-shifting effects of a single 4-hr pulse of bright light in 15 Ss (aged 19–45 yrs). With use of a "constant routine" to estimate circadian phase, the study found that a single 4-hr pulse of light produced significant shifts in the phase of the core temperature (COR) rhythm. The timing of the exposure, relative to the COR rhythm, determinec the degree and direction of the phase shift. Exposure immediately prior to habitual bedtime produced a mean phase delay in the COR of 2.39 hrs. Exposure immediately following habitual wake-up produced a mean phase advance of 1.49 hrs. The magnitude of the shift increased the closer the light pulse was to the S's estimated endogenous COR minimum. There was considerable interindividual variability in this relationship. Results confirm that a single pulse of bright light can produce significant phase shifts in the phase of the circadian pacemaker controlling COR.

Keywords

De Berardis D, Acciavatti T, Di Iorio G, Corbo M, et al. | ***Year*** 2011

Authors Domenico De Berardis, Tiziano Acciavatti, Giuseppe Di Iorio, Mariangela Corbo, Nicola Serroni, Daniela Campanella, Fabiola Di Emidio, Monica Piersanti, Marilde Cavuto, Giova

Report Name The melatonergic system: effects on sleep and implications for the treatment of psychiatric disorders

Publication ChronoPhysiology and Therapy

Issue-page numbers 20 December 2011

URL http://www.dovepress.com/getfile.php?fileID=11679

Abstract Abstract: The circadian pacemaker or biological clock, located in the hypothalamic suprachiasmatic nucleus, is the generation site of circadian rhythms. The light/dark cycle is the circadian pacemaker's dominant synchronizing agent, though it is also influenced by neurotransmitters and the phase-shifting effects of various chemical and pharmacological components,
of which melatonin (N-acetyl-5-methoxytryptamine) is the most well established.
In recent years, melatonin and melatonin analogs have been commercialized in many countries, mainly with hypnotic purposes. A new compound, agomelatine, has been recently synthesized and studied. Among melatonin analogs, this drug possesses unique pharmacological and clinical features; it is an antagonist at 5-HT2B and 5-HT2C receptors and has well established antidepressant and anxiolytic properties. Agomelatine opens new perspectives in the chronobiotic treatment of depression. The purpose of the present review was to elucidate the effects of the melatonergic system on sleep and the implications for the treatment of psychiatric disorders.

Keywords

de Gruijl FR

Year 1997

Authors F.R. de Gruijl

Report Name Health effects from solar UV radiation

Publication Radiat Prot Dosimetry

Issue-page numbers 72 (3-4): 177-196.

URL http://rpd.oxfordjournals.org/content/72/3-4/177

Abstract Solar UV radiation is a ubiquitous challenge to life on earth, and to human health in particular. As UV radiation does not penetrate any deeper than the skin, this organ has to be specifically well adapted. It even exploits UV radiation for a beneficial effect: the formation of vitamin D3. Our day-to-day exposure suffices for the latter effect. Overexposure mainly contributes to adverse effects, such as the formation of skin cancer and the suppression of immunity against infection. Chronic UV exposure is further suspected to affect the eyes, e.g. through the formation of cataracts. A depletion of stratospheric ozone is expected to increase these adverse effects on human health. Virtually nothing is known about the quantitative impacts of this depletion on infections and very little about its impact on eye afflictions, but quantitative estimates of increases in skin carcinomas can be made. As a first approximation, squamous cell carcinomas are expected to increase ultimately by 3%, and basal cell carcinomas by 1.7%, for each per cent of lasting ozone depletion.

Keywords

De Gruijl FR, Van Der Leun JC

Year 1991

Authors F R De Gruijl, J C Van Der Leun

Report Name Development of skin tumors in hairless mice after discontinuation of ultraviolet irradiation

Publication Cancer Research

Issue-page numbers Volume: 51, Issue: 3, Pages: 979-984

URL http://www.mendeley.com/research/development-of-skin-tumors-in-hairless-mice-after-discontinuation-of-ultraviolet-irradiation/

Abstract The development of skin tumors (mainly squamous cell carcinomas) in hairless Skh-HR1 mice after discontinuation of a course of daily UV irradiations (wavelengths, 280-370 nm) is compared to that when the daily irradiations are continued. Under conditions of continued daily exposures 50% of 22 animals contracted tumors with diameters of at least 4 mm in 135 days. With exposures stopped after 35 or 19 days (2 groups with 24 and 23 mice) this time interval increased to 280 and 645 days, respectively; the rate at which multiple tumors developed on the mice was correspondingly lower. A mathematical model, derived from a larger experiment (223 mice) with different levels of chronic UV exposure, successfully predicts the tumor development after discontinuation of UV exposure. This model is similar to those used in risk assessments for skin cancers in human populations, e.g., in relation to stratospheric ozone depletion, sunbeds, etc. The model separates UV-driven processes from purely time-dependent processes. These stochastic processes, described by Weibull statistics, form stages in the tumorigenesis. This interpretation of the data indicates that a late, UV-independent stage occurs between the smallest observable tumors and larger ones with diameters of over 4 mm. This could be a simple growth stage, but histopathology suggests that it may also entail a transition from actinic keratosis to squamous cell carcinoma.

Keywords

de Gruijl FR, van der Leun JC

Year 2002

Authors Frank R. de Gruijl and Jan C. van der Leun

Report Name Physical variables in experimental photocarcinogenesis and quantitative relationships between stages of tumor development

Publication Frontiers in Bioscience

Issue-page numbers 7, d1525-1530, June 1, 2002

URL http://www.bioscience.org/u37153137/gaDTRQo7632rgysaGWQYT64356/2002/v7/d/gruijl/gruijl.pdf

Abstract

Solar ultraviolet (UV) radiation is a prominent environmental carcinogen, but it does not penetrate any deeper than the skin. The UV-related skin cancers are by far the most common form of cancer among white Caucasians in the USA and Australia, and this poses a serious public health problem. Chronic UV exposure of hairless mice is a well established model for squamous cell carcinomas in man. It is important to identify the essential physical variables, and explore fully how photocarcinogenesis evolves in dependence of these variables. The 3 main physical variables in photocarcinogenesis are (i) the wavlength of the radiation, (ii) the exposure and (iii) time. A good quantitative description of tumor induction and precursing stages can be given in terms of these variables. An analysis of this description shows us that the early induction of clusters of epidermal cells that over-express mutant p53 ('p53 patches') are closely and, most likely, causally linked to the eventual tumors. These p53 patches may thus serve as early indicators of tumor risk. The induction of an immunetolerance toward the UV-induced tumors precedes the actual occurrence of the tumors at high daily doses, but extrapolation indicates that this order of events may be reversed at low daily doses. This disparity between the dose-time relationships for the tumor tolerance and the tumors needs to be investigated further. It could imply a shift to non-immunogenic tumors at low daily doses.

Keywords

de Gruijl FR, Van der Leun JC

Year 1994

Authors de Gruijl FR, Van der Leun JC.

Report Name Estimate of the wavelength dependency of ultraviolet carcinogenesis in humans and its relevance to the risk assessment of a stratospheric ozone depletion

Publication Health Phys

Issue-page numbers 1994 Oct;67(4):319-25.

URL http://www.ncbi.nlm.nih.gov/pubmed/8083043

Abstract The wavelength dependency of carcinogenesis is an important factor in risk assessments pertaining to sources of ultraviolet radiation, the most important of which is the sun. This wavelength dependency cannot be measured directly in humans, but it has been measured in hairless mice, and represented in an action spectrum. An estimate of the action spectrum for humans can be produced by correcting for differences in epidermal transmission between mice and humans. This carcinogenic action spectrum for humans resembles the action spectrum for ultraviolet-induced erythema (sunburn), and results in small adjustments of earlier estimates of the effects of a stratospheric ozone depletion on skin cancer incidences.

Keywords

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de Gruijl FR, van Kranen HJ, Mullenders LHF

Year 2001

Authors Frank R de Gruijl, Henk J van Kranen, Leon H.F Mullenders

Report Name UV-induced DNA damage, repair, mutations and oncogenic pathways in skin cancer

Publication Journal of Photochemistry and Photobiology B: Biology

Issue-page numbers Volume 63, Issues 1-3, October 2001, Pages 19-27

URL http://www.sciencedirect.com/science/article/pii/S1011134401001993

Abstract Repair of UV induced DNA damage is of key importance to UV-induced skin carcinogenesis. Specific signal transduction pathways that regulate cell cycling, differentiation and apoptosis are found to be corrupted in skin cancers, e.g., the epidermal growth-stimulating Hedgehog pathway in basal cell carcinomas (BCCs). Mutations in genes coding for proteins in these pathways lead to persistent disturbances that are passed along to daughter cells, e.g., mutations in the gene for the Patched (PTCH) protein in the Hedgehog pathway. Thus far only the point mutations in the P53 gene from squamous cell carcinomas and BCCs, and in PTCH gene from BCC of xeroderma pigmentosum (XP) patients appear to be unambiguously attributable to solar UV radiation. Solar UVB radiation is most effective in causing these point mutations. Other forms of UV-induced genetic changes (e.g., deletions) may, however, contribute to skin carcinogenesis with different wavelength dependencies.

Keywords UV radiation; Skin cancer; Oncogenic pathways; DNA damage; DNA repair

de Vries E, van de Poll-Franse LV, Louwman WJ, et al. **Year** 2005

Authors de Vries E, van de Poll-Franse LV, Louwman WJ, de Gruijl FR, Coebergh JW

Report Name Predictions of skin cancer incidence in the Netherlands up to 2015

Publication British Journal of Dermatology

Issue-page numbers Volume 152, Issue 3, pages 481–488, March 2005

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.2005.06386.x/full

Abstract

Summary Background Skin cancer is an important, growing public health problem among white caucasians, causing a heavy burden on dermatologists and general practitioners.

Objectives To predict the future incidence of skin cancer in the Netherlands up to 2015.

Methods Expected numbers of skin cancer cases in the Netherlands up to 2015 were calculated by trend modelling of observed rates for melanoma and squamous cell carcinoma (SCC) between 1989 and 2000 obtained from the Netherlands Cancer Registry and for basal cell carcinoma (BCC) obtained from the Eindhoven Cancer Registry; these rates were then multiplied by the predicted age distributions. Incidence rates were fitted to four different models, and predictions were based on the best fitting model.

Results An increase of 80% in the total number of skin cancer patients is expected in the Netherlands: from 20 654 in 2000 to 37 342 in 2015. The total number of melanoma cases is expected to increase by 99%, with the largest increase for males (males aged 35–64, 111%; males aged ≥65, 139%). Numbers of patients with SCC will increase overall by 80%, mainly among older males and females (increase of 79%) and females aged 35–64 (increase of 93%). The number of cases of BCC will increase by 78%, with the largest increase for the combined groups, those aged 15–64 (males, 66% increase; females, 94% increase), especially for sites other than the head and neck. The contribution of demographic changes (ageing effect) was largest for males with BCC and SCC (35–44%).

Conclusions If incidence rates for skin cancers in the Netherlands continue to increase and population growth and ageing remain unabated, a rise in annual demand for care of more than 5% could occur, putting a heavy burden on general practitioners and dermatologists. In the absence of marked changes in current ultraviolet radiation exposure, these increases will probably continue after 2015.

Keywords basal cell carcinoma; incidence; melanoma; predictions; squamous cell carcinoma

Authors Deacon S, Arendt J

Report Name Adapting to phase shifts, I. An experimental model for jet lag and shift work

Publication Physiol Behav

Issue-page numbers 59:665–673 doi:10.1016/0031-9384(95)02147-7. PMID:8778850

URL http://www.ncbi.nlm.nih.gov/pubmed/8778850

Abstract An experimental model was developed to measure various behavioral and physiological parameters in a laboratory paradigm mimicking phase shifts that could occur in time-zone transitions and shift work rotas. Volunteers were exposed to 9-h pulses of bright light (1,200 lx) as follows: day (D)1: 1800-0300 h, D2: 2100-0600 h, and D3, 4, 5: 2400-0900 h, each period followed by 8 h darkness. Immediately following the last treatment, subjects resumed their baseline sleep/wake schedule in a normal environment, thus experiencing a rapid 9-h advance phase shift of local time cues. During the gradual delay shift, a progressive delay shift in the rhythms of urinary 6-sulphatoxymelatonin (aMT6s), temperature and alertness was evident (maximum shift: 9.13 +/- 0.83 h, 9.09 +/- 1.06, and 10.62 +/- 0.96 h, mean +/- SD, respectively). There were no important detrimental effects on behavioral variables. After the rapid 9-h phase advance, sleep patterns, temperature amplitude, aMT6s acrophase, alertness, and performance took at least 5 days to reestablish normal baseline patterns. This model provides an effective and inexpensive model to study adaptation strategies in real life.

Keywords

Authors Stephen J. Deacon, Josephine Arendt

Report Name Phase-shifts in melatonin, 6-sulphatoxymelatonin and alertness rhythms after treatment with moderately bright light at night

Publication Clinical Endocrinology

Issue-page numbers Volume 40, Issue 3, pages 413–420, March 1994

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1994.tb03940.x/abstract

Abstract

OBJECTIVES Shift work and rapid travel across several time zones leads to desynchronization of internal circadian rhythms from the external environment and from each other with consequent problems of behaviour, physiology and performance. Field studies of travellers and shift workers are expensive and difficult to control. This investigation concerns the simulation of such rhythm disturbance in a laboratory environment. The main objectives are to assess the ability of controlled exposure to moderately bright light and darkness/sleep to delay circadian rhythms in volunteers without environmental isolation and, secondly, to evaluate the use of different indices of melatonin (MT) secretion together with self-rated alertness as marker rhythms.

PATIENTS Six normal volunteers aged 22–26 years (mean ± SD 24·3 ± 1·4).

DESIGN Subjects were exposed to the following periods of moderately bright light (1200 lux) on three consecutive days in early December 1991: Day (D)1: 2000-0200 h, D2: 2200-0400 h and D3: 2400-0600 h. Each period was followed by 8 hours of darkness (< 1 lux). Hourly blood, sequential 4-hourly urine (8-hourly when asleep) and hourly saliva (except when asleep) samples were taken throughout a 24-hour period on D0 (baseline), D4 (1 day post-light treatment) and D7 (4 days post-light treatment). During waking hours, subjective alertness was rated every 2 hours on a visual analogue scale.

MEASUREMENTS MT was measured in plasma and saliva, and its metabolite, 6-sulphatoxymelatonin (aMT6s), was measured in urine. MT, aMT6s and alertness scores were analysed by ANOVA and a cosinor analysis program.

RESULTS A delay shift was present in the aMT6s, plasma MT and salivary MT rhythms (degree of shift: 2·67 ± 0.3 h ($P<0·001$, n = 5); 2·35±0·29 h ($P<0·001$, n = 6); and 1·97 ± 0·32 h ($P < 0·01$, n = 6), mean ± SEM, respectively) 1 day post-light treatment compared to baseline. Adaptation to the initial phase position was apparent by the 4th post-treatment day. Significant correlations were obtained between plasma MT onset (degree of shift: 3·12 ± 0·74 h ($P < 0·001$, n = 6, mean ± SEM)) and the acrophases (calculated peak times) of plasma MT ($P<0·001$), salivary MT ($P < 0·05$) and urinary aMT6s ($P < 0·01$). A significant phase delay in the alertness rhythm was also evident 1 day post-treatment (3·08 ± 0·67 h ($P < 0·01$, n = 6, mean ± SEM)) with adaptation by the 2nd post-treatment day.

CONCLUSIONS This study suggests that these methods of determining MT secretion are comparable and give reliable assessments of the MT circadian phase position even after a phase-shift. Significant phase-shifts of similar magnitude can be induced in both MT and alertness rhythms using moderate intensity bright light at night.

Keywords

Deacon SJ, Arendt J — *Year* 1995

Authors Deacon SJ, Arendt J

Report Name Melatonin-induced temperature suppression and its acute phase-shifting effects correlate in a dose-dependent manner in humans

Publication Brain Res

Issue-page numbers 688:77–85 doi:10.1016/0006-8993(95)96872-I. PMID:8542325

URL http://www.mendeley.com/research/melatoninduced-temperature-suppression-acute-phaseshifting-effects-correlate-dosedependent-manner-humans/

Abstract Melatonin is able to phase-shift the endogenous circadian clock and can induce acute temperature suppression. It is possible that there is a direct relationship between these phenomena. In a double-blind, placebo-controlled crossover study, 6 healthy volunteers maintained a regular sleep/wake cycle in a normal environment. From dusk until 24:00 h on days (D) 1-4 subjects remained in dim artificial lighting 50 lux) and darkness 1 lux) from 24:00-08:00 h. At 17:00 h on D3 either melatonin (0.05 mg, 0.5 mg or 5 mg) or placebo was administered. Melatonin treatment induced acute, dose-dependent temperature suppression and decrements in alertness and performance efficiency. On the night of D3, earlier sleep onset, offset and better sleep quality were associated with increasing doses of melatonin. The following day, a significant dose-dependent phase-advance in the plasma melatonin onset time and temperature nadir (D4-5) was observed with a trend for the alertness rhythm to phase-advance. A significant dose-response relationship existed between the dose of oral melatonin, the magnitude of temperature suppression and the degree of advance phase shift in the endogenous melatonin and temperature rhythms, suggesting that acute changes in body temperature by melatonin may be a primary event in phase-shifting mechanisms.

Keywords

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deBoer JB, Schreuder DA — *Year* 1967

Authors deBoer, J. B., and D. A. Schreuder

Report Name Glare as a Criterion for Quality in Street Lighting

Publication Transactions of the Illuminating Engineering Society

Issue-page numbers Vol. 32, No. 2, 1967, pp. 117-135

URL http://books.google.com/books/about/Glare_as_a_criterion_for_quality_in_stre.html?id=kslOcgAACAAJ

Abstract N/A

Keywords glare

Deguchi T, Axelrod J

Year 1972

Authors Takeo Deguchi and Julius Axelrod

Report Name Control of Circadian Change of Serotonin N-Acetyltransferase Activity in the Pineal Organ by the β-Adrenergic Receptor

Publication PNAS

Issue-page numbers September 1, 1972 vol. 69 no. 9 2547-2550

URL http://www.pnas.org/content/69/9/2547.short

Abstract Serotonin N-acetyltransferase (EC 2.3.1.5) activity in the rat pineal organ is enhanced 50-fold at night. Rats exposed to light at night or kept in darkness during the daytime do not show any elevation of enzyme activity. Treatment with reserpine, a compound that depletes norepinephrine from nerves, 1-propranolol, a β-adrenergic blocking agent, or cycloheximide, an inhibitor of protein synthesis, abolishes the nocturnal increase in serotonin N-acetyltransferase activity, indicating that the enzyme activity is modulated by neural release of norepinephrine from sympathetic nerves via β-adrenergic receptors, and that the increase in enzyme activity is due to synthesis of new enzyme molecules. When rats are exposed to light at night or injected with 1-propranolol, there is a precipitous fall in serotonin N-acetyltransferase activity (half-life 5 min). Cycloheximide administered at night results in a slow fall in enzyme activity (half-life 60 min). When rats are kept in darkness and then exposed to light for 10 min, L-isoproterenol rapidly initiates the elevation of serotonin N-acetyltransferase activity to the initial level in 60 min. On the other hand, when the rats are kept in continuous light, L-isoproterenol initiates an increase in serotonin N-acetyltransferase activity after a lag phase of 60 min. The results indicate that there are two types of changes in serotonin N-acetyltransferase activity; a rapid increase and decrease mediated by the β-adrenergic receptor, and a slow increase and decrease in enzyme activity that appears to represent the turnover of the enzyme

Keywords diurnal, neural regulation, norepinephrine

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del Gobbo V, Libri V, Villani N et al.

Year 1989

Authors V. Del Gobbo, V. Libri, N. Villani, R. Caliō, G. Nistic

Report Name Pinealectomy inhibits interleukin-2 production and natural killer activity in mice.

Publication Int J Immunopharmacol

Issue-page numbers 11:567–573 doi:10.1016/0192-0561(89)90187-2. PMID:2807631

URL http://www.sciencedirect.com/science/article/pii/0192056189901872

Abstract Four — five-week-old C57BL/6 mice were surgically pinealectomized. At different time intervals after surgery their spleens were removed and assayed for interleukin-2 (IL-2) production and natural killer (NK) cell activity. Non-operated and sham-operated mice were used as controls. The present results indicate that pinealectomy significantly reduced IL-2 production and NK cell activity, in comparison to sham-operated mice. These effects seem to be related to the lack of melatonin. In fact the subcutaneous injection of this hormone (50 or 100 mg/kg at 5 p.m.) in pinealectomized mice was able to restore IL-2 production and NK cell activity. However, chronic treatment with melatonin (10, 20 and 50 mg/kg for 9 consecutive days) failed to reverse the impairment of the immune responses.

Keywords

Authors Susana del Olmo-Aguado, Alberto G. Manso, Neville N. Osborne

Report Name Light might directly affect retinal ganglion cell mitochondria to potentially influence function

Publication Photochemistry and Photobiology

Issue-page numbers Accepted Article (Accepted, unedited articles published online for future issues)

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2012.01120.x/abstract

Abstract

Visible light (360-760nm) entering the eye impinges on the many ganglion cell mitochondria in the non-myelinated part of their axons. The same light also disrupts isolated mitochondrial function in vitro and kills cells in culture with the blue light component being particularly lethal while red light has little effect. Significantly, a defined light insult only affects the survival of fibroblasts in vitro that contain functional mitochondria supporting the view that mitochondrial photosensitizers are influenced by light. Moreover, a blue light insult to cells in culture causes a change in mitochondrial structure and membrane potential and results in a release of cytochrome c. Blue light also causes an alteration in mitochondria located components of the oxidative phosphorylation system (OXPHOS). Complex III and IV as well as complex V are significantly up-regulated while complex I and II are slightly but significantly up- and down regulated, respectively. Also, blue light causes Dexras1 and reactive oxygen species to be up-regulated and for mitochondrial located apoptosis inducing factor (AIF) to be activated. A blue light detrimental insult to cells in culture does not involve the activation of caspases but is known to be attenuated by necrostatin-1, typical of a death mechanism named necroptosis.

Keywords

Authors Susana del Olmo-Aguado and Neville N. Osborne

Report Name In Vitro Evidence To Show That Blue Light Influences Mitochondrial Functions Negatively

Publication Invest Ophthalmol Vis Sci

Issue-page numbers 2012;53: E-Abstract 782.

URL http://abstracts.iovs.org/cgi/content/abstract/53/6/782

Abstract

Purpose:To show that blue light in particular influences mitochondrial functions in vitro to potentially elicit retinal cell death in situ.

Methods:Semi-confluent cultures of RGC-5 (a cell line with certain ganglion cell properties) cells were exposed to blue (465-470nm, 400 lux), white (400-800nm, 1000 lux) or red (625-635nm, 1000 lux) light over 24 or 48 hours. Thereafter cells in 96-well plates were analysed for viability (MTT procedure) and their inner membrane potential (JC-1). Proteins from cells in culture were also extracted and individual oxidative phosphorylation (OXPHOS) complexes quantified by electrophoresis/western blotting. RGC-5 cells on coverslips were also processed for the localisation of mitochondria (mitotracker) or the presence of cytochrome-c. In addition immunocytochemistry was used to localise individual OXPHOS complexes.

Results:Blue and white light caused a loss of cell viability with blue light being much more effective. Red light had a negligible influence on cell viability. Double staining of cells with DAPI and either JC-1, mitotracker or cytochrome-c showed that blue light caused a change in the inner membrane electrochemical potential, mitochondrial morphology and the release of mitochondrial located cytochrome-c into the cytoplasm. Analysis of individual OXPHOS complexes by immunocytochemistry and western blotting showed differential effects. Complex II is down-regulated and complex I unaffected, while complex III, IV and V are up-regulated.

Conclusions:Of the light that impinges on the retina, the blue light component in particular affects mitochondrial functions negatively as might occur with the many mitochondria located to ganglion cells in situ. The present studies also suggest that blue light has a direct influence on fluorophores associated with complex II, III, IV and V of mitochondrial OXPHOS.

Keywords ganglion cells • mitochondria • radiation damage: light/UV

del Río B, García Pedrero JM, Martínez-Campa C et al. **Year** 2004

Authors Beatriz del Río, Juana M. García Pedrero, Carlos Martínez-Campa, Pedro Zuazua, Pedro S. Lazo, and Sofía Ramos

Report Name Melatonin, an endogenous-specific inhibitor of estrogen receptor alpha via calmodulin.

Publication J Biol Chem

Issue-page numbers 279:38294–38302 doi:10.1074/jbc.M403140200. PMID:15229223

URL http://hwmaint.jbc.org/cgi/content/abstract/M403140200v1

Abstract

elatonin is an indolic hormone produced mainly by the pineal gland. We have previously demonstrated that melatonin interferes with estrogen (E2) signaling in MCF7 cells by impairing estrogen receptor (ER) pathways. Here we present the characterization of its mechanism of action showing that melatonin is a specific inhibitor of E2-induced ERalpha -mediated transcription in both ERE- and AP1-containing promoters, whereas ERbeta -mediated transactivation is not inhibited, or even activated at certain promoters. We show that the sensitivity of MCF-7 cells to melatonin depends on the ERalpha /ERbeta ratio and ectopic expression of ERbeta results in MCF-7 cells to become insensitive tc this hormone. Melatonin acts as a calmodulin antagonist inducing conformational changes in the ERalpha -CaM complex thus impairing the binding of E2-ERalpha -CaM complex to DNA and therefore preventing ERalpha -dependent transcription. Moreover the mutant ERalpha (K302G, K303G) unable to bind calmodulin becomes insensitive to melatonin. The effect of melatonin is specific since other related indols neither interact with CaM nor inhibit ERalpha -mediated transactivation. Interestingly, melatonin does not affect the binding of coactivators to ERalpha indicating that melatonin action is different to that of current therapeutic antiestrogens used in breast cancer therapy. Thus, they target ERalpha at different levels, representing two independent ways to control ERalpha activity. It is therefore conceivable a synergistic pharmacological effect of melatonin and current antiestrogen drugs.

Keywords

Authors Delcourt C, Carrière I, Ponton-Sanchez A, Fourrey S, Lacroux A, Papoz L; POLA Study Group.

Report Name Light exposure and the risk of age-related macular degeneration: the Pathologies Oculaires Liées à l'Age

Publication Arch Ophthalmol

Issue-page numbers Oct;119(10):1463-8.

URL http://www.ncbi.nlm.nih.gov/pubmed/11594945

Abstract

BACKGROUND:

The role of light exposure in the development of age-related macular degeneration (ARMD) has been questioned. We present the relationship between lifetime light exposure and ARMD as examined in the Pathologies Oculaires Liées à l'Age (POLA) study.
METHODS:

The POLA study is a population-based study on cataract and ARMD and their risk factors. It included 2584 residents of the town of Sète, located in the South of France. The presence of early and late ARMD was assessed on the basis of 50 degrees color fundus photographs using an international classification system. A questionnaire about light exposure was administered.
RESULTS:

Late ARMD (n = 38) was not significantly associated with any light exposure variable. Subjects exposed to high ambient solar radiation and those with frequent leisure exposure to sunlight had a decreased risk of pigmentary abnormalities (odds ratio [OR] = 0.61; 95% confidence interval [CI], 0.39-0.93, and OR = 0.70; 95% CI, 0.52-0.95, respectively) and of early signs of ARMD (OR = 0.73; 95% CI, 0.54-0.98, and OR = 0.80; 95% CI, 0.64-1.00, respectively). Subjects who had used sunglasses regularly had a decreased risk of soft drusen (OR = 0.81; 95% CI, 0.66-1.00). These relationships were not modified by further adjustments for potential confounders.
CONCLUSION:

Our study does not support a deleterious effect of sunlight exposure in ARMD.

Keywords

Delezie J, Challet E

Year 2011

Authors Julien Delezie,

Report Name Interactions between metabolism and circadian clocks: reciprocal disturbances

Publication Annals of the New York Academy of Sciences

Issue-page numbers Volume 1243, The Year in Diabetes and Obesity pages 30–46, December 2011

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.2011.06246.x/full

Abstract Obesity is a medical condition of excess body fat, recognized as a global epidemic. Besides genetic factors, overconsumption of high-energy food and a sedentary lifestyle are major obesogenic causes. A newly identified determinant is altered circadian rhythmicity. To anticipate and adapt to daily changes in the environment, organisms have developed an endogenous circadian timing system, comprising a main circadian clock, located in the suprachiasmatic nucleus (SCN) of the hypothalamus, principally synchronized to the light–dark cycle. Secondary peripheral clocks are found in various tissues, such as the liver, pancreas, and adipose tissue. These clocks control the rhythmic patterns of myriad metabolic processes. We will review the evidence that metabolic dysfunction is associated with circadian disturbances at both central and peripheral levels and, conversely, that disruption of circadian clock functioning can lead to obesity. The roots of these reciprocal interactions will be illustrated by transcriptional crosstalk between metabolic and circadian systems. Chronotherapeutic approaches of dieting to maintain or restore a proper circadian alignment could be useful to limit the magnitude of metabolic risks.

Keywords circadian rhythm; clock gene; metabolism; obesity; feeding

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Delmelle M

Year 1978

Authors M. Delmelle

Report Name Retinal sensitized photodynamic damage to liposomes

Publication Photochemistry and Photobiology

Issue-page numbers Volume 28, Issue 3, pages 357–360, September 1978

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.1978.tb07718.x/abstract

Abstract All trans-retinal has been introduced (2 mol %) into artificial membranes made up of egg lecithin, cholesterol and dicetyl phosphate. Illumination of retinal-enriched liposomes at 365 nm induced photodynamic damages; it triggered the sensitized oxidation of the lipids measured by the appearance of a 233 nm absorption band or by the formation of malonyl dialdehyde. Illumination produced an increase of the membrane fluidity detected with the spin label technique and led also to the lysis of the liposomes as revealed by the release of entrapped chromate ions or by changes in light scattering. Singlet oxygen is involved in these photodynamic effects. The results have been discussed in connection with the light damage phenomena which may afflict the rod outer segment membranes.

Keywords

Demas GE, Nelson RJ **Year** 1998

Authors Demas GE, Nelson RJ

Report Name Exogenous melatonin enhances cell-mediated, but not humoral, immune function in adult male deer mice (Peromyscus maniculatus)

Publication J Biol Rhythms

Issue-page numbers 13:245–252 doi:10.1177/074873098129000084. PMID:9615288

URL http://www.biomedsearch.com/nih/Exogenous-melatonin-enhances-cell-mediated/9615288.html

Abstract Many nontropical rodent species display seasonal changes in reproductive physiology and metabolism, as well as in immune function. Field studies of seasonal changes in immune function typically report decreased immune function in the short days of winter compared to summer; presumably, reduced immunity in winter reflects increased glucocorticoid secretion in response to environmental stressors. In contrast, laboratory studies of photoperiodic changes in immunity invariably demonstrate increased immune function in short compared to long days. Although the precise mechanisms regulating short-day enhancement of immune function are not known, it is hypothesized that increased immunity is due to the increased duration of melatonin secretion in short compared to long days. However, melatonin can act both directly (i.e, via melatonin receptors located on lymphatic tissue) and indirectly (i.e., via alterations in gonadal steroids) to affect immune function. The present study examined the effects of exogenous melatonin administration on both cell-mediated and humoral immune function in adult male deer mice (Peromyscus maniculatus), as well as the role of gonadal steroid hormones in mediating these effects. Mice either were castrated to remove circulating androgens or received sham operations and were implanted with empty capsules or capsules containing melatonin. Individual mice implanted with melatonin underwent reproductive regression and displayed enhanced splenocyte proliferation to the T-cell mitogen concanavalin A; antigen-specific serum immunoglobulin M production was unaffected by melatonin treatment. Castration had no effect on either cell-mediated or humoral immune function. Taken together, these results suggest that exogenous melatonin enhances cell-mediated, but not humoral, immune function in adult male deer mice and that this effect is independent of gonadal steroid hormones. These results are consistent with a direct effect of melatonin on immunity.

Keywords

Demisch L, Demisch K, Nickelsen T **Year** 1988

Authors Demisch L, Demisch K, Nickelsen T

Report Name Influence of dexamethasone on nocturnal melatonin production in healthy adult subjects.

Publication J Pineal Res

Issue-page numbers 5:317–322 doi:10.1111/j.1600-079X.1988.tb00657.x. PMID:3404401

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1988.tb00657.x/abstract?

Abstract There is no conclusive evidence supporting an interaction between the pineal gland and the hypothalamic-pituitary-adrenal axis. In this study, 11 healthy adults (six women, five men; aged 18–47 years) received a placebo the first night and 1 mg dexamethasone the next night at either 1800 or 2300 h. Administration of 1 mg of dexamethasone was followed by an attenuation of the nocturnal production of melatonin in 9 of 11 subjects. A significant reduction was found between melatonin plasma levels before and after dexamethasone at 0400h ($P < 0.01$, t test for dependent groups). It is suggested that dexamethasone affects nocturnal production of melatonin by means of mechanisms within the pineal gland.

Keywords pineal gland; hypothalamic-pituitary-adrenal axis; glucocorticoids

Denda M, Tsutsumi M, Denda S — **Year** 0

Authors Mitsuhiro Denda, Moe Tsutsumi, Sumiko Denda

Report Name Topical application of TRPM8 agonists accelerates skin permeability barrier recovery and reduces epidermal proliferation induced by barrier insult: role of cold-sensitive TRP rece

Publication Experimental Dermatology

Issue-page numbers Volume 19, Issue 9, pages 791–795, September 2010

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0625.2010.01154.x/abstract

Abstract TRPA1 and TRPM8 receptors are activated at low temperature (A1: below 17°C and M8: below 22°C). Recently, we observed that low temperature (below 22°C) induced elevation of intracellular calcium in keratinocytes. Moreover, we demonstrated that topical application of TRPA1 agonists accelerated the recovery of epidermal permeability barrier function after disruption. In this study, we examined the effect of topical application of TRPM8 modulators on epidermal permeability barrier homoeostasis. Immunohistochemical study and RT-PCR confirmed the expression of TRPM8 or TRPM8-like protein in epidermal keratinocytes. Topical application of TRPM8 agonists, menthol and WS 12 accelerated barrier recovery after tape stripping. The effect of WS12 was blocked by a non-selective TRP antagonist, Ruthenium Red, and a TRPM8-specific antagonist, BTCT. Topical application of WS12 also reduced epidermal proliferation associated with barrier disruption under low humidity, and this effect was blocked by BTCT. Our results indicate that TRPM8 or a closely related protein in epidermal keratinocytes plays a role in epidermal permeability barrier homoeostasis and epidermal proliferation after barrier insult.

Keywords epidermis; keratinocyte; stratum corneum; transient receptor potential; TRP

Dennison E, Hindmarsh P, Fall C et al. — **Year** 1999

Authors E. Dennison, P. Hindmarsh, C. Fall, S. Kellingray, D. Barker, D. Phillips and C. Cooper

Report Name Profiles of endogenous circulating cortisol and bone mineral density in healthy elderly men.

Publication J Clin Endocrinol Metab

Issue-page numbers 84:3058–3063 doi:10.1210/jc.84.9.3058. PMID:10487665

URL http://jcem.endojournals.org/content/84/9/3058

Abstract Exogenous glucocorticoids are known to increase the risk of osteoporosis. However, the contribution made by endogenous circulating cortisol concentrations to adult skeletal status remains unknown. We examined this issue in a sample of 34 healthy men, aged 61–72 yr. Venous blood samples were obtained under standard conditions every 20 min over a 24-h period. Measurements were made of serum cortisol and cortisol-binding globulin. Bone mineral density was measured at the lumbar spine and proximal femur using dual energy x-ray absorptiometry. Measurements were made at baseline and 4 yr later. There was a weak negative association between integrated cortisol concentration and lumbar spine bone density ($r = -0.37$; $P < 0.05$); similar relationships ($P < 0.05$) existed at three of five proximal femoral sites. There were also statistically significant positive associations between the trough cortisol concentration and bone loss rate at the lumbar spine ($r = 0.38$; $P < 0.05$), femoral neck ($r = 0.47$; $P < 0.001$), and the trochanteric region ($r = 0.41$; $P = 0.02$) over the 4-yr follow-up period. The cross-sectional relationships between cortisol concentration and bone density were removed by adjustment for body mass index, but the influence on bone loss rate remained significant after adjusting for adiposity, cigarette smoking, alcohol consumption, dietary calcium intake, physical activity, and serum testosterone and estradiol levels. These observations suggest that the endogenous cortisol profile of healthy elderly men is a determinant of their bone mineral density and their rate of involutional bone loss.

Keywords

Denton ML, Foltz MS, Schuster KJ **Year** 2007

Authors Michael L. Denton, Michael S. Foltz, Kurt J. Schuster, Larry E. Estlack, Robert J. Thomas

Report Name Damage thresholds for cultured retinal pigment epithelial cells exposed to lasers at 532 nm and 458 nm

Publication J. Biomed. Opt

Issue-page numbers 12, 034030 (May 10, 2007); doi:10.1117/1.2737394

URL http://spiedigitallibrary.org/jbo/resource/1/jbopfo/v12/i3/p034030_s1?isAuthorized=no

Abstract The determination of safe exposure levels for lasers has come from damage assessment experiments in live animals, which typically involve correlating visually identifiable damage with laser dosimetry. Studying basic mechanisms of laser damage in animal retinal systems often requires tissue sampling (animal sacrifice), making justification and animal availability problematic. We determined laser damage thresholds in cultured monolayers of a human retinal pigment epithelial (RPE) cell line. By varying exposure duration and laser wavelength, we identified conditions leading to damage by presumed photochemical or thermal mechanisms. A comparison with literature values for ocular damage thresholds validates the in vitro model. The in vitro system described will facilitate molecular and cellular approaches for understanding laser-tissue interaction.

Keywords

Deprés-Brummer P, Bourin P, Pages N et al. **Year** 1997

Authors Petra Deprés-Brummer, Philippe Bourin, Nicole Pages, Gérard Metzger, and Francis Lévi

Report Name Persistent T lymphocyte rhythms despite suppressed circadian clock outputs in rats

Publication Am J Physiol

Issue-page numbers 273:R1891–R1899. PMID:9435642

URL http://ajpregu.physiology.org/content/273/6/R1891.full

Abstract Circadian rhythms in circulating leukocyte and lymphocyte counts persisted with halved amplitudes in constant light (LL) of 300 lx intensity for 8 wk, whereas circadian rhythms in body temperature, locomotor activity, and plasma catecholamines were completely suppressed. Subsequent exposure to constant darkness (DD) normalized all circadian rhythms within 2 wk. Rhythms in circulating T lymphocyte subsets were studied in LL or DD using double labeling with monoclonal antibodies and flow cytometry. Circadian rhythms were suppressed for leukocytes and lymphocytes but were maintained for both T helper cells (Th) and T cytotoxic cells (Ts) lymphocytes after 11 wk in LL. A group 24-h rhythm was only validated for total lymphocytes after 16 wk in LL. However, individual total, Th, and Ts lymphocytes maintained their usual respective phase relationships in each rat. The alteration of immune cell circulatory rhythms likely stemmed from a progressive loss of circadian synchronization among rats kept in LL. Conversely, after 11 or 16 wk in DD, leukocytes and lymphocyte subsets circadian rhythms were maintained. Thus catecholamines do not drive circulatory T cell rhythms. The loss of coupling between T lymphocyte rhythms and three major outputs of the circadian system further supports the hypothesis of an independent immunologic oscillator.

Keywords circadian rhythms, desynchronization, body temperature, locomotor activity, leukocytes, catecholamines

Year 1995

Authors Deprés-Brummer P, Lévi F, Metzger G, Touitou Y

Report Name Light-induced suppression of the rat circadian system

Publication Am J Physiol

Issue-page numbers 268:R1111–R1116. PMID:7771569

URL http://ajpregu.physiology.org/content/268/5/R1111.short

Abstract In a constant environment, circadian rhythms persist with slightly altered period lengths. Results of studies with continuous light exposure are less clear, because of short exposure durations and single-variable monitoring. This study sought to characterize properties of the oscillator(s) controlling the rat's circadian system by monitoring both body temperature and locomotor activity. We observed that prolonged exposure of male Sprague-Dawley rats to continuous light (LL) systematically induced complete suppression of body temperature and locomotor activity circadian rhythms and their replacement by ultradian rhythms. This was preceded by a transient loss of coupling between both functions. Continuous darkness (DD) restored circadian synchronization of temperature and activity circadian rhythms within 1 wk. The absence of circadian rhythms in LL coincided with a mean sixfold decrease in plasma melatonin and a marked dampening but no abolition of its circadian rhythmicity. Restoration of temperature and activity circadian rhythms in DD was associated with normalization of melatonin rhythm. These results demonstrated a transient internal desynchronization of two simultaneously monitored functions in the rat and suggested the existence of two or more circadian oscillators. Such a hypothesis was further strengthened by the observation of a circadian rhythm in melatonin, despite complete suppression of body temperature and locomotor activity rhythms. This rat model should be useful for investigating the physiology of the circadian timing system as well as to identify agents and schedules having specific pharmacological actions on this system.

Keywords

Year 2004

Authors Desmettre T, Lecerf JM, Souied EH.

Report Name Nutrition and age-related macular degeneration

Publication J Fr Ophtalmol. [Article in French]

Issue-page numbers Nov;27(9 Pt 2):3S38-56.

URL http://www.ncbi.nlm.nih.gov/pubmed/15602406

Abstract The nutritional factors involved in the pathogenesis of age-related macular degeneration (AMD) include antioxidants or antioxidant cofactors: vitamins A, C, etc.; zinc, etc.; anti-free-radicals such as beta-carotene and carotenoids, including lutein and zeaxanthin; micronutrients protecting from blue light such as lutein and zeaxanthin; and finally components of the membranes of the photoreceptors docosahexaenoic acid (DHA). These nutritional factors are closely related to environmental risk factors such as smoking and chronic blue light exposure. Although the experimental and epidemiological data are concordant and coherent, the protective role of these micronutrients is not clearly established, mainly because there are very few clinical studies. However, a first observation study showed positive effects at stages 3 and 4 of AMD. Report #8 of the Age-Related Eye Disease Study (AREDS) provides important results for preventing complications of AMD (secondary prevention), and the cocktail of micronutrients proposed even encourages complementary studies on, for example, lutein and zeaxanthin instead of beta-carotene. The outcome of observation studies including a supplementation of long-chain polyunsaturated fatty acids (PUFA) of the omega-3 family (DHA) is also important, as it addresses primary prevention of the disease. A supplementation of omega-3 PUFAs could be proposed to certain subjects at risk for AMD for primary prevention and a supplementation with an antioxidant cocktail of micronutrients could be proposed to patients presenting AMD at stages 3 or 4 or to subjects with a nutritional imbalance. These conceivable supplementations are compatible with simple dietary advice. The supplements currently proposed could be optimized to increase their advantages. New research and new clinical studies are necessary to definitively validate these formulations in order to grant them an authentic drug status.

Keywords

Desotelle JA, Wilking MJ, Ahmad N

Year 2012

Authors Joshua A. Desotelle, Melissa J. Wilking, Nihal Ahmad

Report Name The Circadian Control of Skin and Cutaneous Photodamage

Publication Photochemistry and Photobiology

Issue-page numbers Accepted Article (Accepted, unedited articles published online for future issues)

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2012.01099.x/abstract

Abstract Biologically, light including ultraviolet (UV) radiations is vital for life. However, UV exposure does not come without risk, as it is a major factor in the development of skin cancer. Natural protections against UV damage may have been affected by lifestyle changes over the past century, including changes in our sun exposure due to working environments, and the use of sunscreens. In addition, extended 'day time' through the use of artificial light may contribute to the disruption of our circadian rhythms; the daily cycles of changes in critical bio-factors including gene expression. Circadian disruption has been implicated in many health conditions, including cardiovascular, metabolic, and psychiatric diseases, as well as many cancers. Interestingly, the pineal hormone melatonin plays a role in both circadian regulation, as well as protection from UV skin damage, and is therefore an important factor to consider when studying the impact of UV light. This review discusses the beneficial and deleterious effects of solar exposure, including UV skin damage, Vitamin D production, circadian rhythm disruption, and the impact of melatonin. Understanding of these benefits and risks is critical for the development of protective strategies against solar radiation.

Keywords

Dewan EM

Year 1967

Authors Dewan EM

Report Name On the possibility of a perfect rhythm method of birth control by periodic light stimulation

Publication Am J Obstet Gynecol

Issue-page numbers 99:1016–1019. PMID:6058735

URL http://www.ncbi.nlm.nih.gov/pubmed/6058735

Abstract N/A

Keywords

Di W-L, Kadva A, Djahanbakhch O, Silman R **Year** 1998

Authors Di W-L, Kadva A, Djahanbakhch O, Silman R

Report Name Radioimmunoassay of bound and free melatonin in plasma

Publication Clin Chem

Issue-page numbers 44:304–310. PMID:9474029

URL http://www.clinchem.org/cgi/content/abstract/44/2/304

Abstract We describe a nonextraction procedure, and two extraction procedures, for RIA of melatonin in human plasma. All procedures showed a diurnal rhythm of melatonin in human subjects, with interindividual differences greater than interprocedure differences. However, further investigations demonstrated considerable variability of recovery in the nonextraction procedure, suggesting a variability of binding proteins between samples. Combining recovery and dialysis experiments in the extraction procedures, we demonstrated that chloroform was unable to extract albumin-bound melatonin from a human serum albumin solution but, paradoxically, was able to extract bound and free melatonin from a plasma sample. The methanol extraction procedure extracted free and bound melatonin from all sources. These results indicate that albumin binding can substantially affect the RIA procedures. We conclude that assays should be validated against free and bound melatonin and that the two forms should be independently investigated when assessing bioactivity.

Keywords

Díaz E, Fernández C, Castrillón PO et al. **Year** 1999

Authors Díaz E, Fernández C, Castrillón PO et al.

Report Name Effect of exogenous melatonin on neuroendocrinereproductive function of middle-aged female rats.

Publication J Reprod Fertil

Issue-page numbers 117:331–337 doi:10.1530/jrf.0.1170331. PMID:10690201

URL http://sciencestage.com/d/7758360/effect-of-exogenous-melatonin-on-neuroendocrine-reproductive-function-of-middle-aged-female-rats..html

Abstract The possible role of melatonin in the regulation of the reproductive system of female rats during ageing was investigated in middle-aged female rats showing irregular duration of the oestrous cycle (n = 30). Blood samples were obtained by jugular venepuncture during the oestrous cycle in control rats. After this experiment was completed, the female rats were treated with melatonin for 2 months and blood samples were obtained at different stages of the oestrous cycle. Plasma LH, FSH and prolactin concentrations were significantly increased in the afternoon of the day of pro-oestrus after melatonin treatment compared with control rats. Moreover, FSH concentrations too were significantly increased on the morning of pro-oestrus and oestrus in melatonin treated rats compared with control rats. Similarly, oestradiol concentrations were significantly higher on the morning of pro-oestrus in melatonin treated rats compared with controls. Another group of rats showing irregular duration of the oestrous cycle was used to study the possible effect of melatonin treatment on the timing of pro-oestrous surges of LH and FSH. The results showed that LH and FSH peak values occurred at 5 h after melatonin treatment. Pituitary responsiveness to LHRH in a 90 min test was also studied in middle-aged rats showing irregular duration of the oestrous cycle that had been injected for 1 month with either melatonin or saline. Prolactin response was unaffected by exogenous melatonin, but a stimulatory effect of melatonin on LH and FSH pituitary responsiveness to LHRH was observed. The results indicate an improved function of the neuroendocrine-repro ductive axis in middle-aged rats after melatonin treatment.

Keywords

Diaz E, Pazo D, Esquifino AI, Diaz B **Year** 2000

Authors Diaz E, Pazo D, Esquifino AI, Diaz B

Report Name Effects of ageing and exogenous melatonin on pituitary responsiveness to GnRH in rats

Publication J Reprod Fertil

Issue-page numbers 119:151–156 doi:10.1530/reprod/119.1.151. PMID:10864825

URL http://www.sciencedirect.com/science/article/pii/S0093691X06005826

Abstract The study examined the effect of melatonin implants on in vivo pituitary responsiveness to GnRH in control, fully productive (5.7 ± 0.4 years old, n = 17) and aged (10.7 ± 0.3 years old, n = 14) ovariectomized, estradiol-treated Rasa Aragonesa ewes. On 27 February, eight ewes in each age group received a single implant containing 18 mg melatonin. On 10 April, blood samples to be assayed for LH were collected at 10-min intervals over 4 h (starting at 09:00 and 22:00 h). After samples 6 and 18 were collected, ewes received a single i.v. injection of GnRH (20 ng/kg liveweight). The pituitary response to GnRH was assessed using the difference between plasma LH concentrations before and after (highest value) each injection (DLH1, DLH2)), and the area under the LH response curve for 1 h after each GnRH injection (AUC1, AUC2). On 23 September, the previously implanted ewes received a new melatonin implant and, on 17 November, all of the ewes were subjected to the same diurnal and nocturnal sampling protocols, again. Generally, non-implanted aged ewes exhibited a lower pituitary response to GnRH than did non-implanted control ewes, particularly in November and after the first injection ($P < 0.05$ for DLH1 and AUC1 in both the diurnal and nocturnal tests). The response was significantly affected by the interaction of age and melatonin treatment, particularly in the diurnal tests ($P < 0.1$ for DLH1 and AUC1, and $P < 0.05$ for AUC2 in April; $P < 0.05$ for DLH1, AUC1 and AUC2 in November), which indicated that exogenous melatonin increased LH levels after GnRH injections in aged ewes compared to non-implanted ewes, this effect being the opposite in control females. Thus, melatonin can restore in ewes the functionality of the neuroendocrine system, after it has been reduced by senescence.

Keywords Sheep; Melatonin; Aging; LH

Díaz López B, Díaz Rodríguez E, Urquijo C, Fernández Alvarez C **Year** 2005

Authors Díaz López B, Díaz Rodríguez E, Urquijo C, Fernández Alvarez C

Report Name Melatonin influences on the neuroendocrine-reproductive axis.

Publication Ann N Y Acad Sci

Issue-page numbers 1057:337–364 doi:10.1196/annals.1356.026. PMID:16399905

URL http://www.mendeley.com/research/melatonin-influences-neuroendocrinereproductive-axis/

Abstract The neuroendocrine-reproductive axis designates the functional activity of the hypothalamus-pituitary-gonadal axis. A delicate synchronization of many inputs at these three different levels is vital for normal reproductive function. From the median basal hypothalamus, the median eminence releases gonadotrophin releasing hormone into the portal circulation to reach the anterior pituitary gland. Gonadotrophin releasing hormone is obviously a key hormone for the regulation of the secretion of gonadotrophins LH and FSH.

Keywords

Authors Díaz Rodríguez E, Díaz López B, Debeljuk L et al.

Report Name Developmental changes of hypothalamic, pituitary and striatal tachykinins in response to testosterone: influence of prenatal melatonin.

Publication Peptides

Issue-page numbers 20:501–508 doi:10.1016/S0196-9781(99)00032-7. PMID:10458521

URL http://www.sciencedirect.com/science/article/pii/S0196978199000327

Abstract Substance P (SP) and neurokinin A (NKA), members of the family of mammalian tachykinins, are involved in the regulation of many physiological functions and are widely distributed in mammalian tissues. In this report, the effects of prenatal melatonin on the postnatal developmental pattern of NKA, and SP, and on testosterone secretion were investigated. Also, tachykinin response to the administration of testosterone propionate (TP) was studied. The brain areas studied were medio-basal-hypothalamus, pituitary gland and striatum. Male rat offspring of control or melatonin treated mother rats were studied at different ages of the sexual development: infantile, juvenile or prepubertal periods, and pubertal period. Both groups received exogenous TP (control-offspring+TP and MEL-offspring+TP), or the vehicle (control-offspring+placebo and MEL-offspring+placebo). Hypothalamic concentrations of all peptides studied in control-offspring+placebo remained at low levels until the juvenile period, days 30–31 of age. After this age, increasing concentrations of these peptides were found, with peak values at puberty, 40–41 days of age, then declining until adulthood. In the MEL-offspring+placebo a different pattern of development was observed; hypothalamic concentrations of NKA and SP from the infantile period until the end of juvenile period were significantly higher than in control-offspring+placebo. TP administration exerted a more marked influence on MEL-offspring than on control-offspring and prevented the elevation in tachykinin concentrations associated with prenatal melatonin treatment. TP administration to control-offspring resulted in significantly reduced ($P < 0.05$) tachykinin concentration only at 40–41 days of age, and increased ($P < 0.01$) during infantile period as compared to control-offspring+placebo. Pituitary NKA concentrations were lower than in the hypothalamus. In control-offspring+placebo pituitary NKA levels did not show significant changes throughout sexual development. A different developmental pattern was observed in MEL-offspring+placebo, with significantly increased ($P < 0.05$) pituitary NKA concentrations at 35–36 days of age than in control-offspring+placebo. TP administration to control-offspring influenced pituitary NKA levels at the end of the infantile and pubertal periods, showing at both stages significantly higher ($P < 0.05$) NKA levels as compared to control-offspring+placebo. NKA levels in MEL-offspring+TP were only affected at 21–22 days of age, showing significantly increased ($P < 0.01$) values as compared to MEL-offspring+placebo. Striatal tachykinin concentrations in control-offspring did not undergo important modifications throughout sexual development, but during the prepubertal period they started to increase. Maternal melatonin and TP injections produced short-lived alterations during the infantile period. The results showed that prenatal melatonin delayed the postnatal testosterone secretion pattern until the end of the pubertal period and postnatal peptide secretion in brain structures. Consequently, all functions depending of the affected areas will in turn, be affected.

Keywords NKA; SP; Prenatal melatonin; Hypothalamus; Pituitary; Striatum; Testosterone

Dickerman B, Liu J. **Year** 2012

Authors Dickerman B, Liu J.

Report Name Does current scientific evidence support a link between light at night and breast cancer among female night-shift nurses?: review of evidence and implications for occupational ar

Publication Workplace Health Saf.

Issue-page numbers 2012 Jun;60(6):273-90. doi: 10.3928/21650799-20120529-06.

URL http://www.ncbi.nlm.nih.gov/pubmed/22658734

Abstract Breast cancer is increasingly prevalent in industrialized regions of the world, and exposure to light at night (LAN) has been proposed as a potential risk factor. Epidemiological observations have documented an increased breast cancer risk among female night-shift workers, and strong experimental evidence for this relationship has also been found in rodent models. Indirect support for the LAN hypothesis comes from studies involving blind women, sleep duration, bedroom light levels, and community nighttime light levels. This article reviews the literature, discusses possible mechanisms of action, and provides recommendations for occupational health nursing research, practice, and education. Research is needed to further explore the relationship between exposure to LAN and breast cancer risk and elucidate the mechanisms underlying this relationship before interventions can be designed for prevention and mitigation of breast cancer.

Keywords

Diffey BL **Year** 1991

Authors Diffey BL.

Report Name Solar ultraviolet radiation effects on biological systems.

Publication Phys Med Biol.

Issue-page numbers Mar;36(3):299-328.

URL http://www2.ess.ucla.edu/~ahock/filez/pdfz/diffey%201991%20-%20uv%20effects%20on%20bio.pdf

Abstract Ultraviolet climatology is outlined including atmospheric ozone and factors affecting terrestrial ultraviolet radiation. Solar dosimetry in photobiology and terrestrial UV monitoring are discussed. Molecular and cellular ultraviolet photobiology are described. The effect of solar UV on aquatic life and plants is outlined. The effects of solar UV on human skin such as sunburn, tanning, vitamin D3 production, photo-ageing, melanomas and skin cancer are described. The effect of solar UV on the eye is discussed.

Keywords

Dijk DJ, Lockley SW — *Year* 2002

Authors Dijk DJ, Lockley SW.

Report Name Integration of human sleep-wake regulation and circadian rhythmicity.

Publication Journal of Applied Physiology

Issue-page numbers 2002 Feb;92(2):852-62.

URL http://www.ncbi.nlm.nih.gov/pubmed/11796701

Abstract The human sleep-wake cycle is generated by a circadian process, originating from the suprachiasmatic nuclei, in interaction with a separate oscillatory process: the sleep homeostat. The sleep-wake cycle is normally timed to occur at a specific phase relative to the external cycle of light-dark exposure. It is also timed at a specific phase relative to internal circadian rhythms, such as the pineal melatonin rhythm, the circadian sleep-wake propensity rhythm, and the rhythm of responsiveness of the circadian pacemaker to light. Variations in these internal and external phase relationships, such as those that occur in blindness, aging, morning and evening, and advanced and delayed sleep-phase syndrome, lead to sleep disruptions and complaints. Changes in ocular circadian photoreception, interindividual variation in the near-24-h intrinsic period of the circadian pacemaker, and sleep homeostasis can contribute to variations in external and internal phase. Recent findings on the physiological and molecular-genetic correlates of circadian sleep disorders suggest that the timing of the sleep-wake cycle and circadian rhythms is closely integrated but is, in part, regulated differentially.

Keywords

Dijk DJ, Neri DF, Wyatt JK, et al. — *Year* 0

Authors Derk-Jan Dijk, David F. Neri, James K. Wyatt, Joseph M. Ronda, Eymard Riel, Angela Ritz-De Cecco, Rod J. Hughes, Ann R. Elliott, G. Kim Prisk, John B. West, and

Report Name Sleep, performance, circadian rhythms, and light-dark cycles during two space shuttle flights

Publication AJP - Regu Physiol

Issue-page numbers November 2001 vol. 281 no. 5 R1647-R1664

URL http://ajpregu.physiology.org/content/281/5/R1647.abstract

Abstract Sleep, circadian rhythm, and neurobehavioral performance measures were obtained in five astronauts before, during, and after 16-day or 10-day space missions. In space, scheduled rest-activity cycles were 20–35 min shorter than 24 h. Light-dark cycles were highly variable on the flight deck, and daytime illuminances in other compartments of the spacecraft were very low (5.0–79.4 lx). In space, the amplitude of the body temperature rhythm was reduced and the circadian rhythm of urinary cortisol appeared misaligned relative to the imposed non-24-h sleep-wake schedule. Neurobehavioral performance decrements were observed. Sleep duration, assessed by questionnaires and actigraphy, was only ~6.5 h/day. Subjective sleep quality diminished. Polysomnography revealed more wakefulness and less slow-wave sleep during the final third of sleep episodes. Administration of melatonin (0.3 mg) on alternate nights did not improve sleep. After return to earth, rapid eye movement (REM) sleep was markedly increased. Crewmembers on these flights experienced circadian rhythm disturbances, sleep loss, decrements in neurobehavioral performance, and postflight changes in REM sleep.

Keywords microgravity, entrainment, sleep homeostasis, rapid eye movement sleep, adaptation, melatonin, slow-wave sleep, cortisol, memory

Dillon J, Zheng L, Merriam JC, Gaillard ER

Year 2004

Authors James Dillon, Lei Zheng, John C Merriam, Elizabeth R Gaillard

Report Name Transmission of light to the aging human retina: possible implications for age related macular degeneration

Publication Experimental Eye Research

Issue-page numbers Volume: 79, Issue: 6, Pages: 753-759

URL http://www.mendeley.com/research/transmission-light-aging-human-retina-possible-implications-age-related-macular-degeneration-1/

Abstract The purpose of this study is to determine the transmission properties of the anterior segment of the human eye as a function of age and relate those changes to possible consequences for retinal disorders. For this a new method has been developed. This consists of a probe which is inserted into the posterior sclera and detects light passing through the anterior segment. The probe is connected to a CCD spectrophotometer via a fibre optic bundle. Using this, the transmission properties of human cadaver eyes were determined. A young primate anterior segment has a maximum absorption of 365 nm due to the O-beta-glucoside of 3-hydroxykynurenine (3-HKG) in the lens. There is a steep increase in transmission of the human anterior segment at wavelengths longer than 400 nm. With aging there is an increase in absorption throughout the visible such that by the sixth decade only 20% of blue light is transmitted to the retina compared to the young primate eye. The rate of decrease of blue light was similar to the age related change of the ratio of absorbance at 365/320 nm of the lens. (IOVS 41:1454;1999). The age related rate of decrease in the transmission of blue light to the retina was similar to the rate of increase of lipofuscin formation in the retina, and the amount of light absorbed by A2E in the RPE is constant from the second to seventh decade. Although this yellowing is thought to be detrimental to the lens, it would appear to be beneficial to the retina. It was determined that the implantation of a standard IOL after cataract surgery increased the amount of light absorbed by A2-E by approximately a factor of five.

Keywords

Dilsaver SC

Year 1988

Authors Steven C. Dilsaver

Report Name Artificial light and nicotine subsensitivity

Publication Biological Psychiatry

Issue-page numbers Volume 24, Issue 4, August 1988, Pages 437-440

URL http://www.sciencedirect.com/science/article/pii/0006322388901813

Abstract N/A

Keywords

Dilsaver SC, Majchrzak MJ

Year 1987

Authors Steven C. Dilsaver M.D., Mark J. Majchrzak

Report Name Bright artificial light subsensitizes a central muscarinic mechanism

Publication Life Sciences

Issue-page numbers Volume 41, Issue 24, 14 December 1987, Pages 2607-2614

URL http://www.sciencedirect.com/science/article/pii/0024320587902748

Abstract

Supersensitivity of a muscarinic mechanism is implicated in the pathophysiology of depression. Bright artificial light is efficacious in the treatment of Seasonal Affective Disorder (SAD). We studied the effect of constant bright light (11, 500 lux) on the sensitivity of adult, male rats to oxotremorine, 1.5 mg/kg ip, using a repeated measures design. Oxotremorine challenges were proceeded by the injection of methylscopolamine, 1 mg/kg ip, by 30 minutes. Temperature was telemetrically measured every 10 minutes for 120 minutes starting 10 minutes after the injection of oxotremorine. Prior to and after 7 continuous days of exposure to bright light, the sample exhibited a hypothermic response of 2if2.50 ± 0.48°C (mean ± SEM) and 0.29 ± 0.31°C (mean ± SEM), respectively ($p < 0.0014$). All 7 animals exhibited blunting to the thermic response to oxotremorine. Bright light also blocked the capacity of amitriptyline to supersensitize a central muscarinic mechanism. Exposure to light at an intensity of 300 lux for 7 days had no effect on the thermic response to oxotremorine. These data are consistent with the hypotheses that the biology of depression involves supersensitivity of central muscarinic mechanisms and that the effects of bright artificial light are not the consequence of shifting circadian rhythms.

Keywords

Authors Dimitrov S, Lange T, Fehm HL, Born J

Report Name A regulatory role of prolactin, growth hormone, and corticosteroids for human T-cell production of cytokines

Publication Brain Behav Immun

Issue-page numbers 18:368–374 doi:10.1016/j.bbi.2003.09.014. PMID:15157954

URL http://www.researchgate.net/publication/8548325_A_regulatory_role_of_prolactin_growth_hormone_and_corticosteroids_for_human_T-cell_production_of_cytokines

Abstract

The release of the pituitary hormones, prolactin and growth hormone (GH), and of adrenal corticosteroids is subject to a profound regulation by sleep. In addition these hormones are known to be involved in the regulation of the immune response. Here, we examined their role for in vitro production of T-cell cytokines. Specifically, we hypothesized that increased concentrations of prolactin and GH as well as a decrease in cortisol, i.e., hormonal changes characterizing early nocturnal sleep, could be responsible for a shift towards T helper 1 (Th1) cytokines during this time. Whole blood was sampled from 15 healthy humans in the morning after regular sleep and was activated in vitro with ionomycin and two concentrations of phorbol myrestate acetate (PMA, 8 and 25 ng/ml) in the absence or presence of prolactin, prolactin antibody, GH, glucocorticoid receptor (GR) antagonist RU-486, or mineralocorticoid receptor (MR) antagonist spironolactone. Hormones were examined at physiological concentrations. Production of T-cell derived cytokines was measured at the single cell level using multiparametric flow cytometry. Generally, effects were more pronounced after stimulation with 8 rather than 25 ng/ml PMA. The following changes reached significance ($p < .05$): prolactin (versus prolactin antibody) increased tumor necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma) producing CD4+ and CD8+ cells and interleukin-2 (IL-2) producing CD8+ cells. Compared with control, prolactin antibody decreased, whereas GH increased IFN-gamma+CD4+ cells. RU-486 increased TNF-alpha, IFN-gamma, and IL-2 producing CD4+ and CD8+ cells. Surprisingly strong effects were found after MR blocking with spironolactone which increased TNF-alpha, IFN-gamma, and IL-2 producing CD4+ and CD8+ cells. No effects on IL-4+CD4+ cells were observed, while the IFN-gamma/IL-4 ratio shifted towards Th1 after spironolactone and after RU-486 plus GH. Results suggest that enhanced prolactin and GH concentrations as well as low cortisol levels during early nocturnal sleep synergistically act to enhance Th1 cytokine activity.

Keywords Brain, behavior, immunity

Dimitrov S, Lange T, Tieken S et al. **Year** 2004

Authors Stoyan Dimitrov, Tanja Lange, Swantje Tieken, Horst L Fehm, Jan Born

Report Name Sleep associated regulation of T helper 1/T helper 2 cytokine balance in humans.

Publication Brain Behav Immun

Issue-page numbers 18:341–348 doi:10.1016/j.bbi.2003.08.004. PMID:15157951

URL http://www.mendeley.com/research/sleep-associated-regulation-t-helper-1t-helper-2-cytokine-balance-humans-1/

Abstract

Recent human studies suggested a supportive influence of regular nocturnal sleep on immune responses to experimental infection (vaccination). We hypothesized here that sleep could ease such responses by shifting the balance between T helper 1 (Th1) and T helper 2 (Th2) cytokine activity towards Th1 dominance thereby favoring cellular over humoral responses to infection. We compared the Th1/Th2 cytokine balance in 14 healthy men during regular nocturnal sleep (between 23:00 and 07:00 h) and while remaining awake during the same nocturnal interval, in a within-subject cross-over design. Blood was collected every 2 h. Production of T cell derived cytokines-interferon-gamma (IFN-gamma), interleukin-2 (IL-2), interleukin-4 (IL-4), and tumor necrosis factor-alpha (TNF-alpha)-was measured at the single cell level using multiparametric flow cytometry. Also, several immunoactive hormones-prolactin, growth hormone (GH), thyroid stimulating hormone (TSH), cortisol, and melatonin-were measured, the release of which is known to be regulated by sleep. Compared with wakefulness, early nocturnal sleep induced a shift in the Th1/Th2 cytokine balance towards increased Th1 activity, as indicated by an increased ($p < .05$) ratio of IFN-gamma/IL-4 producing T helper cells. However, the Th1 shift was only of moderate size and replaced by Th2 dominance during late sleep ($p < .05$). It could be mediated via release of prolactin and GH which both were distinctly increased during sleep ($p < .001$). Though unexpected, the most pronounced effect of sleep on T cell cytokine production was a robust decrease in TNF-alpha producing CD8+ cells probably reflecting increased extravasation of cytotoxic effector and memory T cells.

Keywords

Ding JH, Sheckter CB, Drinkwater BL et al. **Year** 1988

Authors JU-HONG DING, M.S., M.D.; CAROL B. SHECKTER, M.D.; BARBARA L. DRINKWATER, Ph.D.; MICHAEL R. SOULES, M.D.; and WILLIAM J. BREMNER

Report Name High serum cortisol levels in exercise-associated amenorrhea.

Publication Ann Intern Med

Issue-page numbers 108:530–534. PMID:3348561

URL http://www.annals.org/content/108/4/530.short

Abstract

Objective: To determine whether basal Cortisol levels are elevated in exercise-associated amenorrhea.

Design: Survey, with hormone levels measured weekly for 1 month and patients followed clinically for 6 months.

Setting: Volunteers were recruited through media advertisements and fliers.

Participants: Ninety-two women were enrolled; 71 (77%) completed the study. Subjects were grouped by menstrual and activity histories reported by a self-administered questionnaire. After 6 months, final groups were assigned: amenorrhea athletes, 19; eumenorrheic athletes, 35; a transition group of amenorrheic athletes who had resumed menses after entering the study, 7; and normal cyclic nonathletes, 10.

Interventions: Four weekly resting blood samples (0800 to 1000 hours) were obtained and measured for Cortisol, estradiol, progesterone, and prolactin levels. Lumbar bone mineral density was measured by dual-photon densitometry.

Measurements and Main Results: Mean (±SE) Cortisol levels were higher in amenorrheic athletes (585±33 nmol/L) than in eumenorrheic athletes (411±14 nmol/L), transition athletes (378±33 nmol/L), or nonathletic women (397±30 nmol/L) ($P < 0.01$). Of nine women with abnormally high Cortisol levels (greater than 579 nmol/L), eight were amenorrheic athletes, and one was a eumenorrheic athlete. Bone mineral density was lower in amenorrheic athletes than in the other three groups ($P < 0.01$).

Conclusions: Increased glucocorticoid levels may be an etiologic factor in exercise-associated amenorrhea. High Cortisol levels could also contribute to decreased bone density. The failure of amenorrheic athletes with hypercortisolemia to regain menses within 6 months suggests that they are at risk for a prolonged acyclic state.

Keywords

Ding JM, Faiman LE, Hurst WJ, et al. ***Year*** 1997

Authors Jian M. Ding, Lia E. Faiman, William J. Hurst, Liana R. Kuriashkina, and Martha U. Gillette

Report Name Resetting the Biological Clock: Mediation of Nocturnal CREB Phosphorylation via Light, Glutamate, and Nitric Oxide

Publication The Journal of Neuroscience

Issue-page numbers January 1997, 17(2): 667-675

URL http://neuro.cjb.net/content/17/2/667.short

Abstract Synchronization between the environmental lighting cycle and the biological clock in the suprachiasmatic nucleus (SCN) is correlated with phosphorylation of the Ca2+/cAMP response element binding protein (CREB) at the transcriptional activating site Ser133. Mechanisms mediating the formation of phospho-CREB (P-CREB) and their relation to clock resetting are unknown. To address these issues, we probed the signaling pathway between light and P-CREB. Nocturnal light rapidly and transiently induced P-CREB-like immunoreactivity (P-CREB-lir) in the rat SCN. Glutamate (Glu) or nitric oxide (NO) donor administration in vitro also induced P-CREB-lir in SCN neurons only during subjective night. Clock-controlled sensitivity to phase resetting by light, Glu, and NO is similarly restricted to subjective night. The effects of NMDA and nitric oxide synthase (NOS) antagonists on Glu-mediated induction of P-CREB-lir paralleled their inhibition of phase shifting. Significantly, among neurons in which P-CREB-lir was induced by light were NADPH-diaphorase-positive neurons of the SCN's retinorecipient area. Glu treatment increased the intensity of a 43 kDa band recognized by anti-P-CREB antibodies in subjective night but not day, whereas anti-αCREB-lir of this band remained constant between night and day. Inhibition of NOS during Glu stimulation diminished the anti-P-CREB lir of this 43 kDa band. Together, these data couple nocturnal light, Glu, NMDA receptor activation and NO signaling to CREB phosphorylation in the transduction of brief environmental light stimulation of the retina into molecular changes in the SCN resulting in phase resetting of the biological clock.

Keywords suprachiasmatic nucleus, circadian rhythm, glutamate, NMDA, nitric oxide, CREB phosphorylation

Dinges DF, Douglas SD, Zaugg L et al. ***Year*** 1994

Authors D F Dinges, S D Douglas, L Zaugg, D E Campbell, J M McMann, W G Whitehouse, E C Orne, S C Kapoor, E Icaza, M T Orne

Report Name Leukocytosis and natural killer cell function parallel neurobehavioral fatigue induced by 64 hours of sleep deprivation.

Publication J Clin Invest

Issue-page numbers 93:1930–1939 doi:10.1172/JCI117184. PMID:7910171

URL http://www.jci.org/articles/view/117184/pdf

Abstract T he hypothesis that sleep deprivation depresses immune function was tested in 20 adults, selected on the basis of their normal blood chemistry, monitored in a laboratory for 7 d, and kept awake for 64 h. At 2200 h each day measurements were taken of total leukocytes (WBC), monocytes, granulocytes, lymphocytes, eosinophils, erythrocytes (RBC), B and T lymphocyte subsets, activated T cells, and natural killer (NK) subpopulations (CD56/CD8 dual-positive cells, CD16-positive cells, CD57-positive cells). Functional tests included NK cytotoxicity, lymphocyte stimulation with mitogens, and DNA analysis of cell cycle. Sleep loss was associated with leukocytosis and increased NK cell activity. At the maximum sleep deprivation, increases were observed in counts of WBC, granulocytes, monocytes, NK activity, and the proportion of lymphocytes in the S phase of the cell cycle. Changes in monocyte counts correlated with changes in other immune parameters. Counts of CD4, CD16, CD56, and CD57 lymphocytes declined after one night without sleep, whereas CD56 and CD57 counts increased after two nights. No changes were observed in other lymphocyte counts, in proliferative responses to mitogens, or in plasma levels of cortisol or adrenocorticotropin hormone. The physiologic leukocytosis and NK activity increases during deprivation were eliminated by recovery sleep in a manner parallel to neurobehavioral function, suggesting that the immune alterations may be associated with biological pressure for sleep.

Keywords

Authors Dinges DF, Graeber RC, Rosekind MR et al.

Report Name Principles and guidelines for duty and rest scheduling in commerical aviation

Publication NASA Technical Memorandum 110404 AMES Research Center Moffett Field CA

Issue-page numbers May 1996

URL http://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/19990063635_1999104236.pdf

Abstract

Twenty-four Hour Requirements of the Aviation Industry
The aviation industry requires 24-hour activities to meet operational demands. Growth in global longhaul, regional, overnight cargo, and short-haul domestic operations will continue to increase these round-the-clock requirements. Flight crews must be available to support 24-hour-a-day operations to meet these industry demands. Both domestic and international aviation can also require crossing multiple time zones. Therefore, shift work, night work, irregular work schedules, unpredictable work schedules, and time zone changes will continue to be commonplace components of the aviation industry. These factors pose known challenges to human physiology, and because they result in performance-impairing fatigue, they pose a risk to safety. It is critical to acknowledge and, whenever possible, incorporate scientific information on fatigue, human sleep, and circadian physiology into 24-hour aviation operations. Utilization of such scientific information can help promote crew performance and alertness during flight operations and thereby maintain and improve the safety margin.

Keywords

Djeridane Y, Touitou Y **Year** 2004

Authors Djeridane Y, Touitou Y

Report Name Ex vivo studies on the acute and chronic effects of DHEA and DHEA-sulfate on melatonin synthesis in young- and old-rat pineal glands

Publication Steroids

Issue-page numbers 69:343–349 doi:10.1016/j.steroids.2004.03.003. PMID:15219412

URL http://www.mendeley.com/research/ex-vivo-studies-acute-chronic-effects-dhea-dheasulfate-melatonin-synthesis-young-oldrat-pineal-glands/

Abstract This study investigates the effects of acute and chronic injections of the neurosteroid dehydroepiandrosterone (DHEA) and its sulfate DHEA-S on pineal gland melatonin synthesis. Pineal melatonin production and plasma melatonin levels were investigated in young (9-week-old) and old (27-month-old) male Wistar rats. DHEA or DHEA-S have been administered acutely in a single intraperitoneal injection at a dosage of 50, 250, or 500 microg per animal, or on a long-term basis, i.e., for 8 days at a dosage of 100 microg per animal, 1 h before the onset of darkness. DHEA, at a dose of 50, 250, or 500 microg per animal, administered acutely to rats had no significant effects on pineal melatonin production whatever the age of the animals. In contrast, 500 microg DHEA-S induced a significant increase in the pineal melatonin content (15% in young animals and 35% in old animals) and the activity of N-acetyltransferase, the rate-limiting enzyme for melatonin synthesis in the pineal gland, (40% in young animals and 20% in old animals), without altering the activity of hydroxyindole-O-methyltransferase whatever the age of the animals. At lower concentrations (50 or 250 microg) DHEA-S had no effect on pineal melatonin production regardless of the age of the rats. Chronic injection of DHEA or DHEA-S at a dose of 100 microg had no effect on pineal melatonin or NAT and HIOMT activities in the two age groups. This work shows that DHEA-S (and not DHEA) is able, at pharmacological concentrations, to stimulate melatonin production by rat pineal glands regardless of the age of the animals.

Keywords

Dolin PJ, Johnson GJ **Year** 1994

Authors Paul J. Dolin and Gordon J. Johnson

Report Name Solar ultraviolet radiation and ocular disease: a review of the epidemiological and experimental evidence

Publication Ophthalmic Epidemiology

Issue-page numbers 1994, Vol. 1, No. 3 , Pages 155-164

URL http://informahealthcare.com/doi/abs/10.3109/09286589409047224?journalCode=ope

Abstract Exposure to solar ultraviolet radiation has been linked, at some point, with more than a dozen eye diseases. Some of these associations are based solely on anecdotes, while others have been subjected to epidemiological investigations. For each eye disease, the evidence for an association with ultraviolet radiation is presented and evaluated. The only eye disease for which there is sufficient evidence of a causal association in humans is photo-keratitis. For several eye diseases (climatic droplet keratopathy, pterygium, cataract) there is limited evidence for an association, while for other diseases (uveal melanoma, macular degeneration) there is either little support for an association or inadequate data on which to base an assessment.

Keywords ultraviolet radiation, climatic droplet keratopathy, keratopathy, pterygium, macular degeneration, eye cancer, epidemiology

Dorn M, Jurk M, Schmieder P — ***Year*** 2012

Authors Matthias Dorn, Marcel Jurk, Peter Schmieder

Report Name Blue News Update: BODIPY-GTP Binds to the Blue-Light Receptor YtvA While GTP Does Not

Publication PLoS ONE

Issue-page numbers 7(1): e29201. doi:10.1371/journal.pone.0029201

URL http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0029201

Abstract Light is an important environmental factor for almost all organisms. It is mainly used as an energy source but it is also a key factor for the regulation of multiple cellular functions. Light as the extracellular stimulus is thereby converted into an intracellular signal by photoreceptors that act as signal transducers. The blue-light receptor YtvA, a bacterial counterpart of plant phototropins, is involved in the stress response of Bacillus subtilis. The mechanism behind its activation, however, remains unknown. It was suggested based on fluorescence spectroscopic studies that YtvA function involves GTP binding and that this interaction is altered by absorption of light. We have investigated this interaction by several biophysical methods and show here using fluorescence spectroscopy, ITC titrations, and three NMR spectroscopic assays that while YtvA interacts with BODIPY-GTP as a fluorescent GTP analogue originally used for the detection of GTP binding, it does not bind GTP.

Keywords

Drazen DL, Bilu D, Bilbo SD, Nelson RJ — ***Year*** 2001

Authors Drazen DL, Bilu D, Bilbo SD, Nelson RJ

Report Name Melatonin enhancement of splenocyte proliferation is attenuated by luzindole, a melatonin receptor antagonist.

Publication Am J Physiol Regul Integr Comp Physiol

Issue-page numbers 280:R1476–R1482. PMID:11294771

URL http://ajpregu.physiology.org/content/280/5/R1476.full.pdf

Abstract Melatonin enhancement of splenocyte proliferation is attenuated by luzindole, a melatonin receptor antagonist. Am J Physiol Regulatory Integrative Comp Physiol 280: R1476–R1482, 2001.—In addition to marked seasonal changes in reproductive, metabolic, and other physiological functions, many vertebrate species undergo seasonal changes in immune function. Despite growing evidence that photoperiod mediates seasonal changes in immune function, little is known regarding the neuroendocrine mechanisms
underlying these changes. Increased immunity in short days is hypothesized to be due to the increase in the
duration of nightly melatonin secretion, and recent studies indicate that melatonin acts directly on immune cells to enhance immune parameters. The present study examined the contribution of melatonin receptors in mediating the enhancement of splenocyte proliferation in response to the T cell mitogen Concanavalin A in mice. The administration of luzindole, a high-affinity melatonin receptor antagonist, either in vitro or in vivo significantly attenuated the ability of in vitro melatonin to enhance splenic lymphocyte proliferation during the day or night. In the absence of melatonin or luzindole, splenocyte proliferation was intrinsically higher during the night than during the day. In the absence of melatonin administration, luzindole reduced the ability of spleen cells to proliferate during the night, when endogenous melatonin concentrations are naturally high. This effect was not observed during the day, when melatonin concentrations are low. Taken together, these results suggest that melatonin enhancement of splenocyte proliferation is mediated directly
by melatonin receptors on splenocytes and that there is diurnal variation in splenocyte proliferation in mice that is also mediated by splenic melatonin receptors.

Keywords

Drobnik J

Year 2012

Authors Jacek Drobnik

Report Name Wound healing and the effect of pineal gland and melatonin

Publication J Exp Integr Med

Issue-page numbers 2012; 2(1): 3-14

URL http://www.scopemed.org/?mno=12299

Abstract Wound healing is a complex phenomenon that is controlled by local and general regulatory mechanisms. The aim of the paper is to analyze recently-published data devoted to the regulation of wound repair by melatonin.
The effect of melatonin has been reported in different wound types healed with various mechanisms. The action of the pineal indoleamine is dependent on the used dose, time of application and target organ. Moreover, melatonin influences different phases of wound repair such as inflammation, by regulating the release of inflammatory mediators, cell proliferation and migration, by influencing angiogenesis, and the proliferation of fibroblasts, as well as the synthesis phase, by regulating collagen and glycosaminoglycan accumulation in the wounded milieu. Thus, healing of the skin wound, myocardial infarction, bone fractures and gastric ulcer is influenced by melatonin.
In patients with low levels of melatonin (elderly or β-blocker treated patients), its regulatory effects are expected to be impaired. Thus, the need for melatonin supplementation in those patients is postulated in the study.

Keywords Angiogenesis; Collagen; Fibroblasts; Glycosaminoglycans; Inflammation; Melatonin

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Dubina MV, Petrishev NN, Panchebko AV et al.

Year 2002

Authors Dubina MV, Petrishev NN, Panchebko AV et al.

Report Name [Circadian features of carcinogenesis of the large intestine induced by 1,2-dimethylhydrazine in rats]

Publication Vopr Onkol

Issue-page numbers 48:331–334. PMID:12455357

URL http://lib.bioinfo.pl/paper:12455357

Abstract The study was concerned with comparison of carcinogenesis induced in the rat large intestine by 5 single doses of 1,2-dimethylhydrazine (DMH) 21 mg/kg injected at different circadian stages--either at 10 a.m. or 10 p.m. Evening injections were followed by significant decrease in incidence (from 91 to 75%) and size of tumor (27.2-15.5 mm2). Also, there were relatively fewer large tumors in the evening series.

Keywords

Dubocovich ML

Year 1995

Authors Dubocovich ML

Report Name Melatonin receptors: are there multiple subtypes?

Publication Trends Pharmacol Sci

Issue-page numbers 16:50–56 doi:10.1016/S0165-6147(00)88978-6. PMID:7762083

URL http://www.sciencedirect.com/science/article/pii/S0165614700889786

Abstract There is now evidence for more than one site of action for the hormone melatonin (N-acetyl-5-methoxytryptamine). Recent pharmacological and molecular advances are providing the tools to address the characterization of melatonin receptor subtypes. The development of novel melatonin receptor agonists and antagonists, high-affinity radioligands, quantitative bioassays, and the recent cloning of melatonin receptors are furthering our understanding of native and recombinant melatonin receptors. In this article, Margarita Dubocovich discusses the properties of melatonin receptors, and the basis for their classification into at least two subtypes, the ML1 and ML2.

Keywords

Dubocovich ML, Markowska M

Year 2005

Authors Dubocovich ML, Markowska M

Report Name Functional MT1 and MT2 melatonin receptors in mammals

Publication Endocrine

Issue-page numbers 27:101–110 doi:10.1385/ENDO:27:2:101. PMID:16217123

URL http://www.springerlink.com/content/k2048v63141qm368/

Abstract Melatonin, dubbed the hormone of darkness, is known to regulate a wide variety of physiological processes in mammals. This review describes well-defined functional responses mediated through activation of high-affinity MT1 and MT2 proteinteoupled receptors viewed as potential targets for drug discovery. MT1 melatonin receptors modulate neuronal firing, arterial vasoconstriction, cell proliferation in cancer cells, and reproductive and metabolic functions. Ativation of MT2 melatonin receptors phase shift circadian rhythms of neuronal firing in the suprachiasmatic nucleus, inhibit dopamine release in retina, induce vasodilation and inhibition of leukocyte rolling in arterial beds, and enhance immune responses. The melatonin-mediated responses elicited by activation of MT1 and MT2 native melatonin receptors are dependent on circadian time, duration and mode of exposure to endogenous or exogenous melatonin, and functional receptor sensitivity. Together, these studies underscore the importance of carefully linking each melatonin receptor type to specific functional responses in target tissues to facilitate the design and development of novel therapeutic agent.

Keywords

Dubocovich ML, Yun K, Al-Ghoul WM et al. **Year** 1998

Authors Dubocovich ML, Yun K, Al-Ghoul WM et al.

Report Name Selective MT2 melatonin receptor antagonists block melatonin-mediated phase advances of circadian rhythms

Publication FASEB J

Issue-page numbers 12:1211–1220. PMID:9737724

URL http://www.fasebj.org/content/12/12/1211.full

Abstract This study demonstrates the involvement of the MT2 (Mel1b) melatonin receptor in mediating phase advances of circadian activity rhythms by melatonin. In situ hybridization histochemistry with digoxigenin-labeled oligonucleotide probes revealed for the first time the expression of mt1 and MT2 melatonin receptor mRNA within the suprachiasmatic nucleus of the C3H/HeN mouse. Melatonin (0.9 to 30 μg/mouse, s.c.) administration during 3 days at the end of the subjective day (CT 10) to C3H/HeN mice kept in constant dark phase advanced circadian rhythms of wheel running activity in a dose-dependent manner [EC50=0.72 μg/mouse; 0.98±0.08 h (n=15) maximal advance at 9 μg/mouse]. Neither the selective MT2 melatonin receptor antagonists 4P-ADOT and 4P-PDOT (90 μ/mouse, s.c.) nor luzindole (300 μg/mouse, s.c.), which shows 25-fold higher affinity for the MT2 than the mt1 subtype, affected the phase of circadian activity rhythms when given alone at CT 10. All three antagonists, however, shifted to the right the dose-response curve to melatonin, as they significantly reduced the phase shifting effects of 0.9 and 3 μg melatonin. This is the first study to demonstrate that melatonin phase advances circadian rhythms by activation of a membrane-bound melatonin receptor and strongly suggests that this effect is mediated through the MT2 melatonin receptor subtype within the circadian timing system. We conclude that the MT2 melatonin receptor subtype is a novel therapeutic target for the development of subtype-selective analogs for the treatment of circadian sleep and mood-related disorders.—Dubocovich, M. L., Yun, K., Al-Ghoul, W. M., Benloucif, S., Masana, M. I. Selective MT2 melatonin receptor antagonists block melatonin-mediated phase advances of circadian rhythms.

Keywords melatonin receptors • suprachiasmatic nucleus • C3H/HeN mouse • luzindole • 4P-ADOT • 4P-PDOT • mt1 • Mel1a • Mel1b

Dubois EL, Tuffanelli DL **Year** 1964

Authors Edmund L. Dubois, Denny L. Tuffanelli

Report Name Clinical manifestations of systemic lupus erythematosus. Computer analysis of 520 cases

Publication JAMA

Issue-page numbers 1964;190(2):104-111. doi: 10.1001/jama.1964.03070150014003

URL http://jama.ama-assn.org/content/190/2/104.abstract

Abstract Diagnosis of systemic lupus erythematosus (SLE) was confirmed by the presence of lupus erythematosus cells in 75.7% of the patients, findings of skin biopsies in 6.0% and of renal biopsies in 1.2%, and by the clinical picture alone in 17.1%. Negroes comprised 34% of the subjects. Spontaneous remissions occurred in 35% of the patients. Proven familial SLE occurred in 2%. Myalgia was present in 48.2%. No history of cutaneous involvement at any time was found in 28%. Classic skin lesions of chronic discoid lupus at the onset of their illness were present in 10.8%. Urinary abnormalities were noted in only 46.1%. Uremia caused 34% of the 135 deaths and progressive central nervous system involvement caused 18.4%. The prognosis has markedly improved. The mean duration is now 94.8 months for the entire series versus 38.5 months in an untreated control group

Keywords

Duffield GE, Best JD, Meurers BH et al. **Year** 2002

Authors Giles E. Duffield, Jonathan D. Best, Bernhard H. Meurers, Anton Bittner, Jennifer J. Loros and Jay C. Dunlap

Report Name Circadian programs of transcriptional activation, signaling, and protein turnover revealed by microarray analysis of mammalian cells.

Publication Curr Biol

Issue-page numbers 12:551–557 doi:10.1016/S0960-9822(02)00765-0. PMID:11937023

URL http://www.cell.com/current-biology/abstract/S0960-9822%2802%2900765-0

Abstract Many aspects of physiology and behavior are temporally organized into daily 24 hr rhythms, driven by an endogenous circadian clock. Studies in eukaryotes have identified a network of interacting genes forming interlocked autoregulatory feedback loops which underlie overt circadian organization in single cells [1,2]. While in mammals the master oscillator resides in the suprachiasmatic nuclei of the hypothalamus [2], semiautonomous circadian oscillators also exist in peripheral tissues [3,4,5] and in immortalized fibroblasts, where rhythmicity is induced following a serum shock [6,7]. We used this model system in combination with high-density cDNA microarrays to examine the magnitude and quality of clock control of gene expression in mammalian cells. Supported by application of novel bioinformatics tools, we find ~2% of genes, including expected canonical clock genes, to show consistent rhythmic circadian expression across five independent experiments. Rhythmicity in most of these genes is novel, and they fall into diverse functional groups, highlighted by a predominance of transcription factors, ubiquitin-associated factors, proteasome components, and Ras/MAPK signaling pathway components. When grouped according to phase, 68% of the genes were found to peak during estimated subjective day, 32% during estimated subjective night, with a tendency to peak at a phase corresponding to anticipation of dawn or dusk.

Keywords

Duffy JF, Czeisler CA **Year** 2009

Authors Jeanne F. Duffy, and Charles A. Czeisler

Report Name Effect of Light on Human Circadian Physiology

Publication Sleep Med Clin

Issue-page numbers June; 4(2): 165–177.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2717723/

Abstract The circadian system in animals and humans, being near but not exactly 24-hours in cycle length, must be reset on a daily basis in order to remain in synchrony with external environmental time. This process of entrainment is achieved in most mammals through regular exposure to light and darkness. In this chapter, we review the results of studies conducted in our laboratory and others over the past 25 years in which the effects of light on the human circadian timing system were investigated. These studies have revealed, how the timing, intensity, duration, and wavelength of light affect the human biological clock. Our most recent studies also demonstrate that there is much yet to learn about the effects of light on the human circadian timing system.

Keywords biological rhythm, core body temperature, illuminance, melatonin, phase response curve

Authors Duffy JF, Dijk DJ, Hall EF, Czeisler CA

Report Name Relationship of endogenous circadian melatonin and temperature rhythms to self-reported preference for morning or evening activity in young and older people.

Publication J Investig Med

Issue-page numbers 47:141–150. PMID:10198570

URL http://www.ncbi.nlm.nih.gov/pubmed/10198570

Abstract

BACKGROUND:

Morningness-eveningness refers to interindividual differences in preferred timing of behavior (i.e., bed and wake times). Older people have earlier wake times and rate themselves as more morning-like than young adults. It has been reported that the phase of circadian rhythms is earlier in morning-types than in evening types, and that older people have earlier phases than young adults. These changes in phase have been considered to be the chronobiological basis of differences in preferred bed and wake times and age-related changes therein. Whether such differences in phase are associated with changes in the phase relationship between endogenous circadian rhythms and the sleep-wake cycle has not been investigated previously.
METHODS:

We investigated the association between circadian phase, the phase relationship between the sleep-wake cycle and circadian rhythms, and morningness-eveningness, and their interaction with aging. In this circadian rhythm study, 68 young and 40 older subjects participated.
RESULTS:

Among the young subjects, the phase of the melatonin and core temperature rhythms occurred earlier in morning than in evening types and the interval between circadian phase and usual wake time was longer in morning types. Thus, while evening types woke at a later clock hour than morning types, morning types actually woke at a later circadian phase. Comparing young and older morning types we found that older morning types had an earlier circadian phase and a shorter phase-wake time interval. The shorter phase-waketime interval in older "morning types" is opposite to the change associated with morningness in young people, and is more similar to young evening types.
CONCLUSIONS:

These findings demonstrate an association between circadian phase, the relationship between the sleep-wake cycle and circadian phase, and morningness-eveningness in young adults. Furthermore, they demonstrate that age-related changes in phase angle cannot be attributed fully to an age-related shift toward morningness. These findings have important implications for understanding individual preferences in sleep-wake timing and age-related changes in the timing of sleep.

Keywords

Duffy JF, Wright KP

Year 2005

Authors Jeanne F. Duffy, Kenneth P. Wright Jr.

Report Name Entrainment of the Human Circadian System by Light

Publication Journal of Biological Rhythms

Issue-page numbers August 2005 vol. 20 no. 4 326-338

URL http://jbr.sagepub.com/content/20/4/326.abstract

Abstract The periodic light-dark cycle is the dominant environmental synchronizer used by humans to entrain to the geophysical 24-h day. Entrainment is a fundamental property of circadian systems by which the period of the internal clock (τ) is synchronized to the period of the entraining stimuli (T cycle). An important aspect of entrainment in humans is the maintenance of an appropriate phase relationship between the circadian system, the timing of sleep and wakefulness, and environmental time (a.k.a. the phase angle of entrainment) to maintain wakefulness throughout the day and consolidated sleep at night. In this article, we review these concepts and the methods for assessing circadian phase and period in humans, as well as discuss findings on the phase angle of entrainment in healthy adults. We review findings from studies that examine how the phase, intensity, duration, and spectral characteristics of light affect the response of the human biological clock and discuss studies on entrainment in humans, including recent studies of the minimum light intensity required for entrainment. We briefly review conditions and disorders in which failure of entrainment occurs. We provide an integrated perspective on circadian entrainment in humans with respect to recent advances in our knowledge of circadian period and of the effects of light on the biological clock in humans.

Keywords light, human, entrainment, circadian rhythm, photic entrainment, period

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Duffy JF, Zeitzer JM, Rimmer DW et al.

Year 2002

Authors Jeanne F. Duffy, Jamie M. Zeitzer, David W. Rimmer, Elizabeth B. Klerman, Derk-Jan Dijk, and Charles A. Czeisler

Report Name Peak of circadian melatonin rhythm occurs later within the sleep of older subjects

Publication Am J Physiol Endocrinol Metab

Issue-page numbers 282:E297–E303. PMID:11788360

URL http://ajpendo.physiology.org/content/282/2/E297.short

Abstract We investigated the relationship between sleep timing and the timing of the circadian rhythm of plasma melatonin secretion in a group of healthy young and older subjects without sleep complaints. The timing of sleep and the phase of the circadian melatonin rhythm were earlier in the older subjects. The relationship between the plasma melatonin rhythm and the timing of sleep was such that the older subjects were sleeping and waking earlier relative to their nightly melatonin secretory episode. Consequently, the older subjects were waking at a time when they had higher relative melatonin levels, in contrast with younger subjects, whose melatonin levels were relatively lower by wake time. Our findings indicate that aging is associated not only with an advance of sleep timing and the timing of circadian rhythms but also with a change in the internal phase relationship between the sleep-wake cycle and the output of the circadian pacemaker. In healthy older subjects, the relative timing of the melatonin rhythm with respect to sleep may not play a causal role in sleep disruption.

Keywords

Authors Dumont M, Benhaberou-Brun D, Paquet J

Report Name Profile of 24-h light exposure and circadian phase of melatonin secretion in night workers

Publication J Biol Rhythms

Issue-page numbers 16:502–511 doi:10.1177/074873001129002178. PMID:11669423

URL http://jbr.sagepub.com/content/16/5/502.abstract

Abstract Light exposure was measured in 30 permanent night nurses to determine if specific light/dark profiles could be associated with a better circadian adaptation. Circadian adaptation was defined as a significant shift in the timing of the episode of melatonin secretion into the daytime. Light exposure was continuously recorded with ambulatory wrist monitors for 56 h, including 3 consecutive nights of work. Participants were then admitted to the laboratory for 24 h where urine was collected every 2 h under dim light for the determination of 6-sulphatoxymelatonin concentration. Cosinor analysis was used to estimate the phase position of the episode of melatonin secretion. Five participants showed a circadian adaptation by phase delay (“delayed participants”) and 3 participants showed a circadian adaptation by phase advance (“advanced participants”). The other 22 participants had a timing of melatonin secretion typical of day-oriented people (“nonshifters”). There was no significant difference between the 3 groups for total light exposure or for bright light exposure in the morning when traveling home. However, the 24-h profiles of light exposure were very distinctive. The timing of the main sleep episode was associated with the timing of light exposure. Delayed participants, however, slept in darker bedrooms, and this had a major impact on their profile of light/dark exposure. Delayed and advanced participants scored as evening and morning types, respectively, on a morningness-eveningness scale. This observation suggests that circadian phase prior to night work may contribute to the initial step toward circadian adaptation, later reinforced by specific patterns of light exposure.

Keywords melatonin, light exposure, night work, morningness-eveningness, circadia rhythms, 6-sulphatoxymelatonin, nurses

Dumont M, Lanctôt V, Cadieux-Viau R, Paquet J

Year 2012

Authors Marie Dumont, Valérie Lanctôt, Raphaëlle Cadieux-Viau, and Jean Paquet

Report Name Melatonin Production and Light Exposure of Rotating Night Workers

Publication Chronobiology International

Issue-page numbers Mar., 2012, Vol. 29, No. 2 , Pages 203-210 (doi:10.3109/07420528.2011.647177)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.647177

Abstract Decreased melatonin production, due to acute suppression of pineal melatonin secretion by light exposure during night work, has been suggested to underlie higher cancer risks associated with prolonged experience of night work. However, the association between light exposure and melatonin production has never been measured in the field. In this study, 24-h melatonin production and ambulatory light exposure were assessed during both night-shift and day/evening-shift periods in 13 full-time rotating shiftworkers. Melatonin production was estimated with the excretion of urinary 6-sulfatoxymelatonin (aMT6s), and light exposure was measured with an ambulatory photometer. There was no difference in total 24-h aMT6s excretion between the two work periods. The night-shift period was characterized by a desynchrony between melatonin and sleep-wake rhythms, as shown by higher melatonin production during work and lower melatonin production during sleep when working night shifts than when working day/evening shifts. Light exposure during night work showed no correlation with aMT6s excreted during the night of work ($p > .5$), or with the difference in 24-h aMT6s excretion between the two work periods ($p > .1$). However, light exposure during night work was negatively correlated with total 24-h aMT6s excretion over the entire night-shift period ($p < .01$). In conclusion, there was no evidence of direct melatonin suppression during night work in this population. However, higher levels of light exposure during night work may have decreased total melatonin production, possibly by initiating re-entrainment and causing internal desynchrony. This interpretation is consistent with the proposition that circadian disruption, of which decreased melatonin production is only one of the adverse consequences, could be the mediator between night shiftwork and cancer risks.

Keywords Cancer, Circadian disruption, Light-at-night, Light exposure, Melatonin suppression, Night shiftwork, 6-Sulfatoxymelatonin

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Dunlap JC

Year 2003

Authors Jay C. Dunlap

Report Name Chronobiology: Biological Timekeeping

Publication Dunlap JC, Loros JJ, DeCoursey PJ, editors.

Issue-page numbers Sunderland,

URL http://www.amazon.com/Chronobiology-Biological-Timekeeping-Jay-Dunlap/dp/087893149X

Abstract The study of how solar and lunar related rhythms are governed by living pacemakers within organisms constitutes the scientific discipline of chronobiology. Few fields encompass the breadth of science that is associated with this subject which is at the cutting edge of fields ranging from microbial genetics to ethology to treatment of human psychiatric illnesses. To recognise that no individual could do justice to the field in writing a comprehensive text, a group of experienced editors and contributors have collaborated to produce "Chronobiology". The text begins with a general introduction to the formalisms and vocabulary which describe circadian rhythmicity, followed by an analysis of behavioural and ecological importance of rhythms and their theoretical bases. A central block of four chapters develops the comparative anatomy, physiology, genetics and molecular biology of organisms within circadian clocks. Examples from the real world and from current and classic research are included and a final chapter looks to the future by exploring six cutting edge areas of research.

Keywords

Dupré SM

Year 2011

Authors Sandrine M. Dupré

Report Name Encoding and Decoding Photoperiod in the Mammalian Pars Tuberalis

Publication Neuroendocrinology

Issue-page numbers 2011;94:101-112 (DOI: 10.1159/000328971)

URL http://content.karger.com/produktedb/produkte.asp?doi=328971

Abstract In mammals, the nocturnal melatonin signal is well established as a key hormonal indicator of seasonal changes in day-length, providing the brain with an internal representation of the external photoperiod. The pars tuberalis (PT) of the pituitary gland is the major site of expression of the G-coupled receptor MT1 in the brain and is considered as the main site of integration of the photoperiodic melatonin signal. Recent studies have revealed how the photoperiodic melatonin signal is encoded and conveyed by the PT to the brain and the pituitary, but much remains to be resolved. The development of new animal models and techniques such as cDNA arrays or high throughput sequencing has recently shed the light onto the regulatory networks that might be involved. This review considers the current understanding of the mechanisms driving photoperiodism in the mammalian PT with a particular focus on the seasonal prolactin secretion.

Keywords Photoperiodism, Melatonin, MT1, Pars tuberalis, Prolactin

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Dutch Cancer Society

Year 2010

Authors Dutch Cancer Society

Report Name De relatie tussen kanker, zonnestraling en vitamine D, Signaleringscommissie Kanker van KWF Kankerbestrijding

Publication Dutch Cancer Society [Dutch]

Issue-page numbers ISBN 978-90-71229-21-3. Amsterdam

URL http://scripts.kwfkankerbestrijding.nl/bestellingen/documents/SCK_rapport_Vitamine_D_aug_2010.pdf

Abstract N/A

Keywords

Authors E. Eadie, J. Ferguson, H. Moseley

Report Name A preliminary investigation into the effect of exposure of photosensitive individuals to light from compact fluorescent lamps

Publication British Journal of Dermatology

Issue-page numbers Volume 160, Issue 3, pages 659–664, March 2009

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.2008.08998.x/full

Abstract

Summary Background Compact fluorescent lamps (CFLs) are due to replace common incandescent lamps over the next few years. There has been no investigation of the possible effect of this on patients with photosensitive disorders.

Objectives To determine the effect of exposure of photosensitive individuals to light from CFLs.

Methods The spectral emission from a sample of CFLs was measured using a calibrated spectroradiometer. The erythemal response was determined in one normal individual and four photosensitive individuals by direct exposure of the skin to light from a CFL. The susceptibility of a wider group of photosensitive individuals was predicted based on the light dose known to elicit a reaction during phototesting at discrete ultraviolet (UV) wavelengths.

Results CFLs emit UV radiation at wavelengths down to 254 nm. Prolonged exposure of a normal individual's skin produced erythema. However, an exposure of only 2·5 min at 5 cm elicited marked erythema in one of the abnormally photosensitive patients.

Conclusions CFLs could be a source of harmful UV radiation to photosensitive individuals. Patients with chronic actinic dermatitis are thought to be at greatest risk. The use of a protective envelope is recommended.

Keywords erythema; fluorescent light; photodermatosis; photosensitivity; spectrum; ultraviolet emission

Eastman CI, Boulos Z, Terman M et al. **Year** 1995

Authors Eastman CI, Boulos Z, Terman M, Scott S. Campbell, Derk-Jan Dijk, Alfred J. Lewy

Report Name Light treatment for sleep disorders: consensus report. VI. Shift work.

Publication J Biol Rhythms

Issue-page numbers 10:157–164 doi:10.1177/074873049501000208. PMID:7632989

URL http://jbr.sagepub.com/content/10/2/157.short

Abstract The unhealthy symptoms and many deleterious consequences of shift work can be explained by a mismatch between the work-sleep schedule and the internal circadian rhythms. This mismatch occurs because the 24-h zeitgebers, such as the natural light-dark cycle, keep the circadian rhythms from phase shifting to align with the night-work, day sleep schedule. This is a review of studies in which the sleep schedule is shifted several hours, as in shift work, and bright light is used to try to phase shift circadian rhythms. Phase shifts can be produced in laboratory studies, when subjects are kept indoors, and faster phase shifting occurs with appropriately timed bright light than with ordinary indoor (dim) light. Bright light field studies, in which subjects live at home, show that the use of artificial nocturnal bright light combined with enforced daytime dark (sleep) periods can phase shift circadian rhythms despite exposure to the conflicting 24-h zeitgebers. So far, the only studies on the use of bright light for real shift workers have been conducted at National Aeronautics and Space Administration (NASA). In general, the bright light studies support the idea that the control of light and dark can be used to overcome many of the problems of shift work. However, despite ongoing pra

Keywords bright light, circadian rhythms, shift work

Eastman CI, Martin SK **Year** 1999

Authors Eastman CI, Martin SK

Report Name How to use light and dark to produce circadian adaptation to night shift work.

Publication Ann Med

Issue-page numbers 31:87–98 doi:10.3109/07853899908998783. PMID:10344580

URL http://www.mendeley.com/research/how-to-use-light-and-dark-to-produce-circadian-adaptation-to-night-shift-work/

Abstract The circadian rhythms of night shift workers do not usually adjust to their unusual work and sleep schedules, reducing their quality of life and producing potentially dangerous health and safety problems. This paper reviews field studies of simulated night work in which shifted light-dark cycles were constructed with artificial bright or medium-intensity light to produce circadian adaptation, ie the shifting of circadian rhythms to align with night work and day sleep schedules. By using these studies we describe fundamental principles of human circadian rhythms relevant to producing circadian adaptation to night shift work at a level designed for the reader with only a basic knowledge of circadian rhythms. These principles should enable the reader to start designing work/sleep-light/dark schedules for producing circadian adaptation in night shift workers. One specific schedule is presented as an example. Finally, we discuss phase-response curves to light and clarify common misconceptions about the production of circadian rhythm phase shifts.

Keywords

Ebert S, Walczak Y, Remé C, Langmann T **Year** 2012

Authors Stefanie Ebert, Yana Walczak, Charlotte Remé and Thomas Langmann

Report Name Microglial Activation and Transcriptomic Changes in the Blue Light-Exposed Mouse Retina

Publication Retinal Degenerative Diseases

Issue-page numbers 2012, Volume 723, Part 8, 619-632, DOI: 10.1007/978-1-4614-0631-0_79

URL http://www.springerlink.com/content/g71364r20834251u/

Abstract Microglia are important components of the ocular immune system and may contribute to age-related macular degeneration. Exposure to blue light induces oxidative protein modifications similar to those observed in drusen and elicits retinal immune responses. To study the underlying cellular events, we analyzed microglial activation and monitored transcriptomic changes in blue light-induced retinal lesions. MacGreen mice with EGFP-tagged retinal microglia were exposed to blue light. At different time intervals, eyes were prepared for immunofluorescence microscopy, microarray analysis, and qRT-PCR. Retinal whole mounts and cross sections showed that EGFP-labeled microglia rapidly migrated toward the retinal lesion. Prominent transcriptomic changes occurred after 12 h, peaked at 24 h, and declined at 72 h. We identified more than 100 differentially expressed genes, including transcripts related to microglial activation, apoptosis, and regenerative signaling. A comparison of our results with published datasets from white light damage indicates overlapping but also distinct molecular mechanisms. This study extends our knowledge of transcriptomic changes in light-induced models of retinal degeneration.

Keywords Mouse retina - Blue light damage - Retinal degeneration - Microglia - MacGreen mice - Transcriptomics - Regeneration - AMD

Ebisawa T, Uchiyama M, Kajimura N et al. **Year** 2001

Authors Ebisawa T, Uchiyama M, Kajimura N et al.

Report Name Association of structural polymorphisms in the human period3 gene with delayed sleep phase syndrome

Publication EMBO Rep

Issue-page numbers 2:342–346 doi:10.1093/embo-reports/kve070. PMID:11306557

URL http://www.nature.com/embor/journal/v2/n4/abs/embor441.html

Abstract Recent progress in biological clock research has facilitated genetic analysis of circadian rhythm sleep disorders, such as delayed sleep phase syndrome (DSPS) and non-24-h sleep–wake syndrome (N-24). We analyzed the human period3 (hPer3) gene, one of the human homologs of the Drosophila clock-gene period (Per), as a possible candidate for rhythm disorder susceptibility. All of the coding exons in the hPer3 gene were screened for polymorphisms by a PCR-based strategy using genomic DNA samples from sleep disorder patients and control subjects. We identified six sequence variations with amino acid changes, of which five were common and predicted four haplotypes of the hPer3 gene. One of the haplotypes was significantly associated with DSPS (Bonferroni's corrected P = 0.037; odds ratio = 7.79; 95% CI 1.59–38.3) in our study population. Our results suggest that structural polymorphisms in the hPer3 gene may be implicated in the pathogenesis of DSPS.

Keywords

Eckel-Mahan K, Sassone-Corsi P

Year 2013

Authors Kristin Eckel-Mahan and Paolo Sassone-Corsi

Report Name Metabolism and the Circadian Clock Converge

Publication Physiol Rev

Issue-page numbers January 1, 2013 vol. 93 no. 1 107-135

URL http://physrev.physiology.org/content/93/1/107.short

Abstract Circadian rhythms occur in almost all species and control vital aspects of our physiology, from sleeping and waking to neurotransmitter secretion and cellular metabolism. Epidemiological studies from recent decades have supported a unique role for circadian rhythm in metabolism. As evidenced by individuals working night or rotating shifts, but also by rodent models of circadian arrhythmia, disruption of the circadian cycle is strongly associated with metabolic imbalance. Some genetically engineered mouse models of circadian rhythmicity are obese and show hallmark signs of the metabolic syndrome. Whether these phenotypes are due to the loss of distinct circadian clock genes within a specific tissue versus the disruption of rhythmic physiological activities (such as eating and sleeping) remains a cynosure within the fields of chronobiology and metabolism. Becoming more apparent is that from metabolites to transcription factors, the circadian clock interfaces with metabolism in numerous ways that are essential for maintaining metabolic homeostasis.

Keywords

Eckel-Mahan KL, Patel VR, Mohney RP

Year 2012

Authors Kristin L. Eckel-Mahan, Vishal R. Patel, Robert P. Mohney, Katie S. Vignola, Pierre Baldi, and

Report Name Coordination of the transcriptome and metabolome by the circadian clock

Publication PNAS

Issue-page numbers print March 19, 2012, doi: 10.1073/pnas.1118726109

URL http://www.pnas.org/content/early/2012/03/14/1118726109.short

Abstract The circadian clock governs a large array of physiological functions through the transcriptional control of a significant fraction of the genome. Disruption of the clock leads to metabolic disorders, including obesity and diabetes. As food is a potent zeitgeber (ZT) for peripheral clocks, metabolites are implicated as cellular transducers of circadian time for tissues such as the liver. From a comprehensive dataset of over 500 metabolites identified by mass spectrometry, we reveal the coordinate clock-controlled oscillation of many metabolites, including those within the amino acid and carbohydrate metabolic pathways as well as the lipid, nucleotide, and xenobiotic metabolic pathways. Using computational modeling, we present evidence of synergistic nodes between the circadian transcriptome and specific metabolic pathways. Validation of these nodes reveals that diverse metabolic pathways, including the uracil salvage pathway, oscillate in a circadian fashion and in a CLOCK-dependent manner. This integrated map illustrates the coherence within the circadian metabolome, transcriptome, and proteome and how these are connected through specific nodes that operate in concert to achieve metabolic homeostasis.

Keywords

Edelstein K, de la Iglesia HO, Schwartz WJ, Mrosovsky N **Year** 2003

Authors K Edelstein, H.O de la Iglesia, W.J Schwartz, N Mrosovsky

Report Name Behavioral arousal blocks light-induced phase advances in locomotor rhythmicity but not light-induced Per1 and Fos expression in the hamster suprachiasmatic nucleus

Publication Neuroscience

Issue-page numbers Volume 118, Issue 1, 25 April 2003, Pages 253-261

URL http://www.sciencedirect.com/science/article/pii/S0306452202009089

Abstract Both photic and nonphotic stimuli entrain circadian rhythms. Although the adaptive significance of nonphotic clock resetting is unknown, one possibility is that nonphotic cues modulate circadian responses to light. Results of studies on the interaction between photic and nonphotic stimuli support this idea. During the day, light blocks the effects of nonphotic stimuli on the phase of locomotor rhythms and on expression of clock genes in suprachiasmatic nucleus (SCN) neurons. At night, novelty-induced activity prior to and during exposure to light attenuates the phase-shifting response to that light, but the effects of this manipulation on clock gene expression are unknown. The present experiments explore the interaction between behavioral state and response to light at the molecular level. We show that confining hamsters to novel wheels immediately after a light pulse during the late subjective night attenuates light-induced phase advances of wheel-running rhythms and the transient effects on circadian period. In contrast to the striking effect of novelty-induced activity on behavioral responses to light, Fos protein and Per1 mRNA were robustly expressed in the SCN of all light-pulsed animals, regardless of behavioral treatment. Our results are inconsistent with the idea that light and nonphotic stimuli block each other's effects on phase shifts by inducing or attenuating transcription of Per1. Photic regulation of clock genes and spontaneous rhythmic expression of clock genes are probably mediated by different mechanisms.

Keywords circadian rhythm; clock gene; immediate early gene; nonphotic; suprachiasmatic nucleus; wheel running

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Edwards C, Gaskell SA, Hill SA, et al. **Year** 1999

Authors Edwards C, Gaskell SA, Hill SA, Heggie R, Pearse AD, Marks R.

Report Name Effects on human epidermis of chronic suberythemal exposure to pure infrared radiation

Publication Arch Dermatol

Issue-page numbers Vol. 135 No. 5, May 1999

URL http://archderm.ama-assn.org/cgi/content/extract/135/5/608

Abstract We studied 8 normal healthy volunteers (4 men, 4 women, age range 28-39 years; skin phototypes I through III) with no history of skin disorders and minimal solar damage.

An infrared lamp (Hydrosun 500; Hydrosun Medizintechnik GmBh, Germany) with single-output band (620-1370 nm) and an irradiance of 440 mW · cm-2 was used. Irradiance between 250 nm and 400 nm is 0.0034 mW · cm-2, but from 250 nm to 340 nm is only 0.00045 mW · cm-2, 106 less than the main infrared band; 9.5 minutes' irradiation at 30 cm is equivalent to a 1-hour exposure to a typical solar spectrum (ASTM).1

Irradiation of buttock skin for 9.5 minutes produced no pain and was administered randomly to either . . .

Keywords

Authors J. Christopher Ehlen and Ketema N. Paul

Report Name Regulation of light's action in the mammalian circadian clock: role of the extrasynaptic GABAA receptor

Publication Am J Physiol Regul Integr Comp Physiol

Issue-page numbers 2009 May; 296(5): R1606–R1612.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2689827/

Abstract

GABAA receptor agonists act in the suprachiasmatic nucleus (SCN) to reset circadian rhythms during the day but inhibit the ability of light to reset rhythms during the night. In the present study, we examined whether these paradoxical differences in the effect of GABAA receptor stimulation on the circadian system are mediated by separate GABAA receptor subtypes. 4,5,6,7-Tetrahydroisoxazolo[5,4-c]pyridin-3-ol (THIP), a GABAA receptor agonist, preferentially activates GABAA receptors in extrasynaptic locations. THIP, muscimol (a GABAA agonist), or vehicle were microinjected into the SCN region of Syrian hamsters free-running in constant darkness during the mid-subjective day, early subjective night, or late subjective night. The subjective night injections were followed by a light pulse or sham control. Behavioral phase shifts of wheel running rhythms and both Period1 (Per1) and Per2 mRNA levels in the SCN were assessed. Animals that received THIP during the subjective day did not exhibit significant phase alterations. During the early and late subjective night, however, THIP abolished the phase-shifting effects of light and the ability of light to increase Per1 and Per2 mRNA levels. The ability of N-methyl-d-aspartic acid to phase-shift wheel running rhythms was also attenuated by THIP. Together these data demonstrate that THIP does not produce phase shifts during the subjective day, but does inhibit the ability of light to produce phase shifts. Thus, extrasynaptic GABAA receptors appear to play a role in regulating light input to the SCN, while a different population of GABAA receptors appears to be responsible for daytime effects of GABA.

Keywords suprachiasmatic nucleus, GABA, THIP, phase shift, circadian rhythm

Eide MJ; Weinstock MA

Year 2005

Authors Melody J. Eide; Martin A. Weinstock

Report Name Association of UV index, latitude, and melanoma incidence in nonwhite

Publication Arch Dermatol

Issue-page numbers 141:477-481.

URL http://archderm.ama-assn.org/cgi/content/abstract/141/4/477

Abstract

Objective To estimate the association between UV index, latitude, and melanoma incidence in different racial and ethnic populations in a high-quality national data set.

Design Descriptive study.

Setting Eleven US cancer registries that constitute the Surveillance, Epidemiology, and End Results Program (SEER-11).

Patients Patients with malignant melanoma of the skin reported between 1992 and 2001.

Main Outcome Measures Pearson correlation coefficients and regression coefficients were used to estimate the relationship of age-adjusted melanoma incidence rates (2000 US standard population) with the UV index or latitude within racial and ethnic groups.

Results A higher mean UV index was significantly associated with an increase in melanoma incidence only in non-Hispanic whites (r = 0.85, P = .001), although a nonsignificant association was noted in Native Americans (r = 0.42, P = .20).Negative, but not significant, correlations with incidence were observed in blacks (r = –0.53, P = .10), Hispanics (r = –0.43, P = .19), and Asians (r = –0.28, P = .41).Latitude also had a significant correlation with incidence only in non-Hispanic whites (r = –0.85, P = .001). A substantial portion of the variance in registry incidence in non-Hispanic whites could be explained by the UV index (R2 = 0.71, P = .001).

Conclusions Melanoma incidence is associated with increased UV index and lower latitude only in non-Hispanic whites. No evidence to support the association of UV exposure and melanoma incidence in black or Hispanic populations was found.

Keywords

Elder GH

Year 1998

Authors Elder GH

Report Name The cutaneous porphyrias

Publication In: Hawk JLM, editor. Photodermatology

Issue-page numbers London: Chapman & Hall; 1998. p.171-97

URL Book

Abstract N/A

Keywords

el-Domeiri AA, Das Gupta TK | *Year* 1973

Authors el-Domeiri AA, Das Gupta TK

Report Name Reversal by melatonin of the effect of pinealectomy on tumor growth

Publication Cancer Res

Issue-page numbers 33:2830–2833. PMID:4748439

URL http://cancerres.aacrjournals.org/content/33/11/2830

Abstract Pinealectomy is known to cause accelerated growth of transplanted melanoma in hamsters. The precise mechanisms involved in this action have not yet been identified. Since the pineal is the only organ that produces melatonin, this investigation was undertaken to determine the effect of this indole in the same tumor model. Administration of 0.1 mg of exogenous melatonin i.p. daily for 3 weeks did not influence the growth rate of tumors at 3- and 6-week intervals in intact animals. Administration of the same dosage of melatonin to pinealectomized animals, however, abolished the accelerating effect of pinealectomy on the growth of melanoma implants. Therefore it is concluded that the effect of pinealectomy on tumor growth is due to a deficiency in endogenous melatonin.

Keywords

Elenkov IJ, Chrousos GP | *Year* 2002

Authors Elenkov IJ, Chrousos GP

Report Name Stress hormones, proinflammatory and antiinflammatory cytokines, and autoimmunity

Publication Ann N Y Acad Sci

Issue-page numbers 966:290–303 doi:10.1111/j.1749-6632.2002.tb04229.x. PMID:12114286

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.2002.tb04229.x/abstract?

Abstract Recent evidence indicates that glucocorticoids and catecholamines, the major stress hormones, inhibit the production of proinflammatory cytokines, such as interleukin (IL)-12, tumor necrosis factor (TNF)-α, and interferon (IFN)-γ, whereas they stimulate the production of antiinflammatory cytokines, such as IL-10, IL-4, and transforming growth factor (TGF)-β. Thus, systemically, an excessive immune response, through activation of the stress system, stimulates an important negative feedback mechanism, which protects the organism from an “overshoot” of proinflammatory cytokines and other products of activated macrophages with tissue-damaging potential. Conversely, in certain local responses and under certain conditions, stress hormones actually may boost regional immune responses, through induction of TNF-α, IL-1, and IL-8, and by inhibiting TGF-β production. Therefore, conditions that are associated with significant changes in stress system activity, such as acute or chronic stress, cessation of chronic stress, severe exercise, and pregnancy and the postpartum period, through modulation of the systemic or local pro/antiinflammatory cytokine balance, may suppress or potentiate autoimmune diseases activity and/or progression.

Keywords stress; glucocorticoids; catecholamines; autoimmunity; inflammation; interleukin-12; rheumatoid arthritis; multiple sclerosis

Eramo LR; Garden JM; Esterly NB

Year 1986

Authors Lynne R. Eramo; Jerome M. Garden; Nancy B. Esterly

Report Name Hydroa vacciniforme. Diagnosis by repetitive ultraviolet-A phototesting

Publication Arch Dermatol

Issue-page numbers 122(11):1310-1313.

URL http://archderm.ama-assn.org/cgi/content/abstract/122/11/1310

Abstract Hydroa vacciniforme is a rare disorder manifested in early childhood by recurrent photoinduced vesicles that heal with scarring. We report a case in which repetitive exposures to artificial ultraviolet light in the A range reproduced the clinical findings induced by natural sunlight. Phototesting may be viewed as an important diagnostic aid, as the induction of lesions clinically identical to hydroa vacciniforme can provide a reliable criterion for the diagnosis.

Keywords

Authors Eriksen CA, Gillberg M, Vestergren P

Report Name Sleepiness and sleep in a simulated “six hours on/six hours off” sea watch system

Publication Chronobiol Int

Issue-page numbers 23:1193–1202 doi:10.1080/07420520601057981. PMID:17190705

URL http://informahealthcare.com/doi/abs/10.1080/07420520601057981

Abstract

Ships are operated around the clock using rapidly rotating shift schedules called sea watch systems. Sea watch systems may cause fatigue, in the same way as other irregular working time arrangements. The present study investigated subjective sleepiness and sleep duration in connection with a 6 h on/6 h off duty system. The study was performed in a bridge simulator, very similar to those found on ships. Twelve officers divided into two groups participated in the study that lasted 66 h. Half of the subjects started with the 06:00–12:00 h watch and the other half with the 12:00–18:00 h watch. The subjects alternated between off-duty and on-duty for the remainder of the experimental period. Approximately halfway through the experiment, the 12:00–18:00 h watch was divided into two 3 h watches/off-duty periods. The effect of this was to reverse the on-duty/off-duty pattern between the two groups. This enabled all subjects to work the four possible watches (00:00–06:00 h, 06:00–12:00 h, 12:00–18:00 h, and 18:00–24:00 h) in an order that was essentially counterbalanced between groups. Ratings of sleepiness (Karolinska Sleepiness Scale; KSS) were obtained every 30 min during on-duty periods and if subjects were awake during off-duty periods. The subjectively rated duration of sleep was recorded after each off-duty period that preceded watch periods when KSS was rated. The results showed that the average level of sleepiness was significantly higher during the 00:00–06:00 h watch compared to the 12:00–18:00 h and 18:00–24:00 h watches, but not to the 06:00–12:00 h watch. Sleepiness also progressed significantly from the start toward the end of each watch, with the exception of the 06:00-12:00 h watch, when levels remained approximately stable. There were no differences between groups (i.e., the order between watches). Sleep duration during the 06:00–12:00 h off-duty period (3 h 29 min) was significantly longer than during the 12:00–18:00 h period (1 h 47 min) and the 18:00–24:00 h period (2 h 7 min). Sleep during the 00:00–06:00 h period (4 h 23 min) was longer than all sleep periods except the 06:00–12:00 h period. There were no differences between groups. In spite of sufficient opportunities for sleep, sleep was on the average around 1–1 h 30 min shorter than the 7–7 h 30 min that is considered “normal” during a 24 h period. This is probably a consequence of the difficulty to sleep during daytime due to the alerting effects of the circadian rhythm. Also, sleepiness during the night and early mornings reached high levels, which may be explained by a combination of working close to or during the circadian trough of alertness and the relatively short sleep periods obtained. An initial suppression of sleepiness was observed during all watches, except for the 06:00–12:00 h watch. This suppression may be explained by the “masking effect” exerted by the relative high levels of activity required when taking over the responsibility of the ship. Toward the end of watches, the levels of sleepiness progressively increased to relatively high levels, at least during the 00:00–06:00 h watch. Presumably, initially high levels of activity are replaced by routine and even boredom.

Keywords

Erren TC

Year 2000

Authors Erren, T.C.

Report Name Winter darkness in the Artic- Cancer in the light of the Melatonin Hypotesis

Publication Proc. of Int. Symp. on Low frequency EMF, Visible Light, Melatonin and Cancer

Issue-page numbers May 4-5, 2000, University of Cologne, Germany

URL http://www.uni-koeln.de/symposium2000/contrib/index.html

Abstract

The melatonin hypothesis states that excess exposure to environmental light may contribute to breast cancer risks via impaired pineal secretion of melatonin.(1, 2) A corollary, not considered previously, is that a net annual increase in oncostatic melatonin would be expected in persons experiencing deficits of daylight during long winter days. Hormone-dependent cancers should therefore occur less frequently in people who reside north, rather than south, of the Arctic circle. We have reviewed descriptive epidemiologic data on cancer incidence during 1960 and 1988 in Greenland, northern Alaska, and the northern part of the Canadian mainland. They show a pattern of uniformly low risks for hormone-dependent cancer consistent with our prediction. SMRs or SIRs ranged between 0.2 and 0.5 for breast cancer, were 0.9 or less for cancer of the ovary and 0.3 or less for cancer of the corpus uteri, and ranged between 0.1 and 0.7 for prostate cancer. However, tobacco, alcohol and diet related cancer risks were high. The latter observations suggest that the low incidence of hormone-dependent cancers is unlikely to be explicable simply in terms of indigenous nutritional and life-style factors. Moreover, the available literature on genetic, reproductive, and environmental risk factors provides no obvious clues to the observed cancer patterns. We note also that melatonin concentrations in volunteers who live in the arctic part of Norway and in northern Finland have been reported as high during the dark season (November-January), when light intensity is low. This too is consistent with our prediction.

Keywords

Erren TC, Falaturi P, Morfeld P, et al. **Year** 2010

Authors Thomas C Erren, Puran Falaturi, Peter Morfeld, Peter Knauth, Russel J Reiter, and Claus Piekarski

Report Name Shift Work and Cancer - The Evidence and the Challenge

Publication Dtsch Arztebl Int.

Issue-page numbers September; 107(38): 657–662.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2954516/

Abstract

Background
In 2007, the International Agency for Research on Cancer (IARC) classified shift work with circadian disruption or chronodisruption as a probable human carcinogen. Short-term disturbances of biological 24-hour-rhythms following exposures to light and darkness at unusual times are well-known as „jet-lag“ and „shift-lag“ symptoms. However, that chronic disturbances or disruptions of timely sequenced circadian rhythms (chronodisruption) should contribute to long-term developments of cancer is a relatively new concept. This review provides background and practical information with regard to the open question „does shift-work cause cancer?“
Methods
Overview on the basis of a selective literature search via Medline and ISI Web of Knowledge until 2009 from the viewpoints of occupational medicine, epidemiology, chronobiology, and occupational science.
Results
The postulated causal links between shift-work and cancer in humans are biologically plausible in the light of experimental findings, but to date we lack epidemiological studies which could describe or exonerate risks in humans. Monetary compensation has already been paid for such cases in at least one country (Denmark). In Germany, however, according to the applicable law, a new occupational disease can only be recognized when certain conditions for the recognition of „general scientific merit“ have been met. We present the current state of knowledge regarding prevention.
Conclusion
While causal links between shift-work and cancer developments are not established, future shift-work planning should pay more attention to insights from occupational medicine, chronobiology, and occupational science.

Keywords Erren TC, Falaturi P, Morfeld P, et al.

Erren TC, Groß JV, Meyer-Rochow VB **Year** 2011

Authors Thomas C. Erren, J. Valérie Groß and V. Benno Meyer-Rochow

Report Name Light, Clocks, Mood, and Cancer: Consolidation and Novel Tests of Latitude and Instability Hypotheses

Publication Chronobiology International

Issue-page numbers 28:5, 471-473

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.577542

Abstract N/A

Keywords

European Council Directive — *Year* 2003

Authors European Council Directive

Report Name No 2003/88/EC of the European Parliament and the council of 4 November 2003 concerning certain aspects of the organisation of the working time

Publication Off J Eur Commun

Issue-page numbers L299: 9–19

URL http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:299:0009:0019:en:PDF

Abstract N/A

Keywords

European Council Directive — *Year* 1992

Authors European Council Directive

Report Name No 92/85/EEC on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are

Publication Off J Eur Commun

Issue-page numbers L348:1–8

URL

Abstract (tenth individual Directive within the meaning of Article 16 (1) of Directive 89/391/EEC)

Keywords

European Council Directive **Year** 1994

Authors European Council Directive

Report Name No 94/33/EC L 216 on the protections of young people at work. 24 June 1994

Publication Off J Eur Commun

Issue-page numbers L216: 12–20

URL http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=31994L0033&model=guichett

Abstract N/A

Keywords

European Council Directive **Year** 1993

Authors European Council Directive

Report Name No 93/104/EC concerning Certain Aspects of the Organization of Working Time

Publication Off J Eur Commun

Issue-page numbers L307: 18–24

URL http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31993L0104:en:HTML

Abstract N/A

Keywords

European Foundation

Year 2007

Authors European Foundation

Report Name Fourth European Working Conditions Survey

Publication (European Foundation for the Improvement of Living and Working Conditions)

Issue-page numbers Loughlinstown, Dublin, Ireland. www.eurofound.europa.eu

URL http://www.eurofound.europa.eu/publications/htmlfiles/ef0698.htm

Abstract EU policymakers recognise that improving working conditions is crucial to achieving a better quality of work, greater productivity and increased employment – the Lisbon objectives. In this context, the Foundation's European Working Conditions Surveys, conducted every five years, have been providing a valuable insight into key aspects of work since 1990. This report analyses the findings of the fourth European Working Conditions Survey, carried out in autumn 2005 across 31 countries, including the 27 EU Member States. Based on workers' responses, it paints a broad and varied picture of the physical, intellectual and psychological dimensions of work and its impact on personal fulfilment and work-life balance.

Keywords

Evans JA, Carter SN, Freeman DA, Gorman MR

Year 2011

Authors J.A. Evans, S.N. Carter, D.A. Freeman, M.R. Gorman

Report Name Dim nighttime illumination alters photoperiodic responses of hamsters through the intergeniculate leaflet and other photic pathways

Publication Neuroscience

Issue-page numbers In Press, Uncorrected Proof - Note to users

URL http://www.sciencedirect.com/science/article/pii/S0306452211013091

Abstract In mammals, light entrains the central pacemaker within the suprachiasmatic nucleus (SCN) through both a direct neuronal projection from the retina and an indirect projection from the intergeniculate leaflet (IGL) of the thalamus. Although light comparable in intensity to moonlight is minimally effective at resetting the phase of the circadian clock, dimly lit and completely dark nights are nevertheless perceived differentially by the circadian system, even when nighttime illumination is below putative thresholds for phase resetting. Under a variety of experimental paradigms, dim nighttime illumination exerts effects that may be characterized as enhancing the plasticity of circadian entrainment. For example, relative to completely dark nights, dimly lit nights accelerate development of photoperiodic responses of Siberian hamsters transferred from summer to winter day lengths. Here we assess the neural pathways underlying this response by testing whether IGL lesions eliminate the effects of dim nighttime illumination under short day lengths. Consistent with previous work, dimly lit nights facilitated the expansion of activity duration under short day lengths. Ablation of the IGL, moreover, did not influence photoperiodic responses in animals held under completely dark nights. However, among animals that were provided dimly lit nights, IGL lesions prevented the short-day typical expansion of activity duration as well as the seasonally appropriate gonadal regression and reduction in body weight. Thus, the present data indicate that the IGL plays a central role in mediating the facilitative effects of dim nighttime illumination under short day lengths, but in the absence of the IGL, dim light at night influences photoperiodic responses through residual photic pathways.

Keywords circadian; intergeniculate leaflet; dim nighttime illumination; short day photoperiod; Siberian hamster

Evans JA, Elliott JA, Gorman MR

Year 2011

Authors Jennifer A. Evans, Jeffrey A. Elliott and Michael R. Gorman

Report Name Dim Nighttime Illumination Interacts With Parametric Effects of Bright Light to Increase the Stability of Circadian Rhythm Bifurcation in Hamsters

Publication Chronobiology International

Issue-page numbers 28:6, 488-496

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.591952

Abstract The endogenous circadian pacemaker of mammals is synchronized to the environmental day by the ambient cycle of relative light and dark. The present studies assessed the actions of light in a novel circadian entrainment paradigm where activity rhythms are bifurcated following exposure to a 24-h light:dark:light:dark (LDLD) cycle. Bifurcated entrainment under LDLD reflects the temporal dissociation of component oscillators that comprise the circadian system and is facilitated when daily scotophases are dimly lit rather than completely dark. Although bifurcation can be stably maintained in LDLD, it is quickly reversed under constant conditions. Here the authors examine whether dim scotophase illumination acts to maintain bifurcated entrainment under LDLD through potential interactions with the parametric actions of bright light during the two daily photophases. In three experiments, wheel-running rhythms of Syrian hamsters were bifurcated under LDLD with dimly lit scotophases, and after several weeks, dim scotophase illumination was either retained or extinguished. Additionally, “full” and “skeleton” photophases were employed under LDLD cycles with dimly lit or completely dark scotophases to distinguish parametric from nonparametric effects of bright light. Rhythm bifurcation was more stable in full versus skeleton LDLD cycles. Dim light facilitated the maintenance of bifurcated entrainment under full LDLD cycles but did not prevent the loss of rhythm bifurcation in skeleton LDLD cycles. These studies indicate that parametric actions of bright light maintain the bifurcated entrainment state; that dim scotophase illumination increases the stability of the bifurcated state; and that dim light interacts with the parametric effects of bright light to increase the stability of rhythm bifurcation under full LDLD cycles. A further understanding of the novel actions of dim light may lead to new strategies for understanding, preventing, and treating chronobiological disturbances.

Keywords Bifurcated rhythms, Circadian coupling, Oscillator interactions, Parametric and nonparametric entrainment, Plasticity, Splitting

Everson CA

Year 1993

Authors Everson CA

Report Name Sustained sleep deprivation impairs host defense

Publication Am J Physiol

Issue-page numbers 265:R1148–R1154. PMID:8238617

URL http://ajpregu.physiology.org/content/265/5/R1148.abstract

Abstract Prolonged sleep deprivation in rats causes an unexplained hypercatabolic state, secondary malnutrition symptoms, and mortality. The nature of the vital impairment has long been a mystery. Its determination would help to elucidate the type of organic dysfunction that sleep prevents. There are no gross detectable disturbances in intermediary metabolism, clinical chemistry, or hematological indexes that provide substantial clues to the mediation of sleep-deprivation effects. Furthermore, postmortem examinations reveal no systematic morphological or histopathological findings. Taken together, the cachexia and the absence of evidence of structural damage or organ dysfunction pointed to involvement of a regulatory system that was diffuse, possibly the immune system. Blood cultures revealed invasion by opportunistic microbes to which there was no febrile response. These results suggest that the life-threatening condition of prolonged sleep deprivation is a breakdown of host defense against indigenous and pathogenic microorganisms.

Keywords

Eysel UT, Burandt U

Year 1984

Authors Ulf Th. Eysel, Ulrich Burandt

Report Name Fluorescent tube light evokes flicker responses in visual neurons

Publication Vision Research

Issue-page numbers Volume 24, Issue 9, 1984, Pages 943-948

URL http://www.sciencedirect.com/science/article/pii/0042698984900695

Abstract Single neurons in the cat visual system respond distinctly to the temporal information present in light from fluorescent tubes driven by 50 or 60 Hz alternating current. Despite the resulting flicker frequencies of 100 or 120 Hz all retinal and most thalamic neurons show strong phase locking of the neuronal responses to the modulation of fluorescent tube light. Some retinal ganglion cells have not yet reached their critical flicker fusion frequency under such conditions. Though usually beyond perception, the frequency and depth of modulation of artificial light thus might well play a role in biological light effects.

Keywords Flicker fusion frequency; Cat Visual neurons Artificial light; Fluorescent tubes

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Falchi F, Cinzano P, Elvidge CD, et al.

Year 2011

Authors Falchi F, Cinzano P, Elvidge CD, Keith DM, Haim A

Report Name Limiting the impact of light pollution on human health, environment and stellar visibility

Publication J Environ Manage

Issue-page numbers Oct;92(10):2714-22. Epub 2011 Jul 13

URL http://www.ncbi.nlm.nih.gov/pubmed/21745709

Abstract Light pollution is one of the most rapidly increasing types of environmental degradation. Its levels have been growing exponentially over the natural nocturnal lighting levels provided by starlight and moonlight. To limit this pollution several effective practices have been defined: the use of shielding on lighting fixture to prevent direct upward light, particularly at low angles above the horizon; no over lighting, i.e. avoid using higher lighting levels than strictly needed for the task, constraining illumination to the area where it is needed and the time it will be used. Nevertheless, even after the best control of the light distribution is reached and when the proper quantity of light is used, some upward light emission remains, due to reflections from the lit surfaces and atmospheric scatter. The environmental impact of this "residual light pollution", cannot be neglected and should be limited too. Here we propose a new way to limit the effects of this residual light pollution on wildlife, human health and stellar visibility. We performed analysis of the spectra of common types of lamps for external use, including the new LEDs. We evaluated their emissions relative to the spectral response functions of human eye photoreceptors, in the photopic, scotopic and the 'meltopic' melatonin suppressing bands. We found that the amount of pollution is strongly dependent on the spectral characteristics of the lamps, with the more environmentally friendly lamps being low pressure sodium, followed by high pressure sodium. Most polluting are the lamps with a strong blue emission, like Metal Halide and white LEDs. Migration from the now widely used sodium lamps to white lamps (MH and LEDs) would produce an increase of pollution in the scotopic and melatonin suppression bands of more than five times the present levels, supposing the same photopic installed flux. This increase will exacerbate known and possible unknown effects of light pollution on human health, environment and on visual perception of the Universe by humans. We present quantitative criteria to evaluate the lamps based on their spectral emissions and we suggest regulatory limits for future lighting.

Keywords light at night, health, stellar visibility

Fan Y, Hida A, Anderson DA et al. *Year* 2007

Authors Fan Y, Hida A, Anderson DA et al.

Report Name Cycling of CRYPTOCHROME proteins is not necessary for circadian-clock function in mammalian fibroblasts

Publication Curr Biol

Issue-page numbers 17:1091–1100 doi:10.1016/j.cub.2007.05.048. PMID:17583506

URL http://www.cell.com/current-biology/retrieve/pii/S0960982207014728

Abstract # Background
An interlocked transcriptional-translational feedback loop (TTFL) is thought to generate the mammalian circadian clockwork in both the central pacemaker residing in the hypothalamic suprachiasmatic nuclei and in peripheral tissues. The core circadian genes, including Period1 and Period2 (Per1 and Per2), Cryptochrome1 and Cryptochrome2 (Cry1 and Cry2), Bmal1, and Clock are indispensable components of this biological clockwork. The cycling of the PER and CRY clock proteins has been thought to be necessary to keep the mammalian clock ticking.
Results
We provide a novel cell-permeant protein approach for manipulating cryptochrome protein levels to evaluate the current transcription and translation feedback model of the circadian clockwork. Cell-permeant cryptochrome proteins appear to be functional on the basis of several criteria, including the abilities to (1) rescue circadian properties in Cry1−/−Cry2−/− mouse fibroblasts, (2) act as transcriptional repressors, and (3) phase shift the circadian oscillator in Rat-1 fibroblasts. By using cell-permeant cryptochrome proteins, we demonstrate that cycling of CRY1, CRY2, and BMAL1 is not necessary for circadian-clock function in fibroblasts.
Conclusions
These results are not supportive of the current version of the transcription and translation feedback-loop model of the mammalian clock mechanism, in which cycling of the essential clock proteins CRY1 and CRY2 is thought to be necessary.

Keywords

Farewell VT, Math B, Math M *Year* 1977

Authors Farewell VT, Math B, Math M

Report Name The combined effect of breast cancer risk factor

Publication Cancer

Issue-page numbers 40:931–936 doi:10.1002/1097-0142(197708)40:2<931::AID-CNCR2820400251>3.0.CO;2-Y. PMID:890675

URL http://www.ncbi.nlm.nih.gov/pubmed/890675

Abstract An extension of the logistic model (Cox, 1970) is applied to the prospective study of breast cancer in Guernsey (Bulbrook and Hayward, 1967). Four important risk factors, age at menarche, family history, age at first birth and etiocholanolone excretion, are identified and shown to have additive effects on a logistic scale for the probability of developing breast cancer. The feasibility of screening a high risk group of women is considered and shown unlikely to be of practical value.

Keywords

Ferguson J

Year 2006

Authors Ferguson J

Report Name Photodermatology. London: Manson Publishing; 2006

Publication London: Manson Publishing; 2006

Issue-page numbers N/A

URL Book N/A

Abstract N/A

Keywords

Ferguson J

Year 2003

Authors Ferguson J

Report Name Phototoxicity due to fluoroquinolones

Publication In: Hooper DC, Rubinstein E, editors. Quinolone

Issue-page numbers Washington DC: ASM Press; 2003.

URL http://books.google.com/books?hl=en&lr=&id=bsVJKmbtgbMC&oi=fnd&pg=PA451&dq=Phototoxicity+due+to+fluoroquinolones&ots=Royja00peG&sig=SQf9Od_A1o21N9x5hfVp

Abstract Book - N/A

Keywords

Ferguson J

Year 1990

Authors Ferguson J.

Report Name Photosensitivity Dermatitis and Actinic Reticuloid Syndrome (Chronic Actinic Dermatitis)

Publication Semin Dermatol

Issue-page numbers 1990 Mar;9(1):47-54.

URL http://www.ncbi.nlm.nih.gov/pubmed/2203443

Abstract The photosensitivity dermatitis and actinic reticuloid syndrome (chronic actinic dermatitis) is a common eczematous photodermatosis of unknown aetiology that in severe form is an extremely disabling condition. It is unclear why males are particularly affected. Difficulties in diagnosis arise in patients who have perennial problems in whom clinical photosensitivity may not be volunteered. An additional problem for the clinician is the finding of contact allergy that is frequently multiple, which further complicates the clinical picture that may, in severe cases, present as an erythroderma or a pseudolymphomatous state. Patch testing and phototesting are the key investigations, with broad ultraviolet (UV) waveband sensitivity occurring as a dermatitis rather than a sunburn response. Contact allergy recognition and avoidance, along with photoprotective measures, are helpful in most cases. Photochemotherapy (PUVA) and systemic immunosuppression may be required in those patients who fail to respond. In some cases, spontaneous resolution follows after a number of years.

Keywords

Ferguson J

Year 1998

Authors Ferguson J.

Report Name Drug and chemical photosensitivity

Publication In: Hawk JLM, editor. Photodermatology

Issue-page numbers London: Chapman & Hall; 1998. p.155-69.

URL Book N/A

Abstract N/A

Keywords

Ferguson J, Addo HA, Jones S, et al. **Year** 1985

Authors J. FERGUSON, H.A. ADDO, S. JONES, B.E. JOHNSON, W. FRAIN-BELL

Report Name A study of cutaneous photosensitivity induced by amiodarone

Publication British Journal of Dermatology

Issue-page numbers Volume 113, Issue 5, pages 537–549, November 1985

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.1985.tb02377.x/abstract?

Abstract Amiodarone-induced cutaneous photosensitivity was studied in 12 subjects treated with the drug. The action spectrum for the abnormal response to sunlight was shown to be within the range of 335–460 (±30) nm. The clinical features of the photosensitivity response suggested that it was most probably a phototoxic reaction, a conclusion supported by the results in in vitro studies which indicated activity mainly against cell membranes. Of the five in vitro models used, three—namely photohaemolysis, the inhibition of DNA synthesis in PHA stimulated lymphocytes and the killing of mouse peritoneal macrophages—provided unequivocal evidence of the phototoxic potential of both amiodarone and its major metabolite, desethylamiodarone. In each model desethylamiodarone produced a greater effect by a factor of between 2 and 10. In vitro, UV-B wavelengths produced a greater effect than UVA but the difference between the effective wavelengths in vivo and in vitro might be explained by the greater absorption of the shorter wavelength UV-B in the opidermis. Zinc oxide-containing preparations appeared to be the most effective in reducing the cutaneous photosensitivity. It is suggested that the long-term cutaneous pigmentation resulting from oral amiodarone has a significant photosensitivity component.

Keywords

Fernández Alvarez C, Díaz Rodriguez E, Pazo Vinuesa D, et al. **Year** 1999

Authors Fernández Alvarez C, Díaz Rodriguez E, Pazo Vinuesa D et al.

Report Name In vitro pituitary responsiveness to LHRH in young and old female rats. Influence of melatonin

Publication Mech Ageing Dev

Issue-page numbers 112:75–83 doi:10.1016/S0047-6374(99)00080-9. PMID:10656184

URL http://www.sciencedirect.com/science/article/pii/S0047637499000809

Abstract The effect of aging and melatonin on in vitro pituitary responsiveness to luteinizing hormone-releasing hormone (LHRH) was studied. Young cyclic (3-months-old) control (cyclic-control, N=15), and melatonin (MEL) treated for 2 months (150 μg/100 g BW) (cyclic-MEL, N=15), old acyclic (23-months-old) control (acyclic-control, N=13), and MEL-treated (acyclic-MEL, N=18) rats were used. The hormones analyzed were luteinizing hormone (LH), follicle stimulating hormone (FSH) and prolactin (PRL). The results showed a different influence of the reproductive status as well as of melatonin on the basal secretion rate of both gonadotropins, i.e. LH and FSH. Only the basal FSH release was significantly reduced in cyclic-MEL and acyclic-controls compared to cyclic-controls. The hemipitutary FSH content raised to values similar to those observed for FSH secretion and only the cyclic-MEL group showed significantly higher FSH pituitary content than for release. LHRH addition to the incubation medium resulted in increased LH release for both cyclic and acyclic rats, but FSH release was only stimulated in acyclic rats. Melatonin treatment blunted this response in both cases. In addition, melatonin treatment inhibited prolactin release in acyclic-MEL group after LHRH stimulation but not the basal levels. Pituitary LH and prolactin contents, were significantly higher than the pituitary LH and prolactin levels released from all groups studied, and were not affected by reproductive senescence nor by exogenous melatonin. These data indicate that aging influences more the secretory than the biosynthetic processes. Melatonin influences is endocrine status-dependent, being inhibitory when pituitary hormones reach their higher values.

Keywords Aging; Melatonin; LHRH; Gonadotropins; Prolactin

Authors Fernández B, Díaz E, Colmenero MD, Díaz B

Report Name Maternal pineal gland participates in prepubertal rats' ovarian oocyte development.

Publication Anat Rec

Issue-page numbers 243:461–465 doi:10.1002/ar.1092430408. PMID:8597292

URL http://onlinelibrary.wiley.com/doi/10.1002/ar.1092430408/abstract?

Abstract

Background: Sexual maturation is a very complex phenomenom that it is mediated by the ontogeny of the hypothalamus-pituitarygonadal axis during intrauterine life. The maternal pineal gland can affect fetal development because the main pineal hormone, melatonin, crosses the placental barrier. We found that melatonin treatment during gestation in the rat produced delayed sexual maturation of the female offspring. The present work was undertaken to study the maturational stage of oocytes of prepubertal female rats when their mothers were either pinealectomized (PIN-X) or treated with melatonin (MEL) during pregnancy.

Methods: Three groups of female Wistar rats were used: control, PIN-X, and those treated (250 µg/100 g body weight) with melatonin throughout pregnancy. Ovaries of 25–30- and 34-day-old female offspring were studied during the prepubertal phase. Morphometric studies of semithin sections (1 µm) of the ovaries were performed. Oocyte, nuclear, and nucleolar volumes were calculated by a computer-assisted program (M.I.P.) in an image analyzer Kontron. Regularity of the structures was determined by the frequency distributions of circular and regular form factors.

Results: Cytometric study of oocyte structure showed a frequency distribution of regular and circular form factors, with a high degree of regularity very close to unit. Cellular and nuclear volumes of follicular oocytes showed a transitory increase at 30 days of age in control rats. In the offspring of MEL-treated mother rats, a pattern of oocyte development showed significantly lower nuclear and nucleolar volumes at 30 days of age than at the other time points and significantly lower cellular volume at 34 days of age than at 25 days of age. In the offspring of PIN-X mother rats, no significant differences in oocyte cellular volumes were observed throughout prepubertal development, but we observed a significantly higher nuclear volume at 25 days of age and a significantly lower nucleolar volume at 30 days of age.

Conclusions: These findings show that the maternal pineal gland participates in cellular and nuclear volumes of prepubertal oocyte development. Melatonin treatment during pregnancy resulted in a redirected postnatal oocyte development.

Keywords

Fernández B, Malde JL, Montero A, Acuña D **Year** 1990

Authors Fernández B, Malde JL, Montero A, Acuña D

Report Name Relationship between adenohypophyseal and steroid hormones and variations in serum and urinary melatonin levels during the ovarian cycle, perimenopause and menopause in

Publication J Steroid Biochem

Issue-page numbers 35:257–262 doi:10.1016/0022-4731(90)90282-W. PMID:2308340

URL http://www.sciencedirect.com/science/article/pii/002247319090282W

Abstract Morning levels of serum melatonin, FSH, LH, prolactin (PRL), progesterone and estradiol were studied by RIA during the ovarian cycle, perimenopause and menopause in 79 healthy women. FSH and LH levels showed a slight nonsignificant increase from the fertile period to perimenopause, exhibiting a significantly greater increase during menopause. PRL, progesterone and estradiol showed parallel changes, reaching lower levels during menopause. Serum melatonin levels decreased with age, attaining minimum levels in menopause. FSH and estradiol were significantly correlated with melatonin in the follicular phase, while in the luteal phase a negative correlation was found between melatonin, progesterone and estradiol. No significant correlations were noted between serum hormone levels during the perimenopausal period. In menopause, as during the follicular phase, melatonin and FSH were negatively correlated. As expected, a significant positive correlation was found between morning serum levels of melatonin and nocturnal urinary excretion of this indoleamine in all groups studied.

Keywords

Ferrari E, Magri F, Dori D et al. **Year** 1995

Authors Ferrari E, Magri F, Dori D et al.

Report Name Neuroendocrine correlates of the aging brain in humans

Publication Neuroendocrinology

Issue-page numbers 61:464–470 doi:10.1159/000126869. PMID:7783860

URL http://www.ncbi.nlm.nih.gov/pubmed/7783860

Abstract Physiological brain aging is characterized by important biochemical and structural changes and by the unbalance among the different neurotransmitters and neuromodulators. The study of the circadian organization of neuroendocrine functions may be considered a clinically reliable tool to investigate the changes of the CNS and particularly of the limbic-hypothalamic system occurring in aged people. The circadian rhythms of plasma melatonin, ACTH and cortisol and of oral temperature were studied in 16 clinically healthy women aged 66-90 years and in 14 young controls aged 20-30. In addition, the effect of dexamethasone on the plasma cortisol circadian rhythm and the cortisol response to Synacthen pulse intravenous injection were evaluated. All subjects were studied as inpatients, with the same synchronization to the hospital life schedule. When compared with young controls, elderly subjects exhibited a reduction of the mean level and of the amplitude of the circadian rhythm of oral temperature, an increase of the mean level of ACTH and cortisol rhythms and a selective impairment of melatonin nocturnal secretion. Furthermore, elderly subjects showed a reduced sensitivity to the dexamethasone suppression test, by comparison to young controls. These changes were age-related and they may depend either on CNS modification or on alterations of the hormonal metabolic clearance.

Keywords

Ferreira ZS, Fernandes PACM, Duma D et al

Year 2005

Authors Zulma S Ferreira, Pedro A C M Fernandes, Danielle Duma, Jamil Assreuy, Maria C W Avellar, Regina P Markus

Report Name Corticosterone modulates noradrenalineinduced melatonin synthesis through inhibition of nuclear factor kappa B

Publication J Pineal Res

Issue-page numbers 38:182– 188 doi:10.1111/j.1600-079X.2004.00191.x. PMID:15725340

URL http://www.mendeley.com/research/corticosterone-modulates-noradrenalineinduced-melatonin-synthesis-through-inhibition-nuclear-factor-kappa-b/

Abstract In chronically inflamed animals, adrenal hormones exert a positive control on the secretion of melatonin by the pineal gland. In this paper, the mechanism of corticosterone as a modulator of melatonin and N-acetylserotonin (NAS) was determined. Rat pineal glands in culture, stimulated for 5 hr with noradrenaline (10 nm), were previously incubated with corticosterone (1.0 nm-1.0 microm) for 48 hr in the presence or absence of the glucocorticoid receptor (GR) antagonist, mifepristone (1.0 microm), the proteasome inhibitor, N-acetyl-leucinyl-leucinyl-norleucinal-H (ALLN, 12.5 microm) or the antagonist of the nuclear factor kappa B (NFkappaB), pyrrolidinedithiocarbamate (PDTC, 12.5 microm). Corticosterone potentiated noradrenaline-induced melatonin and NAS production in a bell-shaped manner. The increase in NAS (12.9 2.7, n=6 versus 34.3 8.3 ng per pineal) and melatonin (16.3 2.0, n=6 versus 44.3 12.9 ng per pineal) content induced by 1 microm corticosterone was blocked by mifepristone, and mimicked by ALLN and PDTC. The presence of GRs was shown by 3H-dexamethasone binding (0.30 0.09 pmol/mg protein) and corticosterone inhibition of NFkappaB nuclear translocation was demonstrated by electromobility shift assay. Therefore, corticosterone potentiates noradrenaline-induced melatonin and NAS production through GR inhibition of NFkappaB nuclear translocation. To the best of our knowledge, this is the first time that this relevant pathway for passive and acquired immune response is shown to modulate melatonin production in pineal gland.

Keywords

Feskanich D, Hankinson SE, Schernhammer ES

Year 2009

Authors D Feskanich, S E Hankinson, E S Schernhammer

Report Name Nightshift work and fracture risk: the Nurses' Health Study

Publication Osteoporosis international

Issue-page numbers Volume: 20, Issue: 4, Pages: 537-542

URL http://www.mendeley.com/research/nightshift-work-and-fracture-risk-the-nurses-health-study/

Abstract SUMMAYR: Nightshift work suppresses melatonin production and has been associated with an increased risk of major diseases including hormonally related tumors. Experimental evidence suggests that light at night acts through endocrine disruption likely mediated by melatonin. To date, no observational study has addressed the effect of night work on osteoporotic fractures, another condition highly sensitive to sex steroid exposure. Our study, to our knowledge, the first to address this question, supports the hypothesis that nightshift work may negatively affect bone health, adding to the growing list of ailments that have been associated with shift work.

Keywords

Fève-Montange M, Abou-Samra AB | ***Year*** 1983

Authors Fève-Montange M, Abou-Samra AB

Report Name Glucocorticoids inhibit the in vivo melatonin production by rat pineal stimulated by norepinephrine (NE) or 8-bromo-cyclic AMP

Publication 14th Acta Endocrinol. Congress Satellite Symposium

Issue-page numbers Abstract 11

URL N/A

Abstract N/A

Keywords

Fève-Montange M, Van Cauter E, Refetoff S et al | ***Year*** 1981

Authors MICHELLE FÈVRE MONTANGE, EVE VAN CAUTER, SAMUEL REFETOFF, DANIEL DÉSIR, . J. TOURNIAIRE and GEORGES COPINSCHI

Report Name Effects of “jet lag” on hormonal patterns. II. Adaptation of melatonin circadian periodicity

Publication J Clin Endocrinol Metab

Issue-page numbers 52:642–649 doi:10.1210/jcem-52-4-642. PMID:7204537

URL http://jcem.endojournals.org/content/52/4/642.short

Abstract

The plasma melatonin concentration was measured by RIA in samples obtained at 15-min intervals during seven 24-h studies staggered over a period of 10 weeks (October to January). The five normal male volunteers underwent a 7-h westward time shift by jet preceding the second study and, 1 month later, a 7-h eastward shift preceding the fifth study. In the basal, unperturbed state, the 24-h plasma melatonin profile was characterized by a nocturnal elevation, approximately 2.5-fold above the mean daytime value, occurring at 0130 ± 0039 local time, thus 2.5 h after exposure to darkness and 1.5 h after sleep onset. Episodic fluctuations occurred throughout the entire 24-h period.

A significant decrease in the 24-h sleep and daytime mean melatonin levels was observed only after the westward trip, during which the difference between sunrise and sunset (daylight duration) was 16 h rather than 10 h. Shifts in the acrophase observed on the day after the westward trip indicated partial adaptation (>2-and <5-h shift), while the eastward trip, which involved 33 h of sleep deprivation, caused a total desynchronization. Eastward displacement was also associated with a significant disruption in the sleep pattern and an increase in the anxiety and depression scores. On the 11th day after trips in both directions, the melatonin acrophases were fully adapted to the local time.

Despite an apparent correlation between the melatonin and cortisol rhythms during the unperturbed state, a lack of relationship is supported on the basis of the following discrepancies: diminished 24-h mean level of melatonin after westward displacement without changes in the 24-h mean levels of ACTH and cortisol, more rapid adaptation of the circadian rhythm of melatonin without the eastward-westward time differences observed for cortisol, and abolishment of the 6-h time difference between melatonin and cortisol rhythms during the period of adaptation after time shift.

The amplitude of the acrophase declined throughout the period of investigation in parallel with the decrease in daylight duration. This change, apparently unrelated to acute time shifts or duration of exposure to artificial light, suggests that daylight may exert a prevailing influence on the amplitude of the melatonin rhythm.

Keywords

Feychting M

Year 2000

Authors Feychting, M.

Report Name Reduced Cancer incidence among the Blind in Sweden

Publication Proc. of Int. Symp. on Low frequency EMF, Visible Light, Melatonin and Cancer

Issue-page numbers May 4-5, 2000, University of Cologne, Germany

URL http://www.uni-koeln.de/symposium2000/contrib/index.html

Abstract

Melatonin is a hormone primarily produced by the pineal gland at night, which is suppressed by exposure to light. Experimental studies have indicated that melatonin may protect against cancer development, and different mechanisms for this effect have been suggested. Reduced melatonin levels increase the level of circulating estrogen, which would increase susceptibility to sex hormone related cancers. Furthermore, an oncostatic effect of melatonin has been demonstrated. Some studies have indicated an effect of melatonin on the immune system, and it has also been suggested that melatonin may act as a potent antioxidant, which means that melatonin would have a protective effect against cancer development in general. The majority of totally blind people, with no light perception, have a free running melatonin cycle, with a period slightly exceeding 24 hours, and melatonin is never suppressed by light exposure.

The aim of this study was to test the hypothesis that totally blind people have a decreased cancer incidence. We identified a cohort of 1,567 totally blind and 13,292 severely visually impaired subjects. In the severely visually impaired, but not blind people we did not hypothesize a decreased risk of cancer development. We assumed that, because they perceive light, they would have a melatonin cycle similar to sighted people. We obtained information about cancer incidence from the Swedish Cancer Registry. A total of 136 cancer cases were identified in the totally blind cohort, and 1,709 in the visually impaired cohort. We calculated standardized incidence ratios based on the number of person years and national age, sex, and calendar year specific incidence rates.

The results of the study showed that totally blind people had a lower incidence of all cancers combined (SIR=0.69; 95% CI 0.59-0.82). The risk reduction was observed in both men and women, and was equally pronounced in hormone dependent tumors as in other types of cancer. For specific cancer sites, the number of cases was too small to allow firm conclusions. Apart from gender, age, and time period, we had no information about potential confounding factors. Separate analyses of smoking related cancers and cancers not related to smoking indicate that difference in smoking habits between blind and sighted people can not explain the findings. In severely visually impaired, SIR was 0.95 (95% CI 0.91-1.00).

The findings support the hypothesis that blind people have a lower cancer incidence. However, other explanations than the higher melatonin exposure must also be considered.

Keywords

Feychting M, Osterlund B, Ahlbom A

Year 1998

Authors M Feychting, B Osterlund, A Ahlbom

Report Name Reduced cancer incidence among the blind

Publication Epidemiology

Issue-page numbers Volume: 9, Issue: 5, Pages: 490-494

URL http://www.mendeley.com/research/reduced-cancer-incidence-among-blind-see-comments/

Abstract Melatonin is a hormone primarily produced by the pineal gland at night and is suppressed by exposure to light. Experimental studies have indicated that melatonin may protect against cancer development. In the majority of totally blind people, melatonin is never suppressed by light exposure. The aim of this study was to test the hypothesis that blind people have a decreased cancer incidence, and that this effect is more pronounced in the totally blind than in the severely visually impaired. We identified a cohort of 1,567 totally blind and 13,292 severely visually impaired subjects and obtained information about cancer incidence from the Swedish Cancer Registry. We calculated standardized incidence ratios (SIRs) based on the number of person-years and incidence rates specific for national age, sex, and calendar year. Totally blind people had a lower incidence of all cancers combined SIR = 0.69; 95% confidence interval (CI) = 0.59-0.82. The risk reduction was observed in both men and women and was equally pronounced in hormone-dependent tumors as in other types of cancer. In the severely visually impaired, SIR was 0.95 (95% CI = 0.91-1.00). The findings support the hypothesis that blind people have a lower cancer incidence, although other explanations than the higher melatonin exposure must also be considered

Keywords

Fideleff H, Aparicio NJ, Guitelman A et al.

Year 1976

Authors Fideleff H, Aparicio NJ, Guitelman A et al.

Report Name Effect of melatonin on the basal and stimulated gonadotropin levels in normal men and postmenopausal women

Publication J Clin Endocrinol Metab

Issue-page numbers 42:1014–1017 doi:10.1210/jcem-42-6-1014. PMID:777019

URL http://www.ncbi.nlm.nih.gov/pubmed/777019

Abstract The effect of melatonin on LH and FSH secretion in basal conditions and after stimulation with synthetic LHRH was studied in 3 volunteer normal men and 3 women two to five years after menopause. During the first three days of study, blood samples were obtained at 8 AM. On the second day, an iv injection of 50 mug LHRH was performed; on the third day, 2 ml of 0.9% saline were injected. In both cases, blood samples were obtained 30 and 60 minutes after the injection. On the fourth day, the subjects began melatonin (10 mg daily im for 13 days). Blood samples at 8 AM were obtained after 5, 11, and 13 days of administration of the drug. On days 5 and 11 of the treatment, iv injections of 50 mug LHRH were performed and on day 13 an iv injection of saline 0.9% was given. Blood samples were obtained 30 and 60 minutes after each injection. In each sample LH and FSH levels were determined by radioimmunoassay. Melatonin treatment did not cause any significant change in basal or post-stimulation LH and FSH levels either in men or in post-menopausal women. These results do not support previous findings of an insults do not support previous findings of an inhibitory effect of melatonin on gonadotropin secretion, even with the same dose as the one used in this study. Further studies with higher doses of melatonin are needed to clarify the action of this drug on gonadotropin secretion.

Keywords

Authors Mariana G Figueiro, Andrew Bierman, Barbara Plitnick, Mark S Rea

Report Name Preliminary evidence that both blue and red light can induce alertness at night

Publication BMC Neuroscience

Issue-page numbers 10:105doi:10.1186/1471-2202-10-105

URL http://www.biomedcentral.com/1471-2202/10/105

Abstract

Background

A variety of studies have demonstrated that retinal light exposure can increase alertness at night. It is now well accepted that the circadian system is maximally sensitive to short-wavelength (blue) light and is quite insensitive to long-wavelength (red) light. Retinal exposures to blue light at night have been recently shown to impact alertness, implicating participation by the circadian system. The present experiment was conducted to look at the impact of both blue and red light at two different levels on nocturnal alertness. Visually effective but moderate levels of red light are ineffective for stimulating the circadian system. If it were shown that a moderate level of red light impacts alertness, it would have had to occur via a pathway other than through the circadian system.

Methods

Fourteen subjects participated in a within-subject two-night study, where each participant was exposed to four experimental lighting conditions. Each night each subject was presented a high (40 lx at the cornea) and a low (10 lx at the cornea) diffuse light exposure condition of the same spectrum (blue, λmax = 470 nm, or red, λmax = 630 nm). The presentation order of the light levels was counterbalanced across sessions for a given subject; light spectra were counterbalanced across subjects within sessions. Prior to each lighting condition, subjects remained in the dark (< 1 lx at the cornea) for 60 minutes. Electroencephalogram (EEG) measurements, electrocardiogram (ECG), psychomotor vigilance tests (PVT), self-reports of sleepiness, and saliva samples for melatonin assays were collected at the end of each dark and light periods.

Results

Exposures to red and to blue light resulted in increased beta and reduced alpha power relative to preceding dark conditions. Exposures to high, but not low, levels of red and of blue light significantly increased heart rate relative to the dark condition. Performance and sleepiness ratings were not strongly affected by the lighting conditions. Only the higher level of blue light resulted in a reduction in melatonin levels relative to the other lighting conditions.

Conclusion

These results support previous findings that alertness may be mediated by the circadian system, but it does not seem to be the only light-sensitive pathway that can affect alertness at night.

Keywords

Figueiro MG, Plitnick B, Rea MS

Year 2012

Authors Mariana G. Figueiro, Barbara Plitnick, and Mark S. Rea

Report Name LightModulates Leptin and Ghrelin in Sleep-Restricted Adults

Publication International Journal of Endocrinology

Issue-page numbers Volume 2012, Article ID 530726, 6 pages

URL http://scholar.google.com/scholar_url?hl=en&q=http://downloads.hindawi.com/journals/ije/2012/530726.pdf&sa=X&scisig=AAGBfm17udnaVXr4bmmiDLErV9WVfkXAcA&oi=scho

Abstract Acute and chronic sleep restrictions cause a reduction in leptin and an increase in ghrelin, both of which are associated with hunger. Given that light/dark patterns are closely tied to sleep/wake patterns, we compared, in a within-subjects study, the impact of morning light exposures (60 lux of 633-nm [red], 532-nm [green], or 475-nm [blue] lights) to dim light exposures on leptin and ghrelin concentrations after subjects experienced 5 consecutive days of both an 8-hour (baseline) and a 5-hour sleep-restricted schedule. In morning dim light, 5-hour sleep restriction significantly reduced leptin concentrations compared to the baseline, 8-hour sleep/dim-light condition ($t_{1,32} = 2.9$; $P = 0.007$). Compared to the 5-hour sleep/dim-light condition, the red, green, and blue morning light exposures significantly increased leptin concentrations ($t_{1,32} = 5.7$; $P < 0.0001$, $t_{1,32} = 3.6$; $P = 0.001$, and $t_{1,32} = 3.0$; $P = 0.005$, resp.). Morning red light and green light exposures significantly decreased ghrelin concentrations ($t_{1,32} = 3.3$; $P < 0.003$ and $t_{1,32} = 2.2$; $P = 0.04$, resp.), but morning blue light exposures did not. This study is the first to demonstrate that morning light can modulate leptin and ghrelin concentrations, which could have an impact on reducing hunger that accompanies sleep deprivation.

Keywords

Figueiro MG, Rea MS

Year 2010

Authors Mariana G Figueiro, Mark S Rea

Report Name The effects of red and blue lights on circadian variations in cortisol, alpha amylase, and melatonin

Publication International journal of endocrinology

Issue-page numbers Volume: 2010, Pages: 829351 DOI: 10.1155/2010/829351

URL http://www.mendeley.com/research/effects-red-blue-lights-circadian-variations-cortisol-alpha-amylase-melatonin/

Abstract The primary purpose of the present study was to expand our understanding of the impact of light exposures on the endocrine and autonomic systems as measured by acute cortisol, alpha amylase, and melatonin responses. We utilized exposures from narrowband long-wavelength (red) and from narrow-band short-wavelength (blue) lights to more precisely understand the role of the suprachiasmatic nuclei (SCN) in these responses. In a within-subjects experimental design, twelve subjects periodically received one-hour corneal exposures of 40 lux from the blue or from the red lights while continuously awake for 27 hours. Results showed-that, as expected, only the blue light reduced nocturnal melatonin. In contrast, both blue and red lights affected cortisol levels and, although less clear, alpha amylase levels as well. The present data bring into question whether the nonvisual pathway mediating nocturnal melatonin suppression is the same as that mediating other responses to light exhibited by the endocrine and the autonomic nervous systems.

Keywords

Authors Mariana G Figueiro, Mark S Rea

Report Name Preliminary evidence that light through the eyelids can suppress melatonin and

Publication BMC Research Notes

Issue-page numbers 2012, 5:221 doi:10.1186/1756-0500-5-221

URL http://www.biomedcentral.com/content/pdf/1756-0500-5-221.pdf

Abstract

Background
A previous study reported a method for measuring the spectral transmittance of individual human eyelids. A prototype light mask using narrow-band “green” light (λmax = 527 nm) was used to deliver light through closed eyelids in two within-subjects studies. The first study investigated whether an individual-specific light dose could suppress melatonin by 40% through the closed eyelid without disrupting sleep. The light doses were delivered at three times during the night: 1) beginning (while subjects were awake), 2) middle (during rapid eye movement (REM) sleep), and 3) end (during non-REM sleep). The second study investigated whether two individual-specific light doses expected to suppress melatonin by 30% and 60% and delivered through subjects’ closed eyelids before the time of their predicted minimum core body temperature would phase delay the timing of their dim light melatonin onset (DLMO).
Findings
Compared to a dark control night, light delivered through eyelids suppressed melatonin by 36% ($p = 0.01$) after 60-minute light exposure at the beginning, 45% ($p = 0.01$) at the middle, and 56% ($p < 0.0001$) at the end of the night. In the second study, compared to a dark control night, melatonin was suppressed by 25% ($p = 0.03$) and by 45% ($p = 0.009$) and circadian phase, as measured by DLMO, was delayed by 17 minutes ($p = 0.03$) and 71 minutes (ns) after 60-minute exposures to light levels 1 and 2, respectively.
Conclusions
These studies demonstrate that individual-specific doses of light delivered through closed eyelids can suppress melatonin and phase shift DLMO and may be used to treat circadian sleep disorders.

Keywords

Authors M. G. Figueiro, M. S. Rea, & R. Hamner

Report Name Calibrated Personal Light Exposures as They Might Affect Melatonin Suppression in Different Populations

Publication Conference: Experiencing Light 2012. Eindhoven, The Netherlands.

Issue-page numbers November 12-13, 2012

URL http://experiencinglight.nl/doc/9.pdf

Abstract

In mammals, melatonin is synthesized by the pineal gland at night and in darkness. Studies with nocturnal rodents have shown that a reduction in melatonin can enhance tumor growth (Blask, Dauchy, & Sauer,
2005). Since light can suppress melatonin at night, concerns have been expressed in the literature about light at night (LAN) as a potential causative agent for breast cancer in humans (Stevens et al., 2007).
Optical radiation incident on the retina will suppress melatonin synthesis if the light levels are sufficiently high and the durations are sufficiently long (Figueiro, Lesniak, & Rea, 2011; Lewy, Wehr, Goodwin, Newsome, & Markey, 1980; Rea, Figueiro, Bierman, & Hamner, 2011; Rea, Figueiro, Bullough, & Bierman, 2005; Zeitzer, Dijk, Kronauer, Brown, & Czeisler, 2000). The amount and duration of light exposure necessary to suppress melatonin production is species specific. The circadian systems of nocturnal rodents are several orders of
magnitude more sensitive to light than that of humans. The spectral sensitivities of species also differ. Rodents are, for example, highly sensitive to ultraviolet radiation while humans are not at all sensitive to radiation in this region of the electromagnetic spectrum (Amir & Robinson, 1995; Benshoff, Brainard, Rollag, & Lynch, 1987; Bullough, Rea, & Figueiro, 2006).
To properly consider LAN as a potential causative agent for breast cancer, it is necessary to, first, properly characterize light as a stimulus for the human circadian system and, second, to measure calibrated personal
light exposures in populations that might be at risk for breast cancer (Figueiro, Rea, & Bullough, 2006; Rea, Brons, & Figueiro, 2011). The goal of the present study was to examine personal calibrated light exposures
in different groups of participants and relate them to predictions of how they might impact melatonin production. All participants had worn the Daysimeter, a personal circadian light meter, for a period of five to seven days, depending on the experimental protocol (Bierman, Klein, & Rea, 2005).

Keywords

Figueiro MG, Wood B, Plitnick B, Rea MS. **Year** 2011

Authors Figueiro MG, Wood B, Plitnick B, Rea MS.

Report Name The impact of light from computer monitors on melatonin levels in college students

Publication Neuro Endocrinol Lett

Issue-page numbers 2011;32(2):158-63.

URL http://www.researchgate.net/publication/51107485_The_impact_of_light_from_computer_monitors_on_melatonin_levels_in_college_students

Abstract OBJECTIVES: Self-luminous electronic devices emit optical radiation at short wavelengths, close to the peak sensitivity of melatonin suppression. Melatonin suppression resulting from exposure to light at night has been linked to increased risk for diseases. The impact of luminous cathode ray tube (CRT) computer monitors on melatonin suppression was investigated. DESIGN: Twenty-one participants experienced three test conditions: 1) computer monitor only, 2) computer monitor viewed through goggles providing 40 lux of short-wavelength (blue; peak λ ≈ 470 nm) light at the cornea from light emitting diodes (LEDs), and 3) computer monitor viewed through orange-tinted safety glasses (optical radiation <525 nm ≈ 0). The blue-light goggles were used as a "true-positive" experimental condition to demonstrate protocol effectiveness; the same light treatment had been shown in a previous study to suppress nocturnal melatonin. The orange-tinted glasses served as a "dark" control condition because the short-wavelength radiation necessary for nocturnal melatonin suppression was eliminated. Saliva samples were collected from subjects at 23:00, before starting computer tasks, and again at midnight and 01:00 while performing computer tasks under all three experimental conditions. RESULTS: Melatonin concentrations after exposure to the blue-light goggle experimental condition were significantly reduced compared to the dark control and to the computer monitor only conditions. Although not statistically significant, the mean melatonin concentration after exposure to the computer monitor only was reduced slightly relative to the dark control condition. CONCLUSIONS: Additional empirical data should be collected to test the effectiveness of different, brighter and larger screens on melatonin suppression.

Keywords

Fildes JE, Yonan N, Keevil BG **Year** 2009

Authors James E Fildes, Nizar Yonan, and Brian G Keevil

Report Name Melatonin – a pleiotropic molecule involved in pathophysiological processes following organ transplantation

Publication Immunology

Issue-page numbers 2009 August; 127(4): 443–449. doi: 10.1111/j.1365-2567.2009.03113.x

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2729521/

Abstract Mammals adjust their physiology in response to seasonal changes to environment (i.e. photoperiod, temperature, food availability). These changes are thought to predominantly occur for the conservation of energy during winter, by pervasive changes such as the inhibition of reproduction. Previous reports have suggested that circannual changes also occur to the immune system. In mammals, this chronological effect may be dependent on photoperiod, and evidence exists to suggest that there is a great deal of immune variation in response to light, or circadian rhythm. This is a clinically relevant, yet under-reported area of human transplantation. The aim of this review is to discuss immune variation, with specific emphasis on melatonin secretion, in the context of organ rejection, infection, neoplasia formation, and immunosuppression.

Keywords cancer, immunomodulation, infection, melatonin, rejection, transplantation

Filipovich AH, Mathur A, Kamat D, Shapiro RS

Year 1992

Authors Filipovich AH, Mathur A, Kamat D, Shapiro RS

Report Name Primary immunodeficiencies: genetic risk factors for lymphoma

Publication Cancer Res

Issue-page numbers 52 Suppl;5465s–5467s. PMID:1327508

URL http://www.ncbi.nlm.nih.gov/pubmed/1327508

Abstract It has been estimated that up to 25% of patients with certain genetically determined immunodeficiencies will develop tumors, primarily B-cell lymphomas, during their lifetime. Epstein-Barr virus appears to be an important cofactor in the development of lymphoproliferative disorders in patients with primary immunodeficiencies, as well as acquired immunodeficiencies. Additionally, host defects in immunoregulation and/or gene rearrangement, which are features of certain primary immunodeficiencies, probably contribute to the risk of lymphomagenesis in patients at risk.

Keywords

Filipski E, Delaunay F, King VM, et al.

Year 2004

Authors Elisabeth Filipski, Franck Delaunay, Verdun M. King, Ming-Wei Wu, Bruno Claustrat, Aline Gréchez-Cassiau, Catherine Guettier, Michael H. Hastings, and Lévi Francis

Report Name Effects of Chronic Jet Lag on Tumor Progression in Mice

Publication Cancer Res

Issue-page numbers November 1, 2004 64; 7879-7885

URL http://cancerres.aacrjournals.org/content/64/21/7879.abstract

Abstract Frequent transmeridian flights or predominant work at night can increase cancer risk. Altered circadian rhythms also predict for poor survival in cancer patients, whereas physical destruction of the suprachiasmatic nuclei (SCN), the hypothalamic circadian pacemaker, accelerates tumor growth in mice. Here we tested the effect of functional disruption of circadian system on tumor progression in a novel experimental model of chronic jet lag. B6D2F1 mice were synchronized with 12 hours of light and 12 hours of darkness or underwent repeat 8-hour advances of the light/dark cycle every 2 days before inoculation of Glasgow osteosarcoma. The 24-hour changes were assessed for plasma corticosterone, clock protein mPER1 expression in the SCN, and mRNA expression of clock genes mPer2 and mRev-erbα in liver and tumor. Time series were analyzed by spectral analysis and/or Cosinor. Differences were compared with analysis of variance (ANOVA). The 24-hour rest/activity cycle was ablated, and the rhythms of body temperature, serum corticosterone, and mPER1 protein expression in the SCN were markedly altered in jet-lagged mice as compared with controls (ANOVA, $P < 0.001$ for corticosterone and $P = 0.01$ for mPER1). Tumor grew faster in the jet-lagged animals as compared with controls (ANOVA, $P < 0.001$), whereas exposure to constant light or darkness had no effect (ANOVA, $P = 0.66$ and $P = 0.8$, respectively). The expression of mPer2 and mRev-erbα mRNAs in controls showed significant circadian rhythms in the liver ($P = 0.006$ and $P = 0.003$, respectively, Cosinor) and in the tumor ($P = 0.04$ and $P < 0.001$). Both rhythms were suppressed in the liver ($P = 0.2$ and $P = 0.1$, respectively, Cosinor) and in the tumor ($P = 0.5$) of jet-lagged mice. Altered environmental conditions can disrupt circadian clock molecular coordination in peripheral organs including tumors and play a significant role in malignant progression.

Keywords cancer, light, dark, light at night

Filipski E, Innominato PF, Wu M, et al. **Year** 2005

Authors Elisabeth Filipski, Pasquale F. Innominato, MingWei Wu, Xiao-Mei Li, Stefano Iacobelli, Li-Jian Xian and Francis Lévi

Report Name Effects of Light and Food Schedules on Liver and Tumor Molecular Clocks in Mice

Publication Journal of the National Cancer Institute

Issue-page numbers (2005) 97 (7): 507-517

URL http://jnci.oxfordjournals.org/content/97/7/507.abstract

Abstract

Background: Disrupted circadian coordination accelerates malignant growth, but the molecular mechanism is unclear. Methods: Healthy or Glasgow osteosarcoma–bearing mice (n = 162) were synchronized with light and darkness over 2–3 weeks, submitted to an 8-hour advance onset of light every 2 days (chronic jet lag) to disrupt circadian coordination, or submitted to chronic jet lag and meal timing to prevent molecular clock alteration. The expression of molecular clock genes and of the cell cycle genes c-Myc and p53 in liver and tumor was determined with quantitative reverse transcription–polymerase chain reaction at six circadian times over a 24-hour period of light and darkness and analyzed with analysis of variance and cosinor. Tumor weight was measured daily over the course of the experiment. All statistical tests were two-sided. Results: In synchronized mice, mean mRNA levels of clock genes Rev-erbα, Per2, and Bmal1 varied by 206-, four-, and 26-fold, respectively, over the 24 hours in healthy mouse liver; by 36-, 35-, and 32-fold in the livers of tumor-bearing mice; and by 9.4-, 5.5-, and sixfold in tumor tissue (P = .046 to <.001). In mice subjected to chronic jet lag, the periodic changes were dampened and the clock gene rhythms were temporally shifted in liver and ablated in tumor, and tumor growth was accelerated. Meal timing reversed the chronic jet lag–induced alterations in Rev-erbα and Per2 expression in liver and of all three clock genes in tumor and slowed tumor growth. Tumor growth differed as a function of light and feeding schedules (P = .04). No obvious rhythm was detected for p53 or c-Myc in liver or tumor tissues of synchronized mice. In healthy mice subjected to chronic jet lag, the mean level of p53 expression was cut in half (P = .002), and a 12-fold circadian variation in c-Myc mRNA level (P = .03) was induced in the liver of healthy mice, whereas complex expression patterns were found in the liver and tumor of tumor-bearing mice. Conclusions: Altered light–dark or feeding schedules modified the expression of molecular clock genes and genes involved in carcinogenesis and tumor progression.

Keywords

Authors Filipski E, King VM, Li X et al.

Report Name Host circadian clock as a control point in tumor progression

Publication J Natl Cancer Inst

Issue-page numbers 94:690–697. PMID:11983758

URL http://jnci.oxfordjournals.org/content/94/9/690.full.pdf

Abstract

The circadian timing system controlled by the suprachiasmatic nuclei (SCN) of the hypothalamus regulates daily rhythms of motor activity and adrenocortical secretion. An alteration in these rhythms is associated with poor survival of patients with metastatic colorectal or breast cancer. We developed a mouse model to investigate the consequences of severe circadian dysfunction upon tumor growth. Methods: The SCN of mice were destroyed by bilateral electrolytic lesions, and body activity and body temperature were recorded with a radio transmitter implanted into the peritoneal cavity. Plasma corticosterone levels and circulating lymphocyte counts were measured (n = 75 with SCN lesions, n = 64 sham-operated). Complete SCN destruction was ascertained postmortem. Mice were inoculated with implants of Glasgow osteosarcoma (n = 16 with SCN lesions, n = 12 sham-operated) or pancreatic adenocarcinoma (n = 13 with SCN lesions, n = 13 sham-operated) tumors to determine the effects of altered circadian rhythms on tumor progression. Time series for body temperature and rest–activity patterns were analyzed by spectral analysis and cosinor analysis. Parametric data were compared by the use of analysis of variance (ANOVA) and survival curves with the log-rank test. All statistical tests were two-sided. Results: The 24-hour rest–activity cycle was ablated and the daily rhythms of serum corticosterone level and lymphocyte count were markedly altered in 75 mice with complete SCN destruction as compared with 64 sham-operated mice (two-way ANOVA for corticosterone: sampling time effect P<.001, lesion effect P = .001, and time × lesion interaction P<.001; for lymphocytes P = .001, .002, and .002 respectively). Body temperature rhythm was suppressed in 60 of the 75 mice with SCN lesions (P<.001). Both types of tumors grew two to three times faster in mice with SCN lesions than in sham-operated mice (two-way ANOVA: P<.001 for lesion and for tumor effects; P = .21 for lesion × tumor effect interaction). Survival of mice with SCN lesions was statistically significantly shorter compared with that of sham-operated mice (log-rank P = .0062). Conclusions: Disruption of circadian rhythms in mice was associated with accelerated growth of malignant tumors of two types, suggesting that the host circadian clock may play an important role in endogenous control of tumor

progression.

Keywords

Finken LK, Nelson RJ — ***Year*** 2011

Authors Laura K. Fonken, Randy J. Nelson

Report Name Illuminating the deleterious effects of light at night

Publication F1000 Med Rep

Issue-page numbers 2011; 3: 18. doi: 10.3410/M3-18

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3169904/

Abstract Technological advances, while providing many benefits, often create circumstances that differ from the conditions in which we evolved. With the wide-spread adoption of electrical lighting during the 20th century, humans became exposed to bright and unnatural light at night for the first time in their evolutionary history. Electrical lighting has led to the wide-scale practice of 24-hour shift-work and has meant that what were once just “daytime” activities now run throughout the night; in many ways Western society now functions on a 24-hour schedule. Recent research suggests that this gain in freedom to function throughout the night may also come with significant repercussions. Disruption of our naturally evolved light and dark cycles can result in a wide range of physiological and behavioral changes with potentially serious medical implications. In this article we will discuss several mechanisms through which light at night may exert its effects on cancer, mood, and obesity, as well as potential ways to ameliorate the impact of light at night.

Keywords light at night, obesity, breast cancer

Flemmer DD, Dilsaver SC, Peck JA — ***Year*** 1991

Authors Duane D. Flemmer, Steven C. Dilsaver, Jason A. Peck

Report Name Exposure to constant darkness enhances the thermic response of the rat to a muscarinic agonist

Publication Pharmacology Biochemistry and Behavior

Issue-page numbers Volume 38, Issue 1, January 1991, Pages 227-230

URL http://www.sciencedirect.com/science/article/pii/009130579190617B

Abstract Bright artificial light is used to treat patients with major depression with a seasonal component (“Winter Depression”). Hyperactivity of muscarinic cholinergic systems is implicated in the pathophysiology of depression. Continual exposure to bright light for 7 days or during discrete portions of the photoperiod blunts the thermic response to a muscarinic agonist (oxotremorine) in the rat. Exposure to either 24 hours per day of bright light (in contrast to periods of circumscribed exposure) or darkness would tend to produce free-running. Observers have suggested that the reduced responsiveness to oxotremorine may result from the induction of free-running (the “free-running hypothesis”). The “free-running hypothesis” leads to the prediction that rats exposed to constant darkness will exhibit a reduction in thermic responsiveness to oxotremorine. The authors hypothesized that constant exposure to darkness would, contrary to the “free-running hypothesis”, enhance the thermic response to oxotremorine. Rats (n=12) exposed to constant darkness for 7 days exhibited supersensitivity to oxotremorine 5 days after return to standard light/dark cycle in the vivarium. This argues against the hypothesis that the induction of free-running enhances sensitivity to the thermic effects of oxotremorine.

Keywords Affective disorders; Acetylcholine; Bright light; Cholinergic; Muscarinic; Receptors; Seasonal affective disorder

Fogle KJ, Parson KG, Dahm NA, Holmes TC

Year 2011

Authors Keri J. Fogle, Kelly G. Parson, Nicole A. Dahm, and Todd C. Holmes

Report Name CRYPTOCHROME Is a Blue-Light Sensor That Regulates Neuronal Firing Rate

Publication Science

Issue-page numbers Vol. 331 no. 6023 pp. 1409-1413 DOI: 10.1126/science.1199702

URL http://www.sciencemag.org/content/331/6023/1409.short

Abstract Light-responsive neural activity in central brain neurons is generally conveyed through opsin-based signaling from external photoreceptors. Large lateral ventral arousal neurons (lLNvs) in Drosophila melanogaster increase action potential firing within seconds in response to light in the absence of all opsin-based photoreceptors. Light-evoked changes in membrane resting potential occur in about 100 milliseconds. The light response is selective for blue wavelengths corresponding to the spectral sensitivity of CRYPTOCHROME (CRY). cry-null lines are light-unresponsive, but restored CRY expression in the lLNv rescues responsiveness. Furthermore, expression of CRY in neurons that are normally unresponsive to light confers responsiveness. The CRY-mediated light response requires a flavin redox-based mechanism and depends on potassium channel conductance, but is independent of the classical circadian CRY-TIMELESS interaction.

Keywords

Folkard S, Akerstedt T

Year 2004

Authors Folkard S, Akerstedt T

Report Name Trends in the risk of accidents and injuries and their implications for models of fatigue and performance

Publication Aviat Space Environ Med

Issue-page numbers 75 Suppl:A161–A167. PMID:15018280

URL http://trid.trb.org/view.aspx?id=704672

Abstract It is assumed that mathematical models based on measures of fatigue and performance will be successful in predicting risk. This study reviews the available literature on shiftwork safety in which real measures of accidents or injuries could be pinpointed in time and in which the a priori risk appeared to be constant. Three main problems for the models emerged from this review: (1) risk was significantly higher on the afternoon shift than on the morning shift; (2) the dominant peak in risk over the course of the night shift occurred at about midnight; (3) risk increased substantially over spans of four successive nights. It is suggested that the relationship between risk and fatigue may be non-linear, that models may overestimate the recovery during short sleeps, and that day sleeps between night shifts may be less recuperative than normally timed night sleeps of the same length. To refine the current models to enable them to predict risk, it may be necessary to incorporate a nonlinear relationship between fatigue and relative risk, add a cumulative fatigue effect, and take into account the time of day at which sleep occurs in determining its recovery value. The findings also suggest the need for more carefully controlled epidemiological studies of the factors that may affect fatigue and risk.

Keywords

Folkard S, Lombardi DA

Year 2004

Authors Folkard S, Lombardi DA

Report Name Toward a “Risk Index” to assess work schedules

Publication Chronobiol Int

Issue-page numbers 21:1063–1072 doi:10.1081/CBI-200036919. PMID:15646251

URL http://informahealthcare.com/doi/abs/10.1081/CBI-200036919

Abstract his article describes our preliminary attempt to develop a Risk Index to estimate the risk of human error on different work schedules based on trends in the relative risk of accidents and injuries, rather than on hypothetical intervening variables such as alertness, fatigue, or performance on interpolated tasks. We briefly review trends in risk from the published epidemiological studies that have ensured that the a priori risk was constant. A simple Risk Index based on an additive model is developed on the basis of these trends, and we illustrate how it may be used to assess work schedules. Finally, we compare the results from this Risk Index with those from the UK HSE's Fatigue Index and point out the discrepancies that emerge. We conclude that our risk-based modeling approach may assist in developing safer work schedules and also increase our understanding of this complex, multifaceted area.

Keywords Work schedules, Worker safety, Occupational injuries, Work-place accidents, Mathematical models

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Follenius M, Brandenberger G, Bandesapt JJ et al.

Year 1992

Authors Follenius M, Brandenberger G, Bandesapt JJ, Libert JP, Ehrhart J.

Report Name Nocturnal cortisol release in relation to sleep structure

Publication Sleep

Issue-page numbers 15:21–27. PMID:1557591

URL http://www.ncbi.nlm.nih.gov/pubmed/1557591

Abstract The relationship between the temporal organization of cortisol secretion and sleep structure is controversial. To determine whether the cortisol profile is modified by 4 hours of sleep deprivation, which shifts slow-wave sleep (SWS) episodes, 12 normal men were studied during a reference night, a sleep deprivation night and a recovery night. Plasma cortisol was measured in 10-minute blood samples. Analysis of the nocturnal cortisol profiles and the concomitant patterns of sleep stage distribution indicates that the cortisol profile is not influenced by sleep deprivation. Neither the starting time of the cortisol increase nor the mean number and amplitude of pulses was significantly different between the three nights. SWS episodes were significantly associated with declining plasma cortisol levels (p less than 0.01). This was especially revealed after sleep deprivation, as SWS episodes were particularly present during the second half of the night, a period of enhanced cortisol secretion. In 73% of cases, rapid eye movement sleep phases started when cortisol was reflecting diminished adrenocortical activity. Cortisol increases were not concomitant with a specific sleep stage but generally accompanied prolonged waking periods. These findings tend to imply that cortisol-releasing mechanisms may be involved in the regulation of sleep.

Keywords

Fonken L

Year 2012

Authors Fonken, Laura

Report Name Impact of Light at Night on Cardiac Arrest Outcome

Publication 2012. Edward F. Hayes Graduate Research Forum. 26th

Issue-page numbers

URL https://kb.osu.edu/dspace/handle/1811/51774

Abstract Little is known about the influence of hospital environment on patient recovery. Nighttime light exposure is particularly prevalent in the hospital setting and may be detrimental because of its neuroinflammatory effects. We used a mouse model of cardiac arrest (CA) to test the hypothesis that exposure to dim light at night after cerebral ischemia impairs recovery. Mice housed in a standard light/dark cycle (LD) underwent a CA or SHAM procedure, then either remained in LD or were exposed to a light/dim light cycle (dLAN). Mortality during the first week after CA was 4-fold higher in mice exposed to dLAN relative to LD. Furthermore, surviving dLAN-CA mice had greater neuroinflammation and hippocampal cell death than LD-CA mice. dLAN likely affects CA recovery by elevating inflammation; selective inhibition of IL-1β or TNFα ameliorated the effects of dLAN light or CA recovery. In addition, restricting the wavelength of the nighttime light exposure to nm, eliminated the detrimental effects of light exposure on CA outcome. Together, these data suggest that lighting in clinical settings may affect patient recovery.

Keywords

Fonken LK, Bedrosian TA, Zhang N, et al.

Year 2012

Authors L.K. Fonken, T.A. Bedrosian, N. Zhang, Z.M. Weil, A.C. DeVries, R.J. Nelson

Report Name 85. Light at night affects cardiac arrest outcome

Publication Brain, Behavior, and Immunity

Issue-page numbers Volume 26, Supplement 1, September 2012, Pages S24

URL http://www.sciencedirect.com/science/article/pii/S0889159112002929

Abstract Most permanent CNS damage following global cerebral ischemia is mediated by endogenous secondary processes. The trajectory of recovery is established early, suggesting that immediate recovery environment may play a critical role in post-ischemic damage. Hospitals are stressful environments, with high noise levels, continuous disruptions by staff, and unpredictable lighting. Physiological processes such as inflammation become deranged in disruptive lighting, which led us to hypothesize that cardiac arrest (CA) outcomes are negatively affected by exposure to light at night. Following a CA and cardiopulmonary resuscitation procedure or a SHAM procedure, mice were exposed to either a standard light/dark cycle (LD) or a light/dim light cycle (dLAN). Mortality was 4-fold higher among dLAN mice compared to LD mice in the week following CA. dLAN increased hippocampal cell death 1 week after CA. Hippocampal expression of pro-inflammatory cytokines was elevated 24 h after CA. Moreover, among CA mice a single night of dLAN was sufficient to upregulate hippocampal expression of IL-1β and TNF-α compared to dark nights. dLAN-CA also increased hippocampal microglia activation and microglial pro-inflammatory cytokine expression compared to LD-CA. Post-CA corticosterone concentrations did not differ suggesting differences in outcome are not due to altered corticosterone. Blocking the inflammatory response and modulating light wavelength minimized light induced damage following CA. These results indicate that dLAN exacerbates damage following CA and may have implications for lighting in clinical settings.

Keywords

Fonken LK, Finy MS, Walton JC, et al. **Year** 2009

Authors Fonken LK, Finy MS, Walton JC, Weil ZM, Workman JL, Ross J, Nelson RJ.

Report Name Influence of light at night on murine anxiety- and depressive-like responses

Publication Behav Brain Res

Issue-page numbers 2009 Dec 28;205(2):349-54. Epub 2009 Jul 8.

URL http://www.ncbi.nlm.nih.gov/pubmed/19591880

Abstract Individuals are increasingly exposed to light at night. Exposure to constant light (LL) disrupts circadian rhythms of locomotor activity, body temperature, hormones, and the sleep-wake cycle in animals. Other behavioural responses to LL have been reported, but are inconsistent. The present experiment sought to determine whether LL produces changes in affective responses and whether behavioural changes are mediated by alterations in glucocorticoid concentrations. Relative to conspecifics maintained in a light/dark cycle (LD, 16:8 light/dark), male Swiss-Webster mice exposed to LL for three weeks increased depressive-like behavioural responses as evaluated by the forced swim test and sucrose anhedonia. Furthermore, providing a light escape tube reversed the effects of LL in the forced swim test. LL mice displayed reduced anxiety as evaluated by the open field and elevated-plus maze. Glucocorticoid concentrations were reduced in the LL group suggesting that the affective behavioural responses to LL are not the result of elevated corticosterone. Additionally, mice housed in LD with a clear tube displayed increased paired testes mass as compared to LL mice. Taken together, these data provide evidence that exposure to unnatural lighting can induce significant changes in affect, increasing depressive-like and decreasing anxiety-like responses.

Keywords

Fonken LK, Kitsmiller E, Smale L, Nelson RJ **Year** 2012

Authors Laura K. Fonken, Emily Kitsmiller, Laura Smale, Randy J. Nelson

Report Name Dim Nighttime Light Impairs Cognition and Provokes Depressive-Like Responses in a Diurnal Rodent

Publication J Biol Rhythms

Issue-page numbers August 2012 vol. 27 no. 4 319-327

URL http://jbr.sagepub.com/content/27/4/319.short

Abstract Circadian disruption is a common by-product of modern life. Although jet lag and shift work are well-documented challenges to circadian organization, many more subtle environmental changes cause circadian disruption. For example, frequent fluctuations in the timing of the sleep/wake schedule, as well as exposure to nighttime lighting, likely affect the circadian system. Most studies of these effects have focused on nocturnal rodents, which are very different from diurnal species with respect to their patterns of light exposure and the effects that light can have on their activity. Thus, the authors investigated the effect of nighttime light on behavior and the brain of a diurnal rodent, the Nile grass rat. Following 3 weeks of exposure to standard light/dark (LD; 14:10 light [~150 lux] /dark [0 lux]) or dim light at night (dLAN; 14:10 light [~150 lux] /dim [5 lux]), rats underwent behavioral testing, and hippocampal neurons within CA1, CA3, and the dentate gyrus (DG) were examined. Three behavioral effects of dLAN were observed: (1) decreased preference for a sucrose solution, (2) increased latency to float in a forced swim test, and (3) impaired learning and memory in the Barnes maze. Light at night also reduced dendritic length in DG and basilar CA1 dendrites. Dendritic length in the DG positively correlated with sucrose consumption in the sucrose anhedonia task. Nighttime light exposure did not disrupt the pattern of circadian locomotor activity, and all grass rats maintained a diurnal activity pattern. Together, these data suggest that exposure to dLAN can alter affective responses and impair cognition in a diurnal animal.

Keywords depression, memory, hippocampus, Arvicanthis niloticus

Fonken LK, Nelson RJ

Year 2011

Authors Laura K. Fonken and Randy J. Nelson

Report Name Illuminating the deleterious effects of light at night

Publication F1000 Med Rep

Issue-page numbers 2011; 3: 18.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3169904/

Abstract Technological advances, while providing many benefits, often create circumstances that differ from the conditions in which we evolved. With the wide-spread adoption of electrical lighting during the 20th century, humans became exposed to bright and unnatural light at night for the first time in their evolutionary history. Electrical lighting has led to the wide-scale practice of 24-hour shift-work and has meant that what were once just “daytime” activities now run throughout the night; in many ways Western society now functions on a 24-hour schedule. Recent research suggests that this gain in freedom to function throughout the night may also come with significant repercussions. Disruption of our naturally evolved light and dark cycles can result in a wide range of physiological and behavioral changes with potentially serious medical implications. In this article we will discuss several mechanisms through which light at night may exert its effects on cancer, mood, and obesity, as well as potential ways to ameliorate the impact of light at night.

Keywords

Fonken LK, Nelson RJ

Year 2013

Authors Laura K. Fonken, Randy J. Nelson

Report Name Dim light at night increases depressive-like responses in male C3H/HeNHsd mice

Publication Behavioural Brain Research

Issue-page numbers Volume 243, 15 April 2013, Pages 74–78

URL http://www.sciencedirect.com/science/article/pii/S0166432812008364

Abstract Daily patterns of light exposure have become increasingly variable since the widespread adoption of electrical lighting during the 20th century. Seasonal fluctuations in light exposure, shift-work, and transmeridian travel are all associated with alterations in mood. These studies implicate fluctuations in environmental lighting in the development of depressive disorders. Here we argue that exposure to light at night (LAN) may be causally linked to depression. Male C3H/HeNHsd mice, which produce nocturnal melatonin, were housed in either a standard light/dark (LD) cycle or exposed to nightly dim (5 lux) LAN (dLAN). After four weeks in lighting conditions mice underwent behavioral testing and hippocampal tissue was collected at the termination of the study for qPCR. Here were report that mice exposed to dLAN increase depressive-like responses in both a sucrose anhedonia and forced swim test. In contrast to findings in diurnal grass rats, dLAN mice perform comparably to mice housed under dark nights in a hippocampus-dependent learning and memory task. TNFα and IL1β gene expression do not differ between groups, demonstrating that changes in these pro-inflammatory cytokines do not mediate dLAN induced depressive-like responses in mice. BDNF expression is reduced in the hippocampus of mice exposed to dLAN. These results indicate that low levels of LAN can alter mood in mice. This study along with previous work implicates LAN as a potential factor contributing to depression. Further understanding of the mechanisms through which LAN contributes to changes in mood is important for characterizing and treating depressive disorders.

Keywords

Authors L.K. Fonken, Z.M. Weil, R.J. Nelson

Report Name Dark nights reverse metabolic disruption caused by dim light at night

Publication Obesity

Issue-page numbers Article first published online: 10 MAY 2013

URL http://onlinelibrary.wiley.com/doi/10.1002/oby.20108/abstract

Abstract

Objective
The increasing prevalence of obesity and related metabolic disorders coincides with increasing exposure to light at night. Previous studies report that mice exposed to dim light at night (dLAN) develop symptoms of metabolic syndrome. This study investigated whether mice returned to dark nights after dLAN exposure recover metabolic function.
Design and Methods

Male Swiss-Webster mice were assigned to either: standard light-dark (LD) conditions for 8 weeks (LD/LD), dLAN for 8 weeks (dLAN/dLAN), LD for 4 weeks followed by 4 weeks of dLAN (LD/dLAN), and dLAN for 4 weeks followed by 4 weeks of LD (dLAN/LD).
Results

After 4 weeks in their respective lighting conditions both groups initially placed in dLAN increased body mass gain compared to LD mice. Half of the dLAN mice (dLAN/LD) were then transferred to LD and vice versa (LD/dLAN). Following the transfer dLAN/dLAN and LD/dLAN mice gained more weight than LD/LD and dLAN/LD mice. At the conclusion of the study dLAN/LD mice did not differ from LD/LD mice with respect to weight gain and had lower fat pad mass compared to dLAN/dLAN mice. Compared to all other groups dLAN/dLAN mice decreased glucose tolerance as indicated by an intraperitoneal glucose tolerance test at week 7, indicating that dLAN/LD mice recovered glucose metabolism. dLAN/dLAN mice also increased MAC1 mRNA expression in peripheral fat as compared to both LD/LD and dLAN/LD mice, suggesting peripheral inflammation is induced by dLAN, but not sustained after return to LD.
Conclusion

These results suggest that re-exposure to dark nights ameliorates metabolic disruption caused by dLAN exposure.

Keywords

Fonken LK, Workman JL, Walton JC, et al. **Year** 2010

Authors Laura K. Fonken, Joanna L. Workman, James C. Walton, Zachary M. Weil, John S. Morris, Abraham Haim, and Randy J. Nelson

Report Name Light at night increases body mass by shifting the time of food intake

Publication Proc Natl Acad Sci U S A

Issue-page numbers 107:18664–9. doi: 10.1073/pnas.1008734107

URL http://www.pnas.org/content/107/43/18664.short

Abstract The global increase in the prevalence of obesity and metabolic disorders coincides with the increase of exposure to light at night (LAN) and shift work. Circadian regulation of energy homeostasis is controlled by an endogenous biological clock that is synchronized by light information. To promote optimal adaptive functioning, the circadian clock prepares individuals for predictable events such as food availability and sleep, and disruption of clock function causes circadian and metabolic disturbances. To determine whether a causal relationship exists between nighttime light exposure and obesity, we examined the effects of LAN on body mass in male mice. Mice housed in either bright (LL) or dim (DM) LAN have significantly increased body mass and reduced glucose tolerance compared with mice in a standard (LD) light/dark cycle, despite equivalent levels of caloric intake and total daily activity output. Furthermore, the timing of food consumption by DM and LL mice differs from that in LD mice. Nocturnal rodents typically eat substantially more food at night; however, DM mice consume 55.5% of their food during the light phase, as compared with 36.5% in LD mice. Restricting food consumption to the active phase in DM mice prevents body mass gain. These results suggest that low levels of light at night disrupt the timing of food intake and other metabolic signals, leading to excess weight gain. These data are relevant to the coincidence between increasing use of light at night and obesity in humans.

Keywords circadian rhythms, light pollution, metabolic syndrome, mice, obesity

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Foret J, Daurat A, Touitou Y, et al. **Year** 1996

Authors Jean Foret, Agnes Daurat, Yvan Touitou, Acacia Aguirre and Odile Benoit

Report Name The Effect on Body Temperature and Melatonin of A 39-H Constant Routine with Two Different Light Levels at Nighttime

Publication Chronobiology International

Issue-page numbers 13:1, 35-45

URL http://informahealthcare.com/doi/abs/10.3109/07420529609040840

Abstract Eight healthy subjects were studied during 39-h spans (from 07:00 on one day until 22:00 the second) in which they remained awake. During one experiment, subjects were exposed to 100 lux of light between 18:00 and 8:00, and during a second experiment, they were exposed to 1000 lux during the same time span. Throughout the daytime period, they were exposed to normal daylight (1500 lux or more). The nighttime 1000-lux light treatment suppressed the melatonin metabolite aMT6s, while the 100 lux treatment did not. On the treatment day, the 1000 lux, in comparison to the 100 lux, light treatment resulted in both an elevated temperature minimum and a delay in its clock-time occurrence overnight. No real circadian phase shift in the temperature, urinary melatonin, or Cortisol rhythms was detected after light treatment. This study confirmed that nocturnal exposure to lower light intensities is capable of modifying circadian variables more than previously estimated. The immediate effects of all-night light treatment are essentially not different from those of evening light. This may be important if bright light is used to improve alertness of night workers. Whether subsequent daytime alertness and sleep recovery are affected by the protocol used in our study remains to be determined.

Keywords Sleep deprivation, Core temperature, Bright light, Melatonin, Cortisol

Foster RG

Year 1998

Authors Foster RG

Report Name Shedding light on the biological clock

Publication Neuron

Issue-page numbers 20:829–832 doi:10.1016/S0896-6273(00)80464-X. PMID:9620688

URL http://www.mendeley.com/research/shedding-light-on-the-biological-clock/

Abstract N/A

Keywords

Foster RG, Hankins MW, Peirson SN

Year 2007

Authors Foster RG, Hankins MW, Peirson SN

Report Name Light, photoreceptors, and circadian clocks. [Review].

Publication Methods Mol Biol

Issue-page numbers 362:3–28 doi:10.1007/978-1-59745-257-1_1. PMID:17416998

URL http://www.springerlink.com/content/h2k1xh53622r2642/

Abstract N/A

Keywords

Foster RG, Provencio I, Hudson D et al. | *Year* 1991

Authors Foster RG, Provencio I, Hudson D et al.

Report Name Circadian photoreception in the retinally degenerate mouse (rd/rd).

Publication J Comp Physiol A Neuroethol Sens Neural Behav Physiol

Issue-page numbers 169:39–50 doi:10.1007/BF00198171. PMID: 1941717

URL http://www.springerlink.com/content/h56l45848637r35h/

Abstract We have examined the effects of light on circadian locomotor rhythms in retinally degenerate mice (C57BL/6J mice homozygous for the rd allele: rd/rd). The sensitivity of circadian photoreception in these mice was determined by varying the irradiance of a 15 min light pulse (515 nm) given at circadian time 16 and meauring the magnitude of the phase shift of the locomotor rhythm. Experiments were performed on animals 80 days of age. Despite the loss of visual photoreceptors in the rd/rd retina, animals showed circadian responses to light that were indistinguishable from mice with normal retinas (rd/+ and +/+).
While no photoreceptor outersegments were identified in the retina of rd/rd animals (80–100 days of age), we did identify a small number of perikarya that were immunoreactive for cone opsins, and even fewer cells that contained rod opsin. Using HPLC, we demonstrated the presence and photoisomerization of the rhodopsin chromophore 11-cis retinaldehyde. The rd/rd retinas contained about 2% of 11-cis retinaldehyde found in +/+ retinas. We have yet to determine whether the opsin immunoreactive perikarya or some other unidentified cell type mediate circadian light detection in the rd/rd retina.

Keywords

Frain-Bell W | *Year* 1985

Authors Frain-Bell W.

Report Name Cutaneous Photobiology

Publication New York: Oxford University Press; 1985.

Issue-page numbers

URL Book

Abstract Book

Keywords

Authors Francl JM, Kaur G, Glass JD.

Report Name Roles of light and serotonin in the regulation of gastrin-releasing peptide and arginine vasopressin output in the hamster SCN circadian clock

Publication Eur J Neurosci

Issue-page numbers Oct;32(7):1170-9. doi: 10.1111/j.1460-9568.2010.07374.x. Epub 2010 Aug 22.

URL http://www.ncbi.nlm.nih.gov/pubmed/20731711

Abstract Daily timing of the mammalian circadian clock of the suprachiasmatic nucleus (SCN) is regulated by photic input from the retina via the retinohypothalamic tract. This signaling is mediated by glutamate, which activates SCN retinorecipient units communicating to pacemaker cells in part through the release of gastrin-releasing peptide (GRP). Efferent signaling from the SCN involves another SCN-containing peptide, arginine vasopressin (AVP). Little is known regarding the mechanisms regulating these peptides, as literature on in vivo peptide release in the SCN is sparse. Here, microdialysis-radioimmunoassay procedures were used to characterize mechanisms controlling GRP and AVP release in the hamster SCN. In animals housed under a 14/10-h light-dark cycle both peptides exhibited daily fluctuations of release, with levels increasing during the morning to peak around midday. Under constant darkness, this pattern persisted for AVP, but rhythmicity was altered for GRP, characterized by a broad plateau throughout the subjective night and early subjective day. Neuronal release of the peptides was confirmed by their suppression with reverse-microdialysis perfusion of calcium blockers and stimulation with depolarizing agents. Reverse-microdialysis perfusion with the 5-HT(1A,7) agonist 8-OH-DPAT ((±)-8-hydroxydipropylaminotetralin hydrobromide) during the day significantly suppressed GRP but had little effect on AVP. Also, perfusion with the glutamate agonist NMDA, or exposure to light at night, increased GRP but did not affect AVP. These analyses reveal distinct daily rhythms of SCN peptidergic activity, with GRP but not AVP release attenuated by serotonergic activation that inhibits photic phase-resetting, and activated by glutamatergic and photic stimulation that mediate this phase-resetting.

Keywords suprachiasmatic, microdialysis, neuropeptide, serotonin, glutamate, photic

Frank DW, Evans JA, Gorman MR

Year 2010

Authors Frank DW, Evans JA, Gorman MR.

Report Name Time-dependent effects of dim light at night on re-entrainment and masking of hamster activity rhythms.

Publication J Biol Rhythms

Issue-page numbers 2010 Apr;25(2):103-12.

URL http://www.ncbi.nlm.nih.gov/pubmed/20348461

Abstract Bright light has been established as the most ubiquitous environmental cue that entrains circadian timing systems under natural conditions. Light equivalent in intensity to moonlight (<1 lux), however, also strongly modulates circadian function in a number of entrainment paradigms. For example, compared to completely dark nights, dim nighttime illumination accelerated re-entrainment of hamster activity rhythms to 4-hour phase advances and delays of an otherwise standard laboratory photocycle. The purpose of this study was to determine if a sensitive period existed in the night during which dim illumination had a robust influence on speed of re-entrainment. Male Siberian hamsters were either exposed to dim light throughout the night, for half of the night, or not at all. Compared to dark nights, dim illumination throughout the entire night decreased by 29% the time for the midpoint of the active phase to re-entrain to a 4-hour phase advance and by 26% for a 4-hour delay. Acceleration of advances and delays were also achieved with 5 hours of dim light per night, but effects depended on whether dim light was present in the first half, second half, or first and last quarters of the night. Both during phase shifting and steady-state entrainment, partially lit nights also produced strong positive and negative masking effects, as well as entrainment aftereffects in constant darkness. Thus, even in the presence of a strong zeitgeber, light that might be encountered under a natural nighttime sky potently modulates the circadian timing system of hamsters.

Keywords

Freedman MS, Lucas RJ, Soni B et al.

Year 1999

Authors Melanie S. Freedman, Robert J. Lucas, Bobby Soni, Malcolm von Schantz, Marta Muñoz, Zoë David-Gray and Russell Foster

Report Name Regulation of mammalian circadian behavior by nonrod, non-cone, ocular photoreceptors

Publication Science

Issue-page numbers 284:502–504 doi:10.1126/science.284.5413.502. PMID:10205061

URL http://www.sciencemag.org/content/284/5413/502.short

Abstract Circadian rhythms of mammals are entrained by light to follow the daily solar cycle (photoentrainment). To determine whether retinal rods and cones are required for this response, the effects of light on the regulation of circadian wheel-running behavior were examined in mice lacking these photoreceptors. Mice without cones (cl) or without both rods and cones (rdta/cl) showed unattenuated phase-shifting responses to light. Removal of the eyes abolishes this behavior. Thus, neither rods nor cones are required for photoentrainment, and the murine eye contains additional photoreceptors that regulate the circadian clock.

Keywords

Freeman RG; Knox JM; Owens DW

Year 1969

Authors Robert G. Freeman; John M. Knox; Donald W. Owens

Report Name Cutaneous lesions of lupus erythematosus induced by monochromatic light

Publication Arch Dermatol

Issue-page numbers 1969;100(6):677-682

URL http://archderm.ama-assn.org/cgi/content/abstract/100/6/677

Abstract Of ten untreated patients with lupus erythematosus subjected to repeated exposures of monochromatic ultraviolet light at 300 nanometer (nm) wavelength, four developed lupus erythematosuslike lesions resembling the patient's natural disease, while four developed a persistent erythema at the test site, and the other two revealed only a normal sunburn response. Of five patients with lupus erythematosus being treated with quinacrine, normal responses were obtained in four and a persistent erythema was observed in the fifth.

Clinically and histologically the lupus erythematosus-like lesions resembled the naturally occurring skin lesions of lupus erythematosus in each patient. The persistent erythemal reactions manifested acanthosis, edema, and cellular infiltration but did not show histologic changes characteristic of lupus erythematosus. Exposure to long-wave ultraviolet and visible light of 340, 360, 400, and 500 nm wavelengths produced no visible response.

Keywords

Frentzel-Beyme R

Year 2001

Authors Frentzel-Beyme R.

Report Name The melatonin hypothesis: a matter of method.

Publication Environ Health Perspec

Issue-page numbers 110(2):A72-3

URL http://www.ncbi.nlm.nih.gov/pubmed/11871346

Abstract Correspondence

Keywords melatonin

Authors Fritschi L, Glass DC, Heyworth JS, Aronson K, Girschik J, Boyle T, Grundy A, Erren TC.

Report Name Hypotheses for mechanisms linking shiftwork and cancer

Publication Med Hypotheses

Issue-page numbers Sep;77(3):430-6. Epub 2011 Jul 1.

URL http://www.sciencedirect.com/science/article/pii/S030698771100260X

Abstract

Shift work has been associated with various adverse health outcomes. In particular, there has been a recent flourish in investigating potential cancer risk associated with working night shifts and other shift schedules. Epidemiologic studies have revealed generally weak associations due to several methodological challenges such as lack of standard classifications of shift or night work. The field also has been hindered by a lack of clarity about the possible mechanisms by which shiftwork could have an effect on cancer risk. One possible mechanism is reduced production of melatonin caused by exposure to light at night. Although there is a growing body of evidence that provides some support for this mechanism, several other mechanisms also make sense from a biological point of view. Further, the relatively weak magnitude of the associations between light at night and melatonin level suggests that multiple factors may be operating along the pathway between shift work and adverse health consequences (including cancer risk). Here we propose four additional mechanisms that should be considered for a comprehensive investigation of these potential pathways. These are: phase shift; sleep disruption; lifestyle factors (such as poor quality diets, less physical activity and higher BMI); and lower vitamin D. Consideration of all these mechanisms is necessary in order to design effective preventative workplace strategies. In developed countries, approximately 20% of the population undertake shiftwork and, while we are unlikely to be able to eliminate shiftwork from current work practices, there are aspects of shiftwork that can be modified and there may be facets of individual susceptibility that we may be able to identify and target for prevention.

Keywords Fritschi L, Glass DC, Heyworth JS, et al.

Frost M, Abrahamsen B, Nielsen TL, et al. **Year** 2010

Authors M. Frost, B. Abrahamsen, T.L. Nielsen, C. Hagen, M. Andersen, K. Brixen

Report Name Vitamin D status and PTH in young men: a cross-sectional study on associations with bone mineral density, body composition and glucose metabolism

Publication Clinical Endocrinology

Issue-page numbers Volume 73, Issue 5, pages 573–580, November 2010

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.2010.03847.x/full

Abstract

Objective Although vitamin D and bone metabolism are closely related, few studies have addressed the effects of vitamin D status on bone in men at time of peak bone mass. The objectives of this study were to evaluate the prevalence of vitamin D inadequacy in a cross-sectional study in young men and the effects of vitamin D and parathyroid hormone (PTH) on bone mass, bone markers and metabolic function.

Design and Participants The study population consisted of 783 men aged 20–29 years.

Measurements Bone mineral density (BMD) of the total hip, femoral neck and lumbar spine was measured. dual-energy X-ray absorptiometry was used to evaluate total body fat mass (BFAT). Visceral fat mass and abdominal subcutaneous fat mass (ViFM and ScFM) were assessed using magnetic resonance imaging. A radioimmunoassay was used to measure the level of 25-hydroxy vitamin D (25OHD).

Results The prevalence of vitamin deficiency (serum 25OHD < 50 nm) was 6·3% during summer and 43·6% during winter. Serum 25OHD was associated with BMD at all sites and inversely associated with bone-specific alkaline phosphatase and directly with carboxyterminal telopeptide of type-1-collagen. 25OHD and PTH were inversely associated with BFAT, whereas 25OHD also was inversely associated with body mass index, waist–hip ratio, ViFM and ScFM after adjustment for confounders. The associations were found only to be present in participants with insufficient levels of 25OHD. 25-Hydroxy vitamin D and PTH were inversely related to insulin resistance in vitamin-insufficient participants only. No associations between PTH or 25OHD and blood pressure were noted.

Conclusion The study showed a high prevalence of 25OHD deficiency in young, northern European men, which was significantly associated with decreased BMD. PTH and 25OHD were found to be inversely related to the markers of insulin resistance.

Keywords

Authors Frost P, Kolstad HA, Bonde JP.

Report Name Shift work and the risk of ischemic heart disease - a systematic review of the epidemiologic evidence

Publication Scand J Work Environ Health

Issue-page numbers 2009 May;35(3):163-79. Epub 2009 Apr 22.

URL http://www.ncbi.nlm.nih.gov/pubmed/19387517

Abstract

OBJECTIVE:

The objective of this review was to evaluate the epidemiologic evidence for a causal relation -between shift work and ischemic heart disease.
METHODS:

We conducted a systematic search until the end of March 2008 for studies providing information on the relative risk of ischemic heart disease in relation to shift work. The quality of included papers was evaluated with respect to design, exposure and outcome information, bias, and exposure response assessment.
RESULTS:

Relevant information was retrieved from 14 studies. Seven of these analyzed fatal events, six -combined fatal and non-fatal events, while one study reported separately on both types of events. Relative risks ranged from 0.6-1.4 in 12 papers while two papers reported relative risks around 2.0. Most studies based on fatal events showed no or weak associations while studies that combined fatal and non-fatal events showed modest positive associations. In a majority of studies, we could not reasonably rule out negative or positive bias due to the quality of outcome or exposure information, or confounder control. Five studies used years in shift work for exposure response analysis and no consistent pattern were seen.
CONCLUSION:

There is limited epidemiological evidence for a causal relation between shift work and ischemic heart disease.

Keywords

Fu L, Lee CC **Year** 2003

Authors Fu L, Lee CC

Report Name The circadian clock: pacemaker and tumour suppressor

Publication Nat Rev Cancer

Issue-page numbers 3:350–361 doi:10.1038/nrc1072. PMID:12724733

URL http://www.nature.com/nrc/journal/v3/n5/full/nrc1072.html

Abstract The circadian rhythms are daily oscillations in various biological processes that are regulated by an endogenous clock. Disruption of these rhythms has been associated with cancer in humans. One of the cellular processes that is regulated by circadian rhythm is cell proliferation, which often shows asynchrony between normal and malignant tissues. This asynchrony highlights the importance of the circadian clock in tumour suppression in vivo and is one of the theoretical foundations for cancer chronotherapy. Investigation of the mechanisms by which the circadian clock controls cell proliferation and other cellular functions might lead to new therapeutic targets.

Keywords

Fu L, Pelicano H, Liu J et al. **Year** 2002

Authors Fu L, Pelicano H, Liu J et al.

Report Name The circadian gene Period2 plays an important role in tumor suppression and DNA damage response in vivo

Publication Cell

Issue-page numbers 111:41–50 doi:10.1016/S0092-8674(02)00961-3. PMID:12372299

URL http://www.cell.com/abstract/S0092-8674%2802%2900961-3

Abstract The Period2 gene plays a key role in controlling circadian rhythm in mice. We report here that mice deficient in the mPer2 gene are cancer prone. After γ radiation, these mice show a marked increase in tumor development and reduced apoptosis in thymocytes. The core circadian genes are induced by γ radiation in wild-type mice but not in mPer2 mutant mice. Temporal expression of genes involved in cell cycle regulation and tumor suppression, such as Cyclin D1, Cyclin A, Mdm-2, and Gadd45α, is deregulated in mPer2 mutant mice. In particular, the transcription of c-myc is controlled directly by circadian regulators and is deregulated in the mPer2 mutant. Our studies suggest that the mPer2 gene functions in tumor suppression by regulating DNA damage-responsive pathways.

Keywords

Fujihara M, Nagai N, Sussan TE, et al. **Year** 2008

Authors Fujihara M, Nagai N, Sussan TE, Biswal S, Handa JT

Report Name Chronic cigarette smoke causes oxidative damage and apoptosis to retinal pigmented epithelial cells in mice

Publication PLoS ONE

Issue-page numbers 3(9): e3119. doi:10.1371/journal.pone.0003119

URL http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0003119

Abstract The purpose of this study was to determine whether mice exposed to chronic cigarette smoke develop features of early age-related macular degeneration (AMD). Two month old C57Bl6 mice were exposed to either filtered air or cigarette smoke in a smoking chamber for 5 h/day, 5 days/week for 6 months. Eyes were fixed in 2.5% glutaraldehyde/2% paraformaldehyde and examined for ultrastructural changes by transmission electron microscopy. The contralateral eye was fixed in 2% paraformaldehyde and examined for oxidative injury to the retinal pigmented epithelium (RPE) by 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-OHdG) immunolabeling and apoptosis by TUNEL labeling. Mice exposed to cigarette smoke had immunolabeling for 8-OHdG in 85±3.7% of RPE cells counted compared to 9.5±3.9% in controls ($p<0.00001$). Bruch membrane was thicker in mice exposed to smoke (1086±332 nm) than those raised in air (543±132 nm; $p = 0.0069$). The two most pronounced ultrastructural changes (severity grading scale from 0–3) seen were a loss of basal infoldings (mean difference in grade = 1.98; $p<0.0001$), and an increase in intracellular vacuoles (mean difference in grade = 1.7; $p<0.0001$). Ultrastructural changes to Bruch membrane in cigarette-smoke exposed mice were smaller in magnitude but consistently demonstrated significantly higher grade injury in cigarette-exposed mice, including basal laminar deposits (mean difference in grade = 0.54; $p<0.0001$), increased outer collagenous layer deposits (mean difference in grade = 0.59; $p = 0.002$), and increased basal laminar deposit continuity (mean difference in grade = 0.4; $p<0.0001$). TUNEL assay showed a higher percentage of apoptotic RPE from mice exposed to cigarette smoke (average 8.0±1.1%) than room air (average 0±0%; $p = 0.043$). Mice exposed to chronic cigarette smoke develop evidence of oxidative damage with ultrastructural degeneration to the RPE and Bruch membrane, and RPE cell apoptosis. This model could be useful for studying the mechanism of smoke induced changes during early AMD.

Keywords

Funk D, Amir S **Year** 1999

Authors Funk D, Amir S

Report Name Conditioned fear attenuates light-induced suppression of melatonin release in rats.

Publication Physiol Behav

Issue-page numbers 67:623–626 doi:10.1016/S0031-9384(99)00073-6. PMID:10549903

URL http://csbn.concordia.ca/Faculty/Amir/docs/Funk-Physiol%20Behav%2067%20%281999%29.pdf

Abstract Male rats were given 5 min of intermittent footshock, or were not shocked, for 3 or 5 consecutive days in a novel context at the midpoint of the dark phase of a 12:12-h light:dark cycle. Six days later, animals were reexposed to the context without footshock and received either a 5-min light pulse or were not disturbed. Reexposure to the context significantly increased plasma corticosterone in animals previously shocked there. Prior context–shock pairings significantly attenuated the suppression of melatonin by light, but did not affect basal levels of melatonin. These results suggest that the circuitry underlying the suppression of melatonin by light can be modified by changes in emotional state produced by aversive conditioning.

Keywords

Gaddy JR, Rollag MD, Brainard GC

Year 1993

Authors J R Gaddy, M D Rollag and G C Brainard

Report Name Pupil size regulation of threshold of light-induced melatonin suppression.

Publication The Journal of Clinical Endocrinology & Metabolism

Issue-page numbers November 1, 1993 vol. 77 no. 5 1398-1401

URL http://jcem.endojournals.org/content/77/5/1398.short

Abstract

The capacity of pupil dilation to affect light-induced plasma melatonin suppression was tested by exposing human subjects with freely constricting or pharmacologically dilated pupils to either 50 (n = 6), 100 (n = 8), or 200 lux (n = 5) of white light presented over the entire visual field. Pupil dilation significantly enhanced low level white light-induced melatonin suppression over that elicited with freely constricting pupils. Although 100 and 200 lux white light exposures resulted in significant melatonin suppression over control (no light) conditions, the effects of 50 lux were not strong enough to demonstrate statistically significant suppression with six subjects. Linear regression did not reveal a systematic relationship between theoretical retinal illuminance in Trolands and magnitude of melatonin suppression. These results suggest that pupil diameter may be a factor in the effectiveness of light stimuli used to shift circadian rhythms or to treat seasonal depression or sleep disorders.

Keywords melatonin, light at night

Authors Anne-Marie Gagné, Frédéric Lévesque, Philippe Gagné, Marc Hébert

Report Name Impact of blue vs red light on retinal response of patients with seasonal affective disorder and healthy controls

Publication Progress in Neuro-Psychopharmacology and Biological Psychiatry

Issue-page numbers Volume 35, Issue 1, 15 January 2011, Pages 227-231

URL http://www.sciencedirect.com/science/article/pii/S0278584610004240

Abstract bjectives

Seasonal affective disorder (SAD) is characterized by a mood lowering in autumn and/or winter followed by spontaneous remission in spring or summer. Bright light (BL) is recognized as the treatment of choice for individuals affected with this disease. It was speculated that BL acts on photosensitive retinal ganglion cells, particularly sensitive to blue light, which led to the emergence of apparatus enriched with blue light. However, blue light is more at risk to cause retinal damage. In addition, we reported using electroretinography (ERG) that a 60 min exposure of BL could reduce rod sensitivity. The goal of the present study was to verify if this decreased in sensitivity could be a consequence of the blue light portion present in the white light therapy lamps. We also wanted to assess the effect of monochromatic blue light vs red light in both healthy controls and patients with SAD.
Method

10 healthy subjects and 10 patients with SAD were exposed in a random order for 60 min to two different light colors (red or blue) separated by an interval of at least 1 day. Cone and rod ERG luminance-response function was assessed after light exposure.
Results

A two-way ANOVA indicates that blue light decreases the maximal ERG response (Vmax) in both groups in photopic ($p < 0.05$) and scotopic conditions ($p < 0.01$).
Conclusion

The main finding of this experiment is that blue light reduces photoreceptor responses after only a single administration. This brings important concerns with regard to blue-enriched light therapy lamps used to treat SAD symptoms and other disorders.
Research Highlights

►Blue light exposure decreases rod ERG response. ►Blue light exposure decreases cone ERG response. ►ERG of SAD and normal controls are similar following a blue light exposure.

Keywords Blue light hazard; Electroretinogram; Light therapy; Seasonal affective disorder

Gagne D, Pons M, Philibert D

Year 1985

Authors Gagne D, Pons M, Philibert D

Report Name RU 38486: a potent antiglucocorticoid in vitro and in vivo.

Publication J Steroid Biochem

Issue-page numbers 23:247–251 doi:10.1016/0022-4731(85)90401-7. PMID:2864478

URL http://www.ncbi.nlm.nih.gov/pubmed/2864478

Abstract The antiglucocorticoid activity of RU 38486, was studied both in vitro and in vivo. In vitro studies, RU 38486 was characterized by a high affinity (3 times higher than that of dexamethasone) for the cytosolic glucocorticoid receptor in rat hepatoma tissue culture (HTC) cells. This high affinity was due to a very low dissociation rate of the complexes formed with the receptor. In whole cells it was a potent full antagonist of dexamethasone-induced tyrosine aminotransferase (TAT) activity: the IC50 was 6-7 times lower than the concentration of the dexamethasone used. It was devoid of any glucocorticoid activity up to a concentration of 10 microM. In in vivo studies using adrenalectomized rats, RU 38486 totally inhibited dexamethasone-induced hepatic tryptophan oxygenase (TO) activity. It is also the first pure antagonist of dexamethasone-induced hepatic TAT. However, doses as high as 5 mg/kg of body weight were required for a 50% inhibition of the effect of dexamethasone at 0.01 mg/kg. RU 38486 did not display any glucocorticoid effect on these two responses up to 50 mg/kg.

Keywords

Gail MH, Brinton LA, Byar DP et al.

Year 1989

Authors Mitchell H. Gail, Louise A. Brinton, David P. Byar, Donald K. Corle, Sylvan B. Green, Catherine Schairer and

Report Name Projecting individualized probabilities of developing breast cancer for white females who are being examined annually

Publication J Natl Cancer Inst

Issue-page numbers 81:1879–1886 doi:10.1093/jnci/81.24.1879. PMID:2593165

URL http://jnci.oxfordjournals.org/content/81/24/1879

Abstract To assist in medical counseling, we present a method to estimate the chance that a woman with given age and risk factors will develop breast cancer over a specified interval. The risk factors used were age at menarche, age at first live birth, number of previous biopsies, and number of first-degree relatives with breast cancer. A model of relative risks for various combinations of these factors was developed from case-control data from the Breast Cancer Detection Demonstration Project (BCDDP). The model allowed for the fact that relative risks associated with previous breast biopsies were smaller for women aged 50 or more than for younger women. Thus, the proportional hazards assumption was relaxed to allow separate proportional hazards models for those under age 50 and for those of age 50 or more. The baseline age-specific hazard rate, which is the rate for a patient without identified risk factors, is computed as the product of the observed age-specific composite hazard rate times the quantity 1 minus the attributable risk. We calculated individualized breast cancer probabilities from information on relative risks and the baseline hazard rate. These calculations take competing risks and the interval of risk into account. Our data were derived from women who participated in the BCDDP and who tended to return for periodic examinations. For this reason, the risk projections given are probably most reliable for counseling women who plan to be examined about once a year.

Keywords

Gaillard ER, Atherton SJ, Eldred G, Dillon J **Year** 1995

Authors Elizabeth R. Gaillard, Stephen J. Atherton, Graig Eldred, James Dillon

Report Name Photophysical studies on human retinal lipofuscin

Publication Photochemistry and Photobiology

Issue-page numbers Volume 61, Issue 5, pages 448–453, May 1995

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.1995.tb02343.x/abstract?

Abstract

Fluorescent material generated in the human retina accumulates within lipofuscin granules of the retinal pigment epithelium (RPE) during aging. Its presence has been suggested to contributed to various diseases including age-related macular degeneration. Because this material absorbs light at wave lengths as long as 550 nm, photophysical studies were performed to determine whether lipofuscin could contribute to light damage and to determine if its composition is similar to a synthetically prepared lipofuscin. Time-resolved experiments were performed to monitor (1) fluorescence decay, (2) the UV-visible absorption of longer-lived excited states and (3) the formation and decay of singlet oxygen at 1270 nm. Steady-state and time-resolved fluorescence studies indicate that human and synthetic lipofuscin have fluorophores in common. Time-resolved absorption experiments on human retinal lipofuscin and synthetic lipofuscin showed the presence of at least two transient species, one absorbing at 430 nm (lifetime caμs) and a second absorbing at 580 nm, which decays via second order kinetics. In addition, there is a third absorbing species stable to several hundred milliseconds. The transient species at 430 nm is quenched by oxygen, suggesting that it is a triplet state. Subsequent studies showed the formation of singlet oxygen, which was monitored by its phosphorescence decay at 1270 nm. These studies demonstrate that lipofuscin can act as a sensitizer for the generation of reactive oxygen species that may contribute to the age-related decline of RPE function and blue light damage.

Keywords

Gaillard ER, Zheng L, Merriam JC, Dillon J

Year 2000

Authors Elizabeth R. Gaillard, Lei Zheng, John C. Merriam and James Dillon

Report Name Age-Related Changes in the Absorption Characteristics of the Primate Lens

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers May 2000 vol. 41 no. 6 1454-1459

URL http://www.iovs.org/content/41/6/1454.full

Abstract

purpose. To quantitate aging of the primate lens by changes in the absorption characteristics that are related to the yellowing of lens protein.

methods. The lenses of lower primates and humans were sectioned anterior to posterior every 0.25 mm, and the UV-visible spectrum of each section was measured to determine the cumulative spectra along the visual axis. The ratio of the absorbance at 320 nm (formed with aging) to the absorbance at 365 nm (present in the young lens) was correlated with the age of the lens.

results. In the young primate UV-B is transmitted to the retina, and UV-A is transmitted to the nucleus of the lens. By puberty, changes in the absorption characteristics of the lens that are associated with the yellowing of lens protein prevented most of the UV-B from reaching the retina and by the eighth decade, the transmittances at 320 and 365 nm to the nucleus of the lens were approximately 40% and 79%, respectively. A linear relationship between the ratio of absorbance at 320 to 365 nm and age was found for both lower primates and humans to the age of 80 years. This is surprising, because the maximum life span of the lower primate is approximately 35 years, whereas humans may live 100 years.

conclusions. These data suggest that the observed spectral changes associated with the yellowing of the lens are the result of a chronological process, such as chemical or photochemical modifications, not biological aging.

Keywords

Year 1991

Authors Gala RR

Report Name Prolactin and growth hormone in the regulation of the immune system

Publication Proc Soc Exp Biol Med

Issue-page numbers 198:513–527. PMID:1891468

URL http://ebm.rsmjournals.com/content/198/1/513.full.pdf

Abstract

Evidence implicating prolactin (PRL) and growth hormone (GH) in the regulation of the immune system has been reviewed. Hypophysectomized animals have deficiencies in both cell-mediated and humoral immunological functions and either PRL or GH corrects these deficiencies. Animals administered bromocryptine, a drug that specifically blocks PRL release, have impaired immune responses similar to hypophysectomized animals, and again both PRL and GH correct these deficiencies. Genetically dwarf animals, which lack both PRL and GH, are also immunocompromised, and once again PRL and GH can correct the deficiencies. In dwarf animals, however, fewer studies have examined PRL actions. In growth-deficient children, immune function is not dramatically altered and basal secretion of GH has been reported. Very few clinical studies have examined whether PRL secretion is also deficient, and this may explain why a clear loss in immune function is not evident in growth-deficient children. In a number of species, including man, both PRL and GH stimulate thymic function and increase the secretion of thymulin, a thymic hormone. No studies, however, have reported on the effects of PRL and GH on other thymic hormones. A number of studies have reported in vitro effects of PRL and GH on cells involved with immunity, and the presence of high-affinity PRL and GH receptors have been observed on a number of these cells. The action of GH on the proliferative response of cells involved with immunity in vitro appears to be mediated by the production of insulin-like growth factor 1. The effect of PRL on insulinlike growth factor I production by these cells has not been examined. One of the most consistent findings from in vitro studies is that prolactin antisera blocked a number of immune reactions. This led to the discovery that cells involved with immunity appear capable of producing PRL and GH, but the physiological significance of these observations have not been explored. There is a great need to identify the cell types responding to PRL and GH and this should be a goal of future investigations. There is also a need for investigators to be aware that both PRL and GH are involved in the regulation of the immune system and to design experiments to elucidate where each functions in the maturation cascade of cells involved with immunity. From the evidence available, it is apparent that PRL and GH have an important function in the immune system and future investigations should be directed toward elucidating their site(s) of action.

Keywords

Authors Gambichler T, Breuckmann F, Boms S, Altmeyer P, Kreuter A.

Report Name Narrowband UVB phototherapy in skin conditions beyond psoriasis

Publication Journal of the American Academy of Dermatology

Issue-page numbers Volume 52, Issue 4 , Pages 660-670, April 2005

URL http://www.eblue.org/article/S0190-9622%2804%2902233-9/abstract

Abstract

Background

Narrowband (NB) UVB phototherapy has been proven to be clearly more effective than broadband UVB and safer and/or more practicable than psoralen-UVA in the management of psoriasis. However, the role of NB UVB seems to be less clear in the management of skin conditions beyond psoriasis.
Objectives

We sought to give an update on clinical experiences in NB UVB of nonpsoriatic skin conditions, and to establish its current position within the spectrum of competing photo(chemo)therapeutic options.
Methods

The computerized bibliographic database PubMed, without time limits, and other sources were screened for clinical trials on NB UVB. Included were research articles of randomized controlled trials, open prospective studies, and retrospective observations on NB UVB in skin disorders other than psoriasis.
Results

A total of 28 articles met our eligibility criteria including 6 randomized controlled studies, 16 open prospective studies, and 6 retrospective observations. NB UVB is effective in patients with chronic atopic dermatitis (AD) (n=719) and generalized vitiligo (n=305) and appears to have some advantages over competing photo(chemo)therapeutic regimens. NB UVB also seems to be effective in patients with polymorphic light eruption (n=25), early stages of cutaneous T-cell lymphoma (n=108), chronic urticaria (n=88), lichen planus (n=15), pruritus associated with polycythemia vera (n=10), seborrheic dermatitis (n=18), actinic prurigo (n=6), and acquired perforating dermatosis (n=5). The quality of evidence determined for the aforementioned diagnoses ranged from high to moderate to very low.
Conclusions

The best currently available data on NB UVB in nonpsoriatic conditions exist for AD and generalized vitiligo. In view of its efficacy, benefit/risk profile, and costs, NB UVB may be considered the first-line photo(chemo)therapeutic option for moderately severe AD and widespread vitiligo. In the treatment of most other nonpsoriatic conditions, NB UVB appears to be effective, but current data allow no definitive conclusions as to whether NB UVB should be preferred to competing photo(chemo)therapeutic options such as UVA1 and psoralen-UVA regimens. Because NB UVB may have a wider indication spectrum, including AD, vitiligo, and early-stage T-cell lymphoma, and appears to be equally effective or even more effective than broadband UVB, a switch from broadband UVB to NB UVB seems to be justified.

Keywords

Gamlin PD, McDougal DH, Pokorny J, et al. **Year** 2007

Authors Paul D. Gamlin, David H. McDougal, Joel Pokorny, Vivianne C. Smith, King-Wai Yau, and Dennis M. Dacey

Report Name Human and Macaque Pupil Responses Driven by Melanopsin-Containing Retinal Ganglion Cells

Publication Vision Res

Issue-page numbers 2007 March; 47(7): 946–954.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1945238/

Abstract Melanopsin, a novel photopigment, has recently been localized to a population of retinal ganglion cells that display inherent photosensitivity. During continuous light and following light offset, primates are known to exhibit sustained pupilloconstriction responses that resemble closely the photoresponses of intrinsically-photoreceptive ganglion cells. We report that, in the behaving macaque, following pharmacological blockade of conventional photoreceptor signals, significant pupillary responses persist during continuous light and following light offset. These pupil responses display the unique spectral tuning, slow kinetics, and irradiance coding of the sustained, melanopsin-derived ganglion cell photoresponses. We extended our observations to humans by using the sustained pupil response following light offset to document the contribution of these novel ganglion cells to human pupillary responses. Our results indicate that the intrinsic photoresponses of intrinsically-photoreceptive retinal ganglion cells play a role in the pupillary light reflex and are primarily responsible for the sustained pupilloconstriction that occurs following light offset.

Keywords Human, macaque, pupil, papillary, melanopsin

Gander PH, Myhre G, Graeber RC et al. **Year** 1989

Authors Philippa H Gander, Grete Myhre, R Curtis Graeber, John K Lauber, Harald T Andersen

Report Name Adjustment of sleep and the circadian temperature rhythm after flights across nine time zones

Publication Aviat Space Environ Med

Issue-page numbers 60:733–743. PMID:2775129

URL http://www.mendeley.com/research/adjustment-sleep-circadian-temperature-rhythm-after-flights-across-nine-time-zones-1/

Abstract The adjustment of sleep-wake patterns and the circadian temperature rhythm was monitored in nine Royal Norwegian Air-force volunteers operating P-3 aircraft during a westward training deployment across nine time zones. Subjects recorded all sleep and nap times, rated nightly sleep quality, and completed personality inventories. Rectal temperature, heart rate, and wrist activity were continuously monitored. Adjustment was slower after the return eastward flight than after the outbound westward flight. The eastward flight produced slower readjustment of sleep timing to local time and greater interindividual variability in the patterns of adjustment of sleep and temperature. One subject apparently exhibited resynchronization by partition, with the temperature rhythm undergoing the reciprocal 15-h delay. In contrast, average heart rates during sleep were significantly elevated only after westward flight. Interindividual differences in adjustment of the temperature rhythm were correlated with some of the personality measures. Larger phase delays in the overall temperature waveform (as measured on the 5th day after westward flight) were exhibited by extraverts, and less consistently by evening types.

Keywords

Gandini S, Sera F, Cattaruzza MS, et al. **Year** 2005

Authors Gandini S, Sera F, Cattaruzza MS, Pasquini P, Picconi O, Boyle P, et al.

Report Name Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure

Publication European Journal of Cancer

Issue-page numbers Volume 41, Issue 1 , Pages 45-60, January 2005

URL http://www.ejcancer.info/article/S0959-8049%2804%2900833-0/abstract

Abstract A systematic revision of the literature was conducted in order to undertake a comprehensive meta-analysis of all published observational studies on melanoma. An extensive analysis of the inconsistencies and variability in the estimates was performed to provide some clues about its Epidemiology. Following a systematic literature search, relative risks (RRs) for sun exposure were extracted from 57 studies published before September 2002. Intermittent sun exposure and sunburn history were shown to play considerable roles as risk factors for melanoma, whereas a high occupational sun exposure seemed to be inversely associated to melanoma. The country of study and adjustment of the estimates adjuste for phenotype and photo-type were significantly associated with the variability of the intermittent sun exposure estimates (P=0.024, 0.003 and 0.030, respectively). For chronic sun exposure, inclusion of controls with dermatological diseases and latitude resulted in significantly different data (P=0.05 and 0.031, respectively). Latitude was also shown to be important (P=0.031) for a history of sunburn; studies conducted at higher latitudes presented higher risks for a history of sunburns. Role of country, inclusion of controls with dermatological diseases and other study features seemed to suggest that “well conducted” studies supported the intermittent sun exposure hypothesis: a positive association for intermittent sun exposure and an inverse association with a high continuous pattern of sun exposure

Keywords Melanoma, Sunlight, Sunburn, Meta-analysis, Epidemiology, Review literature

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Gangwisch JE **Year** 2009

Authors J. E. Gangwisch

Report Name Epidemiological evidence for the links between sleep, circadian rhythms and metabolism

Publication Obesity Reviews

Issue-page numbers Volume 10, Issue Supplement s2, pages 37–45, November 2009

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1467-789X.2009.00663.x/full

Abstract Epidemiological data reveal parallel trends of decreasing sleep duration and increases in metabolic disorders such as obesity, diabetes and hypertension. There is growing evidence that these trends are mechanistically related. The seasonal expression of the thrifty genotype provides a conceptual framework to connect circadian and circannual rhythms, sleep and metabolism. Experimental studies have shown sleep deprivation to decrease leptin, increase ghrelin, increase appetite, compromise insulin sensitivity and raise blood pressure. Habitually short sleep durations could lead to insulin resistance by increasing sympathetic nervous system activity, raising evening cortisol levels and decreasing cerebral glucose utilization that over time could compromise β-cell function and lead to diabetes. Prolonged short sleep durations could lead to hypertension through raised 24-h blood pressure and increased salt retention resulting in structural adaptations and the entrainment of the cardiovascular system to operate at an elevated pressure equilibrium. Cross-sectional and longitudinal epidemiological studies have shown associations between short sleep duration and obesity, diabetes and hypertension. If metabolic changes resulting from sleep restriction function to increase body weight, insulin resistance and blood pressure then interventions designed to increase the amount and improve the quality of sleep could serve as treatments and as primary preventative measures for metabolic disorders.

Keywords Circadian rhythms; epidemiology; metabolism; sleep

Authors Gangwisch JE, Malaspina D, Boden-Albala B, Heymsfield SB

Report Name Inadequate sleep as a risk factor for obesity: analyses of the NHANES I

Publication Sleep

Issue-page numbers 28:1289–1296. PMID:16295214

URL http://www.journalsleep.org/Articles/281017.pdf

Abstract

Study Objectives: Sleep deprivation has been hypothesized to contribute toward obesity by decreasing leptin, increasing ghrelin, and compromising insulin sensitivity. This study examines cross-sectional and longitudinal data from a large United States sample to determine whether sleep duration is associated with obesity and weight gain.
Design: Longitudinal analyses of the 1982-1984, 1987, and 1992 NHANES I Followup Studies and cross-sectional analysis of the 1982-1984 study.
Setting: Probability sample of the civilian noninstitutionalized population of the United States.
Participants: Sample sizes of 9,588 for the cross-sectional analyses, 8,073 for the 1987, and 6,981 for the 1992 longitudinal analyses.
Measurements and Results: Measured weight in 1982-1984 and selfreported weights in 1987 and 1992. Subjects between the ages of 32 and 49 years with self-reported sleep durations at baseline less than 7 hours had higher average body mass indexes and were more likely to be obese than subjects with sleep durations of 7 hours. Sleep durations over 7 hours were not consistently associated with either an increased or decreased likelihood of obesity in the cross-sectional and longitudinal results. Each additional hour of sleep at baseline was negatively associated with change in body mass index over the follow-up period, but this association was small and statistically insignificant.
Conclusions: These findings support the hypothesis that sleep duration is associated with obesity in a large longitudinally monitored United States sample. These observations support earlier experimental sleep studies and provide a basis for future studies on weight control interventions that increase the quantity and quality of sleep.

Keywords Sleep, obesity, insulin resistance

Authors Gao GC, Dashwood MR, Wei ET

Report Name Corticotropin-releasing factor inhibition of substance Pinduced vascular leakage in rats: possible sites of action

Publication Peptides

Issue-page numbers 12:639–644 doi:10.1016/0196-9781(91)90113-4. PMID:1717957

URL http://www.sciencedirect.com/science/article/pii/0196978191901134

Abstract Substance P (SP), 40 µg/kg SC, induced protein leakage in the skin, muscle, trachea and esophagus of the anesthetized rat as measured by Monastral blue B labeling of small blood vessels, CRF, 30 µg/kg SC, injected 30 min before SP, decreased the SP-induced dye leakage. To locate where CRF might act, autoradiographic studies of [125I]-CRF binding to esophageal segments were conducted and displaceable binding of [125I]-CRF to submucosal elements in the esophageal epithelium were revealed, suggesting that CRF acts on selective sites to reduce vascular leakage.

Keywords

Authors Kevin J. Gaston, Thomas W. Davies, Jonathan Bennie, John Hopkins

Report Name REVIEW: Reducing the ecological consequences of night-time light pollution: options and developments

Publication Journal of Applied Ecology

Issue-page numbers Volume 49, Issue 6, pages 1256–1266, December 2012

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2664.2012.02212.x/full

Abstract

Much concern has been expressed about the ecological consequences of night-time light pollution. This concern is most often focused on the encroachment of artificial light into previously unlit areas of the night-time environment, but changes in the spectral composition, duration and spatial pattern of light are also recognized as having ecological effects.

Here, we examine the potential consequences for organisms of five management options to reduce night-time light pollution. These are to (i) prevent areas from being artificially lit; (ii) limit the duration of lighting; (iii) reduce the 'trespass' of lighting into areas that are not intended to be lit (including the night sky); (iv) change the intensity of lighting; and (v) change the spectral composition of lighting.

Maintaining and increasing natural unlit areas is likely to be the most effective option for reducing the ecological effects of lighting. However, this will often conflict with other social and economic objectives. Decreasing the duration of lighting will reduce energy costs and carbon emissions, but is unlikely to alleviate many impacts on nocturnal and crepuscular animals, as peak times of demand for lighting frequently coincide with those in the activities of these species. Reducing the trespass of lighting will maintain heterogeneity even in otherwise well-lit areas, providing dark refuges that mobile animals can exploit. Decreasing the intensity of lighting will reduce energy consumption and limit both skyglow and the area impacted by high-intensity direct light. Shifts towards 'whiter' light are likely to increase the potential range of environmental impacts as light is emitted across a broader range of wavelengths.

Synthesis and applications. The artificial lightscape will change considerably over coming decades with the drive for more cost-effective low-carbon street lighting solutions and growth in the artificially lit area. Developing lighting strategies that minimize adverse ecological impacts while balancing the often conflicting requirements of light for human utility, comfort and safety, aesthetic concerns, energy consumption and carbon emission reduction constitute significant future challenges. However, as both lighting technology and understanding of its ecological effects develop, there is potential to identify adaptive solutions that resolve these conflicts.

Keywords light pollution; lightscape; night-time; nocturnal; spectra; urbanization; vision

Gauger MA, Sancar A

Year 2005

Authors Gauger MA, Sancar A

Report Name Cryptochrome, circadian cycle, cell cycle checkpoints, and cancer

Publication Cancer Res

Issue-page numbers 65:6828–6834 doi:10.1158/0008-5472.CAN-05-1119. PMID:16061665

URL http://cancerres.aacrjournals.org/content/65/15/6828.abstract

Abstract It has been reported that disruption of the circadian clock may lead to increased risk of breast cancer in humans and to a high rate or ionizing radiation–induced tumors and mortality in mice. Cryptochrome 1 and cryptochrome 2 proteins are core components of the mammalian circadian clock and mice mutated in both genes are arrhythmic. We tested Cry1−/−Cry2−/− mice and fibroblasts derived from these mice for radiation-induced cancer and killing and DNA damage checkpoints and killing, respectively. We find that the mutant mice are indistinguishable from the wild-type controls with respect to radiation-induced morbidity and mortality. Similarly, the Cry1−/−Cry2−/− mutant fibroblasts are indistinguishable from the wild-type controls with respect to their sensitivity to ionizing radiation and UV radiation and ionizing radiation–induced DNA damage checkpoint response. Our data suggest that disruption of the circadian clock in itself does not compromise mammalian DNA repair and DNA damage checkpoints and does not predispose mice to spontaneous and ionizing radiation–induced cancers. We conclude that the effect of circadian clock disruption on cellular response to DNA damage and cancer predisposition in mice may depend on the mechanism by which the clock is disrupted.

Keywords cryptochrome, DNA repair, DNA damage checkpoints

Gautherie M

Year 1983

Authors Gautherie M

Report Name Thermobiological assessment of benign and malignant breast diseases

Publication Am J Obstet Gynecol

Issue-page numbers 147:861–869. PMID:6650622

URL http://www.ncbi.nlm.nih.gov/pubmed/6650622

Abstract The recent technical and clinical advances in breast thermography are reviewed in this article. Emphasis is placed upon liquid crystal thermal imaging and computer-assisted analysis of breast thermograms. New data are presented concerning the value of thermography for the early detection of mammary carcinomas, the identification of women at high risk of developing breast cancer, and the detection of cancer in fibrocystic breasts.

Keywords

Gautherie M, Gros C **Year** 1977

Authors Gautherie M, Gros C

Report Name Circadian rhythm alteration of skin temperature in breast cancer

Publication Chronobiologia

Issue-page numbers 4:1–17. PMID:880849

URL http://www.ncbi.nlm.nih.gov/pubmed/880849

Abstract N/A

Keywords

Gautherie M, Gros CM **Year** 1980

Authors Gautherie M, Gros CM

Report Name Breast thermography and cancer risk prediction

Publication Cancer

Issue-page numbers 45:51–56 doi:10.1002/1097-0142(19800101)45:1<51::AID-CNCR2820450110>3.0.CO;2-L. PMID:7351006

URL http://www.medithermclinic.com/Breast/breast%20thermography%20and%20cancer%20risk%20prediction.pdf

Abstract N/A

Keywords

Gauvain H

Year 1926

Authors Henry Gauvain M.D., M.CHIR. (Cantab.), Sir

Report Name Observations on artificial light treatment in surgical tuberculosis

Publication British Journal of Tuberculosis

Issue-page numbers Volume 20, Issue 1, January 1926, Pages 1-11

URL http://www.sciencedirect.com/science/article/pii/S0366085026800328

Abstract N/A

Keywords

Geissmann F, Jung S, Littman DR

Year 2003

Authors Geissmann F, Jung S, Littman DR

Report Name Blood monocytes consist of two principal subsets with distinct migratory properties

Publication Immunity

Issue-page numbers 19:71–82 doi:10.1016/S1074-7613(03)00174-2. PMID:12871640

URL http://www.cell.com/immunity/abstract/S1074-7613%2803%2900174-2

Abstract Peripheral blood monocytes are a heterogeneous population of circulating leukocytes. Using a murine adoptive transfer system to probe monocyte homing and differentiation in vivo, we identified two functional subsets among murine blood monocytes: a short-lived CX3CR1loCCR2+Gr1+ subset that is actively recruited to inflamed tissues and a CX3CR1hiCCR2−Gr1− subset characterized by CX3CR1-dependent recruitment to noninflamed tissues. Both subsets have the potential to differentiate into dendritic cells in vivo. The level of CX3CR1 expression also defines the two major human monocyte subsets, the CD14+CD16− and CD14loCD16+ monocytes, which share phenotype and homing potential with the mouse subsets. These findings raise the potential for novel therapeutic strategies in inflammatory diseases.

Keywords

Gerli R, Riccardi C, Nicoletti I et al. ***Year*** 1987

Authors Gerli R, Riccardi C, Nicoletti I et al.

Report Name Phenotypic and functional abnormalities of T lymphocytes in pathological hyperprolactinemia

Publication J Clin Immunol

Issue-page numbers 7:463–470 doi:10.1007/BF00915056. PMID:2961788

URL http://www.springerlink.com/content/m7xp702r86031523/

Abstract The phenotype and function of T cells circulating in patients with pathological hyperprolactinemia were analyzed and compared to those in sex- and age-matched control subjects. Two-color immunofluorescence study revealed an increased number of CD4+ TQ1+ cells and the presence of phenotypically immature CD1+ T cells, also exhibiting transferrin surface receptor, in peripheral blood of the hyperprolactinemic patients. After chronic treatment with the dopamine agonist bromocriptine, T-cell abnormalities disappeared. In addition, some untreated patients showed enhanced T-cell suppressor activity in anin vitro pokeweed mitogen-driven B-cell transformation assay. These immunological findings confirm a link between neuroendocrine and immune systems in humans.

Keywords Pathological hyperprolactinemia - T lymphocytes - prolactin - neuroendocrine system

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Gery S, Komatsu N, Baldjyan L et al. ***Year*** 2006

Authors Sigal Gery, Naoki Komatsu, Lilit Baldjyan, Andrew Yu, Danielle Koo, H Phillip Koeffler

Report Name The circadian gene per1 plays an important role in cell growth and DNA damage control in human cancer cells

Publication Mol Cell

Issue-page numbers 22:375–382 doi:10.1016/j.molcel.2006.03.038. PMID:16678109

URL http://www.mendeley.com/research/the-circadian-gene-per1-plays-an-important-role-in-cell-growth-and-dna-damage-control-in-human-cancer-cells/

Abstract The Per1 gene is a core clock factor that plays an essential role in generating circadian rhythms. Recent data reveal that major biological pathways, including those critical to cell division, are under circadian control. We report here that Per1 provides an important link between the circadian system and the cell cycle system. Overexpression of Per1 sensitized human cancer cells to DNA damage-induced apoptosis; in contrast, inhibition of Per1 in similarly treated cells blunted apoptosis. The apoptotic phenotype was associated with altered expression of key cell cycle regulators. In addition, Per1 interacted with the checkpoint proteins ATM and Chk2. Ectopic expression of Per1 in human cancer cell lines led to significant growth reduction. Finally, Per1 levels were reduced in human cancer patient samples. Our results highlight the importance of circadian regulation to fundamental cellular functions and support the hypothesis that disruption of core clock genes may lead to cancer development.

Keywords

Gery S, Komatsu N, Kawamata N et al. **Year** 2007

Authors Sigal Gery, Naoki Komatsu, Norihiko Kawamata, Carl W. Miller, Julian Desmond, Renu K. Virk, Alberto Marchevsky, Robert Mckenna, Hirokuni Taguchi and H. Phillip Koeffler

Report Name Epigenetic silencing of the candidate tumor suppressor gene Per1 in non-small cell lung cancer

Publication Clin Cancer Res

Issue-page numbers 13:1399–1404 doi:10.1158/1078-0432.CCR-06-1730. PMID:17332281

URL http://clincancerres.aacrjournals.org/content/13/5/1399.abstract

Abstract

Purpose: Epigenetic events are a critical factor contributing to cancer development. The purpose of this study was to identify tumor suppressor genes silenced by DNA methylation and histone deacetylation in non–small cell lung cancer (NSCLC).

Experimental Design: We used microarray analysis to screen for tumor suppressor genes.

Results: We identified Per1, a core circadian gene, as a candidate tumor suppressor in lung cancer. Although Per1 levels were high in normal lung, its expression was low in a large panel of NSCLC patient samples and cell lines. Forced expression of Per1 in NSCLC cell lines led to significant growth reduction and loss of clonogenic survival. Recent studies showed that epigenetic regulation, particularly histone H3 acetylation, is essential for circadian function. Using bisulfite sequencing and chromatin immunoprecipitation, we found that DNA hypermethylation and histone H3 acetylation are potential mechanisms for silencing Per1 expression NSCLC.

Conclusions: These results support the hypothesis that disruption of circadian rhythms plays an important role in lung tumorigenesis. Moreover, our findings suggest a novel link between circadian epigenetic regulation and cancer development.

Keywords lung cancer

Gibbons RB, Hankey J

Year 2006

Authors Ronald B Gibbons, Jonathan Hankey

Report Name Influence of Vertical Illuminance on Pedestrian Visibility in Crosswalks

Publication Transportation Research Record

Issue-page numbers No. 1973 (2006)

URL http://pubsindex.trb.org/view.aspx?id=777133

Abstract This project investigated the lighting levels required for crosswalk illumination. The current European methods for lighting suggest a crosswalk lighting level of 40 vertical lux for ensured safety. Two major questions were studied: the required vertical illuminance level for adequate pedestrian visibility and the selection of an object that could act as a surrogate for the pedestrian. The vertical illuminance was determined from an experiment that measured the visibility of pedestrians at lighting levels of 5, 20, 40, and 60 vertical lux. During the experiment, a crosswalk scene was presented to the participants and the time taken for identification of an object was measured. In addition to the lighting level, the conditions used in the experiment were lamp type (metal halide versus high-pressure sodium), the presence of glare, the use of overhead lighting, and the type of pedestrian clothing (white, black, and denim). The study found that a lighting design level of 20 vertical lux is likely adequate for proper pedestrian visibility. Except in selected cases, the lamp type was not significant. The impact of glare was not influenced by the lighting design. Three surrogate objects were developed for the experiment and were tested in the same manner as the pedestrians. The surrogates used were an extruded octagon, a cylinder, and a cylinder with a ball on top. These surrogates were selected to allow easy lighting design calculations while best representing a pedestrian. The experiment found that all surrogates performed equally well and that the surrogate can be chosen on the basis of the ease of calculation. It is recommended that a cylinder be used as a pedestrian surrogate.

Keywords lighting

Gibbs M, Hampton S, Morgan L, Arendt J

Year 2007

Authors Gibbs M, Hampton S, Morgan L, Arendt J

Report Name Predicting circadian response to abrupt phase shift: 6-sulphatoxymelatonin rhythms in rotating shift workers offshore

Publication J Biol Rhythms

Issue-page numbers 22:368–370 doi:10.1177/0748730407302843. PMID:17660453

URL http://jbr.sagepub.com/content/22/4/368

Abstract N/A

Keywords

Gibbs M, Hampton S, Morgan L, Arendt J | ***Year*** 2002

Authors Gibbs M, Hampton S, Morgan L, Arendt J

Report Name Adaptation of the circadian rhythm of 6-sulphatoxymelatonin to a shift schedule of seven nights followed by seven days in offshore oil installation workers

Publication Neurosci Lett

Issue-page numbers 325:91–94 doi:10.1016/S0304-3940(02)00247-1. PMID:12044629

URL http://www.sciencedirect.com/science/article/pii/S0304394002002471

Abstract This study evaluated circadian adaptation in a 'swing shift' schedule (seven nights, 18:00–06:00 h; then 7 days, 06:00–18:00 h) on North Sea oil installations. Eleven healthy men provided sequential urine collections for the study period offshore. The urinary melatonin metabolite 6-sulphatoxymelatonin (aMT6s) was used as an index of circadian phase. A significant difference (P=0.0004) was found between the mean aMT6s acrophase (calculated peak time) at the start (±SD: 05:34±2.42 h) and end (±SD: 10.95±3.34 h) of the night shift week, but not between the start (±SD: 11:04±4.03 h) and end (±SD: 12:59±8.83 h) of the day shift week. As a group, the subjects adapted to the night shift but very large individual variations were seen during the day shift. These individual differences clearly require further study.

Keywords Shiftwork; Circadian; Adaptation; 6-Sulphatoxymelatonin; Light

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Gibertini M, Graham C, Cook MR | ***Year*** 1999

Authors Gibertini M, Graham C, Cook MR

Report Name Self-report of circadian type reflects the phase of the melatonin rhythm

Publication Biol Psychol

Issue-page numbers 50:19–33 doi:10.1016/S0301-0511(98)00049-0. PMID:10378437

URL http://www.sciencedirect.com/science/article/pii/S0301051198000490

Abstract This study examined the relationship between circadian rhythm characteristics of the pineal hormone melatonin and individual differences in circadian type and mood. 95 healthy young men and 22 women were assessed each hour (00:00–07:00 h) for blood levels of melatonin throughout one night in the laboratory. Each subject was assessed for circadian type (morning, afternoon, or evening type) and morning mood (PANAS). Circadian type was strongly related to the melatonin acrophase but not to amplitude or time of year of assessment. Also, morning types evidenced a more rapid decline in melatonin levels after the peak than did evening types. Evening types were younger than were morning types. Female morning types reported more positive affect upon waking than did female afternoon or evening types. Males showed no such discrimination. Age was related to both melatonin acrophase and circadian type but did not explain the relationship between them. The results replicate and extend findings on circadian type and psychological and physiological variables.

Keywords

Year 1995

Authors Gilad E, Zisapel N

Report Name High-affinity binding of melatonin to hemoglobin

Publication Biochem Mol Med

Issue-page numbers 56:115–120 doi:10.1006/bmme.1995.1066. PMID:8825074

URL http://www.ncbi.nlm.nih.gov/pubmed/8825074

Abstract Determination of melatonin by radioimmunoassay in plasma samples from hemolyzed blood often yields flawed values. We studied the possibility that hemoglobin can bind melatonin and the iodinated tracer 125I-melatonin. The specific binding of 125I-melatonin to purified bovine hemoglobin was found to be rapid, saturable, and reversible (Kd = 315 pM, Bmax = 58 pmol/mg protein) and was inhibited by 2-iodomelatonin, serotonin, melatonin, and 5-methoxytryptamine. These data are compatible with the concept that hemoglobin can interfere with melatonin determinations by competing for melatonin and the iodinated tracer. Unlike melatonin receptor binding, the binding of 125I-melatonin to hemoglobin was not inhibited by guanine nucleotide analogs (i.e., GTP gamma S, GTP beta S, and Gpp(NH)p). Sodium cyanide had no effect on 125I-melatonin binding, indicating that 125I-melatonin does not bind to the heme group. On the other hand, 2,3-bisphosphoglycerate, at physiological concentrations (3-4 mM), decreased the apparent Bmax and Kd of 125I-melatonin binding to hemoglobin. These data suggest that 125I-melatonin binding to hemoglobin is conformation-specific and is unfavorable in the deoxyhemoglobin state. Hemoglobin may serve as a carrier protein for melatonin in the blood and discharge it in the target organs. Subsequently, the efficacy of melatonin's action as a hormone or antioxidant in target tissues may be enhanced.

Keywords

Gillette MU, Mitchell JW **Year** 2002

Authors Gillette MU, Mitchell JW

Report Name Signaling in the suprachiasmatic nucleus: selectively responsive and integrative

Publication Cell Tissue Res

Issue-page numbers 309:99–107 doi:10.1007/s00441-002-0576-1. PMID:12111540

URL http://www.springerlink.com/content/x8clk254j9c4349v/

Abstract The suprachiasmatic nucleus (SCN) contains a biological clock that generates timing signals that drive daily rhythms in behaviors and homeostatic functions. In addition to this pacemaker function, the SCN gates its own sensitivity to incoming signals, which permits appropriate temporal adjustment to achieve synchrony with environmental and organismic states. A series of time-domains, in which the SCN restricts its own sensitivity to a limited set of stimuli that adjust clock phase, can be distinguished. Pituitary adenylyl cyclase-activating peptide (PACAP) and cAMP directly reset clock phase during the daytime domain; both cause phase advances only during the clock's day-time domain, but are without effect at night. In contrast, acetylcholine and cGMP analogs phase advance the clock only when applied during the night. Sensitivity to light and glutamate arises concomitant with sensitivity to acetylcholine and cGMP. Light and glutamate cause phase delays in the early night, by elevating intracellular Ca2+ via neuronal ryanodine receptors. In late night, light and glutamate utilize a cGMP-mediated mechanism to induce phase advances. Nocturnal responses of SCN primed by light or glutamate can be modulated by effectors of phase-resetting in daytime, namely, PACAP and cAMP. Finally, the dusk and dawn domains are characterized by sensitivity to the pineal hormone, melatonin, acting through protein kinase C. These changing patterns of sensitivities demonstrate that the circadian clock controls multiple intracellular gates, which ensures that they can be opened selectively only at specific points in the circadian cycle. Discerning the molecular bases of these changes is fundamental to understanding integrative and regulatory mechanisms in the circadian system.

Keywords

Gilliam JN, Sontheimer RD **Year** 1982

Authors Gilliam JN, Sontheimer RD

Report Name Skin manifestations of SLE

Publication Clin Rheum Dis

Issue-page numbers 1982; 8:207-18

URL http://www.ncbi.nlm.nih.gov/pubmed/6749395?dopt=Abstract

Abstract N/A

Keywords

Authors Giordano M, Vermeulen M, Palermo MS

Report Name Seasonal variations in antibody-dependent cellular cytotoxicity regulation by melatonin

Publication FASEB J

Issue-page numbers 7:1052–1054. PMID:8370475

URL http://www.fasebj.org/content/7/11/1052.full.pdf

Abstract Data collected over a period of 4 years
show that melatonin (two daily i.v. injections of 0.1 mg/kg
body wt. given at 16:00 h) was able to enhance antibodydependent
cellular cytotoxicity (ADCC) in summer, but
not in winter. Dose-response curves carried out in January,
May, July, and October suggest that the seasonal
effects reported are related to differences in the sensitivity
of mice to melatonin during the course of the year. These
results show seasonal variations in the immune modulatory
action of melatonin.- Giordano, M., Vermeulen,
M., Palermo, M. S. Seasonal variations in antibodydependent
cellular cytotoxicity regulation of melatonin.

Keywords

Girschik J, Heyworth J, Fritschi L

Year 2013

Authors Jennifer Girschik, Jane Heyworth and Lin Fritschi

Report Name Self-reported Sleep Duration, Sleep Quality, and Breast Cancer Risk in a Population-based Case-Control Study

Publication Am. J. Epidemiol.

Issue-page numbers doi: 10.1093/aje/kws422 First published online: January 16, 2013

URL http://aje.oxfordjournals.org/content/early/2013/01/15/aje.kws422.abstract

Abstract Breast cancer is one of the most commonly diagnosed invasive cancers. Established risk factors account for only a small proportion of cases. Previous studies have found reductions in sleep duration and quality in the general population over time. There is evidence to suggest a link between poor sleep and an increased risk of breast cancer. In this study, we investigated the relationship between breast cancer and sleep duration and quality in Western Australian women. Data were obtained from a population-based case-control study conducted from 2009 to 2011. Participants completed a self-administered questionnaire that included questions on sleep. Odds ratios and 95% confidence intervals were calculated using unconditional logistic regression. Sensitivity analysis for potential selection and misclassification bias was also conducted. We found no association between self-reported sleep duration on workdays and risk of breast cancer (for <6 hours, odds ratio (OR) = 1.05 (95% CI: 0.82, 1.33); for 6–7 hours, OR = 0.96 (95% CI: 0.80, 1.16); and for >8 hours, OR = 1.10 (95% CI: 0.87, 1.39), compared with the reference category of 7–8 hours' sleep). In addition, we found no association between sleep duration on nonworkdays, subjective sleep quality, or combined duration and quality and risk of breast cancer. This study does not provide evidence to support an association between self-reported sleep duration or quality and the risk of breast cancer.

Keywords

Gladstone GJ; Tasman W

Year 1978

Authors Geoffrey J. Gladstone; William Tasman

Report Name Solar retinitis after minimal exposure

Publication Arch Ophthalmol.

Issue-page numbers 1978;96(8):1368-1369.

URL http://archopht.ama-assn.org/cgi/content/abstract/96/8/1368

Abstract Solar retinitis after prolonged or purposeful exposure to the sun has been reported many times. In this study, three patients were seen with the clinical diagnosis of solar retinitis but without an initial compatible history. Previously, such persons have frequently been categorized as having foveomacular retinitis. In this study, careful follow-up history was obtained in an attempt to find an origin for the condition of the patients. Evidence for very brief, high-intensity, and long-term low-intensity exposure to the sun's radiant energy was substantiated. Theoretical consideration was made of the mechanisms by which this type of exposure produced retinal damage.

Keywords

Authors Glaser R, MacCallum RC, Laskowski BF et al.

Report Name Evidence for a shift in the Th-1 to Th-2 cytokine response associated with chronic stress and aging

Publication J Gerontol A Biol Sci Med Sci

Issue-page numbers 56:M477–M482. PMID: 11487599

URL http://biomedgerontology.oxfordjournals.org/content/56/8/M477.abstract

Abstract

Background. A number of studies have shown that the chronic stress of caring for persons with dementia can have significant immunological consequences as demonstrated by the down-regulation/dysregulation of the cellular immune response.

Methods. Utilizing flow cytometry to measure the percentages and absolute numbers of CD-4+ and CD-8+ T lymphocytes producing the cytokines indicative of Th-1, Tc1 and Th-2, and Tc2 cells, we compared spousal caregivers and control subjects. The expression of interleukin-2 (IL-2), interferon gamma (IFN-γ), and interleukin-10 (IL-10) in the cytoplasm of CD-4+ and CD-8+ lymphocytes was assessed.

Results. Neither stress nor age was significantly related to the percentage or number of IFNγ+/CD-8+, IL-2+/CD-8+ cells, or IFNγ+, IL-2+, CD-4+ cells. However, the percentage of IL-10+ cells was higher in lymphocytes obtained from caregivers than control subjects. In addition, the significant interaction between stress and aging for IL-10+/CD-4+ and IL 10+/CD-8+ cells demonstrated that the difference between caregivers and control subjects was age dependent; the difference between caregivers and control subjects was substantially larger in younger individuals than in older individuals.

Conclusions. The data are consistent with previous reports on acute stress and suggest that there may also be a shift from a Th-1 to a Th-2 response associated with a chronic stressor such as caregiving. This shift could have implications for an individual's responses to pathogens.

Keywords

Authors Gläser R, Navid F, Schuller W, Jantschitsch C, Harder J, Schröder JM, Schwarz A, Schwarz T.

Report Name UV-B radiation induces the expression of antimicrobial peptides in human keratinocytes in vitro and in vivo

Publication J Allergy Clin Immunol

Issue-page numbers 2009 May;123(5):1117-23. Epub 2009 Apr 1.

URL http://www.ncbi.nlm.nih.gov/pubmed/19342087

Abstract

BACKGROUND:

Suppression of the adaptive immune system by UV radiation plays an important role in photocarcinogenesis. Exacerbation of skin infections has been proposed as a further consequence of UV-induced immunosuppression. Clinically bacterial infections are not a problem. For defense against bacteria, the innate immune response including the release of antimicrobial peptides is much more relevant than the adaptive immune response. Keratinocytes have the capacity to release antimicrobial peptides.
OBJECTIVE:

We asked whether UV radiation induces antimicrobial peptides in vitro and in vivo.
METHODS:

Antimicrobial peptide expression by normal human keratinocytes was measured by real-time PCR and fluorescence-activated cell sorting analysis. Biopsies taken from human volunteers and skin explants were studied with immunohistochemistry.
RESULTS:

Real-time PCR of normal human keratinocytes revealed a dose-dependent increase of human beta-defensin-2, -3, ribonuclease 7, and psoriasin (S100A7) after UV radiation. This was confirmed at the protein level by intracellular fluorescence-activated cell sorting and in vitro immunofluorescence analysis. Immunohistochemistry of biopsies taken from healthy volunteers exposed to different UV radiation doses revealed enhanced epidermal expression of antimicrobial peptides after UV exposure. This was also confirmed by exposing human skin explants to UV radiation.
CONCLUSION:

UV radiation exerts diverse effects on the immune system, suppressing the adaptive but inducing the innate immune response. This may explain why T-cell-mediated immune reactions are suppressed on UV exposure but not host defense reactions against bacterial attacks.

Keywords

Authors Glass JD, Lynch GR

Report Name Melatonin: identification of sites of antigonadal action in mouse brain

Publication Science

Issue-page numbers 214:821–823 doi:10.1126/science.7292016. PMID:7292016

URL http://www.biomedsearch.com/nih/Melatonin-identification-sites-antigonadal-action/7292016.html

Abstract Long-term implants releasing a small quantity of melatonin (45 nanograms per day) were used to determine the brain sites of the hormone's antigonadal action in a photoperiodic species, the white-footed mouse (Peromyscus leucopus). Implants in the medial preoptic and supra- and retrochiasmatic areas elicited completed gonadal regression after 7 weeks. Implants in other brain regions had little effect on the animals' reproductive state.

Keywords

Authors Glickman G, Byrne B, Pineda C, Hauck WW, Brainard GC

Report Name Light therapy for seasonal affective disorder with blue narrow-band light-emitting diodes (LEDs).

Publication Biol Psychiatry

Issue-page numbers 2006 Mar 15;59(6):502-7. Epub 2005 Sep 13.

URL http://www.ncbi.nlm.nih.gov/pubmed/16165105

Abstract

BACKGROUND:

While light has proven an effective treatment for Seasonal Affective Disorder (SAD), an optimal wavelength combination has not been determined. Short wavelength light (blue) has demonstrated potency as a stimulus for acute melatonin suppression and circadian phase shifting.
METHODS:

This study tested the efficacy of short wavelength light therapy for SAD. Blue light emitting diode (LED) units produced 468 nm light at 607 microW/cm2 (27 nm half-peak bandwidth); dim red LED units provided 654 nm at 34 microW/cm2 (21 nm half-peak bandwidth). Patients with major depression with a seasonal pattern, a score of > or =20 on the Structured Interview Guide for the Hamilton Depression Rating Scale-SAD version (SIGH-SAD) and normal sleeping patterns (routine bedtimes between 10:00 pm and midnight) received 45 minutes of morning light treatment daily for 3 weeks. Twenty-four patients completed treatment following random assignment of condition (blue vs. red light). The SIGH-SAD was administered weekly.
RESULTS:

Mixed-effects analyses of covariance determined that the short wavelength light treatment decreased SIGH-SAD scores significantly more than the dimmer red light condition ($F = 6.45$, $p = .019$ for average over the post-treatment times).
CONCLUSIONS:

Narrow bandwidth blue light at 607 microW/cm2 outperforms dimmer red light in reversing symptoms of major depression with a seasonal pattern.

Keywords

Authors Gena Glickman, Ian C. Webb, Jeffrey A. Elliott, Ricardo M. Baltazar, Meghan E. Reale, Michael N. Lehman, Michael R. Gorman

Report Name Photic Sensitivity for Circadian Response to Light Varies with Photoperiod

Publication J Biol Rhythms

Issue-page numbers August 2012 vol. 27 no. 4 308-318

URL http://jbr.sagepub.com/content/27/4/308.short

Abstract The response of the circadian system to light varies markedly depending on photic history. Under short day lengths, hamsters exhibit larger maximal light-induced phase shifts as compared with those under longer photoperiods. However, effects of photoperiod length on sensitivity to subsaturating light remain unknown. Here, Syrian hamsters were entrained to long or short photoperiods and subsequently exposed to a 15-min light pulse across a range of irradiances (0-68.03 μW/cm2) to phase shift activity rhythms. Phase advances exhibited a dose response, with increasing irradiances eliciting greater phase resetting in both conditions. Photic sensitivity, as measured by the half-saturation constant, was increased 40-fold in the short photoperiod condition. In addition, irradiances that generated similar phase advances under short and long days produced equivalent phase delays, and equal photon doses produced larger delays in the short photoperiod condition. Mechanistically, equivalent light exposure induced greater pERK, PER1, and cFOS immunoreactivity in the suprachiasmatic nuclei of animals under shorter days. Patterns of immunoreactivity in all 3 proteins were related to the size of the phase shift rather than the intensity of the photic stimulus, suggesting that photoperiod modulation of light sensitivity lies upstream of these events within the signal transduction cascade. This modulation of light sensitivity by photoperiod means that considerably less light is necessary to elicit a circadian response under the relatively shorter days of winter, extending upon the known seasonal changes in sensitivity of sensory systems. Further characterizing the mechanisms by which photoperiod alters photic response may provide a potent tool for optimizing light treatment for circadian and affective disorders in humans.

Keywords circadian, light, history, photoperiod, sensitivity, winter, phase shift

Glickman RD

Year 2011

Authors Glickman, Randolph D

Report Name Ultraviolet Phototoxicity to the Retina

Publication Eye & Contact Lens: Science & Clinical Practice

Issue-page numbers July 2011 - Volume 37 - Issue 4 - pp 196-205 doi: 10.1097/ICL.0b013e31821e45a9

URL http://journals.lww.com/claojournal/Abstract/2011/07000/Ultraviolet_Phototoxicity_to_the_Retina.6.aspx

Abstract

Objective: This overview of ultraviolet (UV) phototoxicity considers the interaction of UVA and short-wavelength VIS light with the retina and retinal pigment epithelium.

Methods: The damage mechanisms underlying UV retinal phototoxicity are illustrated with a literature survey and presentation of experimental results.

Results: Depending on the wavelength and exposure duration, light interacts with tissue by three general mechanisms: thermal, mechanical, or photochemical. Although the anterior structures of the eye absorb much of the UV component of the optical radiation spectrum, a portion of the UVA band (315-400 nm) penetrates into the retina. Natural sources, such as the sun, emit energetic UV photons in relatively long durations, which typically do not result in energy confinement in the retina, and thus do not produce thermal or mechanical damage but are capable of inducing photochemical damage. Photochemical damage in the retina proceeds through Type 1 (direct reactions involving proton or electron transfers) and Type 2 (reactions involving reactive oxygen species) mechanisms. Commonly used drugs, such as certain antibiotics, nonsteroidal anti-inflammatory drugs, psychotherapeutic agents, and even herbal medicines, may act as photosensitizers that promote retinal UV damage, if they are excited by UVA or visible light and have sufficient retinal penetration.

Conclusions: Although the anterior portion of the eye is the most susceptible to UV damage, the retina is at risk to the longer UV wavelengths that propagate through the ocular media. Some phototoxicity may be counteracted or reduced by dietary intake of antioxidants and protective phytonutrients.

Keywords

Glickman RD

Year 2002

Authors Randolph D. Glickman

Report Name Phototoxicity to the Retina: Mechanisms of Damage

Publication International Journal of Toxicology

Issue-page numbers November 2002 vol. 21 no. 6 473-490

URL http://ijt.sagepub.com/content/21/6/473.abstract

Abstract Light damage to the retina occurs through three general mechanisms involving thermal, mechanical, or photochemical effects. The particular mechanism activated depends on the wavelength and exposure duration of the injuring light. The transitions between the various light damage mechanism may overlap to some extent. Energy confinement is a key concept in understanding or predicting the type of damage mechanism produced by a given light exposure. As light energy (either from a laser or an incoherent source) is deposited in the retina, its penetration through, and its absorption in, various tissue compartments is determined by its wavelength. Strongly absorbing tissue components will tend to “concentrate” the light energy. The effect of absorbed light energy largely depends on the rate of energy deposition, which is correlated with the exposure duration. If the rate of energy deposition is too low to produce an appreciable temperature increase in the tissue, then any resulting tissue damage necessarily occurs because of chemical (oxidative) reactions induced by absorption of energetic photons (photochemical damage). If the rate of energy deposition is faster than the rate of thermal diffusion (thermal confinement), then the temperature of the exposed tissue rises. If a critical temperature is reached (typically about 10° C above basal), then thermal damage occurs. If the light energy is deposited faster than mechanical relaxation can occur (stress confinement), then a thermoelastic pressure wave is produced, and tissue is disrupted by shear forces or by cavitation—nonlinear effects. Very recent evidence suggests that ultrashort laser pulses can produce tissue damage through nonlinear and photochemical mechanisms; the latter because of two-photon excitation of cellular chromophores. In addition to tissue damage caused directly by light absorption, light toxicity can be produced by the presence of photosensitizing agents. Drugs excited to reactive states by ultraviolet (UV) or visible light produce damage by type I (free radical) and type II (oxygen dependent) mechanisms. Some commonly used drugs, such as certain antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and psychotherapeutic agents, as well as some popular herbal medicines, can produce ocular phototoxicity. Specific cellular effects and damage end points characteristic of light damage mechanisms are described.

Keywords

Golan DT, Borel Y

Year 1984

Authors DT Golan and Y Borel

Report Name Increased photosensitivity to near-ultraviolet light in murine SLE

Publication The Journal of Immunology

Issue-page numbers February 1, 1984 vol. 132 no. 2 705-710

URL http://www.jimmunol.org/content/132/2/705.abstract

Abstract We investigated whether there is increased susceptibility to near-UVL in murine SLE. Cultured spleen cells from either strain of mice with lupus disease or conventional strains of mice were exposed to different UVL fractions in vitro. The effect of DNA synthesis, release, and repair was examined. DNA synthesis and release was measured as percent of [3H]thymidine (dT) uptake into either total acid-precipitable radioactive material of cell sediment plus supernatant, or that of the medium alone, whereas hydroxyurea-resistant dT incorporation represented DNA repair. The data indicate that all SLE strains, in contrast to all non-SLE strains, show increased DNA synthesis and release after UV-A exposure. In addition, all murine SLE strains demonstrate increased susceptibility to induction of DNA damage by UV- A. The significance of these observations in relation to the clinical activity of SLE after sunlight exposure is discussed.

Keywords

Goldman BD

Year 1999

Authors Goldman BD

Report Name The circadian timing system and reproduction in mammals

Publication Steroids

Issue-page numbers 64:679–685 doi:10.1016/S0039-128X(99)00052-5. PMID:10503728

URL http://www.sciencedirect.com/science/article/pii/S0039128X99000525

Abstract Circadian systems in a wide variety of organisms all appear to include three basic components: 1) biological oscillators that maintain a self-sustained circadian periodicity in the absence of environmental time cues; 2) input pathways that convey environmental information, especially light cues, that can entrain the circadian oscillations to local time; and 3) output pathways that drive overt circadian rhythms, such as the rhythms of locomotor activity and a variety of endocrine rhythms. In mammals, the circadian system is employed in the regulation of reproductive physiology and behavior in two very important ways. 1) In some species, there is a strong circadian component in the timing of ovulation and reproductive behavior, ensuring that these events will occur at a time when the animal is most likely to encounter a potential mate. 2) Many mammals exhibit seasonal reproductive rhythms that are largely under photoperiod regulation; in these species, the circadian system and the pineal gland are crucial components of the mechanism that is used to measure day length. The rhythm of pineal melatonin secretion is driven by a neural pathway that includes the circadian oscillator(s) in the suprachiasmatic nuclei. Melatonin is secreted at night in all mammals, and the duration of each nocturnal episode of melatonin secretion is inversely related to day length. The pineal melatonin rhythm appears to serve as an internal signal that represents day length and that is capable of regulating a variety of seasonal variations in physiology and behavior.

Keywords Circadian; Photoperiodism; Pineal; Melatonin; Reproduction; Mammals

Authors Goldman BD

Report Name Mammalian photoperiodic system: formal properties and neuroendocrine mechanisms of photoperiodic time measurement

Publication J Biol Rhythms

Issue-page numbers 16:283–301 doi:10.1177/074873001129001980. PMID:11506375

URL http://jbr.sagepub.com/content/16/4/283.short

Abstract Photoperiodism is a process whereby organisms are able to use both absolute measures of day length and the direction of day length change as a basis for regulating seasonal changes in physiology and behavior. The use of day length cues allows organisms to essentially track time-of-year and to “anticipate” relatively predictable annual variations in important environmental parameters. Thus, adaptive types of seasonal biological changes can be molded through evolution to fit annual environmental cycles. Studies of the formal properties of photoperiodic mechanisms have revealed that most organisms use circadian oscillators to measure day length. Two types of paradigms, designated as the external and internal coincidence models, have been proposed to account for photoperiodic time measurement by a circadian mechanism. Both models postulate that the timing of light exposure, rather than the total amount of light, is critical to the organism’s perception of day length. In mammals, a circadian oscillator(s) in the suprachiasmatic nucleus of the hypothalamus receives photic stimuli via the retinohypothalamic tract. The circadian system regulates the rhythmic secretion of the pineal hormone, melatonin. Melatonin is secreted at night, and the duration of secretion varies in inverse relation to day length; thus, photoperiod information is “encoded” in the melatonin signal. The melatonin signal is presumably “decoded” in melatonin target tissues that are involved in the regulation of a variety of seasonal responses. Variations in photoperiodic response are seen not only between species but also between breeding populations within a species and between individuals within single breeding populations. Sometimes these variations appear to be the result of differences in responsiveness to melatonin; in other cases, variations in photoperiod responsiveness may depend on differences in patterns of melatonin secretion related to circadian variation. Sites of action for melatonin in mammals are not yet well characterized, but potential targets of particular interest include the pars tuberalis of the pituitary gland and the suprachiasmatic nuclei. Both these sites exhibit uptake of radiolabeled melatonin in various species, and there is some evidence for direct action of melatonin at these sites. However, it appears that there are species differences with respect to the importance and specific functions of various melatonin target sites.

Keywords photoperiodism, melatonin, pineal, mammal, circadian

Authors Gómez-Abellán P, Hernández-Morante JJ, Luján JA, Madrid JA, Garaulet M

Report Name Clock genes are implicated in the human metabolic syndrome

Publication Int J Obes (Lond)

Issue-page numbers 2008;32:121–8. doi: 10.1038/sj.ijo.0803689

URL http://www.ncbi.nlm.nih.gov/pubmed/17653067

Abstract

BACKGROUND:

Clock genes play a role in adipose tissue (AT) in animal experimental models. However, it remains to be elucidated whether these genes are expressed in human AT.
OBJECTIVE:

We investigated the expression of several clock genes, Bmal1, Per2 and Cry1, in human AT from visceral and subcutaneous abdominal depots. A second objective was to elucidate whether these clock genes expressions were related to the metabolic syndrome features.
METHODS:

Visceral and subcutaneous AT samples were obtained from morbid obese men (n=8), age: 42+/-13 years and body mass index>/=40 kg/m(2), undergoing laparoscopic surgery due to obesity. Biopsies were taken as paired samples at the beginning of the surgical process (1100 hour). Metabolic syndrome features such as waist circumference, plasma glucose, triglycerides, total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein (LDL) cholesterol were also studied. Homeostasis model assessment index of insulin resistance was also calculated. The expression of the different clock genes, hBmal1, hPer2 and hCry1, was determined by quantitative real-time PCR.
RESULTS:

Clock genes were expressed in both human AT depots. hBmal1 expression was significantly lower than hPer2 and hCry1 in both AT (P<0.001). All genes were highly correlated to one another in the subcutaneous fat, while no correlation was found between Bmal1 and Per2 in the visceral AT. Clock genes AT expression was associated with the metabolic syndrome parameters: hPer2 expression level from visceral depot was inversely correlated to waist circumference (P<0.01), while the three clock genes studied were significantly and negatively correlated to total cholesterol and LDL cholesterol (P<0.01).
CONCLUSION:

We have demonstrated for the first time in humans that clock genes are expressed in both subcutaneous and visceral fat. Their association with abdominal fat content and cardiovascular risk factors may be an indicator of the potential role of these clock genes in the metabolic syndrome disturbances.

Keywords

González A, Alvarez-García V, Martínez-Campa C, et al. **Year** 2011

Authors González A, Alvarez-García V, Martínez-Campa C, Alonso-González C, Cos S.

Report Name Melatonin promotes differentiation of 3T3-L1 fibroblasts

Publication J Pineal Res

Issue-page numbers May 26. doi: 10.1111/j.1600-079X.2011.00911.x. [Epub ahead of print]

URL http://www.ncbi.nlm.nih.gov/pubmed/21718362

Abstract

Melatonin inhibits the genesis and growth of breast cancer by interfering at different levels in the estrogen-signaling pathways. Melatonin inhibits aromatase activity and expression in human breast cancer cells, thus behaving as a selective estrogen enzyme modulator. As the adipose tissue adjacent to the tumor seems to account for most aromatase expression and enzyme activity in breast tumors and also mediates the desmoplastic reaction or accumulation of undifferentiated fibroblasts around malignant epithelial cells, in this work, we studied the effects of melatonin on the conversion of preadipocytes (3T3-L1) into adipocytes and on the capability of these cells to synthesize estrogens by regulating the expression and enzyme activity of aromatase, one of the main enzymes that participates in the synthesis of estrogens in the peritumoral adipose tissue. Thus, in both differentiating and differentiated 3T3-L1 adipocytes, high concentrations of melatonin increased intracytoplasmic triglyceride accumulation, an indicator of adipogenic differentiation. Melatonin (1 mm) significantly increased the expression of both CCAAT/enhancer-binding protein α and peroxisome proliferator-activated receptor γ, two main regulators of terminal adipogenesis, in 3T3-L1 cells. The presence of melatonin during differentiation also induced a parallel reduction in aromatase expression and activity and expression of the cells. The effects of melatonin were reversed by luzindole, a melatonin receptor antagonist, indicating that melatonin acts through known receptor-mediated mechanisms. These findings suggest that, in human breast tumors, melatonin could stimulate the differentiation of fibroblasts and reduce the aromatase activity and expression in both fibroblasts and adipocytes, thereby reducing the number of estrogen-producing cells proximal to malignant cells.

Keywords

González A, Martínez-Campa C, Mediavilla MD et al. **Year** 2007

Authors González A, Martínez-Campa C, Mediavilla MD et al.

Report Name Effects of MT1 melatonin receptor overexpression on the aromatase-suppressive effect of melatonin in MCF-7 human breast cancer cells

Publication Oncol Rep

Issue-page numbers 17:947–953. PMID:17342341

URL http://www.ncbi.nlm.nih.gov/pubmed/17342341

Abstract

A major mechanism through which melatonin reduces the development of breast cancer is based on its anti-estrogenic actions by interfering at different levels with the estrogen-signalling pathways. Melatonin inhibits both aromatase activity and expression in vitro (MCF-7 cells) as well as in vivo, thus behaving as a selective estrogen enzyme modulator. The objective of this study was to study the effect of MT1 melatonin receptor overexpression in MCF-7 breast cancer cells on the aromatase-suppressive effects of melatonin. Transfection of the MT1 melatonin receptor in MCF-7 cells significantly decreased aromatase activity of the cells and MT1-transfected cells showed a level of aromatase activity that was 50% of vector-transfected MCF-7 cells. The proliferation of estrogen-sensitive MCF-7 cells in an estradiol-free media but in the presence of testosterone (an indirect measure of aromatase activity) was strongly inhibited by melatonin in those cells overexpressing the MT1 receptor. This inhibitory effect of melatonin on cell growth was higher on MT1 transfected cells than in vector transfected ones. In MT1-transfected cells, aromatase activity (measured by the tritiated water release assay) was inhibited by melatonin (20% at 1 nM; 40% at 10 microM concentrations). The same concentrations of melatonin did not significantly influence the aromatase activity of vector-transfected cells. MT1 melatonin receptor transfection also induced a significant 55% inhibition of aromatase steady-state mRNA expression in comparison to vector-transfected MCF-7 cells ($p<0.001$). In addition, in MT1-transfected cells melatonin treatment inhibited aromatase mRNA expression and 1 nM melatonin induced a higher and significant down-regulation of aromatase mRNA expression ($p<0.05$) than in vector-transfected cells. The findings presented herein point to the importance of MT1 melatonin receptor in mediating the oncostatic action of melatonin in MCF-7 human breast cancer cells and confirm MT1 melatonin receptor as a major mediator in the melatonin signalling pathway in breast cancer

Keywords

Gooley JJ, Chamberlain K, Smith KA, et al. **Year** 2011

Authors Joshua J. Gooley, Kyle Chamberlain, Kurt A. Smith, Sat Bir S. Khalsa, Shantha M. W. Rajaratnam, Eliza Van Reen, Jamie M. Zeitzer, Charles A. Czeisler and Steven W. Lockle

Report Name Exposure to Room Light before Bedtime Suppresses Melatonin Onset and Shortens Melatonin Duration in Humans

Publication Journal of Clinical Endocrinology & Metabolism

Issue-page numbers March 1, 2011 vol. 96 no. 3 E463-E472

URL http://jcem.endojournals.org/content/96/3/E463.abstract

Abstract

Context:Millions of individuals habitually expose themselves to room light in the hours before bedtime, yet the effects of this behavior on melatonin signaling are not well recognized.

Objective:We tested the hypothesis that exposure to room light in the late evening suppresses the onset of melatonin synthesis and shortens the duration of melatonin production.

Design:In a retrospective analysis, we compared daily melatonin profiles in individuals living in room light (<200 lux) vs. dim light (<3 lux).

Patients:Healthy volunteers (n = 116, 18–30 yr) were recruited from the general population to participate in one of two studies.

Setting:Participants lived in a General Clinical Research Center for at least five consecutive days.

Intervention:Individuals were exposed to room light or dim light in the 8 h preceding bedtime.

Outcome Measures:Melatonin duration, onset and offset, suppression, and phase angle of entrainment were determined.

Results:Compared with dim light, exposure to room light before bedtime suppressed melatonin, resulting in a later melatonin onset in 99.0% of individuals and shortening melatonin duration by about 90 min. Also, exposure to room light during the usual hours of sleep suppressed melatonin by greater than 50% in most (85%) trials.

Conclusions:These findings indicate that room light exerts a profound suppressive effect on melatonin levels and shortens the body's internal representation of night duration. Hence, chronically exposing oneself to electrical lighting in the late evening disrupts melatonin signaling and could therefore potentially impact sleep, thermoregulation, blood pressure, and glucose homeostasis.

Keywords

Gooley JJ, Lu J, Chou TC, et al. **Year** 2001

Authors Joshua J. Gooley, Jun Lu, Thomas C. Chou, Thomas E. Scammell, Clifford B. Saper

Report Name Melanopsin in cells of origin of the retinohypothalamic tract

Publication Nature Neuroscience

Issue-page numbers 4, 1165 (2001)

URL http://www.nature.com/neuro/journal/v4/n12/full/nn768.html

Abstract All known eukaryotic organisms exhibit physiological and behavioral rhythms termed circadian rhythms that cycle with a near-24-hour period; in mammals, light is the most poten stimulus for entraining endogenous rhythms to the daily light cycle. Photic information is transmitted via the retinohypothalamic tract (RHT) to the suprachiasmatic nucleus (SCN) in the hypothalamus, where circadian rhythms are generated, but the retinal photopigment that mediates circadian entrainment has remained elusive. Here we show that most retinal ganglion cells (RGCs) that project to the SCN express the photopigment melanopsin.

Keywords melanopsin

Gooley JJ, Rajaratnam SMW, Brainard GC, et al. **Year** 2010

Authors Joshua J. Gooley, Shantha M. W. Rajaratnam, George C. Brainard, Richard E. Kronauer, Charles A. Czeisler and Steven W. Lockle,

Report Name Spectral Responses of the Human Circadian System Depend on the Irradiance and Duration of Exposure to Light

Publication Science Translational Medicine

Issue-page numbers Vol. 2, Issue 31, p. 31ra33

URL http://stm.sciencemag.org/content/2/31/31ra33.abstract

Abstract In humans, modulation of circadian rhythms by light is thought to be mediated primarily by melanopsin-containing retinal ganglion cells, not rods or cones. Melanopsin cells are intrinsically blue light–sensitive but also receive input from visual photoreceptors. We therefore tested in humans whether cone photoreceptors contribute to the regulation of circadian and neuroendocrine light responses. Dose-response curves for melatonin suppression and circadian phase resetting were constructed in subjects exposed to blue (460 nm) or green (555 nm) light near the onset of nocturnal melatonin secretion. At the beginning of the intervention, 555-nm light was equally effective as 460-nm light at suppressing melatonin, suggesting a significant contribution from the three-cone visual system (λmax = 555 nm). During the light exposure, however, the spectral sensitivity to 555-nm light decayed exponentially relative to 460-nm light. For phase-resetting responses, the effects of exposure to low-irradiance 555-nm light were too large relative to 460-nm light to be explained solely by the activation of melanopsin. Our findings suggest that cone photoreceptors contribute substantially to nonvisual responses at the beginning of a light exposure and at low irradiances, whereas melanopsin appears to be the primary circadian photopigment in response to long-duration light exposure and at high irradiances. These results suggest that light therapy for sleep disorders and other indications might be optimized by stimulating both photoreceptor systems.

Keywords

Authors Gooneratne NS, Metlay JP, Guo W et al.

Report Name The validity and feasibility of saliva melatonin assessment in the elderly

Publication J Pineal Res

Issue-page numbers 34:88–94 doi:10.1034/j.1600-079X.2003.02945.x. PMID:12562499

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079X.2003.02945.x/abstract

Abstract ecent work in young and middle-aged subjects suggests that melatonin levels in saliva may represent a viable alternative to serum melatonin measurement. We hypothesized that it may be a valid measure of melatonin levels in older adults as well, but features unique to the elderly may limit its utility. To study this, subjects were admitted to an academic medical center where saliva and serum specimens were collected concurrently in dim light conditions during a 14-hr overnight study period and analyzed for melatonin levels with radioimmunoassays (RIAs). Eighty-five subjects over the age of 65 with a broad range of medical conditions participated in the study. Subjects with dementia, depression and anemia were excluded. We found that saliva volume was inadequate for analysis (<200 μL) in 23.6% of specimens, with the majority of inadequate volume specimens occurring after midnight and inadequate specimens occurring more frequently in females than in males. The correlation coefficient for saliva melatonin and serum melatonin was r = 0.659 (Spearman, P < 0.001), and r = 0.466 for saliva dim light melatonin onset (DLMO) and serum DLMO. Saliva melatonin levels were 30.9% of serum melatonin levels, with a wide range of ratios noted between subjects. Overall melatonin levels influenced both the correlation and ratio of saliva melatonin to serum melatonin; higher correlations and lower ratios were noted when melatonin levels were high. Saliva specimens provide an economical and practical method for melatonin assessment, however, in older adults, issues such as hyposalivation and low melatonin levels limit the feasibility and validity, respectively, of saliva melatonin.

Keywords circadian rhythms; dim light melatonin onset; melatonin; saliva; serum; validation

Gorgels TG, Van Norren D

Year 1998

Authors T G Gorgels, D Van Norren

Report Name Two spectral types of retinal light damage occur in albino as well as in pigmented rat: no essential role for melanin

Publication Experimental Eye Research

Issue-page numbers Volume: 66, Issue: 2, Pages: 155-162

URL http://www.mendeley.com/research/two-spectral-types-of-retinal-light-damage-occur-in-albino-as-well-as-in-pigmented-rat-no-essential-role-in-melanin/

Abstract

Earlier we showed that two spectral types of retinal damage occur in the pigmented rat. In the present study we investigated whether the same is true for albino rats. When investigating this issue we implicitly investigated the role of melanin in both damage types. An albinotic (Wistar) and a pigmented (Long Evans) strain of rats were used. Under anesthesia, a small part of the retina was irradiated at either 380 nm or at 470 nm. Three days later, the retina was analysed by funduscopy and prepared for light microscopy. Funduscopy showed no signs of damage in the albinotic retina. In the pigmented retina a decoloration of the fundus was noticed after irradiations starting from retinal doses of 0.6+/-0.1 J cm-2 at 380 nm, and from 489+/-71 J cm-2 at 470 nm. By light microscopy, retinal damage was found in the albino retina. The histologic manifestations at 380 nm differed from those at 470 nm. Irradiation at 380 nm at a dose of 0. 5-0.9 J cm-2 damaged a few scattered photoreceptor cells. At doses of 1.2-1.6 J cm-2 all rods were damaged while the other retinal layers showed no changes. These findings were similar to those found at 380 nm in the pigmented rat. At 470 nm, damage was found most prominently in the retinal pigment epithelium. These cells showed swelling and an increased number of dark inclusions. Threshold damage occurred at doses of 250-500 J cm-2. Again, the pathology in the pigmented rat was highly similar to that in the albino rat. The results show that both spectral damage types occur in albino as well as in pigmented retina. Therefore, melanin plays no crucial role in these light damage types.

Keywords

Gottsch JD, Pou S, Bynoe LA, Rosen GM **Year** 1990

Authors J D Gottsch, S Pou, L A Bynoe and G M Rosen

Report Name Hematogenous photosensitization. A mechanism for the development of age-related macular degeneration

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers September 1990 vol. 31 no. 9 1674-1682

URL http://www.iovs.org/content/31/9/1674

Abstract

Age-related macular degeneration (ARMD) is one of the leading causes of severe visual loss in the United States. Numerous risk factors have been investigated, but the pathogenesis of ARMD has remained elusive. The authors propose that ARMD develops as a direct result of photosensitization of the vascular endothelium of the choriocapillaris, Bruch's membrane, and the retinal pigment epithelium (RPE) by superoxide anion and singlet oxygen generated by photoactive compounds in blood. Using electron-spin resonance spectrometry, the free-radical trap, 5,5-dimethyl-1-pyrroline-N-oxide, and the singlet-oxygen trap, 2-(9,10-dimethoxyanthracentyl)-t-butylhydroxylamine, the authors demonstrate that the photoactive compound, protoporphyrin IX (PP IX), a naturally occurring precursor molecule of hemoglobin found in erythrocytes and plasma, generates superoxide anion and singlet oxygen. The amount of reactive-oxygen species produced by this system is dependent on the concentration of PP IX and the intensity and wavelength of the light delivered. Furthermore, the production of these photooxidants is significantly reduced by filtering the excitatory wavelengths of PP IX. These photogenerated oxidants could damage the vascular endothelium of the choriocapillaris, Bruch's membrane, and the RPE, necessitating a reparative process. This could result in features characteristically seen in ARMD such as a thickened Bruch's membrane, RPE atrophy, and hyperplasia. Prevention of phototoxic damage by this mechanism could involve enhancing protective enzymes, increasing scavenger substances, or supplying appropriate filters to eliminate the exciting wavelengths of light.

Keywords

Graef K, Schaeffel F

Year 2012

Authors Klaus Graef and Frank Schaeffel

Report Name Control of accommodation by longitudinal chromatic aberration and blue cones

Publication Journal of Vision

Issue-page numbers January 18, 2012 vol. 12 no. 1 article 14

URL http://w.journalofvision.org/content/12/1/14.short

Abstract urpose: To better understand the striking overaccommodation that is triggered at wavelengths below 430 nm (below referred to as OAB). Methods: Fourteen students served as subjects, 6 emmetropic and 8 mildly myopic. They fixated a reading target or a Landolt C at 33-cm distance while the wavelength of light illuminating the target was varied. Their accommodation was continuously monitored with the PowerRefractor (Multichannel Systems, Reutlingen, Germany, 1995). Luminances were matched using a candela meter (Minolta LS100) and neutral density filters. The following experiments were done: (1) confirmation of the effect at 10 cd/m2, (2) comparing 10 and 1 cd/m2, (3) foveal stimulation, (4) parafoveal stimulation, (5) testing independent combinations of the wavelength in the center and periphery, (6) testing accommodation tonus without fixation target while the wavelength is varied. Results: (1) OAB was nicely confirmed as initially described by F. J. Rucker and P. B. Kruger (2004a, 2004b) and A. Seidemann and F. Schaeffel (2002). (2) OAB remained stable at target luminances between 10 and 1 cd/m2. (3, 4) OAB was found to be more pronounced when the parafoveal region was stimulated than when mainly the fovea was stimulated. (5) When fovea and parafovea were illuminated by light of different wavelengths, the wavelength in the foveal region had greater impact on OAB. (6) OAB was not elicited in the absence of an accommodation target. Conclusions: OAB appears to be controlled more by the parafovea than by the fovea. The findings are in line with the assumption that OAB is mediated by the short-wavelength-sensitive cones that are absent from the central fovea in most subjects.

Keywords accommodation, blue cones, chromatic aberration

Graham C

Year 2002

Authors C Graham

Report Name Correspondence: Examination of the Melatonin Hypothesis: Graham et al.'s Response

Publication Environ Health Perspect

Issue-page numbers 2002 February; 110(2): A73

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1240748/

Abstract Correspondence

Keywords melatonin

Graham C, Cook MR, Gerkovich MM, Sastre A **Year** 2001

Authors Graham C, Cook MR, Gerkovich MM, Sastre A.

Report Name Examination of the melatonin hypothesis in women exposed at night to EMF or bright light.

Publication Environ Health Perspect

Issue-page numbers 2001 May;109(5):501-7

URL http://www.ncbi.nlm.nih.gov/pubmed/11401762

Abstract It has been hypothesized that the increased incidence of breast cancer in industrial societies is related to greater exposure to power-frequency electric and magnetic fields (EMF) and/or the presence of high levels of light at night (LAN). EMF and LAN are said to reduce circulating levels of the hormone melatonin which, in turn, allows estrogen levels to rise and stimulate the turnover of breast epithelial stem cells and increase the risk for malignant transformation. Three laboratory-based studies, in which a total of 53 healthy young women were exposed at night to EMF or to LAN under controlled exposure conditions, were performed to determine whether such exposures reduce melatonin and are associated with further alterations in estrogen. All-night exposure to industrial-strength magnetic fields (60 Hz, 28.3 microT) had no effect on the blood levels of melatonin or estradiol. In contrast, nocturnal melatonin levels were profoundly suppressed, and the time of peak concentration was significantly delayed in women exposed to LAN, regardless of whether they were in the follicular or luteal phase of the menstrual cycle. These changes, however, were not associated with alterations in point-for-point matching measures of estradiol. Women who chronically secrete high or low amounts of melatonin each night (area-under-curve range: 86-1,296 pg/mL) also did not differ in their blood levels of estradiol. Taken together, these results are consistent with a growing body of evidence which generally suggests that environmental EMF exposure has little or no effect on the parameters measured in this report.

Keywords emf, light at night

Graham C, Cook MR, Kavet R et al. **Year** 1998

Authors Graham C, Cook MR, Kavet R et al.

Report Name Prediction of nocturnal plasma melatonin from morning urinary measures

Publication J Pineal Res

Issue-page numbers 230–238 doi:10.1111/j.1600-079X.1998.tb00538.x. PMID:9572533

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1998.tb00538.x/abstract?systemMessage=Wiley+Online+Library+will+be+disrupted+8+Oct+from+10-14+BST+for+monthly

Abstract A growing literature indicates that blood levels of the hormone melatonin may have important implications for human health and wellbeing. Melatonin is synthesized and released into the general circulation at night, however, and it is seldom feasible to draw blood samples at night in epidemiological studies. There is some evidence that levels of urinary melatonin and of 6-sulfatoxymelatonin (aMT6s), the major metabolite of melatonin, accurately reflect nocturnal plasma melatonin. If this is the case, urinary assays could be powerful tools for epidemiological studies. A laboratory-based study was performed to examine the relationships between nocturnal plasma melatonin, morning urinary melatonin, and morning urinary aMT6s levels in 78 men. The relationship between total nocturnal plasma melatonin and both urinary aMT6s corrected for creatinine and urinary melatonin is significant. Combining the two urinary measures accounts for 72% of the variance in total plasma melatonin. Peak nocturnal plasma melatonin also was significantly related to urinary melatonin and to aMT6s. The urinary measures show good sensitivity and specificity in identifying individual differences in nocturnal plasma melatonin levels. These results support the inclusion of morning urine samples to assess the contribution of the hormone melatonin in occupational or residential studies involving healthy, young men.

Keywords

Green A, Battistutta D, Hart V, et al. **Year** 1996

Authors Adèle Green, Diana Battistutta, Veronica Hart, David Leslie and David Weedon

Report Name Skin cancer in a subtropical Australian population: incidence and lack of association with occupation

Publication Am. J. Epidemiol.

Issue-page numbers (1996) 144 (11): 1034-1040.

URL http://aje.oxfordjournals.org/content/144/11/1034.full.pdf

Abstract

Because it is not possible to monitor skin cancer accurately using routine methods, special surveys have been undertaken in Nambour, a typical subtropical community in Queensland, Australia. Estimates of incidence reported here are based on skin cancers medically treated between 1985 and 1992 and new cases diagnosed by dermatologists in two examination clinics in 1986 and 1992. Among men and women aged 18–69 years in 1986, age-adjusted incidence rates of basal cell carcinoma were 2,074 and 1,579 per 100,000 per year, respectively—the highest incidence rates of a specific cancer ever reported. Squamous cell carcinoma occurred at half the rate of basal cell carcinoma among men and at about one third the rate among women. Although as expected, fair skin, a history of repeated sunburns, and nonmalignant solar skin damage diagnosed by dermatologists were strongly associated with both types of skin cancer, outdoor occupation was not. Significant self-selection was observed among outdoor workers, whereby people with fair or medium complexions and a tendency to sunburn were systematically underrepresented among those in long-term outdoor occupations although they accounted for more than 80 percent of the community study sample. The mitigating effect of this selection bias may partly explain the paradox of the lack of quantitative evidence of a causal link between sun exposure and skin cancer in humans.

Keywords

Green AC, Williams GM, Logan V, Strutton GM **Year** 2011

Authors Adèle C. Green, Gail M. Williams, Valerie Logan and Geoffrey M. Strutton

Report Name Reduced melanoma after regular sunscreen use: randomized trial follow-up

Publication JCO

Issue-page numbers January 20, 2011 vol. 29 no. 3 257-263

URL http://jco.ascopubs.org/content/29/3/257.abstract

Abstract

Purpose Regular sunscreen use prevents cutaneous squamous cell carcinoma long term, but the effect on melanoma is highly controversial. We evaluated whether long-term application of sunscreen decreases risk of cutaneous melanoma.

Participants and Methods In 1992, 1,621 randomly selected residents of Nambour, a township in Queensland, Australia, age 25 to 75 years, were randomly assigned to daily or discretionary sunscreen application to head and arms in combination with 30 mg beta carotene or placebo supplements until 1996. Participants were observed until 2006 with questionnaires and/or through pathology laboratories and the cancer registry to ascertain primary melanoma occurrence.

Results Ten years after trial cessation, 11 new primary melanomas had been identified in the daily sunscreen group, and 22 had been identified in the discretionary group, which represented a reduction of the observed rate in those randomly assigned to daily sunscreen use (hazard ratio [HR], 0.50; 95% CI, 0.24 to 1.02; P = .051). The reduction in invasive melanomas was substantial (n = 3 in active v 11 in control group; HR, 0.27; 95% CI, 0.08 to 0.97) compared with that for preinvasive melanomas (HR, 0.73; 95% CI, 0.29 to 1.81).

Conclusion Melanoma may be preventable by regular sunscreen use in adults.

Keywords

Greene MW **Year** 2012

Authors Greene MW.

Report Name Circadian Rhythms and Tumor Growth

Publication Cancer Lett

Issue-page numbers 2012 Jan 14. [Epub ahead of print]

URL http://www.ncbi.nlm.nih.gov/pubmed/22252116

Abstract

Hormone secretion, metabolism, and the cell cycle are under rhythmic control. Lack of rhythmic control has been predicted to lead to uncontrolled proliferation and cancer. Consistent with this prediction are findings that circadian disruption by dim light at night or chronic jet lag accelerates tumor growth in desynchronized animals. Circadian controlled factors such as insulin/IGF-1, glucocorticoids, catecholamines, and melatonin have be implicated in controlling tumor growth in the desynchronized animals. Recent attention has focused on the signaling pathways activated by the circadian controlled factors because these pathways hold the potential for the development of novel strategies for cancer prevention and treatment.

Keywords

Authors Greenspan SL, Klibanski A, Rowe JW, Elahi D

Report Name Age alters pulsatile prolactin release: influence of dopaminergic inhibition

Publication Am J Physiol

Issue-page numbers 258:E799–E804. PMID:2333989

URL http://ajpendo.physiology.org/content/258/5/E799

Abstract To determine the effect of age on pulsatile prolactin secretion, we examined prolactin pulse characteristics by cluster analysis in healthy young and old male subjects during the day and night. Pulsatile prolactin secretion was identified in all subjects during the day and night, and prolactin pulse frequency remains stable with age. Younger subjects had a significantly higher prolactin pulse amplitude, area, and peak interval during the night compared with older subjects. In contrast, daytime prolactin pulse characteristics were similar in young and old subjects. Because the major neuroregulator of prolactin is dopamine and because normal aging has been reported to be associated with reductions in hypothalamic dopamine content and effect, we determined whether the mechanism of altered day-night prolactin pulsatile secretion was due to changes in dopaminergic tone. We examined endogenous prolactin secretion after administration of the dopamine antagonist metoclopramide. Metoclopramide significantly increased mean serum prolactin concentration and prolactin pulse height and amplitude in all subjects during the day and night. However, net prolactin pulse amplitude after metoclopramide stimulation at night was significantly higher in older subjects compared with younger subjects. We conclude that prolactin pulse amplitude is blunted in elderly men at night and that daytime pulsatile prolactin secretion is unaltered by age in normal men. The mechanism for this alteration of nighttime prolactin pulsatile secretion in elderly men may be due to age-associated changes in dopaminergic regulation.

Keywords

Authors Griefahn B, Künemund C, Golka K et al

Report Name Melatonin synthesis: a possible indicator of intolerance to shiftwork

Publication Am J Ind Med

Issue-page numbers 42:427–436. PMID:12382256 doi:10.1002/ajim.10122

URL http://onlinelibrary.wiley.com/doi/10.1002/ajim.10122/abstract

Abstract HYPOTHESIS:

Melatonin synthesis, which is directly controlled by the central circadian pacemaker indicates the circadian phase better than rectal temperature.
METHODS:

Thirty four men (16-32 years, 7 morning, 13 neither, 14 evening types) performed a constant routine (24-26-hr bedrest, < 30 lux, 18-20 degrees C, hourly isocaloric diet). Salivary melatonin level was determined hourly and rectal temperature was continuously recorded.
RESULTS:

The nadir of rectal temperature occurred 1.5 hr (P = 0.017), the onset of melatonin synthesis 3 hr earlier (P < 0.0001) in morning than in evening types. Morningness was not related to the quantitative but significantly to the temporal parameters, closer to those of melatonin than of rectal temperature.
CONCLUSIONS:

The melatonin onset is a more reliable indicator of the diurnal type than the nadir of rectal temperature. As morningness has been associated with intolerance to shiftwork, melatonin profiling provides a suitable basis for the establishment of directed preventive measures.

Keywords salivary melatonin concentrations; rectal temperature; diurnal type; shift work; constant routine

Grigore C

Year 2011

Authors Corina Grigore

Report Name THE NEUROHORMONE MELATONIN AND CARDIOVASCULAR RISK

Publication Journal of Internal Medicine Society

Issue-page numbers Nr.4 din luna 2011

URL http://www.medicina-interna.ro/articol.php?articol=674&lang=en

Abstract

Cardiovascular diseases (CVDs) are the first cause of death globally: more people die annually from CVDs than from any other cause. An estimated 17.1 million people died from CVDs in 2004, representing 29% of all global deaths. Of these deaths, an estimated 7.2 million were due to coronary heart disease (CHD) and 5.7 million were due to stroke. Low- and middle-income countries are disproportionally affected: 82% of CVD deaths take place in low- and middle-income countries and occur almost equally in men and women. CVD was the leading cause of death in developing countries, as well as developed ones, in 2010. By 2030, almost 23.6 million people will die from CVDs, mainly from CHD and stroke. These are projected to remain the single leading causes of death. The most important behavioural risk factors are unhealthy diet, physical inactivity and smoking and are responsible for about 80% of CHD and cerebrovascular disease. The effects of unhealthy diet and physical inactivity may show up in individuals as raised blood pressure, raised blood glucose, raised blood lipids, and overweight and obesity; these are called 'intermediate risk factors'(1).
The major and independent risk factors for CVD are cigarette smoking of any amount, hypertension (HBP), elevated serum total cholesterol and low-density lipoprotein cholesterol (LDL-C), low serum high-density lipoprotein cholesterol (HDL-C), diabetes mellitus (DM), and advancing age. The quantitative relationship between these risk factors and CVD risk has been elucidated for the first time by the Framingham Heart Study(2). AHA state another two major risk factors: obesity and physical inactivity(3, 4). The adverse effects of obesity are worsened when it is expressed as abdominal obesity, an indicator of insulin resistance(5). HBP and atherosclerosis (ATS) are both insulin resistance conditions, share similar risk factors and are characterized by structural and functional modification at the level of the arterial wall(6, 7). This group of metabolic risk factors in one person form the metabolic syndrome (MetS), also called the insulin resistance syndrome (NCEP according to ATP III criteria). The molecular relationship between insulin resistance and metabolic risk factors aren't fully understood and appear to be complex and link to endothelial dysfunction (ED). ED is generally defined as the imbalance between growth-promoting and growth-inhibiting factors, proatherogenic and antiatherogenic factors, vasodilators and vasoconstrictors, and procoagulant and anticoagulant factors. Evaluation of ED in patients at risk of developing metabolic syndrome can predict cardiovascular morbidity and mortality(8). Clinical and experimental data demonstrates the involvement of oxidative stress in the development of vascular complications associated with ED and is considered a step by which hyperglycemia promotes and accelerates the development of ATS lesions. The precise molecular mechanisms responsible for the increased production of reactive oxygen species (ROS) are not completely defined(9).
Melatonin was discovered by Lerner et al. in 1958(10) as the hormone of the pineal gland. The hormone received considerably more attention when it was found to regulate and reset circadian rhythms(11, 12) and, in species responding to photoperiodic changes, to be involved in the measurement of daylength, an environmental variable used for seasonal timing of reproduction, metabolism and behavior(13-17). Only many years after then, namely in 2003, it was demonstrate its implication in the regulation of cardiovascular system(18, 19), blood pressure(20), myocardial contractility(21) and increasing the antioxidant reserve(22). Melatonin receptors were discovered in the heart(23) and arteries(24). Moreover, decreased melatonin levels were find in various pathological conditions including hypertension with non-dipper pattern(25), impairment of heart failure(26), ischemic heart disease(27), after acute myocardial infarction(28). Therefore, melatonin is coming to the cutting edge of cardiovascular research and its effects on cardiovascular system in clinical situation are being discussed. The mechanisms behind melatonin influence on cardiovascular system are still not completely understood.

Keywords melatonin, oxidative stress, cardiovascular risk factors, mechanisms

Authors Christian Grimm, Andreas Wenzel, Theodore P. Williams, Pascal O. Rol, Farhad Hafezi and Charlotte E. Remé

Report Name Rhodopsin-mediated blue-light damage to the rat retina: effect of photoreversal of bleaching

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers February 2001 vol. 42 no. 2 497-505

URL http://www.iovs.org/content/42/2/497

Abstract

purpose. Acute white-light damage to rods depends on the amount of rhodopsin available for bleaching during light exposure. Bleached rhodopsin is metabolically regenerated through the visual cycle involving the pigment epithelium, or photochemically by deep blue light through photoreversal of bleaching. Because photoreversal is faster than metabolic regeneration of rhodopsin by several orders of magnitude, the photon catch capacity of the retina is significantly augmented during blue-light illumination, which may explain the greater susceptibility of the retina to blue light than to green light. However, blue light can also affect function of several blue-light–absorbing enzymes that may lead to the induction of retinal damage. Therefore, this study was conducted to test whether rhodopsin and its bleaching intermediates play a role in blue-light–induced retinal degeneration.

methods. Eyes of anesthetized rats and mice that did or did not contain rhodopsin were exposed to green (550 ± 10 nm) or deep blue (403 ± 10 nm) light for up to 2 hours. Rats with nearly rhodopsinless retinas were obtained by bleaching rhodopsin in animals with inhibited metabolic rhodopsin regeneration—that is, under halothane anesthesia. In addition, Rpe65−/− mice that are completely without rhodopsin were used to test the susceptibility to blue-light damage of a rodent retina completely devoid of the visual pigment. Effects of illumination on photoreceptor morphology were assessed 24 hours or 10 days thereafter by morphologic and biochemical methods.

results. Exposure to blue light resulted in severe retinal damage and activation of the transcription factor AP-1 in rats. In contrast, green light had no effect. When rhodopsin was almost completely bleached by short-term green-light exposure while metabolic regeneration (but not photoreversal) was prevented by halothane anesthesia, blue-light exposure induced distinct lesions in rat retinas. When both metabolic rhodopsin regeneration and photoreversal of bleaching were almost completely inhibited, blue-light exposure caused only very moderate lesions. When mice without rhodopsin were exposed to blue light, no damage occurred, in contrast to wild-type control mice.

conclusions. Short time exposure to blue light has deleterious effects on retinal morphology. Because damage was observed only in the presence of the visual pigment, blue-light–induced retinal degeneration is rhodopsin mediated. Absorption of blue light by other proteins is not sufficient to induce light damage. Photoreversal of bleaching, which occurs only in blue but not in green light, increases the photon-catch capacity of the retina and may thus account for the difference in the damage potential between blue and green light.

Keywords

Authors Theodoros B Grivas and Olga D Savvidou

Report Name Melatonin the "light of night" in human biology and adolescent idiopathic scoliosis

Publication Scoliosis

Issue-page numbers 2:6 doi:10.1186/1748-7161-2-6

URL http://www.scoliosisjournal.com/content/2/1/6

Abstract

Melatonin "the light of night" is secreted from the pineal gland principally at night. The hormone is involved in sleep regulation, as well as in a number of other cyclical bodily activities and circadian rhythm in humans. Melatonin is exclusively involved in signalling the 'time of day' and 'time of year' (hence considered to help both clock and calendar functions) to all tissues and is thus considered to be the body's chronological pacemaker or 'Zeitgeber'.

The last decades melatonin has been used as a therapeutic chemical in a large spectrum of diseases, mainly in sleep disturbances and tumours and may play a role in the biologic regulation of mood, affective disorders, cardiovascular system, reproduction and aging. There are few papers regarding melatonin and its role in adolescent idiopathic scoliosis (AIS). Melatonin may play a role in the pathogenesis of scoliosis (neuroendocrine hypothesis) but at present, the data available cannot clearly support this hypothesis. Uncertainties and doubts still surround the role of melatonin in human physiology and pathophysiology and future research is needed.

Keywords

Authors Jolanta Gromadzińska, Beata Peplonska, Wojciech Sobala, Edyta Reszka, Wojciech Wasowicz, Agnieszka Bukowska, Jenny-Anne Lie

Report Name Relationship between intensity of night shift work and antioxidant status in blood of nurses

Publication International Archives of Occupational and Environmental Health

Issue-page numbers November 2012,

URL http://link.springer.com/article/10.1007%2Fs00420-012-0828-7?LI=true

Abstract

Purpose
Light-at-night exposure can disrupt the human circadian rhythm via clock gene expressions. The circadian rhythm influences antioxidant enzymes' activity and cellular mRNA levels of these enzymes. The employees working based on a shift system adjust to the changes occurring both on the cell level and on the level of the whole organism. Therefore, a question should be answered whether shift work disturbs oxidant–antioxidant balance and/or generates oxidative stress.

Methods
A cross-sectional study was conducted among nurses selected from the Local Registry of the Chamber of Nurses and Midwives in Lodz: 359 nurses worked daily only and 349 working rotating night shifts. These two groups differed significantly in respect of age ($p < 0.0001$), menopausal status ($p < 0.0001$), and current smoking habit ($p = 0.02$). The average total work duration was significantly shorter (12.4 years) in nurses working currently rotating night shifts who worked significantly longer on night shifts than day-workers (26.6 years).

Results
We found statistically significant higher red blood cell glutathione peroxidase in nurses working on night shifts (21.0 ± 4.6 vs. 20.0 ± 5.0 U/g Hb, $p < 0.009$) after adjusting for age, oral contraceptive hormone use, smoking, and drinking alcohol during last 24 h. Statistically significant lower vitamin A and E levels were found in the premenopausal women working in rotating system (0.690 ± 0.238 vs. 0.786 ± 0.262 μg/ml, $p < 0.0001$ for vitamin A and 10.93 ± 4.15 vs. 12.78 ± 4.75 μg/ml, $p < 0.0001$ for vitamin E). The marker of lipic peroxidation (TBARS concentration) was significantly lower in the premenopausal nurses than postmenopausal ones working day shifts only (2.06 ± 0.76 vs. 2.21 ± 0.80 nmol/ml, $p < 0.038$). We observed that erythrocyte GSH-Px activity rose statistically significant in nurses working more night shifts per month ($p < 0.01$).

Conclusions
The results quoted above seem to support the existence of an association between light-at-night exposure and blood glutathione peroxidase activity in female shift workers. Nevertheless, in order to explain the mechanisms of this association, we need more studies.

Keywords

Authors C. Gronfier, R. Luthringer, M. Follenius, N. Schaltenbrand, J.P. Macher, A. Muzet and G. Brandenberger

Report Name A quantitative evaluation of the relationships between growth hormone secretion and delta wave electroencephalographic activity during normal sleep and after enrichment in delt

Publication Sleep

Issue-page numbers 19:817–824. PMID:9085491

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24360

Abstract The existence of a relationship between growth hormone (GH) release and slow-wave sleep (SWS), often studied in the past using conventional scoring of sleep stages, remains controversial. In the present study, this relationship was reevaluated by spectral analysis of the sleep electroencephalogram (EEG) and deconvolution analysis of the plasma GH concentrations during normal nocturnal sleep and after enrichment in SWS by means of ritanserin, a selective 5-HT2 receptor antagonist. Eight healthy male subjects each participated in two randomized night studies after having received either a placebo or a 5-mg dose of ritanserin. They were subjected to 8 hours of polysomnography, including spectral analysis of the sleep EEG. Plasma GH levels were measured at 10-minute intervals. The mean delta absolute power and the mean GH secretory rates were significantly higher under ritanserin than under placebo for the first 3 hours after sleep onset (+24% and +29%, respectively). Their nocturnal profiles were significantly and positively correlated in all subjects (average r = 0.710 under placebo, 0.567 under ritanserin; p < 0.0001 in both cases). GH secretory pulses were found to be coincident with delta activity peaks in both directions. The amount of GH secreted during significant GH pulses was correlated with the amount of concomitant delta wave activity (r = 0.803 under placebo, r = 0.764 under ritanserin, p < 0.0001). Similarly, the amount of delta wave activity found during delta wave peaks was correlated with the amount of GH secreted concomitantly (r = 0.715 under placebo, r = 0.723 under ritanserin: p < 0.0001). These results demonstrate a close temporal and quantitative relationship between GH secretion and delta wave activity, which may be evidence of common stimulatory mechanisms.

Keywords

Gronfier C, Wright Jr. KP, Kronauer RE, et al. **Year** 0

Authors Claude Gronfier, Kenneth P. Wright, Jr., Richard E. Kronauer, Megan E. Jewett, and Charles A. Czeisler

Report Name Efficacy of a single sequence of intermittent bright light pulses for delaying circadian phase in humans

Publication AJP - Endo

Issue-page numbers July 2004 vol. 287 no. 1 E174-E181

URL http://ajpendo.physiology.org/content/287/1/E174.full

Abstract It has been shown in animal studies that exposure to brief pulses of bright light can phase shift the circadian pacemaker and that the resetting action of light is most efficient during the first minutes of light exposure. In humans, multiple consecutive days of exposure to brief bright light pulses have been shown to phase shift the circadian pacemaker. The aim of the present study was to determine whether a single sequence of brief bright light pulses administered during the early biological night would phase delay the human circadian pacemaker. Twenty-one healthy young subjects underwent a 6.5-h light exposure session in one of three randomly assigned conditions: 1) continuous bright light of ~9,500 lux, 2) intermittent bright light (six 15-min bright light pulses of ~9,500 lux separated by 60 min of very dim light of <1 lux), and 3) continuous very dim light of <1 lux. Twenty subjects were included in the analysis. Core body temperature (CBT) and melatonin were used as phase markers of the circadian pacemaker. Phase delays of CBT and melatonin rhythms in response to intermittent bright light pulses were comparable to those measured after continuous bright light exposure, even though the total exposure to the intermittent bright light represented only 23% of the 6.5-h continuous exposure. These results demonstrate that a single sequence of intermittent bright light pulses can phase delay the human circadian pacemaker and show that intermittent pulses have a greater resetting efficacy on a per minute basis than does continuous exposure.

Keywords melatonin; circadian pacemaker; photoreception; phase shift

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Gronfier C, Wright KP Jr, Kronauer RE, Czeisler CA. **Year** 2007

Authors Gronfier C, Wright KP Jr, Kronauer RE, Czeisler CA.

Report Name Entrainment of the human circadian pacemaker to longer-than-24-h days

Publication Proc Natl Acad Sci U S A

Issue-page numbers 2007 May 22;104(21):9081-6. Epub 2007 May 14.

URL http://www.ncbi.nlm.nih.gov/pubmed/17502598

Abstract Entrainment of the circadian pacemaker to the light:dark cycle is necessary for rhythmic physiological functions to be appropriately timed over the 24-h day. Nonentrainment results in sleep, endocrine, and neurobehavioral impairments. Exposures to intermittent bright light pulses have been reported to phase shift the circadian pacemaker with great efficacy. Therefore, we tested the hypothesis that a modulated light exposure (MLE) with bright light pulses in the evening would entrain subjects to a light:dark cycle 1 h longer than their own circadian period (tau). Twelve subjects underwent a 65-day inpatient study. Individual subject's circadian period was determined in a forced desynchrony protocol. Subsequently, subjects were released into 30 longer-than-24-h days (daylength of tau + 1 h) in one of three light:dark conditions: (i) approximately 25 lux; (ii) approximately 100 lux; and (iii) MLE: approximately 25 lux followed by approximately 100 lux, plus two 45-min bright light pulses of approximately 9,500 lux near the end of scheduled wakefulness. We found that lighting levels of approximately 25 lux were insufficient to entrain all subjects tested. Exposure to approximately 100 lux was sufficient to entrain subjects, although at a significantly wider phase angle compared with baseline. Exposure to MLE was able to entrain the subjects to the imposed sleep-wake cycles but at a phase angle comparable to baseline. These results suggest that MLE can be used to entrain the circadian pacemaker to non-24-h days. The implications of these findings are important because they could be used to treat circadian misalignment associated with space flight and circadian rhythm sleep disorders such as shift-work disorder.

Keywords

Authors Anne Grundy, Maria Sanchez, Harriet Richardson, Joan Tranmer, Marilyn Borugian, Charles H. Graham and Kristan J. Aronson

Report Name LIGHT INTENSITY EXPOSURE, SLEEP DURATION, PHYSICAL ACTIVITY, AND BIOMARKERS OF MELATONIN AMONG ROTATING SHIFT NURSES

Publication Chronobiology International

Issue-page numbers 26:7, 1443-1461

URL http://informahealthcare.com/doi/abs/10.3109/07420520903399987

Abstract Long-term, night shiftwork has been identified as a potential carcinogenic risk factor. It is hypothesized that increased light at night exposure during shiftwork reduces melatonin production, which is associated with increased cancer risk. Sleep duration has been hypothesized to influence both melatonin levels and cancer risk, and it has been suggested that sleep duration could be used as a proxy for melatonin production. Finally, physical activity has been shown to reduce cancer risk, and laboratory studies indicate it may influence melatonin levels. A cross-sectional study of light exposure, sleep duration, physical activity, and melatonin levels was conducted among 61 female rotating shift nurses (work schedule: two 12 h days, two 12 h nights, five days off). Light intensity was measured using a light-intensity data logger, and sleep duration and physical activity were self-reported in a study diary and questionnaire. Melatonin concentrations were measured from urine and saliva samples. The characteristics of nurses working day and night shifts were similar. Light intensity was significantly higher during sleep for those working at night ($p < 0.0001$), while urinary melatonin levels following sleep were significantly higher among those working days ($p = 0.0003$). Mean sleep duration for nurses working during the day (8.27 h) was significantly longer than for those working at night (4.78 h, $p < 0.0001$). An inverse association ($p = 0.002$) between light exposure and urinary melatonin levels was observed; however, this was not significant when stratified by shift group. There was no significant correlation between sleep duration and melatonin, and no consistent relationship between physical activity and melatonin. Analysis of salivary melatonin levels indicated that the circadian rhythms of night workers were not altered, meaning peak melatonin production occurred at night. This study indicates that two nights of rotating shift work may not change the timing of melatonin production to the day among those working at night. Additionally, in this study, sleep duration was not correlated with urinary melatonin levels, suggesting it may not be a good proxy for melatonin production.

Keywords Lighting, Melatonin, Physical activity, Nurses, Circadian rhythm

Grundy A, Schuetz JM, Lai AS, et al. **Year** 2013

Authors Anne Grundy, Johanna M. Schuetz, Agnes S. Lai, Rozmin Janoo-Gilani, Stephen Leach, Igor Burstyn, Harriet Richardson, Angela Brooks-Wilson, John J. Spinelli, Kristan J. Aro

Report Name Shift work, circadian gene variants and risk of breast cancer

Publication Cancer Epidemiology

Issue-page numbers Available online 28 May 2013

URL http://www.sciencedirect.com/science/article/pii/S1877782113000660

Abstract

Circadian (clock) genes have been linked with several functions relevant to cancer, and epidemiologic research has suggested relationships with breast cancer risk for variants in NPAS2, CLOCK, CRY2 and TIMELESS. Increased breast cancer risk has also been observed among shift workers, suggesting potential interactions in relationships of circadian genes with breast cancer. Relationships with breast cancer of 100 SNPs in 14 clock-related genes, as well as potential interactions with shift work history, were investigated in a case–control study (1042 cases, 1051 controls). Odds ratios in an additive genetic model for European-ancestry participants (645 cases, 806 controls) were calculated, using a two-step correction for multiple testing: within each gene through permutation testing (10,000 permutations), and correcting for the false discovery rate across genes. Interactions of genotypes with ethnicity and shift work (<2 years vs ≥2 years) were evaluated individually. Following permutation analysis, two SNPs (rs3816360 in ARNTL and rs11113179 in CRY1) displayed significant associations with breast cancer and one SNP (rs3027188 in PER1) was marginally significant; however, none were significant following adjustment for the false discovery rate. No significant interaction with shift work history was detected. If shift work causes circadian disruption, this was not reflected in associations between clock gene variants and breast cancer risk in this study. Larger studies are needed to assess interactions with longer durations (>30 years) of shift work that have been associated with breast cancer.

Keywords Clock genes; Shift work; Breast cancer; Interactions; Case–control

Authors Grundy A, Tranmer J, Richardson H, Graham CH, Aronson KJ

Report Name The Influence of Light at Night Exposure on Melatonin Levels among Canadian Rotating Shift Nurses.

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers 2011 Sep 27 doi: 10.1158/1055-9965.EPI-11-0427

URL http://cebp.aacrjournals.org/content/early/2011/08/29/1055-9965.EPI-11-0427.abstract

Abstract

BACKGROUND:

Shift work has been identified as a risk factor for several cancer sites in recent years, with melatonin as a potential intermediate on the proposed causal pathway. This study examined the influence of nighttime light exposure on melatonin levels among 123 rotating shift nurses.
METHODS:

Nurses working a rotating shift schedule (two 12-hour days, two 12-hour nights, and five days off) were recruited and participated on a day and night shift in both the summer and winter seasons. Over each 48-hour study period, nurses wore a light data logger and provided two urine and four saliva samples.
RESULTS:

Saliva measurements showed that the pattern of melatonin production did not differ between day and night shifts. Mean light exposure was significantly higher ($P < 0.0001$) when nurses were working at night, although peak melatonin levels ($P = 0.65$) and the daily change in melatonin levels ($P = 0.80$) were similar across day/night shifts. Multivariate analysis did not show an association between light exposure and melatonin levels when data from both shifts was combined; however, when data from the night shift was considered alone, a statistically significant inverse relationship between light and change in melatonin was observed ($P = 0.04$).
CONCLUSION:

These results show that light exposure does not seem to be strongly related to reduced melatonin production among nurses on this rapidly rotating shift schedule.Impact: Future research considering more extreme shift patterns or brighter lighting conditions could further clarify the relationship between light exposure and melatonin production in observational settings.

Keywords

Grundy, ANNE **Year** 2012

Authors Grundy, ANNE

Report Name The Influence of Shift Work, Light at Night and Clock Gene Polymorphisms on Melatonin Levels and Breast Cancer Risk

Publication Thesis (Ph.D, Community Health & Epidemiology) -- Queen's University, 2012-09-26 20:59:40.209

Issue-page numbers

URL http://qspace.library.queensu.ca/jspui/bitstream/1974/7524/1/Grundy_Anne_L_201209_PhD.pdf

Abstract Background: Shift work has recently been identified as a breast cancer risk factor, where meta-analysis has indicated an approximately 50% increased risk among long-term shift workers. However, additional studies with more comprehensive methods of shift work exposure assessment are needed to capture the diversity of shift patterns. The hypothesized mechanism for this relationship involves chronodisruption (altered circadian rhythms), where increased exposure to light at night during night shifts may decrease production of the cancer-protective hormone melatonin. Further, coordination of circadian rhythms, including melatonin production, is governed by the interactions of a set of central clock genes. Recent studies have suggested that variants in clock genes are associated with cancer risk at multiple sites, including breast cancer, although few studies have considered potential interactions with shift work. Methods: This thesis examined relationships of both shift work and clock gene polymorphisms (and their interactions) with breast cancer risk in a case-control study of 1,142 cases and 1,178 controls. The association between light exposure and melatonin production was also investigated in a longitudinal biomarker study conducted among 123 nurses working a two-day, two-night rotating shift pattern. Results: In the case-control study, an association between breast cancer and ≥30 years of shift work (OR = 2.20, 95%CI = 1.13 – 4.28) was detected, although no relationship with short (0 – 14 years) or medium (15 – 29 years) term shift work was observed. As well, variants in 14 clock-related genes were not associated with breast cancer and there were no apparent interactions with shift work history. In the biomarker study, both peak melatonin levels and daily change in melatonin levels were similar when nurses were working their day and night shifts. Further, on the night shift, a slight inverse relationship between light and change in melatonin was observed (p = 0.04). Conclusions: Taken together, these results contribute to the understanding of both the association between shift work and breast cancer, and the biologic mechanisms underlying this relationship. Since shift work is required for many occupations, understanding the mechanisms through which it impacts breast cancer is important to the development of healthy workplace policy.

Keywords Melatonin, Breast Cancer, Clock Genes, Shift Work, Light at Night

Authors Gundestrup M, Storm HH

Report Name Radiation-induced acute myeloid leukaemia and other cancers in commercial jet cockpit crew: a population-based cohort study

Publication Lancet

Issue-page numbers 354:2029–2031.doi:10.1016/S0140-6736(99)05093-X PMID:10636367

URL http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2899%2905093-X/abstract

Abstract

Background
Cockpit crews receive cosmic radiation during flight operations. The increasing total accumulated dose over the years might be expected to cause increased frequency of radiation-induced cancer. The rate should increase with number of flight hours per year, number of years of flying, and higher flight altitude, If the cumulative radiation exposure during flights is of concern, we would expect an increased cancer risk to be present among those crew members flying jets.
Methods
Cockpit-crew medical records (pilots and flight engineers) from 1946 onwards, holding information on the individual, flight hours, aircraft type, and date of commercial certification and decertification, were linked to the population-based Danish Cancer Registry, the central population registry, and the National Death Index
Findings
Altogether 3877 cockpit crew members could be traced for follow-up, accruing 61 095 person-years at risk in 3790 men and 661 in 87 women. The total number of cancers observed was 169 whereas 153·1 were expected (standardised incidence ratio 1·1 [95% CI 0·94—1·28]). Significantly increased risks of acute myeloid leukaemia (5·1 [1·03—14·91]), skin cancer, excluding melanoma (3·0 [2·12—4·23]), and total cancer (1·2 [1·00—1·53]) were observed among Danish male jet cockpit crew members flying more than 5000 h. Increased risk of malignant melanoma irrespective of aircraft type was also found among those flying more than 5000 h.
Interpretation
Both malignant melanoma and skin cancer were found in excess in cockpit crew members with a long flying history, probably attributable to sun exposure during leisure time at holiday destinations. We cannot confirm previously reported increased risk of brain and rectal cancers in pilots. The study shows that male cockpit crew members in jets flying more than 5000 h have significantly increased frequency of acute myeloid leukaemia.

Keywords

Authors Gupta G, Man I, Kemmett D.

Report Name Hydroa vacciniforme: A clinical and follow-up study of 17 cases

Publication J Am Acad Dermatol.

Issue-page numbers 2000 Feb;42(2 Pt 1):208-13.

URL http://www.ncbi.nlm.nih.gov/pubmed/10642674

Abstract

BACKGROUND:

Hydroa vacciniforme (HV) is a rare, sporadic, idiopathic photodermatosis characterized by vesicles and crust formation after sunlight exposure. The lesions typically heal with vacciniform scarring.
OBJECTIVE:

We identify and review the clinical features and follow-up data of Scottish patients with HV and report on the prevalence of this condition. This is the largest recent study of HV patients from a single center.
METHODS:

In this retrospective study, patients with HV were identified by means of the diagnostic database from the Photobiology Unit, Dundee. Patients were contacted and details of clinical features, duration of disease, results of investigations, and treatment were recorded. At review, disease progress was assessed.
RESULTS:

Between 1973 and 1997, 17 patients (9 males and 8 females) with a diagnosis of HV were investigated. Data from 15 patients showed a mean age at onset of 7.9 years (range, 1 to 16 years), with females (mean, 6.7 years; range, 2 to 12 years) having an earlier onset than males (mean, 8.7 years; range, 1 to 16 years). A bimodal age distribution was also identified with onsets between the ages of 1 and 7 years and 12 and 16 years. At review, spontaneous clearing had occurred in 9 patients (60%) with mean duration of disease being 9 years (range, 4 to 17 years). Males had longer disease duration (mean, 11 years; range, 5 to 17 years) than females (mean, 5 years; range, 4 to 7 years). Eight patients (53%) were sensitive in the UVA wave-band on monochromator phototesting, and 6 (40%) experienced papulovesicular lesions on repetitive broad-spectrum UVA irradiation. All patients received broad-spectrum sunscreens with variable results. Of the 5 patients treated with narrow-band UVB (TL-01) phototherapy, 3 reported beneficial results with an increase in tolerance to sunlight exposure and associated reduction in disease severity.
CONCLUSION:

The estimated prevalence of HV was at least 0.34 cases per 100,000 with an approximately equal sex ratio. Males had a later onset and longer duration of disease than females. Phototesting showed abnormal responses in the UVA wavebands in 53% of cases, whereas 60% of patients treated with prophylactic TL-01 phototherapy found it beneficial.

Keywords

Hagenauer MH, Lee TM

Year 2012

Authors Megan Hastings Hagenauer,Theresa M. Lee

Report Name The neuroendocrine control of the circadian system: Adolescent chronotype

Publication Frontiers in Neuroendocrinology

Issue-page numbers Available online 22 May 2012

URL http://www.sciencedirect.com/science/article/pii/S0091302212000180

Abstract Scientists, public health and school officials are paying growing attention to the mechanism underlying the delayed sleep patterns common in human adolescents. Data suggest that a propensity towards evening chronotype develops during puberty, and may be caused by developmental alterations in internal daily timekeeping. New support for this theory has emerged from recent studies which show that pubertal changes in chronotype occur in many laboratory species similar to human adolescents. Using these species as models, we find that pubertal changes in chronotype differ by sex, are internally generated, and driven by reproductive hormones. These chronotype changes are accompanied by alterations in the fundamental properties of the circadian timekeeping system, including endogenous rhythm period and sensitivity to environmental time cues. After comparing the developmental progression of chronotype in different species, we propose a theory regarding the ecological relevance of adolescent chronotype, and provide suggestions for improving the sleep of human adolescents.

Keywords Biological rhythm; Reproductive hormone; Comparative endocrinology; Sleep; Puberty; Sex; Suprachiasmatic nucleus; Temporal niche; Entrainment; Period

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Hahn RA

Year 1991

Authors Hahn RA

Report Name Profound bilateral blindness and the incidence of breast cancer

Publication Epidemiol

Issue-page numbers 2:208–210 doi:10.1097/00001648-199105000-00008. PMID: 2054403

URL http://www.jstor.org/pss/25759883

Abstract This case-control study addressed the hypothesis that uninterrupted exposure to light is associated with increased rates of breast cancer. We compared the odds of profound binocular blindness among women with a diagnosis of breast cancer with the odds of profound binocular blindness among women with diagnoses of coronary heart disease or stroke. All hospital discharges in the National Hospital Discharge Survey from 1979 through 1987 were analyzed, after exclusion of women with diabetes. Profoundly blind women were half as likely to have breast cancer as women who were not profoundly blind. This effect diminished substantially with increasing age.

Keywords

	Hahn RA	***Year***	1998
Authors	Robert A. Hahn		
Report Name	Does blindness protect against cancers?		
Publication	Epidemiology		
Issue-page numbers	Vol. 9, No. 5 (Sep., 1998), pp. 481-483		
URL	http://www.jstor.org/pss/3702522		
Abstract	N/A		
Keywords			

	Haim A, Portnov BA	***Year***	2011
Authors	Abraham Haim and Boris A. Portnov		
Report Name	LAN and Breast Cancer Risk: Can We See a Forest Through the Trees?—Response to “Measurements of Light at Night (LAN)…		
Publication	Chronobiology International		
Issue-page numbers	28:8, 734-736		
URL	http://informahealthcare.com/doi/abs/10.3109/07420528.2011.604591		
Abstract	Correspondence		
Keywords	Light-at-Night		

Haim A, Portnov BA

Year 2013

Authors Abraham Haim, Boris A. Portnov

Report Name Light Pollution as a New Risk Factor for Human Breast and Prostate Cancers

Publication Book Publisher - Springer Netherlands

Issue-page numbers ISBN: 978-94-007-6219-0 (Print) 978-94-007-6220-6 (Online)

URL http://link.springer.com/book/10.1007/978-94-007-6220-6/page/1

Abstract

Keywords

Hajak G, Rodenbeck A, Ehrenthal HD et al.

Year 1997

Authors Hajak G, Rodenbeck A, Ehrenthal HD et al.

Report Name No evidence for a physiological coupling between melatonin and glucocorticoids

Publication Psychopharmacology (Berl)

Issue-page numbers 133:313–322 doi:10.1007/s002130050408. PMID:9372529

URL http://www.springerlink.com/content/vgrcfd6d2y792a2k/

Abstract Much has been speculated about the existence of a physiological coupling between melatonin and glucocorticoid secretion and about a possible anti-stress action of melatonin. We examined the relationship between melatonin and glucocorticoid secretion under close-to-physiological conditions, when the plasma concentration of either melatonin or glucocorticoids was elevated acutely or chronically in both rats and humans. Tryptophan administration caused a massive rise of plasma melatonin, but had no effect on corticosterone levels in rats or on cortisol levels in humans. The acute and long-lasting exposure of rats to uncontrollable stress resulted in a significant rise of adrenal corticosterone secretion, but had no effect on circulating melatonin levels. Orchectomy caused an initial increase in circulating corticosterone (when melatonin was unaffected) and a delayed rise in circulating melatonin (when corticosterone levels were normalized). In humans, no correlation was found between the nocturnal urinary excretion of melatonin and cortisol, either among healthy subjects, or among patients suffering from panic disorder (with an increased urinary excretion of cortisol) or among insomnia patients (with a high incidence of low melatonin secretion). Furthermore, no evidence was found for a suppressive action of melatonin on dexamethasone-mediated thymus regression in rats and on dexamethasone-mediated suppression of lymphocyte proliferation in vitro. Taken together, the results of this study provide no evidence for the existence of mutual influences between melatonin and glucocorticoid secretion, nor do they support the proposed attenuation of glucocorticoid-mediated effects on target cells or tissues by melatonin under physiological conditions.

Keywords

Year 2012

Authors Hajrasouliha AR, Kaplan HJ.

Report Name Light and ocular immunity.

Publication Curr Opin Allergy Clin Immunol

Issue-page numbers 2012 Aug 21. [Epub ahead of print]

URL http://www.ncbi.nlm.nih.gov/pubmed/22892711

Abstract

PURPOSE OF REVIEW:

Current scientific evidence suggests that the systemic immune response is affected by exposure to light. During the past century man has been exposed for the first time in evolution to light at night, as well as increasing ultraviolet radiation through depletion of the ozone layer in our atmosphere. These ecological changes have enhanced the impact of light on our systemic immune response. We will review the effect of light on the systemic immune response with particular emphasis on ocular immunity.
RECENT FINDINGS:

Visible light is now recognized to be important in the maintenance of immune privilege within the eye; however, little is known about the mechanism through which this effect occurs. Recent studies suggest that the generation of regulatory T cells involved in immune privilege within the eye is dependent on retinoic acid formation by retinal pigment epithelial cells. Light is also important in modulation of multiple pathways including adjustment of circadian rhythm and production of vitamin D.
SUMMARY:

Light regulates our biologic systems in many different ways. Its effect on the systemic immune response suggests that it is important in maintaining health, as well as in the induction of disease. A better understanding of the interaction of light with our biologic systems may allow new preventive measures to avoid disease and novel forms of treatment.

Keywords light; ocular; systemic immune; immune; immune privilege; immunity; immune response; privilege;

Håkansson N, Floderus B, Gustavsson P, et al. **Year** 2001

Authors Håkansson N, Floderus B, Gustavsson P, Feychting M, Hallin N.

Report Name Occupational sunlight exposure and cancer incidence among Swedish construction workers

Publication Epidemiology

Issue-page numbers 2001 Sep;12(5):552-7.

URL http://www.ncbi.nlm.nih.gov/pubmed/11505175

Abstract We studied sunlight exposure from outdoor work in relation to cancer, using data from 323,860 men participating in an occupational health service program of the Swedish construction industry. An experienced industrial hygienist assessed the exposure for 200 job tasks. We estimated relative risks (RRs) adjusted for age, smoking, and magnetic field exposure. There was an increased RR in the high-exposure group for myeloid leukemia [RR = 2.0, 95% confidence interval (95% CI) = 1.1-3.6] and lymphocytic leukemia (RR = 1.7, 95% CI = 0.9-3.2). For non-Hodgkin's lymphoma there was a 30% increase in risk in the high-exposure group (95% CI = 0.9-1.9). There was no increased risk of malignant melanoma, except for tumors of the head, face, and neck in the high-exposure group (RR = 2.0, 95% CI = 0.8-5.2), and we also found an increased risk for malignant melanoma of the eye in this group (RR = 3.4, 95% CI = 1.1-10.5). Outdoor workers had no increased risk of nonmelanoma skin cancer. Nevertheless, the RR for lip cancer (squamous cell carcinoma) among the high-exposure group was estimated at 1.8 (95% CI = 0.8-3.7). Among other sites, an increased risk of stomach cancer was suggested in this group (RR = 1.4, 95% CI = 1.0-1.9). The results for lymphoma, leukemia, and possibly also for stomach cancer might reflect a suppression of the immune system from ultraviolet light in outdoor workers.

Keywords

Haldar C, Rai S, Singh R **Year** 2004

Authors Haldar C, Rai S, Singh R

Report Name Melatonin blocks dexamethasone-induced immunosuppression in a seasonally breeding rodent Indian palm squirrel, Funambulus pennanti

Publication Steroids

Issue-page numbers 69:367–377 doi:10.1016/j.steroids.2004.03.006. PMID:15219786

URL http://www.sciencedirect.com/science/article/pii/S0039128X04000522

Abstract In vivo effect of dexamethasone and melatonin on immunomodulation has been investigated by studying the lymphocyte proliferation to the mitogen Con A from various lymphoid tissues including bone marrow cells of a seasonally breeding rodent adult male F. pennanti during reproductively inactive phase (October to December). During this phase, animal faces the maximum challenges of the nature (hypothermic stress, scarcity of food and shelter). Dexamethasone treatment (60 μg/day/squirrel) for 60 consecutive days significantly decreased the thymus and spleen activity. The lymphoid tissues mass, total leukocyte, lymphocyte count of peripheral blood, bone marrow and T-cell mediated immune function was also significantly suppressed following the dexamethasone treatment but treatment of melatonin (25 μg/squirrel/day) along with dexamethasone significantly restored the suppressed immune status in squirrels. Further, histological study of the thymus showed profound changes in the cellularity with a depletion of thymocytes in the cortex region of thymic lobules and increased in connective tissues and spindle cells. Melatonin treatment alone increased thymocytes density in thymic cortex clearly suggesting that melatonin counteracted the experimentally induced immune stress by dexamethasone. Therefore, in nature during reproductively inactive phase of the squirrel a high level of melatonin was noted, that is required to combat nature’s stress, which might have increased the internal level of corticoids.

Keywords Melatonin; Dexamethasone; Immunity; Funambulus pennanti; Seasonal stress

Authors Haldar C, Singh R, Guchhait P

Report Name Relationship between the annual rhythms in melatonin and immune system status in the tropical palm squirrel, Funambulus pennanti

Publication Chronobiol Int

Issue-page numbers 18:61–69 doi:10.1081/CBI-100001174. PMID:11247114

URL http://www.mendeley.com/research/relationship-between-the-annual-rhythms-in-melatonin-and-immune-system-status-in-the-tropical-palm-squirrel-funambulus-pennanti/

Abstract Melatonin (MEL) regulation of seasonal variation in immunity has been studied extensively in temperate mammals. This report is the first on a tropical mammal, the Indian palm squirrel, F. pennanti. In response to the annual environmental cycle, we studied the rhythms of plasma MEL and the immune parameters of total blood leucocytes, absolute blood lymphocytes and blastogenic responses of blood, thymus and spleen lymphocytes. We found that in parallel with MEL all the immune parameters increased during the month of April onward, when natural day length, temperature, humidity and rainfall were increasing. Maximum values occurred during November (reproductively inactive phase) when the values of all the physical factors were comparatively low. Lowest values occurred during January-March (reproductively active phase) when the values of the physical factors were lowest. In order to establish a clear interrelationship between the pineal MEL and the immune system function, we manipulated these squirrels with exogenous MEL (25mg/100 g B wt/day) at 1730 h during their pineal inactive phase (March) while another group was pinealectomized (Px) during November when their pineal was active. The MEL injection significantly increased all the immune parameters, while Px decreased them significantly. Hence, we suggest that MEL is immuno-enhancing for this tropical squirrel, and plays an important role in the maintenance of its immunity in accordance with the seasonal changes in environmental factors and gonadal status.

Keywords

Authors Haldorsen T, Reitan JB, Tveten U

Report Name Cancer incidence among Norwegian airline pilots

Publication Scand J Work Environ Health

Issue-page numbers 26:106–111. PMID:10817375

URL http://www.sjweh.fi/download.php?abstract_id=519&file_nro=1

Abstract

Objectives In this retrospective cohort study, the cancer incidence of commercial pilots was studied to determine whether exposure at work has any influence on the incidence of cancer.
Methods The cohort was established from the files of the Civil Aviation Administration and included people who had valid licenses as commercial pilots between 1946 and 1994. Basic data about their flight careers were recorded, and exposure to cosmic radiation was estimated. The cohort was linked to the Cancer Register of Norway. The observkd number of cases was compared with that expected based on national rates.
Results A group of 3701 male pilots was followed over 70 560 person-years. There were 200 cases of cancer versus 188.8 expected, with a standardized incidence ratio (SIR) of 1.06 and a 95% confidence interval (95% CI) of 0.92-1.22. No significant decreased risk was found for any cancer site. Excess risks were found for malignant melanoma (22 cases SIR 1.8,95% CI 1.1-2.7) and nonmelanoma skin cancer (14 cases, SIR 2.4,95% CI 1.3-4.0). For malignant melanoma, there was a significant trend for the SIR by cumulative dose.
C O ~ C ~ U SF~orO m~osSt c ancer sites, the incidence among pilots did not deviate from that of the general population and could not be related to block hours of flight time or dose. It seems more likely that the excess risks of malignant melanoma and skin cancer are explained by factors related to life-style rather than by conditions at work.

Keywords

Haldorsen T, Reitan JB, Tveten U

Year 2001

Authors Haldorsen T, Reitan JB, Tveten U

Report Name Cancer incidence among Norwegian airline cabin attendants

Publication Int J Epidemiol

Issue-page numbers 30:825–830.doi:10.1093/ije/30.4.825 PMID:11511611

URL http://ije.oxfordjournals.org/content/30/4/825.full.pdf

Abstract

Background Cabin crews are exposed to cosmic radiation at work and this may increase their incidence of radiation-induced cancers. Former studies indicate an increased risk of breast cancer.

Methods A retrospective cohort study was performed. The cohort was established from the files of the Civil Aviation Administration and included people with a valid licence as a cabin attendant between 1950 and 1994. The cohort was linked to the Cancer Registry of Norway. Observed number of cases was compared with expected, based on national rates. Breast cancer incidence was analysed, adjusting for individual fertility variables.

Results A group of 3693 cabin attendants were followed over 72 804 person-years. Among the women, 38 cases of breast cancer were observed (standardized incidence ratio (SIR) = 1.1, 95% CI : 0.8–1.5). Among men excess risks were found for cancers in the upper respiratory and gastric tract (SIR = 6.0, 95% CI : 2.7–11.4) and cancer of the liver (two cases, SIR = 10.8, 95% CI : 1.3–39.2). For both sexes elevated risks were found for malignant melanoma and non-melanoma skin cancer; for men these were SIR = 2.9 (95% CI : 1.1–6.4) and SIR = 9.9 (95% CI : 4.5–18.8) respectively, while for women these were SIR = 1.7 (95% CI : 1.0–2.7) and SIR = 2.9 (95% CI : 1.0–6.9) respectively. For no cancer site was a significant decreased risk found.

Conclusions An increased risk of radiation-induced cancers was not observed. The excess risks of some other cancers are more probably explained by factors related to lifestyle

Keywords Cabin attendants, cancer, cosmic radiation

Ham JR WT, Mueller HA, Sliney DH

Year 1976

Authors WILLIAM T. HAM JR, HAROLD A. MUELLER & DAVID H. SLINEY

Report Name Retinal sensitivity to damage from short wavelength light

Publication Nature

Issue-page numbers 260, 153 - 155 (11 March 1976); doi:10.1038/260153a0

URL http://www.nature.com/nature/journal/v260/n5547/abs/260153a0.html

Abstract

A GROWING body of literature attests to the deleterious effects of long term exposure to light1–8. To define more critically the differences between thermal and photochemical effects, we have exposed the retinae of rhesus monkeys to eight monochromatic laser lines from 1,064–441.6 nm. Thermal damage to the retina is to be expected for the 1,064-nm line since the photopigments are not involved and energy absorption takes place predominantly in the melanin granules of the pigment epithelium and the choroid. Although data on pathogenesis are not yet available, we found some interesting differences in retinal sensitivity in going from the near infrared to the blue wavelengths in the visible spectrum.

Keywords

Ham WT Jr

Year 1983

Authors Ham WT Jr.

Report Name Ocular hazards of light sources: review of current knowledge

Publication J Occup Med

Issue-page numbers 1983 Feb;25(2):101-3.

URL http://www.ncbi.nlm.nih.gov/pubmed/6834158

Abstract Retinal damage is the most important hazard from light. There are three types of retinal damage classified as structural, thermal and photochemical; damage type depends on wavelength, power level and exposure time. Photochemical damage from blue light produces solar retinitis and is postulated to accelerate aging which leads to senile macular degeneration. The lens protects the retina from blue light and near ultraviolet (UV) but at the expense of cataractogenesis. Lens removal exposes retina to near UV that is six times more dangerous than blue light. Filters are recommended to protect lens and retina from blue light and near UV.

Keywords

Authors Ham WT Jr, Mueller HA, Ruffolo JJ Jr, Clarke AM.

Report Name Sensitivity of the retina to radiation damage as a function of wavelength.

Publication Photochemistry and Photobiology

Issue-page numbers Volume 29, Issue 4, pages 735–743, April 1979

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.1979.tb07759.x/abstract

Abstract

Exposure of the retina of the rhesus monkey to visible and infrared radiation from CW optical sources like the Sun, xenon lamps, etc. produces small lesions or scotomata which may be classified as thermal or photochemical, depending on the wavelength and duration of exposure. The action spectrum for the production of retinal lesions has been determined for eight monochromatic laser wavelengths extending from 1064 to 441 nm. The corneal power required to produce a lesion decreases by three orders of magnitude in going from 1064 to 441 nm. Exposure to 1064 nm radiation for 1000 s produces a typical thermal lesion at elevated retinal temperatures. whereas a 1000 s exposure to 441 nm light produces a photochemical lesion at power levels too low to raise the retinal temperature by an appreciable amount (<0.1°). The two types of lesion have entirely different characteristics as will be discussed in some detail. The photopathology of thc photochemical lesion has been studied at postexposure times ranging from 1 h to 90 days and will be demonstrated in a number of histological slides. Moreover, this photopathology correlates well with monocular visual acuity tests in the rhesus monkey as defined by the Landolt ring technique.

To further elucidate the differential effects on the retina of short vs long wavelength CW radiation, we have divided a simulated solar spectrum at sea level into two spectral bands. 400–800 nm and 700–1400 nm, and determined the radiant exposures required to produce very mild lcsions on the rhesus retina for exposure times of 1, 10, 100 and 1000 s. To correlate our data with solar retinitis and eclipse blindness the image diameter or spot size on the retina was 159 μm, corresponding to the image size of the Sun on the human retina. Exposure to the 400–800 nm spectrum for durations of 10 s or greater required approximately 400 J/cm2 to produce a mild photochemical lesion. Reciprocity is maintained over the exposure range 10–1000 s. Radiant exposure to the 700–1400 nm spectrum, on the other hand, required roughly 69,100 J/cm2 for a 1000 s exposure. This was a mild thermal lesion. We were unable to produce a lesion for exposure times less than 1000 s. We interpret these data to mean that solar retinitis and eclipse blindness are primarily photochemical events produced by the short wavelength component of the solar spectrum, and that the infrared component of the solar spectrum plays only a minor role in these retinal pathologies.

Keywords

Ham WT Jr, Ruffolo JJ Jr , Mueller HA, et al. **Year** 1978

Authors W T Ham Jr, J J Ruffolo Jr, H A Mueller, A M Clarke and M E Moon

Report Name Histologic analysis of photochemical lesions produced in rhesus retina by short-wave-length light.

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers October 1978 vol. 17 no. 10 1029-1035

URL http://www.iovs.org/content/17/10/1029?related-urls=yes&legid=iovs;17/10/1029

Abstract The photopathology of retinal lesions produced by extended exposure (1000 sec) to low corneal power levels (62 microW) of blue light (441 nm) was investigated by light microscopy in 20 rhesus eyes over an interval ranging from 1 hr to 90 days after exposure. Results indicate a nonthermal type of photochemical lesion originating in the retinal pigment epithelium and leading to a histological response with hypopigmentation which requires 48 hr to appear. This type of lesion helps to explain solar retinitis and eclipse blindness and has significance for aging and degenerative changes in the retina.

Keywords

Hamilton T **Year** 2005

Authors T. Hamilton

Report Name Influence of environmental light and melatonin upon mammary tumour induction

Publication British Journal of Surgery

Issue-page numbers Volume 56, Issue 10, pages 764–766, October 1969

URL http://onlinelibrary.wiley.com/doi/10.1002/bjs.1800561018/abstract

Abstract article

Keywords

Authors Hammar N, Linnersjö A, Alfredsson L et al.

Report Name Cancer incidence in airline and military pilots in Sweden 1961–1996

Publication Aviat Space Environ Med

Issue-page numbers 73:2–7. PMID:11817615

URL http://www.ncbi.nlm.nih.gov/pubmed/11817615

Abstract

BACKGROUND:

Aircraft pilots are exposed to several agents that may be associated with an increased risk of cancer. Previous studies regarding cancer incidence and mortality in aircraft pilots have not shown a consistent pattern. The aim of this study was to describe the cancer incidence in male Swedish airline and military pilots considering flight hours and aircraft type.
HYPOTHESIS:

Aircraft pilots have an increased risk of certain types of cancer.
METHODS:

Male aircraft pilots with the Swedish Scandinavian Airline System (SAS) (n = 1,490) and military pilots and navigators in the Swedish Air Force (n = 2,808) employed during 1957 1994 were studied regarding cancer incidence during 1961-1996 using the Swedish National Cancer Register. The cancer incidence was compared with that of the general male Swedish population.
RESULTS:

The standardized incidence ratio (SIR) for cancer overall was 1.00 (95% CI 0.80-1.22) for airline pilots, 0.97 (95% CI 0.83-1.10) for military pilots and 0.98 (95% CI 0.87-1.09) for all pilots. Airline pilots had an increased incidence of malignant melanoma of the skin (SIR 2.54) and military pilots of other skin cancer (SIR 2.10). For airline pilots with > 10,000 block hours or high-altitude long-distance duty results were similar concerning cancer overall and skin cancers.
CONCLUSIONS:

Swedish pilots had an overall cancer incidence similar to the male general population. An increased incidence of malignant melanoma in airline pilots and of other skin cancer in military pilots could be associated with exposure to UV radiation either at work or outside work.

Keywords

Hammer SB, Ruby CL, Brager AJ **Year** 2010

Authors Steven B. Hammer, Christina L. Ruby, Allison J. Brager, Rebecca A. Prosser, and J. David Glass

Report Name ENVIRONMENTAL MODULATION OF ALCOHOL INTAKE IN HAMSTERS: EFFECTS OF WHEEL-RUNNING AND CONSTANT LIGHT EXPOSURE

Publication Alcohol Clin Exp Res

Issue-page numbers September 1; 34(9): 1651–1658.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2929273/

Abstract

BACKGROUND
Alcohol abuse leads to marked disruptions of circadian rhythms, and these disturbances in themselves can increase the drive to drink. Circadian clock timing is regulated by light, as well as by nonphotic influences like food, social interactions, and wheel-running. We previously reported that alcohol markedly disrupts photic and nonphotic modes of circadian rhythm regulation in Syrian hamsters. As an extension of this work, we characterize the hedonic interrelationship between wheel-running and ethanol intake and the effects of environmental circadian disruption (long-term exposure to constant light [LL]) on the drive to drink.
METHODS
First, we tested the effect of wheel running on chronic free-choice consumption of a 20% (v/v) ethanol (EtOH) solution and water. Second, the effect of this alcohol drinking on wheel running in alcohol-naive animals was investigated. Third, we assessed the influence of LL, known to suppress locomotor activity and cause circadian rhythm disruption, on EtOH consumption and wheel-running behavior.
RESULTS
Inhibitory effects of wheel running on EtOH intake and vice versa were observed. Exposure to LL, while not affecting EtOH intake, induced rhythm splitting in 75% of the animals. Notably, the splitting phenotype was associated with lower levels of EtOH consumption and preference prior to, and throughout, the period of LL exposure.
CONCLUSIONS
These results are evidence that exercise may offer an efficacious clinical approach to reducing EtOH intake. Also, predisposition for light-induced (or other) forms of circadian disruption may modulate the drive to drink.

Keywords circadian, ethanol, exercise, constant light, rhythm splitting

Hanifin JP, Stewart KT, Smith P, et al. **Year** 2006

Authors John P. Hanifin, Karen T. Stewart, Peter Smith, Roger Tanner, Mark Rollag and George C. Brainard

Report Name High-intensity red light suppresses melatonin

Publication Chronobiology International

Issue-page numbers 23:1-2, 251-268

URL http://informahealthcare.com/doi/abs/10.1080/07420520500521988

Abstract Early studies on rodents indicated that the long-wavelength portion of the spectrum (orange- and red-appearing light) could influence circadian and neuroendocrine responses. Since then, both polychromatic and analytic action spectra in various rodent species have demonstrated that long-wavelength light is very weak, if not entirely inactive, for regulating neurobehavioral responses. Since testing of monochromatic light wavelengths above 600 nm is uncommon, many researchers have assumed that there is little to no effect of red light on the neuroendocrine or circadian systems. The aims of the following studies were to test the efficacy of monochromatic light above 600 nm for melatonin suppression in hamsters and humans. Results in hamsters show that 640 nm monochromatic light at 1.1×1017 photons/cm2 can acutely suppress pineal melatonin levels. In normal healthy humans, equal photon density exposures of 1.9×1018 photons/cm2 at 460, 630, and 700 nm monochromatic light elicited a significant melatonin suppression at 460 nm and small reductions of plasma melatonin levels at 630 and 700 nm. These findings are discussed relative to the possible roles of classical visual photoreceptors and the recently discovered intrinsically photosensitive retinal ganglion cells for circadian phototransduction. That physiology, and its potential for responding to red light, has implications for domestic applications involving animal care, the lighting of typical human environments, and advanced applications such as space exploration.

Keywords Long-wavelength light, Red light, Circadian rhythm, Melatonin, Pineal gland

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Hansen J **Year** 2001

Authors Hansen J

Report Name Increased breast cancer risk among women who work predominantly at night

Publication Epidemiology

Issue-page numbers 12:74–77.doi:10.1097/00001648-200101000-00013 PMID:11138824

URL http://www.jstor.org/pss/3703682

Abstract Irregular working hours, including working at night, have serious psychological and physiological effects. In a nationwide population-based case-control study, we investigated the breast cancer risk among 30- to 54-year-old Danish women who worked predominantly at night. Individual employment histories were reconstructed back to 1964 for each of 7035 women with breast cancer and their individually matched controls from the records of a nationwide pension scheme with compulsory membership. Odds ratios, including 5 years of induction time and adjusted for socio-economic status, age at the birth of first and last child and number of children, were estimated by conditional logistic regression analysis. The odds ratio for breast cancer among women who worked at night at least half of a year was 1.5 (95% confidence interval, 1.2 to 1.7), and there was a tendency to increasing odds ratio by increasing duration of nighttime employment.

Keywords

Hansen J

Year 2001

Authors Johnni Hansen

Report Name Light at Night, Shiftwork, and Breast Cancer Risk

Publication Journal of the National Cancer Institute

Issue-page numbers Vol. 93, No. 20, October 17, 2001

URL http://jnci.oxfordjournals.org/content/93/20/1513.full.pdf

Abstract Editorial - Breast cancer is the most commonly diagnosed female noncutaneous cancer in the United States and in Europe. The etiology of breast cancer is primarily unknown, with an estimated one quarter of all breast cancers possibly due to heritable factors (1) and only a minor proportion possibly due to already established environmental risk factors, such as early age at menarche, older age at first pregnancy, and delayed menopause (2). Because the incidence of breast cancer in many countries is increasing, for unclear reasons, it is not surprising that society is demanding explanations for the increased incidence of the disease and that researchers are searching for new causes. One avenue of research has been the so-called “man-made endocrine disrupting chemicals,” such as 2-(chlorphenyl)-2-(4-chlorphenyl)-1,1,1-trichlorethan (DDT), polychlorinated biphenyls, or nonyl phenols (3). So far, however, the results from this research have been sparse in expanding our knowledge about risk factors for breast cancer.

Keywords

Hansen J

Year 2001

Authors Hansen J

Report Name Breast Cancer Among Women Who Work at Night

Publication Epidemiology

Issue-page numbers 12:588–599. PMID:11505182

URL http://journals.lww.com/epidem/Fulltext/2001/09000/Breast_Cancer_Among_Women_Who_Work_at_Night.24.aspx

Abstract Although most breast cancers appear to be attributable to environmental exposures, 1 little is known about specific causes for this disease. Therefore, it is important to conduct epidemiologic studies in order to test all biological plausible hypotheses. It has been suggested that light-at-night may cause breast cancer and other hormone-related tumours. 2 Despite the high prevalence of persons who work at night and therefore are exposed to light-at-night, no major study has investigated this hypothesis. As an initial step to evaluate an association between night work and female breast cancer, we used a comprehensive data linkage for this purpose, in which it was possible to control for the major confounder, i.e. the reproductive outcome.

Keywords

Authors Johnni Hansen, Christina F Lassen

Report Name Nested caseecontrol study of night shift work and breast cancer risk among women in the Danish military

Publication Occup Environ Med

Issue-page numbers doi:10.1136/oemed-2011-100240

URL http://press.psprings.co.uk/oem/may/oem100240.pdf

Abstract

Objectives Growing but limited evidence suggests that night shift work is associated with breast cancer. The authors conducted a nationwide caseecontrol study nested within a cohort of 18 551 female military employees born in 1929e1968 to investigate the risk for breast cancer after night shift work and to explore the role of leisure time sun exposure and diurnal preference.
Methods The authors documented 218 cases of breast cancer (1990e2003) and selected 899 age-matched controls from the cohort by incidence density sampling. Information on shift work, sun exposure habits, diurnal preference and other potential confounders was obtained from a structured questionnaire. ORs were estimated by multivariate conditional logistic regression.
Results Overall, the authors observed an adjusted OR of 1.4 (95% CI 0.9 to 2.1) among women with ever compared with never night shifts. The RR for breast cancer tended to increase with increasing number of years of night shift work (p¼0.03) and with cumulative number of shifts (p¼0.02),with a neutral risk for fewer than three night shifts per week. The OR for the group with the highest tertile of cumulative exposure was 2.3 (95% CI 1.2 to 4.6). The most pronounced effect of night shift work on breast cancer risk was observed in women with morning chronotype preference and intense night shifts (OR¼3.9, 95% CI 1.6 to 9.5). Night shift workers tended to sunbathe more frequently than day workers.
Conclusions The results indicate that frequent night shift work increases the risk for breast cancer and suggest a higher risk with longer duration of intense night shifts. Women with morning preference who worked on night shifts tended to have a higher risk than those with evening preference.

Keywords

Authors Johnni Hansen, Richard G. Stevens

Report Name Case-control study of shift-work and breast cancer risk in Danish nurses: Impact of shift systems

Publication European Journal of Cancer

Issue-page numbers August 2011, (in press)

URL http://www.ncbi.nlm.nih.gov/pubmed/21852111

Abstract

BACKGROUND:

Working outside normal daytime hours is increasing worldwide and is now one of the most widespread potential carcinogenic occupational exposures. There is sufficient evidence in experimental animals that light exposure during the biologic night increases tumour growth and limited epidemiologic evidence that night shift-work cause breast cancer. Existing studies had crude definitions of shift-work and did not discriminate between shift-work systems (e.g. permanent versus rotating or evening versus night).
METHODS:

We performed an interview based nested case-control study within a nationwide cohort of Danish nurses, including detailed information on lifetime shift-work and potential confounders. Cases of primary breast cancer (n=310) were identified from the nationwide Danish Cancer Registry. Four control nurses were selected for each case by incidence density sampling. Odds rations (ORs) and 95% confidence intervals (CIs) were estimated by conditional logistic regression, with adjustment for potential confounders.
FINDINGS:

Overall, nurses who worked rotating shifts after midnight had a significantly increased OR (1.8; CI 1.2-2.8) for breast cancer compared to nurses with permanent day work. No association was found in a small group of nurses with evening work and no night work (OR=0.9; 0.4-1.9). The subgroup of nurses with periods of permanent night shift in addition to rotating night and day shifts experienced an OR of 2.9 (1.1-8.0). For nurses working after midnight compared to nurses never ending work before midnight, OR in the third tertile of cumulative number of shifts was 2.2 (1.5-3.2). In an analysis of different rotating shift systems, the highest OR (2.6; 1.8-3.8) was observed for long-term day-night rotating shifts.
INTERPRETATION:

The results provide further evidence that night shift-work may increase the risk for breast cancer and suggest that the largest impact on risk is associated with the most disruptive shifts.
FUNDING:

Danish Cancer Society and National Programme of Environmental Health Research.

Keywords

Hansen MA, Garde HA, Hansen J **Year** 2006

Authors Hansen MA, Garde HA, Hansen J

Report Name Diurnal urinary 6-sulfatoxymelatonin levels among healthy Danish nurses during work and leisure time

Publication Chronobiol Int

Issue-page numbers 23:1203–1215 doi:10.1080/07420520601100955. PMID:17190706

URL http://www.mendeley.com/research/diurnal-urinary-6sulfatoxymelatonin-levels-among-healthy-danish-nurses-during-work-leisure-time/

Abstract The present study aims to examine the influence of evening and night shift work, compared to day shift work, on melatonin secretion in nurses in a field setting. Effects were examined during a workday and during a day off. Both fixed schedules and mixed or rotating schedules were studied. In total, 170 nurses were studied: 89 nurses worked fixed schedules, 27 nurses worked the day shift, 12 nurses worked the evening shift, 50 nurses worked the night shift, and 82 nurses worked mixed schedules, with data collected during a day (n = 17), evening (n = 14), or night shift (n = 50). All spot urine samples were collected during 24 h from the participants on a work day and on a day off and were analyzed for 6-sulphatoxymelatonin. On the day of urine sampling, participants filled in the Karolinska Sleep Diary. Additional information was collected through a telephone interview. Data were analyzed using a mixed procedure with autoregressive covariance structure. The present study showed that shift work affected the concentrations of 6-sulphatoxymelatonin in the short term by lower excretion in urine from nurses working the night compared to day shift on a workday and on a day off as well. No significant differences were observed between a workday and a day off when doing day and evening shifts, irrespective of mixed and fixed schedules. Sleep length was reduced workdays (from 6.1-6.8 h) among all nurses, compared to days off (from 7.8-8.7 h).

Keywords

Hao H, Rivkees SA **Year** 0

Authors Haiping Hao and Scott A. Rivkees

Report Name The biological clock of very premature primate infants is responsive to light

Publication PNAS

Issue-page numbers March 2, 1999 vol. 96 no. 5 2426-2429

URL http://www.pnas.org/content/96/5/2426.short

Abstract Each year more than 250,000 infants in the United States are exposed to artificial lighting in hospital nurseries with little consideration given to environmental lighting cycles. Essential in determining whether environmental lighting cycles need to be considered in hospital nurseries is identifying when the infant's endogenous circadian clock becomes responsive to light. Using a non-human primate model of the developing human, we examined when the circadian clock, located in the hypothalamic suprachiasmatic nuclei (SCN), becomes responsive to light. Preterm infant baboons of different ages were exposed to light (5,000 lux) at night, and then changes in SCN metabolic activity and gene expression were assessed. After exposure to bright light at night, robust increases in SCN metabolic activity and gene expression were seen at ages that were equivalent to human infants at 24 weeks after conception. These data provide direct evidence that the biological clock of very premature primate infants is responsive to light.

Keywords

Authors Hara R, Wan K, Wakamatsu H, Aida R, Moriya T, Akiyama M, Shibata S.

Report Name Restricted feeding entrains liver clock without participation of the suprachiasmatic nucleus

Publication Genes Cells

Issue-page numbers 6:269–278 doi:10.1046/j.1365-2443.2001.00419.x. PMID:11260270

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2443.2001.00419.x/full

Abstract

BACKGROUND:

There are two main stimuli that entrain the circadian rhythm, the light-dark cycle (LD) and restricted feeding (RF). Light-induced entrainment requires induction of the Per1 and Per2 genes in the suprachiasmatic nucleus (SCN), the locus of a main oscillator. In this experiment, we determined whether RF resets the expression of circadian clock genes in the mouse liver with or without participation of the SCN.
RESULTS:

Mice were allowed access to food for 4 h during the daytime (7 h advance of feeding time) under LD or constant darkness (DD). The peaks of mPer1, mPer2, D-site-binding protein (Dbp) and cholesterol 7alpha-hydroxylase (Cyp7A) mRNA in the liver were advanced 6-12 h after 6 days of RF, whereas those in SCN were unaffected. The advance of mPer expression in the liver by RF was still observed in SCN-lesioned mice. A 7 h advance in the LD cycle advanced the peaks of clock gene expression in both the liver and SCN, whereas, a shift in the LD did not move the phase of the liver clock when the shift was carried out under a fixed RF schedule during the night-time.
CONCLUSIONS:

These results suggest that restricted feeding strongly entrained the expression of circadian clock genes in the liver without the participation of an SCN clock function.

Keywords

Harber LC, Whitman GB, Armstrong RB, Deleo VA — *Year* 1985

Authors Harber LC, Whitman GB, Armstrong RB, Deleo VA.

Report Name Photosensitivity diseases related to interior lighting

Publication Annals of the New York Academy of Sciences

Issue-page numbers Volume 453, The Medical and Biological Effects of Light pages 317–327, September 1985

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1985.tb11820.x/abstract

Abstract The most frequently used source of indoor lighting is the fluorescent tube. Although there are major variations in phosphors, the majority of these lamps are safe, efficient, and economical illuminators. These fluorescent light sources are currently our primary source of visible light; however, they emit small amounts of ultraviolet A light (UVA) as well as a somewhat larger percentage of infrared radiation. Photosensitivity diseases have been reported in each of these three broad wavelength bands. Specific examples include heat urticaria from infrared exposure, contact photosensitivity of the phototoxic type following exposure to dyes and visible light, and two relatively rare but disabling conditions from ultraviolet A exposure--solar urticaria and contact photosensitivity of the photoallergic type (persistent light reaction). During the past five years, eight patients with photosensitivity induced by musk ambrette and UVA have been treated at Columbia-Presbyterian Medical Center; six of these have been severely disabled and satisfy the criteria for persistent light reactors. Fifteen patients with solar urticaria have also been observed. Ten of these had reactions in the UVA range. The clinical and laboratory findings of these two groups of patients were presented.

Keywords

Hardeland R — *Year* 2005

Authors Hardeland R

Report Name Antioxidative protection by melatonin: multiplicity of mechanisms from radical detoxification to radical avoidance

Publication Endocrine

Issue-page numbers 27:119–130 doi:10.1385/ENDO:27:2:119. PMID:16217125

URL http://www.springerlink.com/content/c571484q84163611/

Abstract Melatonin has been shown to protect against oxidative stress in various, highly divergent experimental systems. There are many reasons for its remarkable protective potential. Signaling effects comprise the upregulation of antioxidant enzymes, such as superoxide dismutases, peroxidases, and enzymes of glutathione supply, downregulation of prooxidant enzymes, such as nitric oxide synthases and lipoxygenases, and presumably also the control of quinone reductase 2. Other mechanisms are based on direct interactions with several reactive oxygen and nitrogen species. Among these reactions, the capacity of easily undergoing single-electron transfer reactions is of particular importance. Electron donation by melatonin is not only an aspect of direct radical scavenging, but additionally represents the basis for formation of the protective metabolites AMK (N 1-acetyl-N 2-formyl-5methoxykynuramine) and AMK (N 1-acetyl-5methoxykynuramine). Recent investigations on mitochondrial metabolism indicate that melatonin as well as AMK are capable of supporting the electron flux through the respiratory chain, of preventing the breakdown of the mitochondrial membrane potential, and of decreasing electron leakage, thereby reducing the formation of superoxide anions. Radical avoidance is a new line of investigation, which exceeds mitochondrial actions and also comprises antiexcitatory effects and contributions to the maintenance of internal circadian phase relationships.

Keywords ntioxidants - free radicals - kynuramines - melatonin - mitochondria

Hardeland R

Year 2012

Authors Rüdiger Hardeland

Report Name Melatonin in Aging and Disease —Multiple Consequences of Reduced Secretion, Options and Limits of Treatment

Publication Aging and Disease

Issue-page numbers

URL http://www.aginganddisease.org/AD-2012-Hardeland.pdf

Abstract Melatonin is a pleiotropically acting regulator molecule, which influences numerous physiological functions. Its secretion by the pineal gland progressively declines by age. Strong reductions of circulating melatonin are also observed in numerous disorders and diseases, including Alzheimer's disease, various other neurological and stressful conditions, pain, cardiovascular diseases, cases of cancer, endocrine and metabolic disorders, in particular diabetes type 2. The significance of melatonergic signaling is also evident from melatonin receptor polymorphisms associated with several of these pathologies. The article outlines the mutual relationship between circadian oscillators and melatonin secretion, the possibilities for readjustment of rhythms by melatonin and its synthetic analogs, the consequences for circadian rhythm-dependent disorders concerning sleep and mood, and limits of treatment. The necessity of distinguishing between short-acting melatonergic effects, which are successful in sleep initiation and phase adjustments, and attempts of replacement strategies is emphasized. Properties of approved and some investigational melatonergic agonists are compared.

Keywords Alzheimer's Disease; Circadian Rhythms; Diabetes; Melatonin; Mood Disorders; Parkinson's Disease; Sleep

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Hardeland R

Year 2012

Authors R¨udiger Hardeland

Report Name Neurobiology, Pathophysiology, and Treatment of Melatonin

Publication The ScientificWorld Journal

Issue-page numbers Volume 2012, Article ID 640389, 18 pages

URL http://downloads.tswj.com/2012/640389.pdf

Abstract Melatonin is a highly pleiotropic signaling molecule, which is released as a hormone of the pineal gland predominantly during night. Melatonin secretion decreases during aging. Reduced melatonin levels are also observed in various diseases, such as types of dementia, some mood disorders, severe pain, cancer, and diabetes type 2. Melatonin dysfunction is frequently related to deviations in amplitudes, phasing, and coupling of circadian rhythms. Gene polymorphisms of melatonin receptors and circadian oscillator proteins bear risks for several of the diseases mentioned. A common symptom of insufficient melatonin signaling is sleep disturbances. It is necessary to distinguish between symptoms that are curable by short melatonergic actions and others that require extended actions during night.Melatonin immediate release is already effective, atmoderate doses, for reducing difficulties of falling asleep or improving symptoms associated with poorly coupled circadian rhythms, including seasonal affective and bipolar disorders. For purposes of a replacement therapy based on longer-lasting melatonergic actions, melatonin prolonged release and synthetic agonists have been developed. Therapies with melatonin or synthetic melatonergic drugs have to consider that these agents do not only act on the SCN, but also on numerous organs and cells in which melatonin receptors are also expressed.

Keywords

Hardeland R, Poeggeler B **Year** 2003

Authors Hardeland R, Poeggeler B

Report Name Non-vertebrate melatonin

Publication J Pineal Res

Issue-page numbers 34:233–241 doi:10.1034/j.1600-079X.2003.00040.x. PMID:12662344

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079X.2003.00040.x/abstract

Abstract Melatonin has been detected in bacteria, eukaryotic unicells, macroalgae, plants, fungi and various taxa of invertebrates. Although precise determinations are missing in many of these organisms and the roles of melatonin are still unknown, investigations in some species allow more detailed conclusions. Non-vertebrate melatonin is not necessarily circadian, and if so, not always peaking at night, although nocturnal maxima are frequently found. In the cases under study, the major biosynthetic pathway is identical with that of vertebrates. Mimicking of photoperiodic responses and concentration changes upon temperature decreases have been studied in more detail only in dinoflagellates. In plants, an involvement in photoperiodism seems conceivable but requires further support. No stimulation of flowering has been demonstrated to date. A participation in antioxidative protection might be possible in many aerobic non-vertebrates, although evidence for a contribution at physiological levels is mostly missing. Protection from stress by oxidotoxins or/and extensions of lifespan have been shown in very different organisms, such as the dinoflagellate Lingulodinium, the ciliate Paramecium, the rotifer Philodina and Drosophila. Melatonin can be taken up from the food, findings with possible implications in ecophysiology as well as for human nutrition and, with regard to high levels in medicinal plants, also in pharmacology.

Keywords algae; antioxidative protection; circadian rhythms; dinoflagellates; fungi; invertebrates; melatonin; plants

Harmar AJ, Marston HM, Shen S et al. **Year** 2002

Authors Anthony J. Harmar, Hugh M. Marston1, Sanbing Shen, Christopher Spratt, Katrine M. West, W.John Sheward, Christine F. Morrison, Julia R. Dorin, Hugh D. Piggins, Jean-Clauc

Report Name The VPAC(2) receptor is essential for circadian function in the mouse suprachiasmatic nuclei

Publication Cell

Issue-page numbers 109:497–508 doi:10.1016/S0092-8674(02)00736-5. PMID:12086606

URL http://www.cell.com/abstract/S0092-8674%2802%2900736-5

Abstract The neuropeptides pituitary adenylate cyclase-activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP) are implicated in the photic entrainment of circadian rhythms in the suprachiasmatic nuclei (SCN). We now report that mice carrying a null mutation of the VPAC2 receptor for VIP and PACAP (Vipr2−/−) are incapable of sustaining normal circadian rhythms of rest/activity behavior. These mice also fail to exhibit circadian expression of the core clock genes mPer1, mPer2, and mCry1 and the clock-controllec gene arginine vasopressin (AVP) in the SCN. Moreover, the mutants fail to show acute induction of mPer1 and mPer2 by nocturnal illumination. This study highlights the role of intercellular neuropeptidergic signaling in maintenance of circadian function within the SCN.

Keywords

Harrington JM

Year 2001

Authors J M Harrington

Report Name Health effects of shift work and extended hours of work

Publication Occup Environ Med

Issue-page numbers 2001;58:68-72 doi:10.1136/oem.58.1.68

URL http://oem.bmj.com/content/58/1/68.full

Abstract Normal" hours of work are generally taken to mean a working day with hours left for recreation and rest. Rest is a night time activity, work a daytime activity. This review is concerned with those who work other schedules either on shifts or with extended hours which transcend the day-night work-sleep pattern.

Such abnormal" working hours are not a modern phenomenon. Ramazzini (1633–1714) noted that bakers, innkeepers, and soldiers worked such hours. The advent of the industrial revolution led to many people working long hours until legislation was introduced to curtail the worst vicissitudes of the new factory based economy.

Keywords circadian rhythm, shift work

Harris W

Year 1977

Authors Harris W

Report Name Fatigue, circadian rhythms, and truck accidents

Publication In: Vigilance Theory, Operational Performance, and Physiological Correlate

Issue-page numbers New York: Plenum Press. pp. 1033–1046

URL N/A

Abstract N/A

Keywords

Harrison EM, Gorman MR **Year** 2012

Authors Elizabeth M. Harrison and Michael R. Gorman

Report Name Changing the Waveform of Circadian Rhythms: Considerations for Shift-Work

Publication Front Neurol

Issue-page numbers 2012; 3: 72.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3340571/

Abstract Circadian disruption in shift-work is common and has deleterious effects on health and performance. Current efforts to mitigate these harms reasonably focus on the phase of the circadian pacemaker, which unfortunately in humans, shifts slowly and often incompletely. Temporal reorganization of rhythmic waveform (i.e., the shape of its 24 h oscillation), rather than phase, however, may better match performance demands of shift-workers and can be quickly and feasibly implemented in animals. In fact, a bifurcated pacemaker waveform may permit stable entrainment of a bimodal sleep/wake rhythm promoting alertness in both night and daylight hours. Although bifurcation has yet to be formally assessed in humans, evidence of conserved properties of circadian organization and plasticity predict its occurrence: humans respond to conventional manipulations of waveform (e.g., photoperiodism); behaviorally, the sleep/wake rhythm is adaptable; and finally, the human circadian system likely derives from the same multiple cellular oscillators that permit waveform flexibility in the rodent pacemaker. In short, investigation into untried manipulations of waveform in humans to facilitate adjustment to challenging schedules is justified.

Keywords waveform, shift-work, split schedules, dysrhythmia, night shift

Hasan T, Nyberg F, Stephansson E, Puska P, Häkkinen M, Sarna S, Ros AM, Ranki **Year** 1997

Authors Hasan T, Nyberg F, Stephansson E, Puska P, Häkkinen M, Sarna S, Ros AM, Ranki A.

Report Name Photosensitivity in lupus erythematosus, UV photoprovocation results compared with history of photosensitivity and clinical findings

Publication Br J Dermatol

Issue-page numbers 1997 May;136(5):699-705.

URL http://www.ncbi.nlm.nih.gov/pubmed/9205502

Abstract Photosensitivity, one of the presenting symptoms in lupus erythematosus (LE), is still poorly defined and varying prevalence figures have been reported. The possibility of a coexisting photodermatosis, especially polymorphous light eruption (PLE), has often not been taken into account. We report the results of ultraviolet A (UVA) and B (UVB) photoprovocation tests in 67 clinically photosensitive patients who had confirmed discoid LE (DLE), systemic LE (SLE) or subacute cutaneous LE (SCLE). The results are compared with a detailed history of photosensitivity and with clinical and serological findings. A pathological photoprovocation reaction, graded as weak, moderate or strong, was induced with either UVA or UVB in 69% of patients with LE, in 100% of those with SCLE, in 70% of those with SLE and in 64% of those with DLE, but in none of 14 controls. Only 16% of the pathological reactions were strong and long-lasting, resembling LE lesions, while 48% were moderate or weak and transient, clinically like PLE. Fifty-three per cent of the provocation reactions which were biopsied showed a PLE-like histology or a non-specific inflammatory reaction, and most of them were clinically moderate or weak reactions of short duration. In the remaining, mostly clinically strong or long-lasting reactions, the histology was consistent with LE. A history of sunlight sensitivity did not predict a pathological photoprovocation result but a positive association between the presence of SSA/Ro or SSB/La antibodies and a pathological photoprovocation reaction was found. We have shown that PLE coexists with LE and that both PLE- and LE-like lesions can be induced with UV radiation in LE patients.

Keywords

Hashimotoa S, Kohsakab M, Nakamuraa K, et al. ***Year*** 1997

Authors Satoko Hashimotoa, Masako Kohsakab, Kouji Nakamuraa, Hiroshi Honmab, Sato Honmaa, Ken-ichi Honma

Report Name Midday exposure to bright light changes the circadian organization of plasma melatonin rhythm in humans

Publication Neuroscience Letters

Issue-page numbers Volume 221, Issues 2-3, 17 January 1997, Pages 89-92

URL http://www.sciencedirect.com/science/article/pii/S0304394096132912

Abstract

Effects of bright light exposure at midday were examined on plasma melatonin rhythm in humans under controlled living conditions. Bright light of 5000 lx was provided from the ceiling at midday (1100–1700 h) for 3 consecutive days and the circadian rhythm in plasma melatonin was determined from the fourth to fifth day. The control study was performed in the same subjects who spend four days under dim light conditions (less than 200 lx). The subjects were allowed to sleep from 2400 to 0800 h. The onset phase, but not the end phase, of plasma melatonin rhythm was significantly phase-advanced by bright light exposure. Furthermore, the area under the curve of nocturnal melatonin rise was significantly larger under bright light exposure than under dim light. These findings indicate that midday exposure to bright light for 3 consecutive days changes the circadian organization of plasma melatonin rhythm in humans.

Keywords Bright light; Phase-shift; Melatonin; Circadian rhythm; Humans; Multi-oscillator

Hasler G, Buysse DJ, Klaghofer R et al. **Year** 2004

Authors Gregor Hasler; Daniel J. Buysse; Richard Klaghofer; Alex Gamma; Vladeta Ajdacic; Dominique Eich; Wulf Rössler, MA; Jules Angst

Report Name The association between short sleep duration and obesity in young adults: a 13-year prospective study

Publication Sleep

Issue-page numbers 27:661–666. PMID:15283000

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=25997

Abstract

Study Objectives:

Obesity has become a major health problem with increasing prevalence. Given the limited availability of effective treatment of weight problems, the identification of potentially modifiable risk factors may lead to preventive approaches to obesity. The objective of this study was to test the hypothesis that short sleep duration is associated with obesity and weight gain during young adulthood.
Design:

Prospective single-age cohort study of young adults. Information was derived from 4 interviews when participants were ages 27, 29, 34, and 40 years.
Setting:

Community setting.
Participants:

496 young adults.
Measurements and Results:

Trained health professionals administered a semistructured interview for psychiatric and medical conditions and health habits. This study showed an association between short sleep duration and obesity (at age 27 years, odds ratio: 7.4, 95% confidence interval: 1.3-43.1) and a negative association between sleep duration and body mass index in young adults. These associations persisted after controlling for a variety of potentially confounding variables, including family history of weight problems, levels of physical activity, and demographic variables. Associations between sleep duration and obesity diminished after age 34 years. There was a trend (P = .08) for average change rate of weight gain to be negatively associated with average change rate of sleep duration.
Conclusions:

Because sleep duration is a potentially modifiable risk factor, these findings might have important clinical implications for the prevention and treatment of obesity.

Keywords

Hastings MH

Year 2000

Authors Hastings MH

Report Name Circadian clockwork: two loops are better than one

Publication Nat Rev Neurosci

Issue-page numbers 1:143–146 doi:10.1038/35039080. PMID:11252777

URL http://www.nature.com/nrn/journal/v1/n2/abs/nrn1100_143a.html

Abstract The spectacularly successful race over the past three years to place our understanding of the circadian clockwork of mammals into a molecular framework is beginning to yield the cardinal example of the molecular-genetic control of behaviour. This perspective describes recent evidence for the conservation of a double-loop, autoregulatory feedback mechanism across the best understood eukaryotic circadian systems, and discusses how these findings may illuminate some long-standing puzzles concerning our subliminal sense of circadian time.

Keywords

Hastings MH, Herzog ED

Year 2004

Authors Hastings MH, Herzog ED

Report Name Clock genes, oscillators, and cellular networks in the suprachiasmatic nuclei

Publication J Biol Rhythms

Issue-page numbers 19:400–413 doi:10.1177/0748730404268786. PMID:15534320

URL http://jbr.sagepub.com/content/19/5/400

Abstract The mammalian SCN contains a biological clock that drives remarkably precise circadian rhythms in vivo and in vitro. Recent advances have revealed molecular and cellular mechanisms required for the generation of these daily rhythms and their synchronization between SCN neurons and to the environmental light cycle. This review of the evidence for a cell-autonomous circadian pacemaker within specialized neurons of the SCN focuses on 6 genes implicated within the pace making mechanism, an additional 4 genes implicated in pathways from the pacemaker, and the intercellular and intracellular mechanisms that synchronize SCN neurons to each other and to solar time.

Keywords entrainment, stability, Period gene, BMAL1, vasopressin, vasoactive intestinal polypeptide, Cryptochrome, multielectrode

Hastings MH, Reddy AB, Maywood ES **Year** 2003

Authors Hastings MH, Reddy AB, Maywood ES

Report Name A clockwork web: circadian timing in brain and periphery, in health and disease

Publication Nat Rev Neurosci

Issue-page numbers 4:649–661 doi:10.1038/nrn1177. PMID:12894240

URL http://www.nature.com/nrn/journal/v4/n8/links/nrn1177_l.html

Abstract The hypothalamic suprachiasmatic nuclei (SCN) are our principal circadian oscillator, coordinating daily cycles of physiology and behaviour that adapt us to the world. Local versions of the SCN clockwork are also active in peripheral, non-neural tissues, driving the tissue-specific cycles of gene expression that underpin circadian organization. These local oscillators are tuned to each other, and to solar time, by neuroendocrine and metabolic cues that depend on the SCN. The discovery of these local circadian clocks forces a re-appraisal of established models of circadian biology. It also presents new avenues for therapeutic intervention in conditions where disturbance of circadian gene expression is an important cause of morbidity.

Keywords

Hätönena T, Alila-Johanssona A, Mustanojaa S, Laakso M **Year** 1999

Authors Taina Hätönena, a, Aino Alila-Johanssona, a, Satu Mustanojaa, a, Maija-Liisa Laakso

Report Name Suppression of melatonin by 2000-lux light in humans with closed eyelids

Publication Biological Psychiatry

Issue-page numbers Volume 46, Issue 6, 15 September 1999, Pages 827-831

URL http://www.sciencedirect.com/science/article/pii/S0006322398003576

Abstract Background: In order to clarify the role of light in regulating body functions in sleeping humans, we studied whether the light-sensitive pineal hormone melatonin can be suppressed by facial light exposure in subjects with closed eyelids.

Methods: Eight healthy volunteers participated in 3 nightly sessions: a dim-light control session (<10 lux) and two light-exposure sessions (2000 lux, 60 min between 2400 and 0200 h). One light exposure occurred with eyes open and the other with eyes closed. Saliva samples were collected at least every hour from 1900 to 0300 h. Melatonin concentrations were measured by radioimmunoassay.

Results: Salivary melatonin concentrations decreased only in 2 of the 8 volunteers during light-exposure sessions with eyes closed. On average, light exposure did not decrease the salivary melatonin concentration.

Conclusions: Because indoor illuminance is usually much lower than 2000 lux, light is probably ineffective in regulating the neuroendocrine hypothalamic functions in people during their sleep. Nevertheless, the possibility remains that higher illuminances, often used for therapeutic purposes, can inhibit the secretion of melatonin even in sleeping patients.

Keywords Melatonin; pineal gland; circadian rhythms; lighting; light therapy

Authors Hatori M, Hirota T, Iitsuka M, Kurabayashi N, Haraguchi S, Kokame K, Sato R, Nakai A, Miyata T, Tsutsui K, Fukada Y.

Report Name Light-dependent and circadian clock-regulated activation of sterol regulatory element-binding protein, X-box-binding protein 1, and heat shock factor pathways.

Publication Proc Natl Acad Sci U S A

Issue-page numbers 2011 Mar 22;108(12):4864-9. Epub 2011 Mar 7

URL http://www.ncbi.nlm.nih.gov/pubmed/21383147

Abstract

The circadian clock is phase-delayed or -advanced by light when given at early or late subjective night, respectively. Despite the importance of the time-of-day-dependent phase responses to light, the underlying molecular mechanism is poorly understood. Here, we performed a comprehensive analysis of light-inducible genes in the chicken pineal gland, which consists of light-sensitive clock cells representing a prototype of the clock system. Light stimulated expression of 62 genes and 40 ESTs by >2.5-fold, among which genes responsive to the heat shock and endoplasmic reticulum stress as well as their regulatory transcription factors heat shock factor (HSF)1, HSF2, and X-box-binding protein 1 (XBP1) were strongly activated when a light pulse was given at late subjective night. In contrast, the light pulse at early subjective night caused prominent induction of E4bp4, a key regulator in the phase-delaying mechanism of the pineal clock, along with activation of a large group of cholesterol biosynthetic genes that are targets of sterol regulatory element-binding protein (SREBP) transcription factor. We found that the light pulse stimulated proteolytic formation of active SREBP-1 that, in turn, transactivated E4bp4 expression, linking SREBP with the light-input pathway of the pineal clock. As an output of light activation of cholesterol biosynthetic genes, we found light-stimulated pineal production of a neurosteroid, 7α-hydroxypregnenolone, demonstrating a unique endocrine function of the pineal gland. Intracerebroventricular injection of 7α-hydroxypregnenolone activated locomotor activities of chicks. Our study on the genome-wide gene expression analysis revealed time-of-day-dependent light activation of signaling pathways and provided molecular connection between gene expression and behavior through neurosteroid release from the pineal gland.

Keywords

Hattar S, Kumar M, Park A, et al. **Year** 2006

Authors SAMER HATTAR, MONICA KUMAR, ALEXANDER PARK, PATRICK TONG, JONATHAN TUNG, KING-WAI YAU, AND DAVID M. BERSON

Report Name Central Projections of Melanopsin-Expressing Retinal Ganglion Cells in the Mouse

Publication THE JOURNAL OF COMPARATIVE NEUROLOGY

Issue-page numbers 497:326–349 (2006)

URL http://neuroscience.jhu.edu/hattar%20papers/JCNsamer.pdf

Abstract

A rare type of ganglion cell in mammalian retina is directly photosensitive. These novel retinal photoreceptors express the photopigment melanopsin. They send axons directly to the suprachiasmatic nucleus (SCN), intergeniculate leaflet (IGL), and olivary pretectal nucleus (OPN), thereby contributing to photic synchronization of circadian rhythms and the pupillary light reflex. Here, we sought to characterize more fully the projections of these cells to the brain. By targeting tau-lacZ to the melanopsin gene locus in mice, ganglion cells that would normally express melanopsin were induced to express, instead, the marker enzyme -galactosidase. Their axons were visualized by X-gal histochemistry or anti- -galactosidase immunofluorescence. Established targets were confirmed, including the SCN, IGL, OPN, ventral division of the lateral geniculate nucleus (LGv), and preoptic area, but the overall projections were more widespread than previously recognized. Targets included the lateral nucleus, peri-supraoptic nucleus, and subparaventricular zone of the hypothalamus, medial amygdala, margin of the lateral habenula, posterior limitans nucleus, superior colliculus, and periaqueductal gray. There were also weak projections to the margins of the dorsal lateral geniculate nucleus. Co-staining with the cholera toxin B subunit to label all retinal afferents showed that melanopsin ganglion cells provide most of the retinal input to the SCN, IGL, and lateral habenula and much of that to the OPN, but that other ganglion cells do contribute at least some retinal input to these targets. Staining patterns after monocular enucleation revealed that the projections of these cells are overwhelmingly crossed except for the projection to the SCN, which is bilaterally symmetrical.

Keywords melanopsin; circadian; retinofugal; pupil; suprachiasmatic nucleus; retinal

Hattar S, Liao HW, Takao M, et al. **Year** 2002

Authors S. Hattar, H.-W. Liao, M. Takao, D. M. Berson and K.-W. Yau

Report Name Melanopsin-Containing Retinal Ganglion Cells: Architecture, Projections, and Intrinsic Photosensitivity

Publication Science

Issue-page numbers February 2002: Vol. 295 no. 5557 pp. 1065-1070

URL http://www.sciencemag.org/content/295/5557/1065

Abstract The primary circadian pacemaker, in the suprachiasmatic nucleus (SCN) of the mammalian brain, is photoentrained by light signals from the eyes through the retinohypothalamic tract. Retinal rod and cone cells are not required for photoentrainment. Recent evidence suggests that the entraining photoreceptors are retinal ganglion cells (RGCs) that project to the SCN. The visual pigment for this photoreceptor may be melanopsin, an opsin-like protein whose coding messenger RNA is found in a subset of mammalian RGCs. By cloning rat melanopsin and generating specific antibodies, we show that melanopsin is present in cell bodies, dendrites, and proximal axonal segments of a subset of rat RGCs. In mice heterozygous for tau-lacZ targeted to the melanopsin gene locus, β-galactosidase–positive RGC axons projected to the SCN and other brain nuclei involved in circadian photoentrainment or the pupillary light reflex. Rat RGCs that exhibited intrinsic photosensitivity invariably expressed melanopsin. Hence, melanopsin is most likely the visual pigment of phototransducing RGCs that set the circadian clock and initiate other non–image-forming visual functions.

Keywords

Hattar S, Lucas RJ, Mrosovsky N et al. **Year** 2003

Authors S. Hattar, R. J. Lucas, N. Mrosovsky, S. Thompson, R. H. Douglas, M. W. Hankins, J. Lem, M. Biel, F. Hofmann, R. G. Foster & K.-W. Yau

Report Name Melanopsin and rod-cone photoreceptive systems account for all major accessory visual functions in mice

Publication Nature

Issue-page numbers 424:76–81 doi:10.1038/nature01761. PMID:12808468

URL http://www.nature.com/nature/journal/v424/n6944/abs/nature01761.html

Abstract In the mammalian retina, besides the conventional rod–cone system, a melanopsin-associated photoreceptive system exists that conveys photic information for accessory visual functions such as pupillary light reflex and circadian photo-entrainment1, 2, 3, 4, 5, 6, 7. On ablation of the melanopsin gene, retinal ganglion cells that normally express melanopsin are no longer intrinsically photosensitive8. Furthermore, pupil reflex8, light-induced phase delays of the circadian clock9, 10 and period lengthening of the circadian rhythm in constant light9, 10 are all partially impaired. Here, we investigated whether additional photoreceptive systems participate in these responses. Using mice lacking rods and cones, we measured the action spectrum for phase-shifting the circadian rhythm of locomotor behaviour. This spectrum matches that for the pupillary light reflex in mice of the same genotype11, and that for the intrinsic photosensitivity of the melanopsin-expressing retinal ganglion cells7. We have also generated mice lacking melanopsin coupled with disabled rod and cone phototransduction mechanisms. These animals have an intact retina but fail to show any significant pupil reflex, to entrain to light/dark cycles, and to show any masking response to light. Thus, the rod–cone and melanopsin systems together seem to provide all of the photic input for these accessory visual functions.

Keywords

Haus E

Year 2007

Authors Haus E

Report Name Chronobiology in the endocrine system

Publication Adv Drug Deliv Rev

Issue-page numbers 59:985–1014 doi:10.1016/j.addr.2007.01.001. PMID:17804113

URL http://www.chrono-biology.net/paper/Chronobiology%20in%20the%20endocrine%20system.pdf

Abstract Biological signaling occurs in a complex web with participation and interaction of the central nervous system, the autonomous nervous system, the endocrine glands, peripheral endocrine tissues including the intestinal tract and adipose tissue, and the immune system. All of these show an intricate time structure with rhythms and pulsatile variations in multiple frequencies. Circadian (about 24-hour) and circannual (about 1-year) rhythms are kept in step with the cyclic environmental surrounding by the timing and length of the daily light span. Rhythmicity of many endocrine variables is essential for their efficacy and, even in some instances, for the qualitative nature of their effects. Indeed, the continuous administration of certain hormones and their synthetic analogues may show substantially different effects than expected. In the design of drugdelivery systems and treatment schedules involving directly or indirectly the endocrine system, consideration of the human time organization is essential. A large amount of information on the endocrine time structure has accumulated, some of which is discussed in this review.

Keywords

Haus E

Year 1964

Authors Haus E

Report Name Periodicity in response and susceptibility to environmental stimuli

Publication Ann N Y Acad Sci

Issue-page numbers 117:292–319 doi:10.1111/j.1749-6632.1964.tb48187.x. PMID:14196650

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1964.tb48187.x/abstract?

Abstract Indirect periodicity analysis shows spontaneous responsiveness changes to physical and hormonal stimuli and potentially traumatic agents. These changes persist as circadian rhythms under experimental changes of environmental stimuli. Implications for bioassays and pharmacology are noted.

Keywords

Haus E

Year 1996

Authors Haus E

Report Name Biologic rhythms in hematology

Publication Pathol Biol (Paris)

Issue-page numbers 44:618–630. PMID:8977919

URL http://www.ncbi.nlm.nih.gov/pubmed/8977919

Abstract The number of circulating blood cells and their function, as expressed by phagocytosis, the response to mitogens or by the natural killer cell activity, and the formation of blood cells in the bone marrow, and their response to toxic (e.g. chemotherapeutic) agents show biologic rhythms in several frequencies of which the circadian rhythms are most extensively explored. Some of these rhythms show large enough amplitudes to be clinically important, especially if consecutive samples of the same patients are to be evaluated. Rhythm disturbances characterize hematologic and immune related disease states like, e.g., infection with HIV. Circadian rhythms in the aggregability and adhesiveness of blood platelets contribute to the transient state of hypercoagulability during the morning hours which is thought to lead to the peak incidence at this time of myocardial infarction, cerebral infarct, and sudden cardiac death. The rhythmic, and thus in their timing to a certain degree, predictable changes in responsiveness of the hematopoietic and immune system provide an opportunity to improve the effects of growth factors and cytokines, and decrease their undesirable side effects. Timing of cancer chemotherapy at the time of maximal resistance of the hematopoietic system to a certain drug may improve the often dose limiting toxicity of the agent. Some preliminary results suggest that not only treatment toxicity may be diminished, but also efficacy may be improved. This approach is made difficult by the large individual differences in the timing of the rhythms, and by the interaction of circadian, circaseptan, and circannual rhythms which have, thus far, been only incompletely explored.

Keywords

Haus E, Halberg F

Year 1969

Authors Haus E, Halberg F

Report Name Phase-shifting of circadian rhythms in rectal temperature, serum corticosterone and liver glycogen of the male C-mouse

Publication Rass Neurol Veg

Issue-page numbers 23:83–112. PMID:5398839

URL http://www.ncbi.nlm.nih.gov/pubmed/5398839

Abstract N/A

Keywords

Haus E, Lakatua D, Halberg F — *Year* 1967

Authors Haus E, Lakatua D, Halberg F

Report Name The internal timing of several circadian rhythms in the blinded mouse

Publication Exp Med Surg

Issue-page numbers 25:7–45. PMID:5625877

URL http://www.ncbi.nlm.nih.gov/pubmed/5625877

Abstract N/A

Keywords

Haus E, Nicolau GY, Ghinea E et al. — *Year* 1996

Authors Haus E, Nicolau GY, Ghinea E et al.

Report Name Stimulation of the secretion of dehydroepiandrosterone by melatonin in mouse adrenals in vitro

Publication Life Sci

Issue-page numbers 58:PL263–PL276 doi:10.1016/0024-3205(96)00079-3. PMID: 8614260

URL http://www.mendeley.com/research/stimulation-secretion-dehydroepiandrosterone-melatonin-mouse-adrenals-vitro/

Abstract Adrenals of young adult male mice kept on a LD 12:12 lighting regimen for three weeks prior to study and harvested at four different circadian stages were incubated for 2 hours with 0.4 IU synthetic ACTH in 2 ml Krebs-Ringer buffer (KR), or with 50, 150, and 450 microM of melatonin in KR containing 0.4 IU ACTH. The addition of melatonin to ACTH leads to a dose dependent stimulation of production and/or secretion of DHEA into the incubation medium irrespective of the circadian stage of harvesting of the adrenals. This relationship is of interest in view of the simultaneous decrease of dehydroepiandrosterone and melatonin in the course of aging, and the effects of these compounds upon aging related changes.

Keywords

	Haus E, Nicolau GY, Lakatua D, Sackett-Lundeen L	***Year***	1988
Authors	Haus E, Nicolau GY, Lakatua D, Sackett-Lundeen L		
Report Name	Reference values for chronopharmacology		
Publication	Annu Rev Chronopharm		
Issue-page numbers	4:333–424		
URL	http://cat.inist.fr/?aModele=afficheN&cpsidt=7102884		
Abstract	N/A		
Keywords			

	Haus E, Smolensky M	***Year***	2006
Authors	Erhard Haus and Michael Smolensky		
Report Name	Biological Clocks and Shift Work: Circadian Dysregulation and Potential Long-term Effects		
Publication	Cancer Causes and Control		
Issue-page numbers	Volume 17, Number 4, 489-500,		
URL	http://www.springerlink.com/content/w57m0451647x5444/		
Abstract	Long-term epidemiologic studies on large numbers of night and rotating shift workers have suggested an increase in the incidence of breast and colon cancer in these populations. These studies suffer from poor definition and quantification of the work schedules of the exposed subjects. Against this background, the pathophysiology of phase shift and phase adaptation is reviewed. A phase shift as experienced in night and rotating shift work involves desynchronization at the molecular level in the circadian oscillators in the central nervous tissue and in most peripheral tissues of the body. There is a change in the coordination between oscillators with transient loss of control by the master-oscillator (the Suprachiasmatic Nucleus, SCN) in the hypothalamus. The implications of the pathophysiology of phase shift are discussed for long-term health effects and for the design of ergonomic work schedules minimizing the adverse health effects upon the worker.		
Keywords	Shift work, Circadian desynchronization, Risk factors, Heart disease, Cancer, Ergonomics		

Haus E, Smolensky MH

Year 1999

Authors Haus E, Smolensky MH

Report Name Biologic rhythms in the immune system

Publication Chronobiol Int

Issue-page numbers 16:581–622 doi:10.3109/07420529908998730. PMID:10513884

URL http://informahealthcare.com/doi/abs/10.3109/07420529908998730?journalCode=cbi

Abstract In all of its components, the immune system shows regularly recurring, rhythmic variations in numerous frequencies; the circadian (about 24h) rhythms are the best explored. The circadian variations in immunocompetent cells circulating in the peripheral blood are of a magnitude to require attention in medical diagnostics. Both the humoral arm and the delayed (cellular) arm of the immune system function in a rhythmic manner. The response of the immune system to introduction of an antigen and to challenge of the sensitized organism varies in extent in the circadian frequency range and also in lower frequencies, for example, of about a week (circaseptan) or seasonally (circannual). The medical application of the biologic rhythms of the immune system extends to diagnostic measures, as well as treatment.

Keywords Allergy, Asthma, Cellular immune response, Cytokines,

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Haus E, Touitou Y

Year 1992

Authors Haus E, Touitou Y

Report Name Principles of clinical chronobiology

Publication In: Touitou Y & Haus E, Eds. Biologic Rhythms in Clinical and Laboratory Medicine

Issue-page numbers Berlin, Heidelberg, Paris: Springer-Verlag. pp. 6–34

URL N/A

Abstract N/A

Keywords

Haus EL, Smolensky MH

Year 2013

Authors Erhard L. Haus, Michael H. Smolensky

Report Name Shift work and cancer risk: Potential mechanistic roles of circadian disruption, light at night, and sleep deprivation

Publication Sleep Medicine Reviews

Issue-page numbers Volume 17, Issue 4, August 2013, Pages 273–284

URL http://www.sciencedirect.com/science/article/pii/S1087079212000986

Abstract Shift work that includes a nighttime rotation has become an unavoidable attribute of today's 24-h society. The related disruption of the human circadian time organization leads in the short-term to an array of jet-lag-like symptoms, and in the long-run it may contribute to weight gain/obesity, metabolic syndrome/type II diabetes, and cardiovascular disease. Epidemiologic studies also suggest increased cancer risk, especially for breast cancer, in night and rotating female shift workers. If confirmed in more controlled and detailed studies, the carcinogenic effect of night and shift work will constitute additional serious medical, economic, and social problems for a substantial proportion of the working population. Here, we examine the possible multiple and interconnected cancer-promoting mechanisms as a consequence of shift work, i.e., repeated disruption of the circadian system, pineal hormone melatonin suppression by exposure to light at night, sleep-deprivation-caused impairment of the immune system, plus metabolic changes favoring obesity and generation of proinflammatory reactive oxygen species.

Keywords Shift work; Sleep deprivation; Circadian disruption; Melatonin; Cancer

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Hawk JLM and Lim HW

Year 2007

Authors Hawk JLM and Lim HW

Report Name Chronic actinic dermatitis

Publication In: Lim HW, Honigsmann H, Hawk JLM, editors. Photodermatology

Issue-page numbers New York: Informa; 2007. p.169-83.

URL Book

Abstract Book

Keywords

Hazlerigg DG, Andersson H, Johnston JD, Lincoln G **Year** 2004

Authors Hazlerigg DG, Andersson H, Johnston JD, Lincoln G

Report Name Molecular characterization of the longday response in the Soay sheep, a seasonal mammal

Publication Curr Biol

Issue-page numbers 14:334–339. PMID:14972686

URL http://www.sciencedirect.com/science/article/pii/S0960982204000818

Abstract In mammals, seasonal timekeeping depends on the generation of a nocturnal melatonin signal that reflects nightlength/daylength [1]. To understand the mechanisms by which the melatonin signal is decoded, we studied the photoperiodic control of prolactin secretion in Soay sheep, which is mediated via melatonin responsive cells in the pars tuberalis of the pituitary [2]. We demonstrate that the phases of peak expression of the clock genes Cryptochrome1 (Cry1), Period1 (Per1), and RevErbα respond acutely to altered melatonin secretion after a switch from short to long days. Cry1 is activated by melatonin onset, forming the dusk component of the molecular decoder, while Per1 expression at dawn reflects the offset of melatonin secretion. The Cry1-Per1 interval immediately adjusts to the melatonin signal on the first long day, and this is followed within 24 hr by an increase in prolactin secretion. The timing of peak RevErbα expression also responds to a switch to long days due to altered melatonin secretion but does not immediately reset to an entrained long-day state. These data suggest that effects of melatonin on clock gene expression are pivotal events in the neuroendocrine response and that pars tuberalis cells can act as molecular calendars, carrying a form of “photoperiodic memory.”

Keywords

Hazlerigg DG, Morgan PJ, Messager S **Year** 2001

Authors Hazlerigg DG, Morgan PJ, Messager S

Report Name Decoding photoperiodic time and melatonin in mammals: what can we learn from the pars tuberalis?

Publication J Biol Rhythms

Issue-page numbers 16:326–335 doi:10.1177/074873001129002042. PMID:11506378

URL http://jbr.sagepub.com/content/16/4/326.short

Abstract The cellular and molecular mechanisms through which the melatonin signal is decoded to drive/synchronize photoperiodic responses remain unclear. Much of our current understanding of the processes involved in this readout derives from studies of melatonin action in the pars tuberalis of the anterior pituitary. Here, the authors review current knowledge and highlight critical gaps in our present understanding.

Keywords Melatonin, photoperiod, pars tuberalis seasonality, prolactin

Hébert M, Martin SK, Lee C, Eastman CI

Year 2002

Authors Marc Hébert, Stacia K. Martin, Clara Lee, Charmane I. Eastman

Report Name The effects of prior light history on the suppression of melatonin by light in humans

Publication Journal of Pineal Research

Issue-page numbers Volume 33, Issue 4, pages 198-203, November 2002

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079X.2002.01885.x/abstract

Abstract We investigated the impact of light exposure history on light sensitivity in humans, as assessed by the magnitude of the suppression of melatonin secretion by nocturnal light. The hypothesis was that following a week of increased daytime bright-light exposure, subjects would become less sensitive to light, and that after a week of restriction to dimmer light they would become more sensitive. During the bright week, subjects (n = 12) obtained 4.3 ± 0.4 hr of bright light per day (by going outside and using light boxes indoors). During the dim week, they wore dark goggles (about 2% light transmission) when outside during daylight and spent 1.4 ± 0.9 hr per day outside. Saliva samples were obtained every 30 min for 7 hr in dim light (<15 lux) on two consecutive nights (baseline and test night) at the end of each week. On the test night, 500 lux was presented for 3 hr in the middle of the collection period to suppress melatonin. There was significantly more suppression after the dim week compared with after the bright week (to 53 versus 41% of the baseline night values, $P < 0.05$). However, there were large individual differences, and the difference between the bright and dim weeks was most pronounced in seven of the 12 subjects. Possible reasons for these individual differences are discussed, including the possibility that 1 wk was not long enough to change light sensitivity in some subjects. In conclusion, this study suggests that the circadian system's sensitivity to light can be affected by a recent change in light history.

Keywords circadian rhythms; human; light; light sensitivity; melatonin; melatonin suppression

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Herljevic M, Middleton B, Thapan K, Skene DJ

Year 2005

Authors Herljevic M, Middleton B, Thapan K, Skene DJ

Report Name Light-induced melatonin suppression: agerelated reduction in response to short wavelength light

Publication Exp Gerontol

Issue-page numbers 40:237–242 doi:10.1016/j.exger.2004.12.001. PMID:15763401

URL http://www.sciencedirect.com/science/article/pii/S0531556504003481

Abstract One of the possible causes of disturbed circadian rhythms and sleep in the elderly may be impaired photic input to the circadian clock. Age-related changes in lens density are known to reduce the transmission of short wavelength light, which has been shown to be most effective in suppressing nocturnal melatonin. The aim of the study therefore was tc investigate age-related changes in melatonin suppression in response to short and medium wavelength light.

Young premenopausal (n=13) and postmenopausal (n=21) women were exposed to 30 min of monochromatic light at two different wavelengths and irradiances (λmax 456 nm: 3.8 and 9.8 μW/cm2; λmax 548 nm: 28 and 62 μW/cm2). Melatonin suppression was compared across light treatments and between age groups.

Significantly reduced melatonin suppression was noted in the elderly subjects following exposure to short wavelength (456 nm) light compared to the young subjects. These results are likely to reflect age-related changes in lens density.

Keywords Short wavelength light; Melatonin suppression; Ageing; Women; Postmenopausal

Hettiaratchy S, Clarke J, Taubel J, Besa C

Year 2000

Authors Shehan Hettiaratchy, John Clarke, Jorg Taubel, Chola Besa

Report Name Burns after photodynamic therapy

Publication BMJ

Issue-page numbers 320 : 1245 doi: 10.1136/bmj.320.7244.1245

URL http://www.bmj.com/content/320/7244/1245.1.full

Abstract Photodynamic therapy comprises a photosensitising agent, which accumulates in malignant tissue, and a light source, which activates the photosensitiser, causing it to generate highly reactive oxygen species that destroy malignant cells. Temoporfin is a second generation photosensitiser that has a shorter half life than its predecessors and is thought to be more selective towards tumours. These two factors should decrease the incidence of photosensitivity, one of the main side effects of photodynamic therapy. We report on a group of patients who received a single dose of temoporfin (Foscan, Scotia Pharmaceuticals) and developed partial thickness burns after minimal exposure to light.

Keywords

Hiestand PC, Mekler P, Nordmann R et al.

Year 1986

Authors Hiestand PC, Mekler P, Nordmann R et al.

Report Name Prolactin as a modulator of lymphocyte responsiveness provides a possible mechanism of action for cyclosporine

Publication Proc Natl Acad Sci USA

Issue-page numbers 83:2599–2603 doi:10.1073/pnas.83.8.2599. PMID:2939454

URL http://www.pnas.org/content/83/8/2599.short

Abstract Lymphocyte responsiveness in rats was found to depend on serum prolactin levels. Blocking pituitary prolactin release with bromocriptine severely reduces lymphocyte reactivity in vitro (mixed lymphocyte reaction) as well as in vivo (graft-versus-host reaction). In addition, evidence for a prolactin/growth hormone-related mRNA species produced in mitogen- and antigen-stimulated lymphocytes has been obtained. Prolactin was shown to compete in a dose-dependent fashion with the immunosuppressant cyclosporine (cyclosporin A) for a common binding site on the surface of T lymphocytes. Further, stimulation of prolactin secretion reversed the immunosuppression induced by cyclosporine. We conclude that prolactin is involved in the maintenance of T-cell immunocompetence and that the immunosuppressive effects of cyclosporine may be mediated by the displacement of prolactin from binding sites on lymphocytes.

Keywords

Higlett MP, O'Hagan JB, Khazova M

Year 2012

Authors M P Higlett, J B O'Hagan and M Khazova

Report Name Safety of light emitting diodes in toys

Publication J. Radiol. Prot.

Issue-page numbers 32 51 doi:10.1088/0952-4746/32/1/51

URL http://iopscience.iop.org/0952-4746/32/1/51

Abstract Light emitting diodes (LEDs) are increasingly being used in toys. An assessment methodology is described for determining the accessible emission limits for the optical radiation from the toys, which takes account of expected use and reasonably foreseeable misuse of toys. Where data are available, it may be possible to assess the toy from the data sheet alone. If this information is not available, a simple measurement protocol is proposed.

Keywords

Higuchi S, Fukuda T, Kozaki T, et al.

Year 2011

Authors Higuchi S, Fukuda T, Kozaki T, Takahashi M, Miura N.

Report Name Effectiveness of a Red-visor Cap for Preventing Light-induced Melatonin Suppression during Simulated Night Work.

Publication J Physiol Anthropol

Issue-page numbers 2011;30(6):251-8.

URL http://www.ncbi.nlm.nih.gov/pubmed/22197958

Abstract Bright light at night improves the alertness of night workers. Melatonin suppression induced by light at night is, however, reported to be a possible risk factor for breast cancer. Short-wavelength light has a strong impact on melatonin suppression. A red-visor cap can cut the short-wavelength light from the upper visual field selectively with no adverse effects on visibility. The purpose of this study was to investigate the effects of a red-visor cap on light-induced melatonin suppression, performance, and sleepiness at night. Eleven healthy young male adults (mean age: 21.2±0.9 yr) volunteered to participate in this study. On the first day, the subjects spent time in dim light (<15 lx) from 20:00 to 03:00 to measure baseline data of nocturnal salivary melatonin concentration. On the second day, the subjects were exposed to light for four hours from 23:00 to 03:00 with a nonvisor cap (500 lx), red-visor cap (approx. 160 lx) and blue-visor cap (approx. 160 lx). Subjective sleepiness and performance of a psychomotor vigilance task (PVT) were also measured on the second day. Compared to salivary melatonin concentration under dim light, the decrease in melatonin concentration was significant in a nonvisor cap condition but was not significant in a red-visor cap condition. The percentages of melatonin suppression in the nonvisor cap and red-visor cap conditions at 4 hours after exposure to light were 52.6±22.4% and 7.7±3.3%, respectively. The red-visor cap had no adverse effect on performance of the PVT, brightness and visual comfort, though it tended to increase subjective sleepiness. These results suggest that a red-visor cap is effective in preventing melatonin suppression with no adverse effects on vigilance performance, brightness and visibility.

Keywords

Authors Shigekazu Higuchi, Yutaka Motohashi, Yang Liu, Mio Ahara, Yoshihiro Kaneko

Report Name Effects of VDT tasks with a bright display at night on melatonin, core temperature, heart rate, and sleepiness

Publication Journal of Applied Physiology

Issue-page numbers May 2003 vol. 94 no. 5 1773-1776

URL http://jap.physiology.org/content/94/5/1773.short

Abstract The effects of performing video display terminal (VDT) tasks with a bright display (BD) at night on nocturnal salivary melatonin concentration, rectal temperature, heart rate, and sleepiness were examined. Seven healthy male adults performed exciting VDT tasks with a BD and a dark display (DD) and boring VDT tasks with a BD and a DD from 2300 to 0200. The light intensities of the BD and DD were 45 and 15 lx at each subject's eye level, respectively. The exciting VDT task with both BD and DD significantly suppressed the nocturnal decrease in rectal temperature and heart rate and the nocturnal increase in sleepiness. The BD significantly suppressed the nocturnal decrease in rectal temperature during both exciting and boring VDT tasks. The nocturnal salivary melatonin concentration was significantly suppressed by the combination of the exciting task and BD. The results suggest that performing an exciting VDT task with a BD suppresses the nocturnal changes in melatonin concentration and other physiological indicators of human biological clocks.

Keywords

Hikichi T,Tateda N, Miura T | *Year* 2011

Authors Taiichi Hikichi,1 Naohiro Tateda,2 and Toshiaki Miura3

Report Name Alteration of melatonin secretion in patients with type 2 diabetes and proliferative diabetic retinopathy

Publication Clin Ophthalmol

Issue-page numbers 2011; 5: 655–660 doi: 10.2147/OPTH.S19559

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3104794/

Abstract

Background:
The purpose of this study was to evaluate the dynamics of plasma melatonin secretion in patients with type 2 diabetes mellitus and diabetic retinopathy.
Methods:
Plasma melatonin levels were measured by high-performance liquid chromatography in 56 patients. Patients were divided into a diabetic group (30 patients) and a nondiabetic group (26 patients). The diabetic group was divided further into a proliferative diabetic retinopathy (PDR) group (n = 14) and a nonproliferative diabetic retinopathy (NPDR) group (n = 16). Plasma melatonin levels obtained at midnight and 3 am were compared between the groups.
Results:
Nighttime melatonin levels were significantly lower in the diabetic group than in the nondiabetic group ($P < 0.03$) and lower in the PDR group than in the nondiabetic and NPDR groups ($P < 0.01$ and $P < 0.03$, respectively), but no significant difference was found between the nondiabetic and NPDR groups. The daytime melatonin level did not significantly differ between the nondiabetic and diabetic groups or between the nondiabetic, NPDR, and PDR groups.
Conclusion:
The nighttime melatonin level is altered in patients with diabetes and PDR but not in diabetic patients without PDR. Although patients with PDR may have various dysfunctions that affect melatonin secretion more severely, advanced dysfunction of retinal light perception may cause altered melatonin secretion. Alteration of melatonin secretion may accelerate further occurrence of complications in diabetic patients.

Keywords circadian rhythm, diabetes, proliferative diabetic retinopathy, melatonin

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Hildebrandt G, Moser M, Lehofer M | *Year* 1998

Authors Hildebrandt G, Moser M, Lehofer M

Report Name Chronobiology and Chronomedicine - Biologic Rhythms Medical Consequences (German)

Publication Stuttgart: Hippokrates

Issue-page numbers

URL N/A

Abstract N/A

Keywords

Hildebrandt G, Rohmert W, Rutenfranz J | *Year* 1974

Authors Hildebrandt G, Rohmert W, Rutenfranz J

Report Name 12 and 24 h Rhythms in error frequency of locomotive drivers and the influence of tiredness

Publication Int J Chronobiol

Issue-page numbers 2:175–180. PMID:4422310

URL http://www.ncbi.nlm.nih.gov/pubmed/4422310

Abstract N/A

Keywords

Hill SM, Blask DE | *Year* 1988

Authors Hill SM, Blask DE

Report Name Effects of the pineal hormone melatonin on the proliferation and morphological characteristics of human breast cancer cells (MCF-7) in culture

Publication Cancer Res

Issue-page numbers 48:6121–6126. PMID:3167858

URL http://cancerres.aacrjournals.org/content/48/21/6121.full.pdf

Abstract Since melatonin, the major hormone of the pineal gland, has been shown to inhibit the growth of mammary tumors in animal models of human breast cancer, we examined the hypothesis that this indoleamine has the potential to inhibit breast cancer growth by directly inhibiting cell proliferation as exemplified by the growth of the estrogen-responsive human breast cancer cell line MCF-7 in culture. Concentrations of melatonin (10(-9) M; 10(-11) M), corresponding to the physiological levels present in human blood during the evening hours, significantly inhibited (P less than 0.001) cell proliferation by as much as 60% to 78% as measured by either DNA content or hemocytometer cell counts. Melatonin's inhibitory effect was reversible since the logarithmic growth of MCF-7 cells was restored after melatonin-containing medium was replaced with fresh medium lacking melatonin. Not only was the inhibitory effect of melatonin absent at either pharmacological (10(-7) M; 10(-5) M) or subphysiological (10(-15) M; 10(-13) M) concentrations, but melatonin also failed to inhibit the proliferation of either human foreskin fibroblasts or the estrogen receptor-positive human endometrial cancer cell line RL95-2. Both transmission and scanning electron microscopy revealed several morphological changes that correlated with melatonin's inhibition of cell growth. After just 4 days of exposure to melatonin, MCF-7 cells exhibited reduced numbers of surface microvilli, nuclear swelling, cytoplasmic and ribosomal shedding, disruption of mitochondrial cristae, vesiculation of the smooth endoplasmic reticulum, and an increase in the numbers of autophagic vacuoles. These results support the hypothesis that melatonin, at physiological concentrations, exerts a direct but reversible, antiproliferative effect on MCF-7 cell growth in culture. This antiproliferative effect is associated with striking changes in the ultrastructural features of these cells suggestive of a sublethal but reversible cellular injury.

Keywords

Hill SM, Blask DE, Xiang S, et al. **Year** 2011

Authors Steven M. Hill, David E. Blask, Shulin Xiang, Lin Yuan, Lulu Mao, Robert T. Dauchy, Erin M. Dauchy, Tripp Frasch and Tamika Duplesis

Report Name Melatonin and associated signaling pathways that control normal breast epithelium and breast cancer

Publication Journal of Mammary Gland Biology and Neoplasia

Issue-page numbers Volume 16, Number 3, 235-245, DOI: 10.1007/s10911-011-9222-4

URL http://www.springerlink.com/content/x6k257t4010u13h7/

Abstract This review article discusses recent work on the melatonin-mediated circadian regulation and integration of molecular and metabolic signaling mechanisms involved in human breast cancer growth and the associated consequences of circadian disruption by exposure to light-at-night (LAN). The anti-proliferative effects of the circadian melatonin signal are, in general, mediated through mechanisms involving the activation of MT1 melatonin receptors expressed in human breast cancer cell lines and xenografts. In estrogen receptor-positive (ERα+) human breast cancer cells, melatonin suppresses both ERα mRNA expression and estrogen-induced transcriptional activity of the ERα via MT1-induced activation of Gαi2 signaling and reduction of cAMP levels. Melatonin also regulates the transcriptional activity of additional members of the nuclear receptor super-family, enzymes involved in estrogen metabolism, and the expression of core clock and clock-related genes. The anti-invasive/anti-metastatic actions of melatonin involve the blockade of p38 phosphorylation and matrix metalloproteinase expression. Melatonin also inhibits the growth of human breast cancer xenografts via MT1-mediated suppression of cAMP leading to a blockade of linoleic acid (LA) uptake and its metabolism to the mitogenic signaling molecule 13-hydroxyoctadecadienoic acid (13-HODE). Down-regulation of 13-HODE reduces the activation of growth factor pathways supporting cell proliferation and survival. Finally, studies in both rats and humans indicate that light-at-night (LAN) induced circadian disruption of the nocturnal melatonin signal activates human breast cancer growth, metabolism, and signaling, providing the strongest mechanistic support, thus far, for epidemiological studies demonstrating the elevated breast cancer risk in night shift workers and other individuals increasingly exposed to LAN.

Keywords Melatonin – Breast cancer – Nuclear receptors – Molecular signaling – Circadian disruption – Clock

Hill SM, Spriggs LL, Simon MA et al. **Year** 1992

Authors Hill SM, Spriggs LL, Simon MA et al.

Report Name The growth inhibitory action of melatonin on human breast cancer cells is linked to the estrogen response system

Publication Cancer Lett

Issue-page numbers 64:249–256 doi:10.1016/0304-3835(92)90050-6. PMID:1638517

URL http://www.sciencedirect.com/science/article/pii/0304383592900506

Abstract The pineal hormone, melatonin, was examined for its capacity to modulate the proliferation of a panel of human breast cancer cell lines. Melatonin inhibited, to a varying extent, the proliferation of all three estrogen-responsive cell lines, but had no effect on estrogen-insensitive breast tumor cell lines. Melatonin was also able to specifically block estrogen-induced proliferation in MCF-7 breast cancer cells. However, this action was abolished in the presence of tamoxifen. Therefore, it appears that the antiproliferative effects of melatonin are mediated through the estrogen-response pathway.

Keywords antiproliferative effect; breast cancer cells; melatonin; estrogen response pathway

Authors K. Y. HO, W. S. EVANS, R. M. BLIZZARD, J. D. VELDHUIS, G. R. MERRIAM, E. SAMOJLIK, R. FURLANETTO, A. D ROGOL, D. L. KAISER and M. O. THORNER

Report Name Effects of sex and age on the 24-hour profile of growth hormone secretion in man: importance of endogenous estradiol concentrations

Publication J Clin Endocrinol Metab

Issue-page numbers 64:51–58 doi:10.1210/jcem-64-1-51. PMID:3782436

URL http://jcem.endojournals.org/content/64/1/51.short

Abstract

We undertook a study of the separate and combined effects of age and sex on the pulsatile pattern of GH secretion. The 24-h secretory profile of GH was generated by 20-min sampling in 10 young women (aged 18–33 yr), 10 young men (aged 18–33 yr), 8 postmenopausal women (aged >55 yr), and 8 older men (aged >55 yr). A computer-assisted pulse analysis program was used to assess both total GH secretion, as reflected in the 24-h integrated GH concentration (IGHC), and pulsatile secretion, as denoted by pulse frequency, duration, amplitude, and the fraction of GH secreted in pulses during the 24-h period (FGHP).

IGHC was significantly greater in women than in men ($P < 0.025$) and greater in the young than in the old ($P < 0.003$). The mean pulse amplitude, duration, and FGHP were each greater in the young ($P < 0.006$, $P < 0.03$, and $P < 0.0001$, respectively), but not significantly different between the sexes. The mean pulse frequency was not affected by sex or age. The serum concentration of free estradiol, but not free testosterone, correlated with IGHC ($r = 0.46$; $P < 0.005$), pulse amplitude ($r = 0.53$; $P < 0.001$), and FGHP ($r = 0.59$; $P < 0.0002$). After correcting for the effects of estradiol, neither sex nor age influenced IGHC or mean pulse amplitude, while the effect of age on FGHP was reduced from 81% to 29%. Of the indices of GH secretion, FGHP had the strongest correlation ($r = 0.43$; $P < 0.006$) with somatomedin-C. Somatomedin-C declined significantly with age in both sexes

Our results indicate that sex and age have independent and interrelated effects on GH secretion. These effects can be largely accounted for by corresponding variations in endogenous estra-diol levels. These observations suggest an amplifying action of estradiol on the neuroendocrine regulation of pulsatile GH release.

Keywords

Hockwin O, Kojima M, Sakamoto Y, Wegener A, Shui YB, Sasaki K

Year 1999

Authors Hockwin O, Kojima M, Sakamoto Y, Wegener A, Shui YB, Sasaki K.

Report Name UV damage to the eye lens: further results from animal model studies: a review

Publication J Epidemiol

Issue-page numbers 1999 Dec;9(6 Suppl):S39-47.

URL http://www.ncbi.nlm.nih.gov/pubmed/10709349

Abstract UV irradiation has the potential to induce the development of lens opacities. This has been demonstrated since long with animal experiments. Unfortunately these animal cataracts did not explain or elucidate the epidemiological observation that the frequency of human cataracts--such as the so called senile cataract--is remarkably higher in regions with increased cosmic UV irradiation or in the population being in close professional contact with UV-irradiation. The main problem was that the type of UV induced animal cataracts differs remarkably with respect to onset, localization of the opacity, size and its timely progression from the cataract classes observed in human. The research o the last 10 years comes to the conclusion that beside the direct (acute) damage--as seen in animal studies due to high UV dosages--we have to realize a syn- or co-cataractogenic potential of UV irradiation even below the threshold dose which is able to accumulate in the lens and to initiate together with other risk factors (chronic damage) the opacification of the lens. The mechanism for the animal cataract and the human cataract (with an UV risk participation) are different. The epidemiological research about cataract frequency in different regions of the world have to take into account that UV irradiation--even below a threshold dose--is a possible risk among the multifactorial pathogenesis of human cataract.

Keywords

Hoffman AE, Yi C, Zheng T, et al.

Year 2010

Authors Aaron E. Hoffman, Chun-Hui Yi, Tongzhang Zheng, Richard G. Stevens, Derek Leaderer, Yawei Zhang, Theodore R. Holford, Johnni Hansen, Jennifer Paulson, and Yong Zhu

Report Name CLOCK in Breast Tumorigenesis: evidence from Genetic, Epigenetic, and Transcriptional Profiling Analyses

Publication Cancer Research

Issue-page numbers February 15, 2010 70; 1459-68

URL http://cancerres.aacrjournals.org/content/70/4/1459.full

Abstract The transcription factors responsible for maintaining circadian rhythm influence a variety of biological processes. Recently, it has been suggested that the core circadian genes may play a role in breast tumorigenesis, possibly by influencing hormone regulation or other pathways relevant to cancer. To evaluate this hypothesis, we conducted a genetic and epigenetic association study, as well as a transcriptional profiling array and a pathway-based network analysis. We report significant correlations between single nucleotide polymorphisms associated with the central circadian regulator CLOCK and breast cancer risk, with apparent effect modification by estrogen receptor/progesterone receptor status. We also found that hypermethylation in the CLOCK promoter reduced the risk of breast cancer, and lower levels of CLOCK expression were documented in healthy controls relative to normal or tumor tissue from patients with breast cancer. Finally, we silenced CLOCK in vitro and performed a whole-genome expression microarray and pathway analysis, which identified a cancer-relevant network of transcripts with altered expression following CLOCK gene knockdown. Our findings support the hypothesis that circadian genes influence tumorigenesis, and identify a set of circadian gene variants as candidate breast cancer susceptibility biomarkers.

Keywords CLOCK, Circadian genetics, Breast cancer, Genetic variants, Epigenetic variants

Hoffman AE, Zheng T, Stevens RG, et al. **Year** 2009

Authors Aaron E. Hoffman,1 Tongzhang Zheng,1 Richard G. Stevens,2 Yue Ba,1 Yawei Zhang,1 Derek Leaderer,1 Chunhui Yi,1 Theodore R. Holford,1 and Yong Zhu1

Report Name Clock-cancer connection in Non-Hodgkin's Lymphoma: a genetic association study and pathway analysis of the circadian gene Cryptochrome 2

Publication Cancer Res

Issue-page numbers April 15; 69(8): 3605–3613.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3175639/

Abstract

Circadian genes have the potential to influence a variety of cancer-related biological pathways, including immune regulation, which may influence susceptibility to non-Hodgkin's lymphoma (NHL). However, few studies have examined the role of circadian genes in lymphomagenesis. The current study examined Cryptochrome 2 (CRY2), a core circadian gene and transcriptional repressor, as a potential circadian biomarker for NHL. We first performed genetic association analyses of tagging SNPs in CRY2 and NHL risk using DNA samples from a population-based case-control study (N= 455 cases and 527 controls). Three SNPs were found to be significantly associated with risk of NHL when combining all subtypes (dbSNP IDs, odds ratios (ORs), and 95% confidence intervals: rs11038689, OR=2.34 (1.28-4.27), P=0.006; rs7123390, OR=2.40 (1.39-4.13), P=0.002; and rs1401417, OR=2.97 (1.57-5.63), P=0.001). Each of these associations remained significant when restricting the analysis to B-Cell cases and when further restricting to follicular lymphomas. An analysis of CRY2 diplotypes confirmed these significant findings. To further determine the functional impact of CRY2, we silenced the gene in vitro and performed a whole genome expression microarray. A pathway-based analysis showed that genes significantly altered by CRY2 knockdown formed networks associated with immune response and hematological system development. In addition, these genes were predicted to have significant impacts on several disease processes, including cancer (B-H P-value=3.75E-9) and hematological disease (B-H P=8.01E-8). In conclusion, both genetic association and functional analyses suggest that the circadian gene CRY2 may play an important role in NHL development.

Keywords CRY2, NHL, Circadian Genetics

Authors Hoffman K

Report Name The influence of photoperiod and melatonin on testis size and body weight in the Djungarian hamster

Publication J Comp Physiol

Issue-page numbers 85:267–282. doi:10.1007/BF00694233

URL http://www.springerlink.com/content/m3373033x57l0524/

Abstract

The responses of testes, body weight, and pelage colour to short and long photoperiods in winter were determined in adult male hamsters with and without the implantation of melatonin. Animals in winter condition, with involuted testes and winter pelage, were kept at 20 °C under conditions of either long (16 h per day) or short (8 h per day) photoperiods beginning on 2 January. In each condition one group was implanted three times at weekly intervals with melatonin in beeswax, a control group was implanted with beeswax only, and another control group was left untreated. A further control group remained in natural day light. After 37 days testes of the control groups in long photoperiods had reached summer condition, while the group treated with melatonin was delayed in testicular development, and closely resembled both the three shortday groups and the group kept in natural daylight (Fig. 2–4). In short photoperiods there was no difference between the group treated with melatonin and the two control groups. All groups showed some testis development as compared to animals killed at the beginning of the experiment. Hamsters kept under natural daylight showed a marked annual cycle of body weight which closely paralleled gonadal activity (Fig. 5). In the experimental groups there was a corresponding increase in body weight paralleling testicular development (Fig. 6). The two control groups in long photoperiods had a significantly higher increase in body weight than all other groups, while there were no significant differences between the groups treated with melatonin, the two short-day groups and the group under natural daylight. Testis size at the end of the experiment was highly correlated with increase in body weight (Fig. 7, and Table 1).
Molt into summer pelage had started in all groups at the end of the experiment. Colour change was most advanced in the two control groups under long photoperiods, while the long-day group treated with melatonin resembled the short-day groups (Figs. 9 and 10).
It is concluded that the change in physiological state from winter to summer is based on an endogenous mechanism, which is accelerated by long photoperiods, and that melatonin inhibits or greatly diminishes this acceleration while it does not inhibit spontaneous development towards summer condition.

Keywords

Hoffmann K, Illnerova H, Vanecek J

Year 1981

Authors KLAUS HOFFMANN,

Report Name Effect of Photoperiod and of One Minute Light at Night-time on the Pineal Rhythm on N-Acetyltransferase Activity in the Djungarian Hamster Phodopus sungorus

Publication Biology of Reproduction

Issue-page numbers April 1, 1981 vol. 24 no. 3 551-556

URL http://www.biolreprod.org/content/24/3/551.short

Abstract The proposition that the temporal pattern of pineal melatonin formation and release may serve as a transducer of photic into humoral stimuli was tested. Adult male Djungarian hamsters were maintained for 3-4 weeks under 16L:8D, 8L:16D, and 8L:16D with additional 1 min light in the middle of the dark period. Pineal N-acetyltransferase activity was estimated at different daytimes as an indicator of melatonin synthesis. The pattern of the rhythms in N-acetyltransferase was similar under 16L:8D and 8L:16D + 1 min light and dissimilar to the pattern under 8L:16D. The high nocturnal N-acetyltransferase activity lasted for ~5 h under 16L:8D, 6 h under 8L:16D + 1 min light, and 12 h under 8L:16D. The demonstration that the regimens 16L:8D and 8L:16D + 1 min light lead to similar rhythms in N-acetyltransferase and hence in melatonin formation, together with our previous finding that the same regimen (8L:16D + 1 min light in the middle of the dark period) mimics the effect of long photoperiods on gonadal development and body weight, further supports the hypothesis that the changing rhythmic pattern of melatonin formation may be involved in conveying the photoperiodic effects.

Keywords

Hoffmann-Dörr S, Greinert R, Volkmer B, Epe B

Year 2005

Authors Hoffmann-Dörr S, Greinert R, Volkmer B, Epe B.

Report Name Visible light (>395 nm) causes micronuclei formation in mammalian cells without generation of cyclobutane pyrimidine dimers.

Publication Mutat Res

Issue-page numbers 2005 May 2;572(1-2):142-9.

URL http://www.ncbi.nlm.nih.gov/pubmed/15790497?dopt=abstract

Abstract Solar radiation gives rise to DNA damage in mammalian cells not only directly by excitation of DNA, which generates predominantly pyrimidine dimers, but also indirectly by the excitation of endogenous photosensitizers, which causes oxidative DNA modifications. The latter mechanism has a low quantum yield, but it is the only one proceeding in the visible range of the spectrum. To investigate its relevance for the genotoxicity of sunlight, we have analysed the generation of micronuclei associated with the induction of oxidative DNA damage by visible light in melanoma cells and primary human skin fibroblasts. Similar yields of light-induced oxidative DNA base modifications sensitive to the repair glycosylase Fpg (7,8-dihydro-8-oxoguanine and other oxidative purine modifications) were observed in the normal fibroblasts and the malignant melanoma cells of the same donor. When irradiations were carried out at intervals to compensate for a photodecomposition of the endogenous chromophore, a significant generation of micronuclei was observed in both cell types. Cyclobutane pyrimidine dimers could be excluded to be responsible for the micronuclei induction at wavelengths >395 nm. Experiments with a cut-off filter indicate that the ratio of pyrimidine dimers and Fpg-sensitive oxidative modifications in irradiated cells not only reflects the relative contributions of direct and indirect mechanisms, but is also similar to the ratio by which the two mechanisms contribute to the generation of the micronuclei. The results suggest that indirectly generated oxidative DNA modifications can contribute significantly to the adverse effects of sunlight.

Keywords

Hogenesch JB, Gu YZ, Jain S, Bradfield CA **Year** 1998

Authors Hogenesch JB, Gu YZ, Jain S, Bradfield CA

Report Name The basic-helix-loop-helix-PAS orphan MOP3 forms transcriptionally active complexes with circadian and hypoxia factors

Publication Proc Natl Acad Sci USA

Issue-page numbers 95:5474–5479 doi:10.1073/pnas.95.10.5474. PMID:9576906

URL http://www.pnas.org/content/95/10/5474.abstract

Abstract We report that MOP3 is a general dimerization partner for a subset of the basic-helix–loop–helix (bHLH)-PER–ARNT–SIM (PAS) superfamily of transcriptional regulators. We demonstrated that MOP3 interacts with MOP4, CLOCK, hypoxia-inducible factor 1α (HIF1α), and HIF2α. A DNA selection protocol revealed that the MOP3-MOP4 heterodimer bound a CACGTGA-containing DNA element. Transient transfection experiments demonstrated that the MOP3-MOP4 and MOP3-CLOCK complexes bound this element in COS 1 cells and drove transcription from a linked luciferase reporter gene. We also deduced the high-affinity DNA binding sites for MOP3-HIF1α complex (TACGTGA) and used transient transfection experiments to demonstrate that the MOP3-HIF1α and MOP3-HIF2α heterodimers bound this element, drove transcription, and responded to cellular hypoxia. Finally, we found that MOP3 mRNA expression overlaps in a number of tissues with each of its four potential partner molecules in vivo.

Keywords

Holick MF **Year** 0

Authors Michael F Holick

Report Name Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis.

Publication Am J Clin Nutr

Issue-page numbers March 2004 vol. 79 no. 3 362-371

URL http://www.ajcn.org/content/79/3/362.abstract

Abstract The purpose of this review is to put into perspective the many health benefits of vitamin D and the role of vitamin D deficiency in increasing the risk of many common and serious diseases, including some common cancers, type 1 diabetes, cardiovascular disease, and osteoporosis. Numerous epidemiologic studies suggest that exposure to sunlight, which enhances the production of vitamin D3 in the skin, is important in preventing many chronic diseases. Because very few foods naturally contain vitamin D, sunlight supplies most of our vitamin D requirement. 25-Hydroxyvitamin D [25(OH)D] is the metabolite that should be measured in the blood to determine vitamin D status. Vitamin D deficiency is prevalent in infants who are solely breastfed and who do not receive vitamin D supplementation and in adults of all ages who have increased skin pigmentation or who always wear sun protection or limit their outdoor activities. Vitamin D deficiency is often misdiagnosed as fibromyalgia. A new dietary source of vitamin D is orange juice fortified with vitamin D. Studies in both human and animal models add strength to the hypothesis that the unrecognized epidemic of vitamin D deficiency worldwide is a contributing factor of many chronic debilitating diseases. Greater awareness of the insidious consequences of vitamin D deficiency is needed. Annual measurement of serum 25(OH)D is a reasonable approach to monitoring for vitamin D deficiency. The recommended adequate intakes for vitamin D are inadequate, and, in the absence of exposure to sunlight, a minimum of 1000 IU vitamin D/d is required to maintain a healthy concentration of 25(OH)D in the blood.

Keywords Vitamin D • sunlight • 25-hydroxyvitamin D • cancer • bone health • diabetes

Hölker F, Moss T, Griefahn B, et al. **Year** 2010

Authors Franz Hölker, Timothy Moss, Barbara Griefahn, Werner Kloas, Christian C. Voigt, Dietrich Henckel, Andreas Hänel, Peter M. Kappeler, Stephan Völker, et al.

Report Name The Dark Side of Light: A Transdisciplinary Research Agenda for Light Pollution Policy

Publication Ecology and Society

Issue-page numbers 15(4): 13.

URL http://www.ecologyandsociety.org/vol15/iss4/art13/

Abstract Although the invention and widespread use of artificial light is clearly one of the most important human technological advances, the transformation of nightscapes is increasingly recognized as having adverse effects. Night lighting may have serious physiological consequences for humans, ecological and evolutionary implications for animal and plant populations, and may reshape entire ecosystems. However, knowledge on the adverse effects of light pollution is vague. In response to climate change and energy shortages, many countries, regions, and communities are developing new lighting programs and concepts with a strong focus on energy efficiency and greenhouse gas emissions. Given the dramatic increase in artificial light at night (0 - 20% per year, depending on geographic region), we see an urgent need for light pollution policies that go beyond energy efficiency to include human well-being, the structure and functioning of ecosystems, and inter-related socioeconomic consequences. Such a policy shift will require a sound transdisciplinary understanding of the significance of the night, and its loss, for humans and the natural systems upon which we depend. Knowledge is also urgently needed on suitable lighting technologies and concepts which are ecologically, socially, and economically sustainable. Unless managing darkness becomes an integral part of future conservation and lighting policies, modern society may run into a global self-experiment with unpredictable outcomes.

Keywords

Holmbäck U, Forslund A, Forslund J et al. **Year** 2002

Authors Holmbäck U, Forslund A, Forslund J et al.

Report Name Metabolic responses to nocturnal eating in men are affected by sources of dietary energy

Publication J Nutr

Issue-page numbers 132:1892–1899. PMID:12097665

URL http://jn.nutrition.org/content/132/7/1892.short

Abstract Because night work is becoming more prevalent, we studied whether feeding at different times of a 24-h period would elicit different metabolic responses and whether dietary macronutrient composition would affect these responses. Seven men (26–43 y, 19.9–26.6 kg/m2) consumed two isocaloric diets, in a crossover design. The diets were a high carbohydrate (HC) diet [65 energy % (E%) carbohydrates, 20E% fat] and a high fat (HF) diet (40E% carbohydrates, 45E% fat). After a 6-d diet-adjustment period, the men were kept awake for 24 h and the food (continuation of respective diet) was provided as six isocaloric meals (i.e., every 4 h). Energy and substrate turnover, heart rate, mean arterial pressure (MAP), blood glucose, triacylglycerol (TAG), nonesterified fatty acid (NEFA) and glycerol were measured throughout the 24-h period. Significantly higher energy expenditure and NEFA concentration, and lower blood glucose and TAG concentrations were observed when the men consumed the HF diet than when they consumed the HC diet. Significant circadian patterns were seen in body and skin temperature (nadir, 0400–0500 h). When the men consumed the HF diet, significant circadian patterns were seen in fat oxidation (nadir, 0800–1200 h; plateau, 1200–0800 h), heat release (nadir, 0800–1200 h; plateau, 1600–0800 h), heart rate (nadir, 0000 h), blood glucose (nadir, 0800–1200 h; peak, 0000–0400 h), NEFA (nadir, 0800–1200 h; peak, 1200–2000 h) and TAG (nadir, 0800–1200 h; peak, 0400–0800 h) concentrations. Energy expenditure, carbohydrate oxidation, MAP and glycerol concentration did not display circadian patterns. Unequal variances eradicated most circadian effects in the HC-diet data. The increased TAG concentration in response to feeding at 0400 h might be involved in the higher TAG concentrations seen in shift workers. Distinct macronutrient/circadian-dependent postprandial responses were seen in most studied variables.

Keywords circadian • macronutrient • triacylglycerols • postprandial • meal • substrate utilization

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Holzman DC **Year** 2010

Authors David C. Holzman

Report Name What's in a Color? The Unique Human Health Effects of Blue Light

Publication Environ Health Perspect

Issue-page numbers 118:A22-A27

URL http://dx.doi.org/10.1289/ehp.118-a22

Abstract Article - The irony of blue as an environmental agent is that before the industrial age, it was merely a color. The unnatural lighting conditions we created turned it into both a potential hazard and a treatment for the ailments it brought about. In addition to the traditional architectural values of visual comfort, aesthetics, and energy efficiency, Brainard says architectural lighting must be redesigned to account for its biological and behavioral impact on humans. “Ultimately that should improve people’s health and well-being in the built environment,” he says.

Keywords Blue, light at night, cancer

Honigsmann H, Hojyo-Tomoka MT | *Year* 2007

Authors Honigsmann H, Hojyo-Tomoka MT

Report Name Polymorphous light eruption, hydroa vacciniforme, and actinic prurigo

Publication In: Lim HW, Honigsmann H, Hawk JLM, editors. Photodermatology

Issue-page numbers New York: Informa; 2007. p.149-67

URL Book

Abstract Book

Keywords

Honma K, Honma S, Wada T | *Year* 1987

Authors Honma K, Honma S, Wada T

Report Name Phase-dependent shift of free-running human circadian rhythms in response to a single bright light pulse

Publication Experientia

Issue-page numbers 43:1205–1207 doi:10.1007/BF01945525. PMID:3691737

URL http://www.springerlink.com/content/j63452q13381371v/

Abstract Responsiveness of free-running human circadian rhythms to a single pulse of bright light was examined in a temporal isolation unit. Bright light (5000 lx) of either 3 or 6 h duration, applied during the early subjective day, produced phase-advance shifts in both the sleep-wake cycle and the rhythm of rectal temperature; the light pulse had essentially no effect on the phase of the circadian rhythms, when it was introduced during the late subjective day or the early subjective night. The results indicate that bright light can reset the human circadian pacemaker.

Keywords

Honma S, Ikeda M, Abe H et al. **Year** 1998

Authors Honma S, Ikeda M, Abe H et al.

Report Name Circadian oscillation of BMAL1, a partner of a mammalian clock gene Clock, in rat suprachiasmatic nucleus

Publication Biochem Biophys Res Commun

Issue-page numbers 250:83–87 doi:10.1006/bbrc.1998.9275. PMID:9735336

URL http://www.uniprot.org/citations/9735336

Abstract A superfamily gene which encodes a bHLH (basic helix-loop-helix)/PAS transcription factor, BMAL1, was cloned and sequenced from rat cDNA. A robust circadian rhythm of rat BMAL1 expression was detected by in situ hybridization in the suprachiasmatic nucleus (SCN), the site of the circadian clock, with the highest level at the subjective night. Less prominent and completely reversed circadian rhythms of rBMAL1 mRNA were observed in the piriform and parietal cortices. The hybridization signals of rBMAL1 mRNA were also detected in the olfactory bulb, hippocampus, and cerebellum. Since the product of rBMAL1 was recently demonstrated to dimerize with the protein of a mammalian clock gene, Clock, and the protein complex was shown to bind the E Box in the promoter region of mPer1 (a mouse homologue to Drosophila clock gene, Per), rBMAL1 possibly plays a critical role in the clock mechanism generating the circadian oscillation in rats.

Keywords

Horio T, Holzle E **Year** 0

Authors Horio T, Holzle E

Report Name Solar urticaria

Publication In: Lim HW, Honigsmann H, Hawk JLM, editors. Photodermatology

Issue-page numbers New York: Informa; 2007. p.186-97

URL Book

Abstract Book

Keywords

Horne JA, Ostberg O **Year** 1976

Authors Horne JA, Ostberg O

Report Name A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms

Publication Int J Chronobiol

Issue-page numbers 4:97–110. PMID:1027738

URL http://www.ncbi.nlm.nih.gov/pubmed/1027738

Abstract An English language self-assessment Morningness-Eveningness questionnaire is presented and evaluated against individual differences in the circadian vatiation of oral temperature. 48 subjects falling into Morning, Evening and Intermediate type categories regularly took their temperature. Circadian peak time were identified from the smoothed temperature curves of each subject. Results showed that Morning types and a significantly earlier peak time than Evening types and tended to have a higher daytime temperature and lower post peak temperature. The Intermediate type had temperatures between those of the other groups. Although no significant differences in sleep lengths were found between the three types, Morning types retired and arose significantly earlier than Evening types. Whilst these time significatly correlated with peak time, the questionnaire showed a higher peak time correlation. Although sleep habits are an important déterminant of peak time there are other contibutory factors, and these appear to be partly covered by the questionnaire. Although the questionnaire appears to be valid, further evaluation using a wider subject population is required.

Keywords

Houdelier C, Bertin A, Guyomarc'h C, et al. **Year** 2007

Authors Cécilia Houdelier, Aline Bertin, Catherine Guyomarc'h, Marie-Annick Richard and Sophie Lumineau

Report Name Daily Laying Time in Free-Living European Starlings: Solar Noon, a Potential Synchronizer

Publication Chronobiology International

Issue-page numbers 24:2, 235-252

URL http://informahealthcare.com/doi/abs/10.1080/07420520701283701

Abstract Reproduction is generally controlled by important temporal constraints involving complex adaptive mechanisms. Birds, in temperate zones, present marked breeding seasonality as well as marked daily organization of reproductive behavior, especially laying. Intra-specific variability and determinants of this pattern have been investigated mainly in domestic non-passerine birds. The present study analyzed the daily temporal organization of laying in a free-living species, the European starling, Sturnus vulgaris. Breeding in a starling colony was monitored for five consecutive years using a non-invasive method (infrared video camera) to precisely estimate laying times. European starlings present a marked daily laying rhythm, ovipositions occurring only during a morning species-specific temporal window. Inside this laying window, time intervals between successive eggs varied greatly among females. Contrary to many species, the light/dark cycle did not appear to control laying time in European starlings, but daily variations of the ultraviolet composition of the solar spectrum appeared to be a possible Zeitgeber of this behavior.

Keywords Daily rhythm, Egg laying, Synchronization, Solar noon, Starling

Howe GR

Year 1984

Authors Howe GR

Report Name Epidemiology of radiogenic breast cancer

Publication In: Boice JD& Fraumeni JF, Eds. Radiation Carcinogenesis: Epidemiology and Biological Significance

Issue-page numbers Raven: New York. pp. 119–129.

URL N/A

Abstract N/A

Keywords

Howland RH

Year 2009

Authors Howland RH.

Report Name An overview of seasonal affective disorder and its treatment options

Publication Phys Sportsmed

Issue-page numbers 2009 Dec;37(4):104-15.

URL http://www.ncbi.nlm.nih.gov/pubmed/20048547

Abstract Seasonal affective disorder (SAD) is defined as a history of major depressive episodes that recur regularly at a particular time of year. Depending on the diagnostic instruments and criteria available, the reported prevalence (1%-10%) varies. Neurotransmitter abnormalities have been implicated in the pathophysiology, but they do not necessarily explain the seasonal pattern or the known chronobiological abnormalities in SAD compared with nonseasonal depression. Circadian rhythm abnormalities have been hypothesized to account for these aspects of SAD, and they provide a rationale for the therapeutic use of light therapy. Family history, twin, and molecular genetics studies suggest that hereditary factors are also involved. Light therapy and antidepressant medication are effective treatment options, with limited evidence for the efficacy of psychotherapy. Some studies demonstrate that narrow-band short wavelength "blue" light, naturalistic dawn simulation, and high-density negative air ionization are effective. Patients should be informed of the benefits of diet and exercise. Light therapy should be clinically monitored in the same manner, as it is done for other antidepressant treatments.

Keywords

Hriscu M, Saulea G, Ostriceanu S, Baciu I **Year** 2002

Authors Hriscu M, Saulea G, Ostriceanu S, Baciu I

Report Name Circadian phagocytic activity in rats under light-dark and constant light regimens

Publication Rom J Physiol

Issue-page numbers 39-40:17–26. PMID:15984664

URL http://www.mendeley.com/research/circadian-phagocytic-activity-rats-under-lightdark-constant-light-regimens/

Abstract The phagocytic function was proved to be a periodic, circadian process. Its acrophase appears to be differently timed in species with different activity type, occurring in the evening in diurnal species and at night in nocturnal ones. The main pineal hormone melatonin, whose secretion occurs strictly at dark, has been shown to play a role in the control of inflammation and to exert a certain stimulatory effect upon phagocytosis in vitro. The aim of the present study was to assess whether the phagocytic activity of neutrophils in the blood of rats exhibits a circadian rhythmicity similar to that of other nocturnal rodents (mice) and also if a constant light regimen alters its amplitude and/or chronostructure. Wistar rats were submitted to either an artificial light-dark 12/12 regimen (LD) or to constant light (LL), for 15 days. In vitro phagocytosis of the neutrophils in whole blood against E.coli was assessed at 10:00, 16:00, 22:00, and 04:00 hours. In LD, phagocytosis appears to be a rhythmical function, with statistically significant differences between the highest value at 04:00 hrs and the lowest at 10:00 hrs. Constant light induces a 30% depression of the phagocytic ability throughout the whole 24 hours cycle, without altering its oscillations. The darkness period appears to play the role of a synchronizer; in its absence the rhythm tends to free-run. It may be stated that rhythmical melatonin secretion is responsible only for maintenance of the phagocytic level, probably via the anterior hypothalamic area and thymus, while it cannot account directly for the nocturnal increase of phagocytosis.

Keywords

Hsu DS, Zhao X, Zhao S et al. **Year** 1996

Authors Hsu DS, Zhao X, Zhao S et al.

Report Name Putative human blue-light photoreceptors hCRY1 and hCRY2 are flavoproteins

Publication Biochemistry

Issue-page numbers 35:13871–13877 doi:10.1021/bi962209o. PMID:8909283

URL http://pubs.acs.org/doi/abs/10.1021/bi962209o

Abstract Recently, a human cDNA clone with high sequence homology to the photolyase/blue-light photoreceptor family was identified. The putative protein encoded by this gene exhibited a strikingly high (48% identity) degree of homology to the Drosophila melanogaster (6−4) photolyase [Todo et al. (1996) Science 272, 109−112]. We have now identified a second human gene whose amino acid sequence displays 73% identity to the first one and have named the two genes CRY1 and CRY2, respectively. The corresponding proteins hCRY1 and hCRY2 were purified and characterized as maltose-binding fusion proteins. Similar to other members of the photolyase/blue-light photoreceptor family, both proteins were found to contain FAD and a pterin cofactor. Like the plant blue-light photoreceptors, both hCRY1 and hCRY2 lacked photolyase activity on the cyclobutane pyrimidine dimer and the (6−4) photoproduct. We conclude that these newly discovered members of the photolyase/photoreceptor family are not photolyases and instead may function as blue-light photoreceptors in humans.

Keywords

Hu R, Jiang X, Zeng Y, et al. ***Year*** 2010

Authors Rong-fang Hu, Xiao-ying Jiang, Yi-ming Zeng, Xiao-yang Chen, and You-hua Zhang

Report Name Effects of earplugs and eye masks on nocturnal sleep, melatonin and cortisol in a simulated intensive care unit environment

Publication Crit Care.

Issue-page numbers 2010; 14(2): R66. Published online 2010 April 18. doi: 10.1186/cc8965

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2887188/

Abstract

Introduction
Environmental stimulus, especially noise and light, is thought to disrupt sleep in patients in the intensive care unit (ICU). This study aimed to determine the physiological and psychological effects of ICU noise and light, and of earplugs and eye masks, used in these conditions in healthy subjects.
Methods
Fourteen subjects underwent polysomnography under four conditions: adaptation, baseline, exposure to recorded ICU noise and light (NL), and NL plus use of earplugs and eye masks (NLEE). Urine was analyzed for melatonin and cortisol levels. Subjects rated their perceived sleep quality, anxiety levels and perception of environmental stimuli.
Results
Subjects had poorer perceived sleep quality, more light sleep, longer rapid eye movement (REM) latency, less REM sleep when exposed to simulated ICU noise and light ($P < 0.05$). Nocturnal melatonin ($P = 0.007$) and cortisol secretion levels ($P = 0.004$) differed significantly by condition but anxiety levels did not ($P = 0.06$). Use of earplugs and eye masks resulted in more REM time, shorter REM latency, less arousal ($P < 0.05$) and elevated melatonin levels ($P = 0.002$).
Conclusions
Earplugs and eye masks promote sleep and hormone balance in healthy subjects exposed to simulated ICU noise and light, making their promotion in ICU patients reasonable.

Keywords

Hua H, Wang Y, Wan C et al. ***Year*** 2006

Authors Hui Hua, Yueqi Wang, Chaomin Wan, Yanyou Liu, Bin Zhu, Chunlei Yang, Xiaojia Wang, Zhengrong Wang, Germaine Cornelissen–Guillaume, Franz Halberg

Report Name Circadian gene mPer2 overexpression induces cancer cell apoptosis

Publication Cancer Sci

Issue-page numbers 97:589–596 doi:10.1111/j.1349-7006.2006.00225.x. PMID:16827798

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1349-7006.2006.00225.x/abstract

Abstract

The Period2 gene, an indispensable component of the circadian clock, not only modulates circadian oscillations, but also regulates organic function. We examined whether overexpression of the mouse Period2 gene (mPer2) in tumor cells influences cell growth and induces apoptosis. Overexpression of PERIOD2 in the mouse Lewis lung carcinoma cell line (LLC) and mammary carcinoma cell line (EMT6) results in reduced cellular proliferation and rapid apoptosis, but not in NIH 3T3 cells. Overexpressed mPER2 also altered the expression of apoptosis-related genes. The mRNA and protein levels of c-Myc, Bcl-XL and Bcl-2 were downregulated, whereas the expression of p53 and bax was upregulated in mPER2-overexpressing LLC cells compared with control cells transferred with empty plasmid. Our results suggest that the circadian gene mPeriod2 may play an important role in tumor suppression by inducing apoptotic cell death, which is attributable to enhanced pro-apoptotis signaling and attenuated anti-apoptosis processes.

Keywords

Authors Jeffrey Hubbard, Elisabeth Ruppert, Claire-Marie Gropp, Patrice Bourgin

Report Name Non-circadian direct effects of light on sleep and alertness: Lessons from transgenic mouse models

Publication Sleep Medicine Reviews

Issue-page numbers Available online 16 April 2013

URL http://www.sciencedirect.com/science/article/pii/S1087079213000026

Abstract Light exerts a strong non-visual influence on human physiology and behavior. Additionally light is known to affect sleep indirectly through the phase shifting of circadian rhythms, and directly, promoting alertness in humans and sleep in nocturnal species. Little attention has been paid to the direct non-image-forming influence of light until recently with the discovery and emerging knowledge on melanopsin, a photopigment which is maximally sensitive to the blue spectrum of light and expressed in a subset of intrinsically photosensitive retinal ganglion cells. Indeed, the development of transgenic mouse models targeting different phototransduction pathways has allowed researchers to decipher the mechanisms by which mammals adapt sleep to their light environment. This review summarizes the novel concepts and discrepancies from recent publications relating to the non-circadian effects of light on sleep and waking. Specifically, we discuss whether darkness, in addition to light, affects their quality. Furthermore, we seek to understand whether longer sustained periods of light exposure can influence sleep, if the direct photic regulation depends on time of day, and whether this affects the homeostatic sleep process. Moreover, the neural pathways by which light exerts a direct influence on sleep will be discussed including the respective role of rods/cones and melanopsin. Finally, we suggest that light weighs on the components of the flip-flop switch model to induce respectively sleep or waking, in nocturnal and diurnal animals. Taking these data into account we therefore propose a novel model of sleep regulation based on three processes; the direct photic regulation interacting with the circadian and homeostatic drives to determine the timing and quality of sleep and waking. An outlook of promising clinical and non-clinical applications of these findings will be considered as well as directions for future animal and human research.

Keywords Light; Sleep regulation; Direct non-circadian non-image-forming effects; Melanopsin; Transgenic mice Model

Hughes PC, Neer RM

Year 1981

Authors Philip C. Hughes, Robert M. Neer

Report Name Lighting for the elderly: a psychobiological approach to lighting.

Publication Human Factors: The Journal of the Human Factors and Ergonomics Society

Issue-page numbers February 1981 vol. 23 no. 1 65-85

URL http://hfs.sagepub.com/content/23/1/65

Abstract

The present paper reviews the role of illumination in shaping the indoor environment of the elderly person. The approach is that lighting has a twofold impact on the individual. One is as a source of information about the environment, i.e., visual, and the other is photobiological through the skin or photoreceptor.

The visually lighted environment is reviewed, discussing first the physiological changes that occur during the aging process, then the effect of aging on visual performance, and finally the importance of qualitative factors in assessing the adequacy of an illuminated environment for the elderly. Special attention is given to application problems in lighting for the elderly, i.e., excessive brightness differences, discomfort glare, veiling reflections, and the importance of color and the spectral power distribution of the light source. The advantages of a full-spectrum light source which simulates natural sunlight for indoor illumination is discussed in light of recent research.

The biologically lighted environment is reviewed in terms of the potential role that indoor illumination can play in regulating important biochemical processes in the elderly population, i.e., neuroendocrine control, vitamin D3 synthesis, immunologic mechanisms, and cardiovascular regulation.

Keywords

Humpel C, Saria A

Year 1991

Authors C. Humpel, A. Saria

Report Name Retinal lesion by bright artificial light increases vasoactive intestinal polypeptide in the rat ventral tegmental area/substantia nigra

Publication Neuroscience Letters

Issue-page numbers Volume 130, Issue 1, 2 September 1991, Pages 92-94

URL http://www.sciencedirect.com/science/article/pii/030439409190235L

Abstract

Sprague-Dawley rats were treated with bright light to induce retinal lesions and vasoactive intestinal polypeptide in the ventral tegmental area/substantia nigra was measured by radioimmunoassay. In Sprague-Dawley rats, but not in Brown Norway rats where light did not induce retinal lesions, significantly increased concentrations of vasoactive intestinal polypeptide were found 21 days after exposure with bright light. This increase declined to control values 60 days after the treatment. Our studies indicate that vasoactive intestinal polypeptide may be involved in visual neurotransmission and that the ventral tegmental area/substantia nigra may be connected to retinal input.

Keywords Vasoactive intestinal polypeptide; Ventral tegmental area; Substantia nigra; Light; Retinal lesion

Hunter JJ, Morgan JIW, Merigan WH, et al. **Year** 2011

Authors Jennifer J. Hunter, Jessica I.W. Morgan, William H. Merigan, David H. Sliney, Janet R. Sparrow, David R. Williams

Report Name The susceptibility of the retina to photochemical damage from visible light

Publication Progress in Retinal and Eye Research

Issue-page numbers In Press, Uncorrected Proof - Note to users

URL http://www.sciencedirect.com/science/article/pii/S135094621100067X

Abstract

The photoreceptor/RPE complex must maintain a delicate balance between maximizing the absorption of photons for vision and retinal image quality while simultaneously minimizing the risk of photodamage when exposed to bright light. We review the recent discovery of two new effects of light exposure on the photoreceptor/RPE complex in the context of current thinking about the causes of retinal phototoxicity. These effects are autofluorescence photobleaching in which exposure to bright light reduces lipofuscin autofluorescence and, at higher light levels, RPE disruption in which the pattern of autofluorescence is permanently altered following light exposure. Both effects occur following exposure to visible light at irradiances that were previously thought to be safe. Photopigment, retinoids involved in the visual cycle, and bisretinoids in lipofuscin have been implicated as possible photosensitizers for photochemical damage. The mechanism of RPE disruption may follow either of these paths. On the other hand, autofluorescence photobleaching is likely an indicator of photooxidation of lipofuscin. The permanent changes inherent in RPE disruption might require modification of the light safety standards. AF photobleaching recovers after several hours possibly as a result of molecular migration and it is not yet clear whether it has any sequelae deleterious to retinal health. Understanding the mechanisms of phototoxicity is all the more important given the potential for increased susceptibility in the presence of ocular diseases that affect either the visual cycle and/or lipofuscin accumulation. In addition, knowledge of photochemical mechanisms can improve our understanding of some disease processes that may be influenced by light exposure, such as some forms of Leber's congenital amaurosis, and aid in the development of new therapies. Such treatment prior to intentional light exposures, as in ophthalmic examinations or surgeries, could provide an effective preventative strategy.

Keywords Phototoxicity; Photochemical; Retina; Retinal pigment epithelium; Autofluorescence; Visual cycle; Lipofuscin; Bisretinoids

Authors Jana Husse, Sophie Charlotte Hintze, Gregor Eichele, Hendrik Lehnert, Henrik Oster

Report Name Circadian Clock Genes Per1 and Per2 Regulate the Response of Metabolism-Associated Transcripts to Sleep Disruption

Publication PLoS ONE

Issue-page numbers 7(12): e52983. doi:10.1371/journal.pone.0052983

URL http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0052983

Abstract Human and animal studies demonstrate that short sleep or poor sleep quality, e.g. in night shift workers, promote the development of obesity and diabetes. Effects of sleep disruption on glucose homeostasis and liver physiology are well documented. However, changes in adipokine levels after sleep disruption suggest that adipocytes might be another important peripheral target of sleep. Circadian clocks regulate metabolic homeostasis and clock disruption can result in obesity and the metabolic syndrome. The finding that sleep and clock disruption have very similar metabolic effects prompted us to ask whether the circadian clock machinery may mediate the metabolic consequences of sleep disruption. To test this we analyzed energy homeostasis and adipocyte transcriptome regulation in a mouse model of shift work, in which we prevented mice from sleeping during the first six hours of their normal inactive phase for five consecutive days (timed sleep restriction – TSR). We compared the effects of TSR between wild-type and Per1/2 double mutant mice with the prediction that the absence of a circadian clock in Per1/2 mutants would result in a blunted metabolic response to TSR. In wild-types, TSR induces significant transcriptional reprogramming of white adipose tissue, suggestive of increased lipogenesis, together with increased secretion of the adipokine leptin and increased food intake, hallmarks of obesity and associated leptin resistance. Some of these changes persist for at least one week after the end of TSR, indicating that even short episodes of sleep disruption can induce prolonged physiological impairments. In contrast, Per1/2 deficient mice show blunted effects of TSR on food intake, leptin levels and adipose transcription. We conclude that the absence of a functional clock in Per1/2 double mutants protects these mice from TSR-induced metabolic reprogramming, suggesting a role of the circadian timing system in regulating the physiological effects of sleep disruption.

Keywords

Hyppönen E, Power C

Year 2007

Authors Elina Hyppönen and Chris Power

Report Name Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors

Publication Am J Clin Nutr

Issue-page numbers March 2007 vol. 85 no. 3 860-868

URL http://www.ajcn.org/content/85/3/860.abstract

Abstract

Background: Increased awareness of the importance of vitamin D to health has led to concerns about the prevalence of hypovitaminosis D in many parts of the world.

Objectives: We aimed to determine the prevalence of hypovitaminosis D in the white British population and to evaluate the influence of key dietary and lifestyle risk factors.

Design: We measured 25-hydroxyvitamin D [25(OH)D] in 7437 whites from the 1958 British birth cohort when they were 45 y old.

Results: The prevalence of hypovitaminosis D was highest during the winter and spring, when 25(OH)D concentrations <25, <40, and <75 nmol/L were found in 15.5%, 46.6%, and 87.1% of participants, respectively; the proportions were 3.2%, 15.4%, and 60.9%, respectively, during the summer and fall. Men had higher 25(OH)D concentrations, on average, than did women during the summer and fall but not during the winter and spring (P = 0.006, likelihood ratio test for interaction). 25(OH)D concentrations were significantly higher in participants who used vitamin D supplements or oily fish than in those who did not (P < 0.0001 for both) but were not significantly higher in participants who consumed vitamin D–fortified margarine than in those who did not (P = 0.10). 25(OH)D concentrations <40 nmol/L were twice as likely in the obese as in the nonobese and in Scottish participants as in those from other parts of Great Britain (ie, England and Wales) (P < 0.0001 for both).

Conclusion: Prevalence of hypovitaminosis D in the general population was alarmingly high during the winter and spring, which warrants action at a population level rather than at a risk group level.

Keywords 25-Hydroxyvitamin D • vitamin D status • vitamin D supplements • vitamin D deficiency • seasonality • fortified food • population studies

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IAOPA

Year 2007

Authors IAOPA

Report Name International Council of Aircraft Owner and Pilot

Publication http://www.iaopa.org/welcome/

Issue-page numbers

URL

Abstract

Keywords

IARC

Year 2010

Authors International Agency for Research on Cancer

Report Name Shiftwork

Publication IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

Issue-page numbers Volume 98 (2010) Painting, Firefighting, and Shiftwork

URL http://monographs.iarc.fr/ENG/Monographs/vol98/mono98-8.pdf

Abstract Shiftwork that involves circadian disruption is probably carcinogenic to humans (Group 2A)

Keywords Shiftwork, cancer, carcinogenic, circadian distruption

ICNIRP **Year** 2000

Authors ICNIRP

Report Name ICNIRP STATEMENT ON LIGHT-EMITTING DIODES (LEDS) AND LASER DIODES: IMPLICATIONS FOR HAZARD ASSESSMENT

Publication ICNIRP Statement - Health Physics Society

Issue-page numbers June 2000, Volume 78, Number 6

URL http://icnirp.org/documents/Led.pdf

Abstract

BOTH VISIBLE and infrared laser diodes and light-emitting diodes (LEDs, or sometimes referred to as IREDs in the infrared) are widely used in displays and in many home entertainment systems, toys, signal lamps, optical fiber communication, and optical surveillance systems. Collectively these are referred to as diode emitters (DEs). While the higher power laser diodes have routinely been considered to be “eye hazards,” traditional LEDs have been regarded as safe. However, with the recent development of higher power LEDs, there has been an effort to develop LED safety standards. There are a variety of LED types ranging from surface emitters to superluminescent diodes (SLDs). The latter have some characteristics more typical of diode lasers. Questions have therefore arisen as to whether laser or incoherent radiation exposure limits (ELs) should be applied to each type of emitter. Based upon current exposure limits, most LEDs—particularly surface-emitting LEDs—pose no clear hazard to the eye. Current surface-emitting LEDs produce exposure levels at the retina that are less than 1% of the levels that are known to cause retinal injury (WHO 1982; Sliney and Wolbarsht 1980) even when the LEDs are viewed at extremely close distances (e.g., at 10 cm)
(Sliney and Wolbarsht 1980). At typical viewing distances of 0.5 to 2 m, the levels are less than 0.1% of
retinal injury levels. Even lengthy exposures of the cornea and lens of the eye pose no hazards whatsoever.
From a safety standpoint, LEDs have been treated both as lasers (e.g., in IEC standard 60825-1) (IEC 1998; ANSI 1988) and as lamps (CIE 1999; ANSI/IESNA 1996a,b). Because of some confusion relating to the actual risk, ICNIRP organized a panel of experts to review the potential hazards of current DEs.
Laser diodes are constructed with miniature resonant cavities with gain, produce a very narrow spectral
bandwidth, can generally achieve shorter pulse durations, are not limited in radiance, and can emit much higher radiant powers than LEDs. Light-emitting diodes of low to moderate brightness
(luminance) are used in many types of visual displays as indicator lights and many related products. Higher power LEDs and IREDs are used as signal lamps and in a wide variety of domestic and industrial products, and can compete with laser diodes in limited optical communications systems, i.e., in local-area networks (LANs). They are generally not competitive with laser diodes because of different output characteristics. These differences in output characteristics define both their uses and their potential eye hazards. Most current LEDs have very limited radiance and do not pose a clear eye hazard, despite the fact that they have been included in some laser safety standards in the past few years.

Keywords

ICNIRP **Year** 2005

Authors ICNIRP

Report Name Adjustment of guidelines for exposure of the eye to optical radiation from ocular instruments:

Publication APPLIED OPTICS

Issue-page numbers Vol. 44, No. 11 10 April 2005

URL http://www.icnirp.de/documents/OcularInstruments0405.pdf

Abstract

A variety of optical and electro-optical instruments are used for both diagnostic and therapeutic applications to the human eye. These generally expose ocular structures to either coherent or incoherent optical radiation (ultraviolet, visible, or infrared radiation) under unique conditions. We convert both laser and incoherent exposure guidelines derived for normal exposure conditions to the application of ophthalmic sources.

Keywords

ICNIRP **Year** 2000

Authors ICNIRP

Report Name REVISION OF GUIDELINES ON LIMITS OF EXPOSURE TO LASER RADIATION OF WAVELENGTHS BETWEEN 400 nm AND 1.4 mm

Publication ICNIRP Guidelines Health Physics

Issue-page numbers October 2000, Volume 79, Number 4

URL http://www.icnirp.de/documents/laser400nm+.pdf

Abstract

SINCE THE publication of the ICNIRP Guidelines on Limits of Exposure to Laser Radiation of Wavelengths between 180 nm and 1,000 mm (1996), recent research has made it appropriate to update the laser retinal protection guidelines for ultrashort (sub-nanosecond) pulse durations and for continuous-wave (CW) exposures lasting 10 s or longer. These revisions are limited to the retinal hazard spectral region (400 nm to 1,400 nm). No changes in the limits are recommended for any exposure duration between 1 nanosecond (ns) and 10 s for intrabeam viewing (nor to 0.7 s for viewing extended sources). Studies of laser-induced retinal injury from modelocked laser pulses have been carried out for more than two decades (Goldman et al. 1977); however, until recently threshold data have not appeared to be consistent, nor have the underlying damage mechanisms for sub-nanosecond (sub-ns) laser-induced injury been well understood. The Commission organized a task group† on ophthalmic biophysics to review the scientific data and
current knowledge of retinal injury mechanisms to consider recommending an extension of the laser guidelines to pulse durations less than 1 ns. The result of this review is that the Commission believes that for ultrashort laser pulses there is now a reasonably consistent explanation of the non-linear optical phenomena that occur in the eye which cause retinal damage. Thus it is appropriate to recommend limits of exposure for pulse durations between 100 femtoseconds (fs) and 1 ns.
Inconsistencies had been discovered in CW laser exposure limits (ELs) when these limits were applied to
intentional viewing of light emitting diodes (LEDs) and diode lasers. Consequently, the Commission also requested the ophthalmic biophysics task group to study the validity of the current guidelines for CW exposures. Prior to the extension of the scope of some laser safety standards to apply to LEDs, general guidance in all laser safety standards was never to view a laser beam directly (intrabeam viewing) and serious efforts to derive accurate ELs for durations exceeding ;10 s did not occur. Indeed, the previous effort had been to simplify the expression, combining both thermal and photochemical damage mechanisms. This approach necessitated very large safety factors to accommodate both injury mechanisms within a single mathematical formulation. The task group reviewed the past criteria and the effects of eye movements, source size, pupillary response, spectral absorption, and the two competing retinal damage mechanisms (photochemical and thermochemical) upon the potential for retinal injury when
viewing a CW laser beam or any small light source. The group recommended splitting the ocular ELs into dual limits: one for photoretinitis (photochemical) and one for retinal burns (thermochemical injury) to eliminate highly inconsistent safety factors. The review showed that the impact of eye movements is greatest for small light sources, but least fo large sources. This dual-limit approach follows the same approach used to evaluate incoherent sources.

Keywords

ICNIRP

Year 2010

Authors ICNIRP

Report Name Protection of Workers against Ultraviolet Radiation

Publication Health Physics

Issue-page numbers 99(1):66-87

URL http://www.icnirp.de/documents/UVWorkersHP.pdf

Abstract OCCUPATIONAL EXPOSURES to ultraviolet radiation (UVR) can originate from the sun and from artificial sources such as specialized lamps and open arcs processes, e.g., welding (Tenkate and Collins 1997; Hietanen and von Nandelstadh 1998). Although indoor workers are normally protected by clothing and eyewear, the same level of protection is not generally achieved for outdoor workers. Most often, over-exposures of indoor workers arise from accidental failures of safety measures or protective equipment. Outdoor workers receive significant exposure to solar UVR and are thereby at increased risk of suffering the adverse consequences associated with excessive UVR exposure of the eyes and skin. The magnitude of the risk for the skin depends greatly upon climatological factors and personal sensitivity to UVR, the latter incorporating both the skin “phototype” and degree of acclimatization, or adaptation, to UVR. However, this great range of individual susceptibility does not exist for the eye, and people of all racial types are usceptible to cataract and other UVR-related eye diseases.

Keywords

ICNIRP

Year 2004

Authors ICNIRP

Report Name GUIDELINES ON LIMITS OF EXPOSURE TO ULTRAVIOLET RADIATION OF WAVELENGTHS BETWEEN 180 NM AND 400 NM (INCOHERENT OPTICAL RADIATION)

Publication Health Physics

Issue-page numbers August 2004, Volume 87, Number 2

URL http://www.icnirp.de/documents/UV2004.pdf

Abstract SINCE THE publication of the ICNIRP Guidelines on UV Radiation Limits (ICNIRP 1996),† recent research has made it appropriate to update the guidelines for protection. While no significant changes are made in the values, the biological basis can be strengthened, and the limitations on use can be clarified.

Keywords

ICNIRP

Year 2001

Authors International Commission for Non-Ionizing Radiation Protection, Standing Committee on Epidemiology, Anders Ahlbom, Elisabeth Cardis, Adele Green, Martha Linet, David Savil

Report Name Review of the Epidemiologic Literature on EMF and Health

Publication Environ Health Perspect

Issue-page numbers 109:911-933

URL http://dx.doi.org/10.1289/ehp.01109s6911

Abstract Review Exposures to extremely low-frequency electric and magnetic fields (EMF) emanating from the generation, transmission, and use of electricity are a ubiquitous part of modern life. Concern about potential adverse health effects was initially brought to prominence by an epidemiologic report two decades ago from Denver on childhood cancer. We reviewed the now voluminous epidemiologic literature on EMF and risks of chronic disease and conclude the following: a) The quality of epidemiologic studies on this topic has improved over time and several of the recent studies on childhood leukemia and on cancer associated with occupational exposure are close to the limit of what can realistically be achieved in terms of size of study and methodological rigor. b) Exposure assessment is a particular difficulty of EMF epidemiology, in several respects: i) The exposure is imperceptible, ubiquitous, has multiple sources, and can vary greatly over time and short distances. ii) The exposure period of relevance is before the date at which measurements can realistically be obtained and of unknown duration and induction period. iii) The appropriate exposure metric is not known and there are no biological data from which to impute it. c) In the absence of experimental evidence and given the methodological uncertainties in the epidemiologic literature, there is no chronic disease for which an etiological relation to EMF can be regarded as established. d) There has been a large body of high quality data for childhood cancer, and also for adult leukemia and brain tumor in relation to occupational exposure. Among all the outcomes evaluated in epidemiologic studies of EMF, childhood leukemia in relation to postnatal exposures above 0.4 μT is the one for which there is most evidence of an association. The relative risk has been estimated at 2.0 (95% confidence limit: 1.27-3.13) in a large pooled analysis. This is unlikely to be due to chance but, may be, in part, due to bias. This is difficult to interpret in the absence of a known mechanism or reproducible experimental support. In the large pooled analysis only 0.8% of all children were exposed above 0.4 μT. Further studies need to be designed to test specific hypotheses such as aspects of selection bias or exposure. On the basis of epidemiologic findings, evidence shows an association of amyotrophic lateral sclerosis with occupational EMF exposure although confounding is a potential explanation. Breast cancer, cardiovascular disease, and suicide and depression remain unresolved.

Keywords cancer, chronic disease, epidemiology, extremely low-frequency EMF, review

ICNIRP

Year 2006

Authors ICNIRP - The International Commission on Non-Ionizing Radiation Protection

Report Name ICNIRP STATEMENT ON FAR INFRARED RADIATION EXPOSURE

Publication Bulletin

Issue-page numbers

URL http://www.icnirp.de/documents/infrared.pdf

Abstract THE INTERNATIONAL Commission on Non Ionizing Radiation Protection (ICNIRP) currently provides guidelines to limit human exposure to intense, broadband infrared radiation (ICNIRP 1997). The guidelines that pertained to infrared radiation (IR) were developed initially with an aim to provide guidance for protecting against hazards from high-intensity artificial sources and to protect workers in hot industries. Detailed guidance for exposure to longer far-infrared wavelengths (referred to as IR-C radiation) was not provided because the energy at longer wavelengths from most lamps and industrial infrared sources of concern actually contribute only a small fraction of the total radiant heat energy and did not require measurement. Based upon the total optical emission of industrial sources and high intensity lamps, the limited IR-C contribution was incorporated into the derivation of the limits. Furthermore, when the limits were developed, the glass or quartz windows used with most portable thermal radiometers blocked most energy beyond 3–4 m; thus, it was reasoned that the appropriate field measurements of IR sources could best be accomplished by limiting the measurements for risk assessments to wavelengths less than 3 m. Therefore, ICNIRP previously did not provide specific guidance for IR-C (3 m–1,000 m) radiation; although, it was recommended that IR-C radiation should be included in measurements if this was of concern

Keywords

ICNRP

Year 1997

Authors ICNRP

Report Name Guidelines on Limits of Exposure to Broad-Band Incoherent Optical Radiation (0.38 to 3μm)

Publication Health Physics

Issue-page numbers 73 (3): 539-554

URL http://www.icnirp.de/documents/broadband.pdf

Abstract

Keywords

IDA

Year 2008

Authors IDA (International Dark-Sky Association)

Report Name Effects of Artificial Light at Night on Wildlife

Publication IDA

Issue-page numbers Practical Guide 2

URL http://docs.darksky.org/PG/PG2-wildlife.pdf

Abstract

From the beginning of existence, humans have controlled their immediate environment, building shelters to keep out the elements and fires to banish the darkness. As civilizations continue to develop, humans are able to affect dizzying change on habitats in all corners of the globe. Though agreeable to us, many of the comforts of advanced society are devastating to the creatures that share the earth. A growing body of data suggests that artificial night lighting has negative and deadly effects on a wide range of creatures, including amphibians, birds, mammals, insects, and even plants.

Keywords

IDA

Year 0

Authors IDA

Report Name Economic Issues in Wasted and Inefficient Outdoor Lighting

Publication IDA (International Dark-Sky Association)

Issue-page numbers Information Sheet #26

URL http://www.darksky.org/assets/documents/is026.pdf

Abstract Let's consider the energy use of inefficient outdoor lighting fixtures. A very common fixture seen everywhere throughout the United States, in cities and in the country, is the 175 watt dusk-to-dawn mercury vapor light. It is used for yard lighting, security lighting, and street lighting. It contains a photocell sensor switch to turn it on at dusk and off at dawn, hence the name "dusk to dawn". Quite a number of fixture manufacturers make such a unit, and many utility companies promote its use for "security" or "safety" at night. We see ads proclaiming "Light Up the Night", all in the interest of security or safety or some such thing. All this is in light of the fact that there is more crime in the daytime than at night, that there is more crime in well-lit areas than in dark areas (compare the light level in New York City to that in a typical rural Midwestern city, and the crime level in both locations, for example).

Keywords economic

IEA/OECD

Year 2006

Authors IEA/OECD

Report Name Light's labour's lost: policies for energy-efficient lighting

Publication IEA/OECD: Paris; 2006

Issue-page numbers

URL http://www.iea.org/papers/2008/cd_energy_efficiency_policy/4-Lighting/4-light2006.pdf

Abstract When the incandescent lamp was first commercialised the main mode of transport was the horse, trains were powered by steam, balloons were the only means of flight and the telegraph was the state of the art for long-distance communication. Much has changed in the intervening 127 years, but much has also remained the same. In 1879 the incandescent lamp set a new standard in energy-efficient lighting technology, but today good-quality compact fluorescent lamps need only onequarter of the power to provide the same amount of light. Yet most of us continue to rely on the "horse" of the incandescent lamp instead of the "internal combustion engine" of the compact fluorescent lamp. Nor is this the only way in which lighting energy is being wasted. We illuminate rooms when we're not there, we over-light spaces, we squander available daylight and we underutilise the most efficient street lighting and non-residential building lighting technologies. …

Keywords

IESNA

Year 2008

Authors IESNA (Illuminating Engineering Society of North America)

Report Name Light and Human Health: An Overview of the Impact of Light on Visual, Circadian, Neuroendocrine and Neurobehavioral Responses

Publication IESNA

Issue-page numbers TM-18-08

URL http://www.ies.org/store/product/light-and-human-health-an-overview-of-the-impact-of-light-on-visual-circadian-neuroendocrine-and-neurobehavioral-responses-1175.cfm

Abstract The aim of this document is twofold:

1. to explain the physiology by which the retina converts optical radiation (visual spectrum of light) signals into neural signals for visional and for circadian, neuroendocrine, and neurobehaviorial responses, and
2. to discuss the responses of these systems to optical radiation stimuli.

Keywords

Iglesias R, Terrés A, Chavarria A **Year** 1980

Authors Iglesias R, Terrés A, Chavarria A

Report Name Disorders of the menstrual cycle in airline stewardesses

Publication Aviat Space Environ Med

Issue-page numbers 51:518–520. PMID:7387577

URL http://www.ncbi.nlm.nih.gov/pubmed/7387577

Abstract Of 200 airline stewardesses, 39% underwent unfavourable changes in the menstrual cycle after commencing aeronautical activities while 11% who had previous disorders healed soon after joining the company. Although 48% of the stewardesses underwent changes in menstruation during flight, in about half of these the menstrual flow increased and in the other half it decreased or disappeared, only to reappear with greater intensity after the flight; 38% of the stewardesses manifected suffering from pelvic discomfort after long flights. Sufficient research in this field has not been done. Therefore, it is difficult to trace the exact origin and mechanism of these changes in the menstrual cycle. Stress and internal desynchronitation due to disruption of circadian rhythm may intervene in generating these disorders.

Keywords

Illnerova H, Vaněeccek J, Křeček J **Year** 1979

Authors Helena Illnerova, J. Vaněeccek, J. Křeček, L. Wetterberg, J. Sääf

Report Name Effect of one minute exposure to light at night on rat pineal serotonin N-acetyltransferase and melatonin

Publication Journal of Neurochemistry

Issue-page numbers Volume 32, Issue 2, pages 673–675, February 1979

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1471-4159.1979.tb00407.x/abstract

Abstract N/A

Keywords

Illnerová H, Zvolsky P, Vaněcek J **Year** 1985

Authors Illnerová H, Zvolsky P, Vaněcek J

Report Name The circadian rhythm in plasma melatonin concentration of the urbanized man: the effect of summer and winter time

Publication Brain Res

Issue-page numbers 328:186–189 doi:10.1016/0006-8993(85)91342-3. PMID:3971177

URL http://www.sciencedirect.com/science/article/pii/0006899385913423

Abstract Plasma melatonin rhythms were measured in healthy urbanized persons between July 4 and 5 and between January 13 and 14. In contrast to findings in other mammals studied thus far, no difference in the duration of elevated night melatonin concentration was observed between summer and winter. In winter, melatonin rhythms were phase-delayed by about 1.5 h as compared with summer patterns.

Keywords circadian; photoperiod; pineal; melatonin; human

International Labour Organization **Year** 2006

Authors International Labour Organization

Report Name LABORSTA Internet

Publication Yearly statistics

Issue-page numbers Geneva ILO

URL http://laborsta.ilo.org/

Abstract N/A

Keywords

	International Labour Organization	***Year***	1948
Authors	International Labour Organization		
Report Name	Night Work of Young Persons (Industry) Convention (Revised)		
Publication	C90 Geneva, ILO		
Issue-page numbers			
URL	http://www.ilo.org/ilolex/cgi-lex/convde.pl?C090		
Abstract	N/A		
Keywords			

	International Labour Organization	***Year***	1990
Authors	International Labour Organization		
Report Name	Night Work Recommendation		
Publication	R178		
Issue-page numbers	Geneva, ILO		
URL	http://www.ilo.org/ilolex/cgi-lex/convde.pl?R178		
Abstract	N/A		
Keywords			

	International Labour Organization	***Year***	1990
Authors	International Labour Organization		
Report Name	Night Work Convention		
Publication	C171		
Issue-page numbers	Geneva, ILO.		
URL	http://www.ilo.org/ilolex/cgi-lex/convde.pl?C171		
Abstract	N/A		
Keywords			

	International Labour Organization	***Year***	1995
Authors	International Labour Organization		
Report Name	Working time around the world		
Publication	Conditions of Work Digest. - (International Labour Office)		
Issue-page numbers	Vol 14, Geneva, ILO		
URL	http://www.ilo.org/ilolex/english/index.htm		
Abstract	N/A		
Keywords			

International Labour Organization

Year 1996

Authors International Labour Organization

Report Name Seafarers' Hours of Work and the Manning of Ships Convention

Publication ILO convention No 180

Issue-page numbers Geneva, 22 October 1996

URL http://www.ilo.org/ilolex/cgi-lex/convde.pl?C180

Abstract N/A

Keywords

Year 1999

Authors Irvine D, Davies DM

Report Name British Airways flightdeck mortality study, 1950–1992

Publication Aviat Space Environ Med

Issue-page numbers 70:548–555. PMID:10373044

URL http://www.ncbi.nlm.nih.gov/pubmed/10373044

Abstract

OBJECTIVE:

To study the mortality and life expectancy of male British Airways flightdeck crew and to establish whether proportionate mortality excesses shown earlier for brain/CNS cancer, colon cancer and melanoma remained evident.
METHODS:

A Standardized Mortality Ratio study (SMR) using England and Wales as the comparison population was carried out for 6209 male pilots and 1153 male flight engineers employed for at least 1 yr between January 1, 1950 and December 31, 1992. Internal relative risk comparisons were made between shorthaul and longhaul operations defined broadly as flights within Europe and beyond Europe, respectively.
RESULTS:

The all-causes SMR for pilots of 61 (592 deaths) and 56 for flight engineers (127 deaths) confirmed the expected Healthy Worker Effect. In pilots apart from the known excess of deaths from aircraft accidents (SMR 14694), most of the comparisons showed significant deficits in mortality. The SMR's for brain/CNS cancer (143) and colon cancer (111) were no longer statistically significant. The SMR of 333 for melanoma was significantly raised in pilots but was not evident in flight engineers. Life expectancy for longhaul pilots and flight engineers was 4-5 yr better than England and Wales for ages 55-65 while the advantage for shorthaul pilots was reduced to between 2-3 yr. Cases of leukemia and aleukaemia in pilots were less than expected and less than the positive excess predicted from modeling based on radiation dose.
CONCLUSION:

The study confirms that flightdeck crew live longer than the England and Wales population and do not exhibit patterns of death that could be directly attributable to occupation.

Keywords

Authors Irvine D, Davies DM

Report Name The mortality of British Airways pilots, 1966–1989: a proportional mortality study

Publication Aviat Space Environ Med

Issue-page numbers 63:276–279. PMID:1610337

URL http://www.ncbi.nlm.nih.gov/pubmed/1610337

Abstract Of 446 deaths among serving and retired British Airways pilots between 1966 and 1989, 411 were analysed using the Proportional Mortality Ratio (PMR) technique. After removal of the predictable excess of aircraft accidents, excesses of cancer (PMR 1.31) and other accidents (1.60) were balanced by deficits in diseases of the circulatory (0.83) and respiratory (0.49) systems. While lung cancer was close to expectation (1.10), consistent excesses were shown in all analyses for malignant melanoma (6.68), cirrhosis of the liver (2.88), colon cancer (2.30) and brain/CNS cancer (2.68). Consideration of these ratios in relation to pilots' lifestyle and occupation leads to the conclusion that the brain/CNS cancer excess must be studied further.

Keywords

Authors Irwin M, Brown M, Patterson T et al.

Report Name Neuropeptide Y and natural killer cell activity: findings in depression and Alzheimer caregiver stress

Publication FASEB J

Issue-page numbers 5:3100–3107. PMID:1743441

URL http://www.fasebj.org/content/5/15/3100.full.pdf

Abstract

ABSTRACT A reduction in immune function has been found in patients with a major depressive disorder and in persons undergoing severe life stress. This study investigated the association between increased sympathetic nervous system activity and reduced natural killer (NK) cytotoxicity in depression and Alzheimer caregiver stress. NK activity and plasma concentrations of epinephrine, norepinephrine, and neuropeptide Y were measured in depressed patients (n =19) and age- and gender-matched controls (n = 19), and in Alzheimer spousal caregivers (n =48) and matched noncaregiver controls (n =17). Plasma levels of neuropeptide Y, but not circulating basal levels of catecholamines, were significantly ($P < 0.01$) elevated in the depressed patients and in the caregivers compared with respective controls. NK activity was significantly ($P < 0.001$) lower in the depressed patients than in their controls, but not different between the caregivers and the noncaregiver controls. Circulating concentrations of neuropeptide Y, but not catecholamines, were inversely correlated ($r = -0.31$, $P < 0.001$) with NK activity. In addition, multiple regression analyses demonstrated that the significant ($P < 0.01$) association between neuropeptide Y and natural cytotoxicity was independent of the relative contribution of age and basal and dynamic levels of epinephrine and norepinephrine. These findings suggest that increased sympathetic nervous system activity and the release of neuropeptide Y may be associated with the modulation of NK cytotoxicity. - Irwin, M.; Brown, M.; Patterson, T.; Hauger, R.; Mascovich, A.; Grant, I. Neuropeptide Y and natural killer cell activity: findings in depression and Alzheimer caregiver stress.

Keywords depression, life, stress, sympathetic nervous system activation, neural modulation of immunity

Irwin M, Hauger RL, Brown MR, Britton KT | ***Year*** 1988

Authors Irwin M, Hauger RL, Brown MR, Britton KT

Report Name CRF activates autonomic nervous system and reduces natural killer cytotoxicity

Publication Am J Physiol

Issue-page numbers 255:R744–R747. PMID:2847561

URL http://ajpregu.physiology.org/content/255/5/R744.short

Abstract Corticotropin-releasing factor (CRF) acts within the brain to elicit changes in neuroendocrine, autonomic, and behavioral activity similar to those observed after stress. A reduction of immune function has also been described following central administration of CRF. In this study, we examined whether autonomic nervous system activation plays a role in CRF-induced suppression of natural killer (NK) cytotoxicity. synthetic rat CRF (1.0 microgram) microinjected into the lateral ventricle significantly increased plasma concentrations of norepinephrine and reduced splenic NK cell activity in the rat. Pretreatment of the animals with the ganglionic-blocking agent chlorisondamine completely abolished the CRF-induced increase in plasma norepinephrine levels and reduction in NK activity. However, CRF-induced elevations in plasma levels of adrenocorticotropic hormone and corticosterone were not affected by chlorisondamine. The results of this study suggest that activation of the sympathetic nervous system plays a role in CRF-induced suppression of NK cytotoxicity.

Keywords

Irwin M, Hauger RL, Jones L et al. | ***Year*** 1990

Authors Irwin M, Hauger RL, Jones L et al.

Report Name Sympathetic nervous system mediates central corticotropin-releasing factor induced suppression of natural killer cytotoxicity

Publication J Pharmacol Exp Ther

Issue-page numbers 255:101–107. PMID: 2120421

URL http://jpet.aspetjournals.org/content/255/1/101.abstract

Abstract Corticotropin-releasing factor (CRF) acts within the brain to elicit changes in neuroendocrine, autonomic and behavioral activity similar to those observed after stress. A reduction of cellular immune function as measured by splenic natural killer cell activity has also been described following the central administration of CRF. In this study we evaluated the role of the sympathetic nervous system in mediating CRF-induced suppression of natural killer (NK) cytotoxicity. Synthetic rat CRF (1.0 microgram) microinjected into the lateral ventricle increased noradrenergic function and reduced NK activity in the rat spleen. Pretreatment of the animals by chemical sympathectomy (6-hydroxy-dopamine, 100 mg/kg i.p. daily over 10 days) produced a greater than 95% reduction of splenic norepinephrine concentration and abolished completely both the CRF-induced increase in plasma catecholamine levels and the reduction in splenic NK activity. In addition, beta adrenergic receptor blockade (either propranolol, 10 mg/kg i.p., or butoxamine, 25 mg/kg i.p. 30 min before i.c.v. infusion) antagonized the CRF-induced reduction in NK activity. Measurement of circulating levels of adrenocorticotrophic hormone and corticosterone demonstrated that activation of the pituitary adrenal axis by CRF was dissociated from changes in NK activity. These findings suggest that the sympathetic nervous system mediates the suppression of splenic NK cytotoxicity after i.c.v. CRF.

Keywords

Irwin M, Mascovich A, Gillin JC et al. ***Year*** 1994

Authors Irwin M, Mascovich A, Gillin JC et al.

Report Name Partial sleep deprivation reduces natural killer cell activity in humans

Publication Psychosom Med

Issue-page numbers 56:493–498. PMID:7871104

URL http://www.psychosomaticmedicine.org/content/56/6/493.abstract

Abstract Sleep disturbance, measured by either subjective report or electroencephalographic (EEG) assessment of sleep, correlates with a reduction of natural killer (NK) cell activity in major depression. To test whether sleep loss independent of mood disturbance alters daytime values of cellular immune function, the effect of late-night partial sleep deprivation on NK cell activity was studied in 23 medically and psychiatrically healthy male volunteers. After a night of sleep deprivation between 3 and 7 AM, NK cell activity was reduced in 18 of the 23 subjects with average lytic activity reduced significantly ($p < .01$) to a level 72% of the mean of three separate baseline values. After a night of resumed nocturnal sleep, NK cell activity had returned to baseline levels. These data implicate sleep in the modulation of natural immunity and demonstrate that even modest disturbances of sleep produce a reduction of NK cell activity.

Keywords

Irwin M, McClintick J, Costlow C et al. ***Year*** 1996

Authors Irwin M, McClintick J, Costlow C et al.

Report Name Partial night sleep deprivation reduces natural killer and cellular immune responses in humans

Publication FASEB J

Issue-page numbers 10:643–653. PMID:8621064

URL http://www.fasebj.org/content/10/5/643.abstract

Abstract Prolonged and severe sleep deprivation is associated with alterations of natural and cellular immune function. To determine whether alterations of immune function also occur after even a modest loss of sleep, the effects of early-night partial sleep deprivation on circulating numbers of white blood cells, natural killer (NK) cell number and cytotoxicity, lymphokine-activated killer (LAK) cell number and activity, and stimulated interleukin-2 (IL-2) production were studied in 42 medically and psychiatrically healthy male volunteers. After a night of sleep deprivation between 10 P.M. and 3 A.M., a reduction of natural immune responses as measured by NK cell activity, NK activity per number of NK cells, LAK activity, and LAK activity per number of LAK precursors (CD16,56, CD25) was found. In addition, concanavalin A-stimulated IL-2 production was suppressed after sleep deprivation due to changes in both adherent and nonadherent cell populations. After a night of recovery sleep, NK activity returned to baseline levels and IL-2 production remained suppressed. These data implicate sleep in the modulation of immunity and demonstrate that even a modest disturbance of sleep produces a reduction of natural immune responses and T cell cytokine production.

Keywords

Authors Irwin M, Vale W, Rivier C

Report Name Central corticotropin-releasing factor mediates the suppressive effect of stress on natural killer cytotoxicity

Publication Endocrinology

Issue-page numbers 126:2837–2844 doi:10.1210/endo-126-6-2837. PMID:2161737

URL http://endo.endojournals.org/content/126/6/2837

Abstract

CRF acts within the brain to elicit changes in neuroendocrine, autonomic, and behavioral activity similar to that observed after stress. A reduction of splenic natural killer (NK) activity has also been described after the central administration of CRF. In this study we examined whether the central release of CRF plays a physiological role in mediating stressinduced suppression of NK cytotoxicity. Four sessions of footshock stress (1.5 mamp; 1-sec duration; 60-Hz sine wave; delivered randomly twice per min for 30 min) over a 48-h period significantly ($P < 0.001$) reduced splenic NK activity in the rat. Pretreatment of the animals by central administration of polyclonal CRF antibodies completely antagonized the stress-induced suppression of NK cell activity. In contrast, the peripheral immunoneutralization of CRF was ineffective. Measurement of circulating levels of ACTH and corticosterone demonstrated that stress-induced elevations of ACTH and corticosterone were significantly ($P < 0.05$) attenuated by peripheral anti-CRF serum, but not by centrally administered anti-CRF. These findings suggest that endogenous brain CRF coordinates the suppressive effect of footshock stress on NK cytotoxicity independently of pituitary-adrenal activation.

Keywords

Authors Irwin MR, Wang M, Campomayor CO et al.

Report Name Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation

Publication Arch Intern Med

Issue-page numbers 166:1756–1762 doi:10.1001/archinte.166.16.1756. PMID:16983055

URL http://archinte.ama-assn.org/cgi/content/abstract/166/16/1756

Abstract

Background Inflammation is associated with increased risk of cardiovascular disorders, arthritis, diabetes mellitus, and mortality. The effects of sleep loss on the cellular and genomic mechanisms that contribute to inflammatory cytokine activity are not known.

Methods In 30 healthy adults, monocyte intracellular proinflammatory cytokine production was repeatedly assessed during the day across 3 baseline periods and after partial sleep deprivation (awake from 11 PM to 3 AM). We analyzed the impact of sleep loss on transcription of proinflammatory cytokine genes and used DNA microarray analyses to characterize candidate transcription-control pathways that might mediate the effects of sleep loss on leukocyte gene expression.

Results In the morning after a night of sleep loss, monocyte production of interleukin 6 and tumor necrosis factor {alpha} was significantly greater compared with morning levels following uninterrupted sleep. In addition, sleep loss induced a more than 3-fold increase in transcription of interleukin 6 messenger RNA and a 2-fold increase in tumor necrosis factor {alpha} messenger RNA. Bioinformatics analyses suggested that the inflammatory response was mediated by the nuclear factor {kappa}B inflammatory signaling system as well as through classic hormone and growth factor response pathways.

Conclusions Sleep loss induces a functional alteration of the monocyte proinflammatory cytokine response. A modest amount of sleep loss also alters molecular processes that drive cellular immune activation and induce inflammatory cytokines; mapping the dynamics of sleep loss on molecular signaling pathways has implications for understanding the role of sleep in altering immune cell physiologic characteristics. Interventions that target sleep might constitute new strategies to constrain inflammation with effects on inflammatory disease risk.

Keywords

Ishida A, Mutoh T, Ueyama T et al. ***Year*** 2005

Authors Atsushi Ishida, Tatsushi Mutoh, Tomoko Ueyama, Hideki Bando, Satoru Masubuchi, Daiichiro Nakahara, Gozoh Tsujimoto, Hitoshi Okamura

Report Name Light activates the adrenal gland: timing of gene expression and glucocorticoid release

Publication Cell Metab

Issue-page numbers 2:297–307 doi:10.1016/j.cmet.2005.09.009. PMID:16271530

URL http://www.sciencedirect.com/science/article/pii/S155041310500269X

Abstract

Light is a powerful synchronizer of the circadian rhythms, and bright light therapy is known to improve metabolic and hormonal status of circadian rhythm sleep disorders, although its mechanism is poorly understood. In the present study, we revealed that light induces gene expression in the adrenal gland via the suprachiasmatic nucleus (SCN)-sympathetic nervous system. Moreover, this gene expression accompanies the surge of plasma and brain corticosterone levels without accompanying activation of the hypothalamo-adenohypophysial axis. The abolishment after SCN lesioning, and the day-night difference of light-induced adrenal gene expression and corticosterone release, clearly indicate that this phenomenon is closely linked to the circadian clock. The magnitude of corticostereone response is dose dependently correlated with the light intensity. The light-induced clock-dependent secretion of glucocorticoids adjusts cellular metabolisms to the new light-on environment.

Keywords

Authors Hitoshi Ishikawa, Asami Onodera, Ken Asakawa, Satoshi Nakadomari and Kimiya Shimizu

Report Name Effects of selective-wavelength block filters on pupillary light reflex under red and blue light stimuli

Publication Japanese Journal of Ophthalmology

Issue-page numbers DOI: 10.1007/s10384-011-0116-1

URL http://www.springerlink.com/content/246n76421757635v/

Abstract

Purpose
To investigate at which wavelength melanopsin-containing retinal ganglion cells (mRGCs) depolarize and how they affect pupillary constriction induced by light stimulation in humans.
Methods
The pupil light reflex was evaluated for 30 normal subjects by use of an infrared pupillometer. Blue light stimulation (470 nm) and red light stimulation (635 nm) of 100 cd/m2 were selected. Selective-wavelength block filters which can selectively remove the wavelengths 440 and 470 nm were used. Visual tests were also performed to observe the effects of the filters on visual acuity, color vision, and contrast sensitivity.
Results
The pupil transiently constricts and then settles toward a steady-state diameter when stimulated with the light. When the 470-nm-block filter was worn, the sustained phase of pupillary constriction, thought to be mediated by the mRGCs, was not stable but there was no effect on the initial phase of pupillary constriction under blue light stimulation. Visual acuity, color vision, and contrast sensitivity were not affected by the 470-nm-block filter.
Conclusions
These results suggest that the mRGC in humans may respond to 470-nm-wavelength light at 100 cd/m2, and there is a possibility of affecting the sustained phase of the light reflex without changing visual performance.

Keywords Pupil light reflex – Melanopsin – Melanopsin-containing retinal ganglion cells (mRGCs) – Selective-wavelength block filters

Ishikawa T, Matsumoto A, Kato T, et al. **Year** 0

Authors T Ishikawa, A Matsumoto, T Kato, S Togashi, H Ryo, … M Ikenaga, T Todo, R Ueda, T Tanimura

Report Name DCRY is a Drosophila photoreceptor protein implicated in light entrainment of circadian rhythm

Publication Genes to cells devoted to molecular cellular mechanisms

Issue-page numbers Volume: 4, Issue: 1, Publisher: John Wiley & Sons, Pages: 57-65

URL http://www.mendeley.com/research/dcry-drosophila-photoreceptor-protein-implicated-light-entrainment-circadian-rhythm/

Abstract BACKGROUND: Light is the major environmental signal for the entrainment of circadian rhythms. In Drosophila melanogaster, the period(per) and timeless (tim) genes are required for circadian behavioural rhythms and their expression levels undergo circadian fluctuations. Light signals can entrain these rhythms by shifting their phases. However, little is known about the molecular mechanism for the perception and transduction of the light signal. The members of the photolyase/cryptochrome family contain flavin adenine dinucleotide (FAD) as chromophore and are involved in two diverse functions, DNA repair and photoreception of environmental light signals. RESULTS: We report the cloning of a new member of this family, dcry, from Drosophila. Northern blot analysis shows that this gene is expressed in various tissues. The dcry mRNA is expressed in a circadian manner in adult heads, while such rhythmic fluctuation is abolished in the clock-defective per0 and tim0 mutants. The circadian expression is dampened down in constant darkness. The over-expression of the dcry gene alters the light-induced phase delay in the locomotor activity rhythms of flies. CONCLUSION: These results suggest that DCRY is a circadian photoreceptor and that its expression is regulated by circadian clock genes.

Keywords

Authors Iversen OH, Iversen UM

Report Name A diurnal variation in the tumorigenic response of mouse epidermis to a single application of the strong short-acting chemical carcinogen methylnitrosourea. A doseresponse stuc

Publication In Vivo

Issue-page numbers 9:117–132. PMID:7548787

URL http://www.ncbi.nlm.nih.gov/pubmed/7548787

Abstract A total of 670 hairless mice (hr/hr Oslo strain, 50% females) were exposed to a single topical application of two doses of MNU dissolved in 100 microliters reagent grade acetone in order to study whether there really is a diurnal variation in the sensitivity of epidermal cells to the short-acting alkylating carcinogen methylnitrosourea (MNU). Three hundred and fifty-one mice were exposed in groups to a single application of 1 mg MNU at either 04:00, 08:00, 12:00, 16:00, 20:00 or 24:00 Central European time. A number of 287 mice were exposed in three groups to single application of 2 mg MNU at 8:00, 12:00 or 20:00. To look at the dose-response relationship we also treated an additional group of 32 mice with 10 mg MNU at 12:00. The mice were kept in plastic cages located in the same room in an animal department with controlled temperature, air flow, humidity and a constant light/darkness rhythm (07:30 - 19:30). The development of all types of skin tumors was observed and the results presented as tumor rates (percentage of tumor-bearing animals in relation to the number of animals alive a appearance of the first tumor related to time), and tumor yields (the cumulative occurrence of all skin tumors standardized for comparison of groups of 32 mice related to time). Most animals were examined once a week for 54 weeks, but those to which 10 mg MNU was applied were observed for only 34 weeks. Modern, well accepted statistical methods were used to analyse the significance of differences between the results. A diurnal variation in tumor production after a single application of 1 mg MNU was demonstrated with a relatively high tumor crop after application in the period from 24:00 to a peak at 08:00, and a lower crop at 12:00 to 20:00 with a trough at 16:00. When 2 mg MNU was applied, there was definitely a low tumor production after application at 12:00 compared to the two other times. There was a good and almost straight-line dose-response relationship after 1, 2 and 10 mg MNU. The results give a strong support to the hypothesis that there is a diurnal variation in the sensitivity of epidermal cells to the short-acting alkylating carcinogen MNU.(ABSTRACT TRUNCATED AT 400 WORDS)

Keywords

Jaffe F, Roszkowski JR, Bercz PA, et al. ***Year*** 2012

Authors Fredric Jaffe, Jennifer R. Roszkowski, Peter A. Bercz, Marcel Junqueira, Gonzalo A. Salgado

Report Name Shift work and sleep disorders

Publication Dialogue and Diagnosis

Issue-page numbers Volume 2 Number 1 March 2012

URL http://www.osteopathic.org/inside-aoa/news-and-publications/Documents/dialogue-and-diagnosis-march-2012.pdf

Abstract

For centuries we lived in a world without artificial light. Thus, when the sun set in the west we stopped working and attempted to sleep. The discovery and the proliferation of artificial light over the last 100 years has allowed work to bleed into the nighttime. The freeing of the workday from daylight hours allowed society and the individual the chance to increase productivity during the whole of that 24-hour period. Unfortunately, with that increased productivity came a price to pay. We, as humans, are not nocturnal and our circadian physiology guides us to be awake during daylight hours and asleep when it is night. Opposing this biological system has far reaching consequences.

Keywords

Jagger J

Year 1967

Authors John Jagger

Report Name Introduction to Research in Ultraviolet Photobiology

Publication Prentice Hall, Englewood Cliffs, New Jersey; 1967.

Issue-page numbers

URL http://books.google.com/books/about/Introduction_to_research_in_ultra_violet.html?id=E9U9AAAAIAAJ

Abstract Book

Keywords Book

Jakubcakova V, Oster H, Tamanini F et al.

Year 2007

Authors Jakubcakova V, Oster H, Tamanini F et al.

Report Name Light entrainment of the mammalian circadian clock by a PRKCA-dependent posttranslational mechanism

Publication Neuron

Issue-page numbers 54:831–843 doi:10.1016/j.neuron.2007.04.031. PMID:17553429

URL http://www.cell.com/neuron/abstract/S0896-6273%2807%2900335-2

Abstract Light is the most potent stimulus for synchronizing endogenous circadian rhythms with external time. Photic clock resetting in mammals involves cAMP-responsive element binding protein (CREB)-mediated transcriptional activation of Period clock genes in the suprachiasmatic nuclei (SCN). Here we provide evidence for an additional photic input pathway to the mammalian circadian clock based on Protein Kinase C α (PRKCA). We found that Prkca-deficient mice show an impairment of light-mediated clock resetting. In the SCN of wild-type mice, light exposure evokes a transient interaction between PRKCA and PERIOD 2 (PER2) proteins that affects PER2 stability and nucleocytoplasmic distribution. These posttranslational events, together with CREB-mediated transcriptional regulation, are key factors in the molecular mechanism of photic clock resetting.

Keywords

Janković BD, Knezević Z, Kojić L, Nikolić V | ***Year*** 1994

Authors Janković BD, Knezević Z, Kojić L, Nikolić V

Report Name Pineal gland and immune system. Immune functions in the chick embryo pinealectomized at 96 hours of incubation

Publication Ann N Y Acad Sci

Issue-page numbers 719:398–409. PMID:8010609

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1994.tb56845.x/abstract?

Abstract N/A

Keywords

Jansen B, Kroon H | ***Year*** 1995

Authors Jansen B, Kroon H

Report Name Rota-risk-profile-analysis

Publication Work Stress

Issue-page numbers 9:245–255 doi:10.1080/02678379508256560

URL http://www.tandfonline.com/doi/abs/10.1080/02678379508256560

Abstract In this article an update of the Rota-Risk-Profile-Analysis (RRPA) is presented. This RRPA is based on 9 rota-risk criteria that are central to a more encompassing rota theory. The RRPA allows coherent assessment of the physical and social risks of a working-time schedule (rota). comparison of schedules with one another in quantitative terms and interpretations of possible differential effects more adequately. First, a closer look at the instrument-a computer program-is taken. Afterwards the criteria and their way of implementation are discussed briefly. To get an impression of the way that RRPA functions an example will be given by applying the instrument to the working rotas from a study on shiftwork in the Netherlands.

Keywords

Jardim ACN, Pawley MDM, Cheeseman JF, et al. ***Year*** 2011

Authors Anisoara C. N. Jardim, Matthew D. M. Pawley, James F. Cheeseman, Mirjam J. Guesgen, Christopher T. Steele and Guy R. Warman

Report Name Validating the Use of Wrist-Level Light Monitoring for In-Hospital Circadian Studies

Publication Chronobiology International

Issue-page numbers Nov., 2011, Vol. 28, No. 9 , Pages 834-840 (doi:10.3109/07420528.2011.611603)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.611603?prevSearch=allfield%253A%2528light-at-night%2529&searchHistoryKey=

Abstract

This clinical methods comparison study describes the difference between light levels measured at the wrist (Actiwatch-L) and at the eye (Daysimeter) in a postoperative in-patient population. The mean difference between the two devices was less than 10 lux at light levels less than 5000 lux. Agreement between the devices was found to decrease as eye-level light exposure increased. Measurements at eye level of 5000 lux or more corresponded to a difference between the devices of greater than 100 lux. Agreement between the eye- and wrist-level light measurements also appears to be influenced by time of day. During the day, the measurement differences were on average 50 lux higher at eye level, whereas at night they were on average 50 lux lower. Although the wrist-level monitor was found to underestimate light exposure at higher light levels, it was well tolerated by participants in the clinical setting. In contrast, the eye-level monitor was cumbersome and uncomfortable for the patients to wear. This study provides light-exposure data on patients in real conditions in the clinical environment. The results show that wrist-level monitoring provides an adequate estimate of light exposure for in-hospital circadian studies.

Keywords

Jasser SA, Hanifin JP, Rollag MD, Brainard GC **Year** 2006

Authors Samar A. Jasser, John P. Hanifin, Mark D. Rollag, George C. Brainard

Report Name Dim Light Adaptation Attenuates Acute Melatonin Suppression in Humans

Publication J Biol Rhythms

Issue-page numbers October 2006 vol. 21 no. 5 394-404

URL http://jbr.sagepub.com/content/21/5/394.abstract

Abstract

Abstract Studies in rodents with retinal degeneration indicated that neither the rod nor the cone photoreceptors obligatorily participate in circadian responses to light, including melatonin suppression and photoperiodic response. Yet there is a residual phase-shifting response in melanopsin knockout mice, which suggests an alternate or redundant means for light input to the SCN of the hypothalamus. The findings of Aggelopoulos and Meissl suggest a complex, dynamic interrelationship between the classic visual photoreceptors and SCN cell sensitivity to light stimuli, relative to various adaptive lighting conditions. These studies raised the possibility that the phototransductive physiology of the retinohypothalamic tract in humans might be modulated by the visual rod and cone photoreceptors. The aim of the following two-part study was to test the hypothesis that dim light adaptation will dampen the subsequent suppression of melatonin by monochromatic light in healthy human subjects. Each experiment included 5 female and 3 male human subjects between the ages of 18 and 30 years, with normal color vision. Dim white light and darkness adaptation exposures occurred between midnight and 0200 h, and a full-field 460-nm light exposure subsequently occurred between 0200 and 0330-h for each adaptation condition, at 2 different intensities. Plasma samples were drawn following the 2-h adaptation, as well as after the 460-nm monochromatic light exposure, and melatonin was measured by radioimmunoassay. Comparison of melatonin suppression responses to monochromatic light in both studies revealed a loss of significant suppression after dim white light adaptation compared with dark adaptation ($p < 0.04$ and $p < 0.01$). These findings indicate that the activity of the novel circadian photoreceptive system in humans is subject to subthreshold modulation of its sensitivity to subsequent monochromatic light exposure, varying with the conditions of light adaptation prior to exposure.

Keywords adaptation, circadian rhythm, melanopsin, melatonin, pineal, photoreception, suprachiasmatic nucleus

Jay SM, Dawson D, Lamond N **Year** 2006

Authors Jay SM, Dawson D, Lamond N

Report Name Train drivers' sleep quality and quantity during extended relay operations

Publication Chronobiol Int

Issue-page numbers 23:1241–1252 doi:10.1080/07420520601083409. PMID:17190709

URL http://trid.trb.org/view.aspx?id=811382

Abstract This article reports on a study of train drivers' sleep quality and quantity during extended (4-day) relay operations, an important mode of freight transportation in Australia. Relay work requires multiple crews to drive the train continuously from one specified destination to another and then return. Drivers (n = 9) working the Port Augusta to Darwin relay operation volunteered to participate. The first leg of the trip typically took 40 hours, followed by an overnight stay in Darwin (8-12 hours), prior to return. Two crews, each consisting of two drivers, changed every 8 hours, giving the crew an 8 hour rest in the relay van prior to each 8 hour working shift. The authors used polysomnography to collect home sleep data prior to and following each trip. All sleep periods during the relay trip, including the overnight in Darwin, were also recorded. Results showed that the quantity of sleep obtained in the relay vans (3.3 hours) was significantly reduced compared to home (6.8 hours). In general, the total sleep time was increased at night and reduced during the day. In terms of quality, sleep onset latency, sleep efficiency, and amount of slow wave and rapid eye movement sleep did not differ significantly between home and the relay vans.

Keywords

JBR **Year** 2005

Authors Special Issue, Sage

Report Name Human circadian rhythms: regulation and impact

Publication Journal of Biological Rhythms

Issue-page numbers Volume 20, Issue 4

URL http://books.google.com/books/about/Human_circadian_rhythms.html?id=AGwsMwAACAAJ

Abstract N/A

Keywords

Jensen LD, Cao Z, Nakamura M, et al. ***Year*** 2012

Authors Lasse Dahl Jensen, Ziquan Cao, Masaki Nakamura, Yunlong Yang, Lars Bräutigam, Patrik Andersson, Yin Zhang, Eric Wahlberg, Toste Länne, Kayoko Hosaka, Yihai Cao

Report Name Opposing Effects of Circadian Clock Genes Bmal1 and Period2 in Regulation of VEGF-Dependent Angiogenesis in Developing Zebrafish

Publication Cell Reports

Issue-page numbers 09 August 2012

URL http://www.cell.com/cell-reports/fulltext/S2211-1247%2812%2900201-X?large_figure=true

Abstract Molecular mechanisms underlying circadian-regulated physiological processes remain largely unknown. Here, we show that disruption of the circadian clock by both constant exposure to light and genetic manipulation of key genes in zebrafish led to impaired developmental angiogenesis. A bmal1-specific morpholino inhibited developmental angiogenesis in zebrafish embryos without causing obvious nonvascular phenotypes. Conversely, a period2 morpholino accelerated angiogenic vessel growth, suggesting that Bmal1 and Period2 display opposing angiogenic effects. Using a promoter-reporter system consisting of various deleted vegf-promoter mutants, we show that Bmal1 directly binds to and activates the vegf promoter via E-boxes. Additionally, we provide evidence that knockdown of Bmal1 leads to impaired Notch-inhibition-induced vascular sprouting. These results shed mechanistic insight on the role of the circadian clock in regulation of developmental angiogenesis, and our findings may be reasonably extended to other types of physiological or pathological angiogenesis.

Keywords

Jöchle W ***Year*** 1964

Authors Wolfgang Jöchle

Report Name Trends in Photophysiologic Concepts

Publication Annals of the New York Academy of Sciences

Issue-page numbers vol. 117, issue 1 Photo-Neuro-E, pp. 88-104

URL http://adsabs.harvard.edu/abs/1964NYASA.117...88J

Abstract N/A

Keywords

Jöchle W **Year** 1963

Authors Wolfgang Jöchle

Report Name Wirkungen von Dauerbelichtung und Sulfonamidverabreichung auf Cyclus und

Publication Deutsche Gesellschaft fur Endokrinologie

Issue-page numbers Symposion 10: 305–308

URL http://www.endokrinologie.net/

Abstract Symposium

Keywords

Johansson C, Willeit M, Smedh C et al. **Year** 2003

Authors Johansson C, Willeit M, Smedh C et al.

Report Name Circadian clock-related polymorphisms in seasonal affective disorder and their relevance to diurnal preference

Publication Neuropsychopharmacology

Issue-page numbers 28:734–739 doi:10.1038/sj.npp.1300121. PMID:12655319

URL http://www.nature.com/?file=/npp/journal/v28/n4/full/1300121a.html

Abstract Disturbed circadian rhythms have been observed in seasonal affective disorder (SAD). The aim of this study was to further investigate this connection, and to test for potential association between polymorphisms in circadian clock-related genes and SAD, seasonality (seasonal variations in mood and behavior), or diurnal preference (morningness–eveningness tendencies). A total of 159 European SAD patients and 159 matched controls were included in the genetic analysis, and subsets were screened for seasonality (n=177) and diurnal preference (n=92). We found that diurnal preference was associated with both SAD and seasonality, supporting the hypothesis of a link between circadian rhythms and seasonal depression. The complete case–control material was genotyped for polymorphisms in the CLOCK, Period2, Period3, and NPAS2 genes. A significant difference between patients and controls was found for NPAS2 471 Leu/Ser (chi2=9.90, Bonferroni corrected P=0.035), indicating a recessive effect of the leucine allele on disease susceptibility (chi2=6.61, Bonferroni corrected P=0.050). Period3 647 Val/Gly was associated with self-reported morningness–eveningness scores (n=92, one-way ANOVA: F=4.99, Bonferroni corrected P=0.044), with higher scores found in individuals with at least one glycine allele (t=3.1, Bonferroni corrected P=0.013). A second, population-based sample of individuals selected for high (n=127) or low (n=98) degrees of seasonality, was also genotyped for NPAS2 471 Leu/Ser. There was no significant difference between these seasonality extreme groups, and none of the polymorphisms studied were associated with seasonality in the SAD case–control material (n=177). In conclusion, our results suggest involvement of circadian clock-related polymorphisms both in susceptibility to SAD and diurnal preference.

Keywords seasonal affective disorder, seasonality, morningness–eveningness, CLOCK, period2, period3, NPAS2

Johnson CH

Year 2010

Authors Carl Hirschie Johnson

Report Name Circadian clocks and cell division

Publication Cell Cycle.

Issue-page numbers 2010 October 1; 9(19): 3864–3873. Published online 2010 October 1. doi: 10.4161/cc.9.19.13205

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3047750/

Abstract Evolution has selected a system of two intertwined cell cycles: the cell division cycle (CDC) and the daily (circadian) biological clock. The circadian clock keeps track of solar time and programs biological processes to occur at environmentally appropriate times. One of these processes is the CDC, which is often gated by the circadian clock. The intermeshing of these two cell cycles is probably responsible for the observation that disruption of the circadian system enhances susceptibility to some kinds of cancer. The core mechanism underlying the circadian clockwork has been thought to be a transcription and translation feedback loop (TTFL), but recent evidence from studies with cyanobacteria, synthetic oscillators and immortalized cell lines suggests that the core circadian pacemaking mechanism that gates cell division in mammalian cells could be a post-translational oscillator (PTO).

Keywords circadian, cell division, cancer, cyanobacteria, KaiABC, synthetic oscillators

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Johnson HM, Torres BA, Smith EM et al.

Year 1984

Authors M Johnson, BA Torres, EM Smith, LD Dion and JE Blalock

Report Name Regulation of lymphokine (gamma-interferon) production by corticotropin

Publication J Immunol

Issue-page numbers 132:246–250. PMID:6317743

URL http://www.jimmunol.org/content/132/1/246.abstract?related-urls=yes&legid=jimmunol;132/1/246

Abstract We have shown that corticotropin (ACTH), alpha-endorphin, and enkephalins can regulate antibody responses, which suggested a role for neuropeptides in a regulatory circuit between the immune and neuroendocrine systems. ACTH and structurally related peptides were examined here for regulation of mitogen induction of the lymphokine gamma-interferon (IFN gamma) in C57BL/6 mouse spleen cell cultures. Synthetic ACTH1-39 and a porcine pituitary extract containing ACTH activity were potent suppressors of the IFN gamma response. Synthetic ACTH1-39 suppressed the response by approximately 62% at 1 to 3 microM, whereas the porcine extract suppressed by greater than 90% at 1 to 3 microM ACTH. The greater potency of the pituitary extract was shown to be due to the presence of an additional peptide of Mr 2100 that was reactive with antibodies to the N-terminal region of ACTH (ACTH1-13), possessed potent anti-cellular activity against L cells and various transformed cells, but lacked ACTH biologic activity. The anti-cellular peptide suppressed the IFN gamma response by greater than 99% at 0.05 microM. The ACTH1-39 cleavage products, alpha-melanocyte stimulating hormone (alpha MSH; acetylated and amidated ACTH1-13), and corticotropin-like intermediate lobe peptide (CLIP; ACTH18-39) had no effect on IFN gamma production. ACTH1-24, like ACTH1-39, has full steroidogenesis activity but also had no effect on IFN gamma production, which suggests a dissociation of the immunoregulatory and steroidogenic properties of ACTH1-39. ACTH1-39, and possibly also the anti-cellular 2100 Mr peptide, is initially synthesized as the precursor polyprotein pro-opiomelanocortin (POMC). Enzymatic processing of POMC, first to the active ACTH1-39 or the anti-cellular peptide and then to the inactive smaller peptides, probably plays an important role in regulation of lymphokine and antibody production by ACTH and ACTH- related neuropeptides. This is consistent with the recent demonstration of the production of ACTH-like peptides by lymphocytes.

Keywords

Johnston JD, Ebling FJ, Hazlerigg DG **Year** 2005

Authors Johnston JD, Ebling FJ, Hazlerigg DG

Report Name Photoperiod regulates multiple gene expression in the suprachiasmatic nuclei and pars tuberalis of the Siberian hamster (Phodopus sungorus)

Publication Eur J Neurosci

Issue-page numbers 21:2967–2974 doi:10.1111/j.1460-9568.2005.04148.x. PMID:15978008

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1460-9568.2005.04148.x/abstract?

Abstract Photoperiod regulates the seasonal physiology of many mammals living in temperate latitudes. Photoperiodic information is decoded by the master circadian clock in the suprachiasmatic nuclei (SCN) of the hypothalamus and then transduced via pineal melatonin secretion. This neurochemical signal is interpreted by tissues expressing melatonin receptors (e.g. the pituitary pars tuberalis, PT) to drive physiological changes. In this study we analysed the photoperiodic regulation of the circadian clockwork in the SCN and PT of the Siberian hamster. Female hamsters were exposed to either long or short photoperiod for 8 weeks and sampled at 2-h intervals across the 24-h cycle. In the SCN, rhythmic expression of the clock genes Per1, Per2, Cry1, Rev-erbα, and the clock-controlled genes arginine vasopressin (AVP) and d-element binding protein (DBP) was modulated by photoperiod. All of these E-box-containing genes tracked dawn, with earlier peak mRNA expression in long, compared to short, photoperiod. This response occurred irrespective of the presence of additional regulatory cis-elements, suggesting photoperiodic regulation of SCN gene expression through a common E-box-related mechanism. In long photoperiod, expression of Cry1 and Per1 in the PT tracked the onset and offset of melatonin secretion, respectively. However, whereas Cry1 tracked melatonin onset in short period, Per1 expression was not detectably rhythmic. We therefore propose that, in the SCN, photoperiodic regulation of clock gene expression primarily occurs via E-boxes, whereas melatonin-driven signal transduction drives the phasing of a subset of clock genes in the PT, independently of the E-box.

Keywords biological rhythms; clock-controlled gene; clock gene; E-box; melatonin

Johnston JD, Messager S, Barrett P, Hazlerigg DG **Year** 2003

Authors Johnston JD, Messager S, Barrett P, Hazlerigg DG

Report Name Melatonin action in the pituitary: neuroendocrine synchronizer and developmental modulator?

Publication J Neuroendocrinol

Issue-page numbers 15:405–408. PMID:12622841 doi:10.1046/j.1365-2826.2003.00972.x

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2826.2003.00972.x/abstract

Abstract Melatonin inhibits the gonadotropin-releasing hormone (GnRH)-stimulated secretion of luteinizing hormone and follicle-stimulating hormone from the pars distalis region of the neonatal rat pituitary gland. Over the initial weeks of postnatal life, this response to melatonin declines in parallel with a loss of iodo-melatonin binding sites. Although neonatal gonadotrophs have since been extensively used to study melatonin receptor signalling pathways, the mechanisms driving this phenomenon, together with its physiological significance, remain unknown. Melatonin receptors are expressed in the foetal pars distalis before activation of the GnRH system. Furthermore, the MT1 melatonin receptor promoter contains response elements for transcription factors involved in both pituitary differentiation and gonadotroph regulation. These data, coupled with the known ability of melatonin to regulate rhythmical gene expression in adult pars tuberalis cells, leads us to propose that melatonin acts in the developing animal as a regulator of internal synchrony between tissues.

Keywords melatonin; pituitary; development; gonadotroph; Pitx1

Authors Johnston JD, Messager S, Ebling FJP et al.

Report Name Gonadotrophin-releasing hormone drives melatonin receptor down-regulation in the developing pituitary gland

Publication Proc Natl Acad Sci USA

Issue-page numbers 100:2831–2835 doi:10.1073/pnas.0436184100. PMID:12598657

URL Gonadotrophin-releasing hormone drives melatonin receptor down-regulation in the developing pituitary gland

Abstract Melatonin is produced nocturnally by the pineal gland and is a neurochemical representation of time. It regulates neuroendocrine target tissues through G-protein-coupled receptors, of which MT1 is the predominant subtype. These receptors are transiently expressed in several fetal and neonatal tissues, suggesting distinct roles for melatonin in development and that specific developmental cues define time windows for melatonin sensitivity. We have investigated MT1 gene expression in the rat pituitary gland. MT1 mRNA is confined to the pars tuberalis region of the adult pituitary, but in neonates extends into the ventral pars distalis and colocalizes with luteinizing hormone β-subunit (LHβ) expression. This accounts for the well documented transient sensitivity of rat gonadotrophs to melatonin in the neonatal period. Analysis of an upstream fragment of the rat MT1 gene revealed multiple putative response elements for the transcription factor pituitary homeobox-1 (Pitx-1), which is expressed in the anterior pituitary from Rathke's pouch formation. A Pitx-1 expression vector potently stimulated expression of both MT1-luciferase and LHβ-luciferase reporter constructs in COS-7 cells. Interestingly, transcription factors that synergize with Pitx-1 to trans-activate gonadotroph-associated genes did not potentiate Pitx-1-induced MT1-luciferase activity. Moreover, the transcription factor, early growth response factor-1, which is induced by gonadotrophin-releasing hormone (GnRH) and trans-activates LHβ expression, attenuated Pitx-1-induced MT1-luciferase activity. Finally, pituitary MT1 gene expression was 4-fold higher in hypogonadal (hpg) mice, which do not synthesize GnRH, than in their wild-type littermates. These data suggest that establishment of a mature hypothalamic GnRH input drives the postnatal decline in pituitary MT1 gene expression.

Keywords

Authors Johnston JD, Schuster C, Barrett P, Hazlerigg DG

Report Name Regulation of the ovine MT1 melatonin receptor promoter: interaction between multiple pituitary transcription factors at different phases of development

Publication Mol Cell Endocrinol

Issue-page numbers 268:59–66 doi:10.1016/j.mce.2007.01.015. PMID:17337323

URL http://www.sciencedirect.com/science/article/pii/S0303720707000342

Abstract

Pineal secretion of melatonin provides a neuroendocrine representation of the light–dark cycle, which is used to synchronise daily and annual rhythms of physiology and behaviour. In mammals, melatonin primarily acts through MT1 melatonin receptors that exhibit a highly restricted tissue distribution. Expression of MT1 receptors is subject to developmental and circadian control, which likely modulates the physiological actions of melatonin. To investigate the mechanisms controlling MT1 expression we cloned the proximal 1.5 kb region of the ovine MT1 promoter.

Sequence analysis revealed putative cis-elements for transcription factors involved in pituitary development, namely Pitx-1 and Egr-1, and multiple putative E-boxes, which are involved in both circadian and developmental gene regulation. Nuclear protein from ovine pars tuberalis (PT) cells, a site of high endogenous MT1 expression, stimulated gene expression from a MT1 expression construct, indicating the presence of a functional promoter. Pitx-1 was strongly expressed in the ovine PT and stimulated MT1 promoter activity in transfection assays. Co-transfection with Egr-1 induced promoter-specific effects: Pitx-1-stimulated MT1 activity was inhibited, whereas βLH promoter activity was enhanced.

In addition to Pitx-1 the circadian clock genes Clock and Bmal1 were also expressed in the PT. However, despite multiple putative E-boxes in the MT1 promoter, transfected Clock and Bmal1 were unable to regulate either basal or Pitx-1-stimulated MT1 promoter activity.

The current data, in conjunction with our previous study of the rat MT1 promoter, suggests a general model in which melatonin receptor expression in the mammalian pituitary is determined by the developmentally changing balance between stimulatory and inhibitory transcription factors. Furthermore, our data suggest that circadian variation in MT1 gene expression does not depend upon the direct action of circadian clock genes on E-box cis-elements.

Keywords Pitx-1; Egr-1; Pars distalis; Gonadotroph; Pars tuberalis; E-box

Authors Johnston JD, Tournier BB, Andersson H et al.

Report Name Multiple effects of melatonin on rhythmic clock gene expression in the mammalian pars tuberalis

Publication Endocrinology

Issue-page numbers 147:959–965 doi:10.1210/en.2005-1100. PMID:16269454

URL http://endo.endojournals.org/content/147/2/959.full

Abstract In mammals, changing day length modulates endocrine rhythms via nocturnal melatonin secretion. Studies of the pituitary pars tuberalis (PT) suggest that melatonin-regulated clock gene expression is critical to this process. Here, we considered whether clock gene rhythms continue in the PT in the absence of melatonin and whether the effects of melatonin on the expression of these genes are temporally gated. Soay sheep acclimated to long photoperiod (LP) were transferred to constant light for 24 h, suppressing endogenous melatonin secretion. Animals were infused with melatonin at 4-h intervals across the final 24 h, and killed 3 h after infusion. The expression of five clock genes (Per1, Per2, Cry1, Rev-erbα, and Bmal1) was measured by in situ hybridization. In sham-treated animals, PT expression of Per1, Per2, and Rev-erbα showed pronounced temporal variation despite the absence of melatonin, with peak times occurring earlier than predicted under LP. The time of peak Bmal1 expression remained LP-like, whereas Cry1 expression was continually low. Melatonin infusion induced Cry1 expression at all times and suppressed other genes, but only when they showed high expression in sham-treated animals. Hence, 3 h after melatonin treatment, clock gene profiles were driven to a similar state, irrespective of infusion time. In contrast to the PT, melatonin infusions had no clear effect on clock gene expression in the suprachiasmatic nuclei. Our results provide the first example of acute sensitivity of multiple clock genes to one endocrine stimulus and suggest that rising melatonin levels may reset circadian rhythms in the PT, independently of previous phase.

Keywords

Jones L

Year 2009

Authors Jones L.

Report Name Thermal touch

Publication Scholarpedia - Web Page

Issue-page numbers 2009; 4:7955

URL http://www.scholarpedia.org/article/Thermal_touch

Abstract

When the hand grasps an object, changes in skin temperature can assist in identifying the object and discriminating between different types of objects. These cues become especially important when objects must be identified without visual feedback, such as when reaching for objects in the dark. The thermal cues that assist in identifying an object arise from the changes in skin temperature that occur when the object and hand are in contact. The thermal properties of the object, such as its conductivity and specific heat capacity, the initial temperatures of the skin and object, the thermal contact resistance between the skin and object, and the object's size and shape all determine the rate at which heat is conducted out of the skin or object during contact. Because of the differences in the thermal properties of materials, when an object made from plastic is held in the hand, skin temperature changes much more slowly than when the hand grasps an object made from stainless steel or copper. This means that the metal object feels “cooler” than one made from plastic, even though both objects are at the same temperature. After 10 seconds of contact with a copper object at room temperature, skin temperature can decrease by as much as 5 °C, whereas it changes by less than 2 °C after 10 seconds of contact with a plastic object (Ho & Jones, 2006). The temperature of the skin is usually higher than the temperature of objects encountered in the environment, and so it is the decrease in skin temperature on contact that is used to identify whether an object is made from metal, wood or plastic. For objects warmer than the hand, such as the water in a shower or the handle of a pot on a stove, increases in skin temperature are typically used to evaluate the temperature of the object, and not to identify it.

Keywords

Authors Joshi BN, Troiani ME, Milin J et al.

Report Name Adrenal-mediated depression of N-acetyltransferase activity and melatonin levels in the rat pineal gland

Publication Life Sci

Issue-page numbers 38:1573–1580 doi:10.1016/0024-3205(86)90496-0. PMID:3702592

URL http://www.sciencedirect.com/science/article/pii/0024320586904960

Abstract

N-acetyltransferase (NAT) is believed to be the rate-limiting enzyme in the synthesis of melatonin from serotonin in the pineal gland. Norepinephrine released from sympathetic nerve endings within the pineal gland stimulates NAT activity and, therefore, melatonin synthesis. When an animal is subjected to a stressful stimulus, it would be expected that the increase in plasma catecholamines originating from the adrenal medulla and/or the sympathetic nervous system would result in a stimulation of pineal NAT activity. Adult male rats were given a 1.5cc injection of physiological saline subcutaneously into the back leg. Compared to non-injected controls, animals stressed in this manner were shown to have significantly lower pineal melatonin content 10 min after the saline injection late in the light phase of the light/dark cycle (at 18.30 h - lights on at 07.00 h). To test this more thoroughly, a time course study was conducted during the dark phase (at 02.00 h - 5 hours after lights out) when pineal NAT activity and melatonin levels are either increasing or elevated. NAT activity and melatonin levels in the pineal were significantly depressed in stressed animals as compared to controls by 10 min after the saline injection, and remained so until 60 min after injection. By 90 min they had returned to control values. In the next study the nighttime response of the pineal to stress was compared in intact and adrenalectomized rats. Adrenalectomy prevented the changes in NAT activity and melatonin content associated with the saline injection. Some factor, such as a catecholamine or corticosterone from the adrenal, seems to be eliciting the response in the pineal to the saline injection. It is not known if the factor is acting centrally or directly on the pineal gland.

Keywords

Jung CM, Khalsa SBS, Scheer FAJL, et al. **Year** 0

Authors Christopher M. Jung, Sat Bir S. Khalsa, Frank A. J. L. Scheer, Christian Cajochen, Steven W. Lockley, Charles A. Czeisler, Kenneth P. Wright Jr

Report Name Acute Effects of Bright Light Exposure on Cortisol Levels

Publication J Biol Rhythms

Issue-page numbers June 2010 vol. 25 no. 3 208-216

URL http://jbr.sagepub.com/content/25/3/208.abstract

Abstract Multisynaptic neural and endocrine pathways from the suprachiasmatic nucleus of the hypothalamus have been hypothesized to communicate circadian and photic information to the adrenal glands. In humans, light exposure has been reported to have no effect, increase, or decrease cortisol levels. These inconsistent findings in humans may be related to differences among studies including the intensity (~500 to 5500 lux), duration (15 min to 4 h), and circadian phase of light exposure. The authors assessed the influence of exposure to bright light on cortisol levels in humans during the rising and descending phases of the circadian rhythm of cortisol, that is, when cortisol levels are high. Twenty healthy men and women were studied using a within-subject research design. Subjects were studied in an environment free of time cues for 9 to 10 days. Subjects received a 6.7-h exposure of bright light (~10,000 lux; equivalent to ambient light intensity just after sunrise or just before sunset) or dim light (~3 lux; equivalent to candlelight) during the biological night and morning. Bright light exposure significantly reduced plasma cortisol levels at both circadian phases studied, whereas dim light exposure had little effect on cortisol levels. The finding of an acute suppressive effect of bright light exposure on cortisol levels supports the existence of a mechanism by which photic information can acutely influence the human adrenal glands.

Keywords circadian rhythm, biological clock, diurnal, circadian phase, adrenal gland

Jungers P, Dougados M, Pélissier C et al. **Year** 1982

Authors Jungers P, Dougados M, Pélissier C et al.

Report Name Lupus nephropathy and pregnancy. Report of 104 cases in 36 patients

Publication Arch Intern Med

Issue-page numbers 142:771–776 doi:10.1001/archinte.142.4.771. PMID:7073417

URL http://archinte.ama-assn.org/cgi/content/abstract/142/4/771

Abstract The reciprocal influence of lupus nephropathy on the outcome of pregnancy and of pregnancy on the course of renal involvement was studied retrospectively in a series of 106 pregnancies observed during the past two decades in 36 patients with lupus nephropathy. The overall incidence of live births, corrected for induced abortions, was 54 (84%) in 64 pregnancies that began before clinical onset of systemic lupus erythematosus (SLE), 20 (87%) in 23 pregnancies that began after onset of SLE, and only four (57%) in seven cases where SLE was first manifested during or after gestation. Relapse or exacerbation of disease activity occurred in 12 (46%) of 26 pregnancies antedated by clinical onset of SLE, more frequently during gestation than post partum, with two cases (8%) of irreversible deterioration of renal function; clinical exacerbation of lupus disease was observed in 11 (66%) of 15 cases where SLE was clinically active at the time of conception, and in only one (9%) of 11 cases where SLE nephritis was in stable clinical remission for at least five months before conception. The data indicate that successful outcome of pregnancy may be expected even in the more severe forms of lupus nephritis if gestation begins after a sustained, complete clinical remission.

Keywords

Jung-Hynes B, Huang W, Reiter RJ, Ahmad N **Year** 2010

Authors Brittney Jung-Hynes, Wei Huang, Russel J. Reiter, and Nihal Ahmad

Report Name Melatonin resynchronizes dysregulated circadian rhythm circuitry in human prostate cancer cells

Publication J Pineal Res

Issue-page numbers 2010 August; 49(1): 60–68.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3158680/

Abstract Prostate cancer (PCa) is a major age-related malignancy as increasing age correlates with increased risk for developing this neoplasm. Similarly, alterations in circadian rhythms have also been associated with the aging population and cancer risk. The pineal hormone melatonin is known to regulate circadian rhythms, which are under the control of a core set of genes: Period 1, 2, 3 (Per 1 – 3); Cryptochrome 1, 2 (Cry 1, 2); Clock, and Bmal 1, 2. Melatonin levels have been shown to decrease in cancer patients and exogenous melatonin exhibits anti-proliferative effects against certain cancers. In this study, we challenged the hypothesis that melatonin imparts anti-proliferative effects in prostate cancer via resynchronization of deregulated core clock circuitry. We found that Clock and Per2 protein levels were downregulated whereas Bmal1 protein levels were upregulated in PCa cells, compared to normal prostate cells. Additionally, employing automated quantitative analysis of a microarray containing human tissues, we found that compared to benign tissues, Clock and Per2 levels were downregulated whereas Bmal1 levels were upregulated in PCa and other proliferative prostatic conditions. Overexpression of Per2 was found to result in a significant loss of PCa cell growth and viability. Interestingly, melatonin treatment resulted in an increase in Per2 and Clock and a reduction in Bmal1 in PCa cells. Further, melatonin treatment resulted in a resynchronization of oscillatory circadian rhythm genes (Dbp and Per2). Our data support our hypothesis and suggest that melatonin should be thoroughly investigated as an agent for the management of PCa and other age-related malignancies.

Keywords circadian rhythm, prostate cancer, melatonin

Jung-Hynes B, Reiter RJ, Ahmad N **Year** 2010

Authors Brittney Jung-Hynes, Russel J. Reiter, and Nihal Ahmad

Report Name Sirtuins, Melatonin and Circadian Rhythms: Building a Bridge between Aging and Cancer

Publication J Pineal Res

Issue-page numbers January; 48(1): 9–19.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2948667/

Abstract Histone deacetylases (HDACs) have been under intense scientific investigation for a number of years. However, only recently the unique class III HDACs, sirtuins, have gained increasing investigational momentum. Originally linked to longevity in yeast, sirtuins and more specifically, SIRT1 have been implicated in numerous biological processes having both protective and/or detrimental effects. SIRT1 appears to play a critical role in the process of carcinogenesis, especially in age-related neoplasms. Similarly, alterations in circadian rhythms as well as production of the pineal hormone melatonin have been linked to aging and cancer risk. Melatonin has been found act as a differentiating agent in some cancer cells and to lower their invasive and metastatic status. In addition, melatonin synthesis and release occurs in a circadian rhythm fashion and it has been linked to the core circadian machinery genes (Clock, Bmal1, Periods, and Cryptochromes). Melatonin has also been associated with chronotherapy, the timely administration of chemotherapy agents to optimize trends in biological cycles. Interestingly, a recent set of studies have linked SIRT1 to the circadian rhythm machinery through direct deacetylation activity as well as through the NAD+ salvage pathway. In this review, we provide evidence for a possible connection between sirtuins, melatonin, and the circadian rhythm circuitry and their implications in aging, chronomodulation and cancer.

Keywords Sirtuins, circadian rhythm, melatonin, cancer, aging, chronotherapy

Jung-Hynes BB, Ahmad N

Year 2009

Authors Brittney Jung-Hynes and Nihal Ahmad

Report Name SIRT1 controls circadian clock circuitry and promotes cell survival: a connection with age-related neoplasms

Publication FASEB J.

Issue-page numbers 2009 September; 23(9): 2803–2809.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2796903/

Abstract Aging is believed to be a primary risk factor for cancer. Interestingly, the sirtuin family of class III histone deacetylases (HDACs) has been implicated in the regulation of longevity and may be a lost link between aging and cancer. SIRT1, a nicotinamide adenine dinucleotide (NAD+)-dependent sirtuin, has been shown to promote cell survival by inhibiting apoptosis or cellular senescence in mammalian cells. Recent studies have provided a link between the cellular metabolic function of SIRT1 and the circadian rhythm (controlled by a clock machinery), which, if deregulated, may lead to an increased risk for some cancers. Interestingly, the loss of the pineal hormone melatonin, a known regulator of circadian rhythm, has been shown to cause deregulation in the circadian rhythm machinery and an increase in susceptibility to cancer. On the basis of scientific evidence, we propose a hypothesis that SIRT1 inhibition will impart an antiproliferative response in age-related cancers via resynchronization of deregulated core clock circuitry at the cellular level. If this hypothesis is found valid, it may ultimately lead to the development of novel approaches toward management of age-related malignancies and possibly other diseases.—Jung-Hynes, B., Ahmad, N. SIRT1 controls circadian clock circuitry and promotes cell survival: a connection with age-related neoplasms.

Keywords sirtuins, melatonin, cancer, HDACs

Kahn SE, Prigeon RL, McCulloch DK et al.

Year 1993

Authors Kahn SE, Prigeon RL, McCulloch DK et al.

Report Name Quantification of the relationship between insulin sensitivity and beta-cell function in human subjects. Evidence for a hyperbolic function.

Publication Diabetes

Issue-page numbers 42:1663–1672 doi:10.2337/diabetes.42.11.1663. PMID:8405710

URL http://www.ncbi.nlm.nih.gov/pubmed/8405710

Abstract To determine the relationship between insulin sensitivity and beta-cell function, we quantified the insulin sensitivity index using the minimal model in 93 relatively young, apparently healthy human subjects of varying degrees of obesity (55 male, 38 female; 18-44 yr of age; body mass index 19.5-52.2 kg/m2) and with fasting glucose levels < 6.4 mM. SI was compared with measures of body adiposity and beta-cell function. Although lean individuals showed a wide range of SI, body mass index and SI were related in a curvilinear manner ($P < 0.0001$) so that on average, an increase in body mass index was associated generally with a lower value for SI. The relationship between the SI and the beta-cell measures was more clearly curvilinear and reciprocal for fasting insulin ($P < 0.0001$), first-phase insulin response (AIRglucose; $P < 0.0001$), glucose potentiation slope ($n = 56$; $P < 0.005$), and beta-cell secretory capacity (AIRmax; $n = 43$; $P < 0.0001$). The curvilinear relationship between SI and the beta-cell measures could not be distinguished from a hyperbola, i.e., SI x beta-cell function = constant. This hyperbolic relationship described the data significantly better than a linear function ($P < 0.05$). The nature of this relationship is consistent with a regulated feedback loop control system such that for any difference in SI, a proportionate reciprocal difference occurs in insulin levels and responses in subjects with similar carbohydrate tolerance. We conclude that in human subjects with normal glucose tolerance and varying degrees of obesity, beta-cell function varies quantitatively with differences in insulin sensitivity.(ABSTRACT TRUNCATED AT 250 WORDS)

Keywords

Authors Kalsbeek A, Buijs RM

Report Name Output pathways of the mammalian suprachiasmatic nucleus: coding circadian time by transmitter selection and specific targeting

Publication Cell Tissue Res

Issue-page numbers 309:109–118 doi:10.1007/s00441-002-0577-0. PMID:12111541

URL http://www.springerlink.com/content/v9un0h5lep0h0ryh/

Abstract Every day, we experience profound changes in our mental and physical condition as body and brain alternate between states of high activity during the waking day and rest during night-time sleep. The fundamental evolutionary adaptation to these profound daily changes in our physiological state is an endogenous 24-h clock. This biological clock enables us to prepare ourselves to these daily changes, instead of only being able to show a passive and delayed response. During the past decade, enormous progress has been made in determining possible molecular components of the biological clock. An important question remains, however, regarding how the rhythmic signal from the biological clock is spread throughout the body to control its physiology and behavior. Indeed, ultimately, the only raison d'etre for the biological clock is its output (Green 1998). In the present review, we propose that the main mechanism for the spreading time-of-day information throughout the body consists of different circadian waves of suprachiasmatic nucleus (SCN) transmitter release, directed to a restricted number of specific SCN target areas, and affecting both neuroendocrine mechanisms and the peripheral autonomic nervous system.

Keywords

Kampinga HH, Brunsting JF, Stege GJ, et al. **Year** 1995

Authors Kampinga HH, Brunsting JF, Stege GJ, Burgman PW, Konings AW.

Report Name Thermal protein denaturation and protein aggregation in cells made thermotolerant by various chemicals: role of heat shock proteins

Publication Exp Cell Res

Issue-page numbers 1995 Aug;219(2):536-46.

URL http://www.ncbi.nlm.nih.gov/pubmed/7641806

Abstract Thermotolerance (TT) induced by sodium arsenite (A-TT: 100 microM, 1 h, 37 degrees C) was compared to heat-induced thermotolerance (H-TT: 15 min, 44 degrees C) using HeLa S3 cells. All four pretreatments led to comparable levels of thermotolerance and also induced resistance to arsenite-, ethanol-, and diamide-induced toxicity (clonogenic ability). Stress-induced expression of the major heat shock proteins (hsp27, hsc70(p73), hsp70(p72), and hsp90) was generally highest in H-TT cells and lowest in A-TT cells. Interestingly, the four types of TT cells showed distinct differences in certain aspects of resistance against thermal protein damage. Thermal protein denaturation and aggregation determined in isolated cellular membrane fractions was found to be attenuated when they were isolated from H-TT and A-TT cells but not when isolated from E-TT and D-TT cells. The heat resistance in the proteins of the membrane fraction corresponded with elevated levels of hsp70(p72) associated with the isolated membrane fractions. In the nuclear fraction, only marginal (not significant) attenuation of the formation of protein aggregates (as determined by TX-100 (in)solubility) was observed. However, the postheat recovery from heat-induced protein aggregation in the nucleus was faster in H-TT, E-TT, and D-TT cells, but not in A-TT cells. Despite the fact that elevated levels of hsp27, hsp70(p73), and hsp70(p72) were found in the TX-100 insoluble nuclear fraction derived from all TT cells, no correlation was found with the degree of resistance in terms of the accelerated recovery from nuclear protein aggregation. The only correlation between accelerated recovery from nuclear protein aggregates was that with total cellular levels of hsp27. The data indicate that heat-induced loss of clonogenic ability may be a multitarget rather than a single target event. A threshold of damage may exist in cells after exposure to heat; multiple sets of proteins in (different compartments of) the cell need to be damaged before this threshold is exceeded and the cell dies. As a consequence, stabilization of only one of these sets of proteins is already sufficient to render cells thermotolerant at the clonogenic level.

Keywords

Kanavy HE, Gerstenblith MR **Year** 2011

Authors Holly E. Kanavy, Meg R. Gerstenblith

Report Name Melanoma and ultraviolet radiation

Publication Seminars in Cutaneous Medicine and Surgery

Issue-page numbers Volume 30, Issue 4, December 2011, Pages 222-228

URL http://www.sciencedirect.com/science/article/pii/S1085562911001301

Abstract Melanoma is a particularly aggressive type of skin cancer, and its incidence has been increasing steadily since the 1970s. This article will review the extensive epidemiologic data demonstrating that ultraviolet radiation (UVR) exposure, from the sun or artificial tanning beds, is the most important environmental risk factor for melanoma; the multiple detrimental effects of UVR on human skin, including DNA damage through the formation of dimeric photoproducts, gene mutations, oxidative stress, inflammation, and immunosuppression, all of which contribute to melanomagenesis; and the evidence that protection from UVR exposure, whether by melanin or by sunscreen, reduces the risk of developing melanoma.

Keywords melanoma; ultraviolet radiation; ultraviolet light; skin cancer

Kanazawa T, Ren S, Maekawa M, et al. **Year** 2010

Authors Takuya Kanazawa, Shukun Ren, Mikika Maekawa, Koji Hasegawa, Fumio Arisaka, Mamoru Hyodo, Yoshihiro Hayakawa, Hiroyuki Ohta, and Shinji Masuda

Report Name Biochemical and Physiological Characterization of a BLUF Protein−EAL Protein Complex Involved in Blue Light-Dependent Degradation of Cyclic Diguanylate in the Purple Bacte

Publication Biochemistry

Issue-page numbers 2010, 49 (50), pp 10647–10655 DOI: 10.1021/bi101448t

URL http://pubs.acs.org/doi/abs/10.1021/bi101448t

Abstract Organisms adapt their physiologies in response to the quality and quantity of environmental light. Members of a recently identified photoreceptor protein family, BLUF domain proteins, use a flavin chromophore to sense blue light. Herein, we report that PapB, which contains a BLUF domain, controls the biofilm formation of the purple photosynthetic bacterium Rhodopseudomonas palustris. Purified PapB undergoes a typical BLUF-type photocycle, and light-excited PapB enhances the phosphodiesterase activity of the EAL domain protein, PapA, which degrades the second messenger, cyclic dimeric GMP (c-di-GMP). PapB directly interacts with PapA in vitro in a light-independent manner and induces a conformational change in the preformed PapA−PapB complex. A PapA−PapB docking simulation, as well as a site-directed mutagenesis study, identified amino acids partially responsible for the interaction between the PapA EAL domain and the two C-terminal α-helices of the PapB BLUF domain. Thus, the conformational change, which involves the C-terminal α-helices, transfers the flavin-sensed blue light signal to PapA. Deletion of papB in R. palustris enhances biofilm formation under high-intensity blue light conditions, indicating that PapB functions as a blue light sensor, which negatively regulates biofilm formation. These results demonstrate that R. palustris can control biofilm formation via a blue light-dependent modulation of its c-di-GMP level by the BLUF domain protein, PapB.

Keywords

Kannen V, Marini T, Zanette DL **Year** 2011

Authors Vinicius Kannen, Tassiana Marini, Dalila L. Zanette, Fernando T. Frajacomo, Gyl E.B. Silva, Wilson A. Silva Jr., Sérgio B. Garcia

Report Name The melatonin action on stromal stem cells within pericryptal area in colon cancer model under constant light

Publication Biochemical and Biophysical Research Communications

Issue-page numbers Volume 405, Issue 4, 25 February 2011, Pages 593-598

URL http://www.sciencedirect.com/science/article/pii/S0006291X11001173

Abstract Constant light (LL) is associated with high incidence of colon cancer. MLT supplementation was related to the significant control of preneoplastic patterns. We sought to analyze preneoplastic patterns in colon tissue from animals exposed to LL environment (14 days; 300 lx), MLT-supplementation (10 mg/kg/day) and DMH-treatment (1,2 dimethylhydrazine; 125 mg/kg). Rodents were sacrificed and MLT serum levels were measured by radioimmunoassay. Our results indicated that LL induced ACF development ($p < 0.001$) with a great potential to increase the number of CD133(+) and CD68(+) cells ($p < 0.05$ and $p < 0.001$). LL also increased the proliferative process (PCNA-Li; $p < 0.001$) as well as decreased caspase-3 protein ($p < 0.001$), related to higher COX-2 protein expression ($p < 0.001$) within pericryptal colonic stroma (PCCS). However, MLT-supplementation controlled the development of dysplastic ACF ($p < 0.001$) diminishing preneoplastic patterns into PCCS as CD133 and CD68 ($p < 0.05$ and $p < 0.001$). These events were relative to decreased PCNA-Li index and higher expression of caspase-3 protein. Thus, MLT showed a great potential to control the preneoplastic patterns induced by LL.

Keywords Colon cancer; Melatonin; Constant light; Cancer stem cells; Aberrant crypt foci

Kant GJ, Genser SG, Thorne DR et al. *Year* 1984

Authors Kant GJ, Genser SG, Thorne DR et al.

Report Name Effects of 72 hour sleep deprivation on urinary cortisol and indices of metabolism

Publication Sleep

Issue-page numbers 7:142–146. PMID:6740058

URL http://www.biomedsearch.com/nih/Effects-72-hour-sleep-deprivation/6740058.html

Abstract Cortisol, urea, glucose, electrolytes, and other compounds were measured in five consecutive 24 h urine collections during a 72 h sleep deprivation study in six young men. Urine was collected during a 24 h predeprivation day, 3 days of sleep deprivation, and a recovery day. Whereas urinary cortisol decreased only slightly, marked changes in other urinary constituents were observed. During sleep deprivation, urinary urea rose markedly, glucose decreased, and urinary electrolytes decreased. These data indicate that sleep deprivation under ad lib food and water conditions can cause disturbances in normal metabolism.

Keywords

Kantermann T, Roenneberg T *Year* 2009

Authors Thomas Kantermann and Till Roenneberg

Report Name IS LIGHT-AT-NIGHT A HEALTH RISK FACTOR OR A HEALTH RISK PREDICTOR?

Publication Chronobiology International

Issue-page numbers 26:6, 1069-1074

URL http://informahealthcare.com/doi/abs/10.3109/07420520903223984

Abstract In 2007, the IARC (WHO) has classified “shift-work that involves circadian disruption” as potentially carcinogenic. Ample evidence leaves no doubt that shift-work is detrimental for health, but the mechanisms behind this effect are not well understood. The hormone melatonin is often considered to be a causal link between night shift and tumor development. The underlying “light-at-night” (LAN) hypothesis is based on the following chain of arguments: melatonin is a hormone produced under the control of the circadian clock at night, and its synthesis can be suppressed by light; as an indolamine, it potentially acts as a scavenger of oxygen radicals, which in turn can damage DNA, which in turn can cause cancer. Although there is no experimental evidence that LAN is at the basis of increased cancer rates in shiftworkers, the scenario “light at night can cause cancer” influences research, medicine, the lighting industry and (via the media) also the general public, well beyond shiftwork. It is even suggested that baby-lights, TVs, computers, streetlights, moonlight, emergency lights, or any so-called “light pollution” by urban developments cause cancer via the mechanisms proposed by the LAN hypothesis. Our commentary addresses the growing concern surrounding light pollution. We revisit the arguments of the LAN theory and put them into perspective regarding circadian physiology, physical likelihood (e.g., what intensities reach the retina), and potential risks, specifically in non-shiftworkers.

Keywords Light-at-night, Cancer, Light pollution, Shift work, Melatonin, Health

Karatsoreos IN

Year 0

Authors Ilia N. Karatsoreos

Report Name Effects of Circadian Disruption on Mental and Physical Health

Publication Current Neurology and Neuroscience Reports

Issue-page numbers DOI: 10.1007/s11910-012-0252-0

URL http://www.springerlink.com/content/e243140351474541/

Abstract Circadian (daily) rhythms in physiology and behavior are phylogenetically ancient and are present in almost all plants and animals. In mammals, these rhythms are generated by a master circadian clock in the suprachiasmatic nucleus of the hypothalamus, which in turn synchronizes “peripheral oscillators” throughout the brain and body in almost all cell types and organ systems. Although circadian rhythms are phylogenetically ancient, modern industrialized society and the ubiquity of electric lighting has resulted in a fundamental alteration in the relationship between an individual’s endogenous circadian rhythmicity and the external environment. The ramifications of this desynchronization for mental and physical health are not fully understood, although numerous lines of evidence are emerging that link defects in circadian timing with negative health outcomes. This article explores the function of the circadian system, the effects of disrupted clocks on the brain and body, and how these effects impact mental and physical health.

Keywords Biological rhythms, Sleep, Aging, Obesity, Metabolic syndrome, Plasticity, Prefrontal, Hippocampus, Learning, Depression, Circadian disruption

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Karbownik M, Reiter RJ

Year 2002

Authors Karbownik M, Reiter RJ

Report Name Melatonin protects against oxidative stress caused by delta-aminolevulinic acid: implications for cancer reduction.

Publication Cancer Invest

Issue-page numbers 2002;20(2):276-86.

URL http://www.ncbi.nlm.nih.gov/pubmed/11901547

Abstract delta-Aminolevulinic acid (ALA) is a precursor of haem. The increased concentration of ALA is typically related to acute intermittent porphyria, hereditary tyrosinemia, and lead poisoning. delta-Aminolevulinic acid produced in excess accumulates in a number of organs, causes oxidative damage, and often leads to cancer. Melatonin (N-acetyl-5-methoxytryptamine) is a well-known antioxidant, free radical scavenger, and exhibits anticarcinogenic properties. It protects DNA, lipids, and proteins from oxidative damage. The protective effects of melatonin against ALA-induced oxidation of guanine bases, lipid peroxidation, and alterations in membrane fluidity in several organs have been documented. There is an inverse relationship between melatonin and ALA concentrations in both experimental and clinical conditions of porphyria. The marked efficacy of melatonin in protecting against ALA-related oxidative stress, its oncostatic properties, and low toxicity constitute reasons to consider the use of this indoleamine as a co-treatment in patients suffering from disturbances related to ALA accumulation.

Keywords

Kardon R, Anderson SC, Damarjian TG, et al. ***Year*** 2009

Authors Randy Kardon, Susan C Anderson, Tina G Damarjian, Elizabeth M Grace, Edwin Stone, Aki Kawasaki

Report Name Chromatic pupil responses: preferential activation of the melanopsin-mediated versus outer photoreceptormediated pupil light reflex.

Publication Ophthalmology

Issue-page numbers Volume: 116, Issue: 8, Publisher: American Academy of Ophthalmology, Pages: 1564-1573

URL http://www.mendeley.com/research/chromatic-pupil-responses-preferential-activation-of-the-melanopsinmediated-versus-outer-photoreceptormediated-pupil-light-reflex/

Abstract

OBJECTIVE: To weight the rod-, cone-, and melanopsin-mediated activation of the retinal ganglion cells, which drive the pupil light reflex by varying the light stimulus wavelength, intensity, and duration. DESIGN: Experimental study. PARTICIPANTS: Forty-three subjects with normal eyes and 3 patients with neuroretinal visual loss. METHODS: A novel stimulus paradigm was developed using either a long wavelength (red) or short wavelength (blue) light given as a continuous Ganzfeld stimulus with stepwise increases over a 2 log-unit range. The pupillary movement before, during, and after the light stimulus was recorded in real time with an infrared illuminated video camera. MAIN OUTCOME MEASURES: The percent pupil contraction of the transient and sustained pupil response to a low- (1 cd/m(2)), medium- (10 cd/m(2)), and high-intensity (100 cd/m(2)) red- and blue-light stimulus was calculated for 1 eye of each subject. From the 43 normal eyes, median and 25th, 75th, 5th, and 95th percentile values were obtained for each stimulus condition. RESULTS: In normal eyes at lower intensities, blue light evoked much greater pupil responses compared with red light when matched for photopic luminance. The transient pupil contraction was generally greater than the sustained contraction, and this disparity was greatest at the lowest light intensity and least apparent with bright (100 cd/m(2)) blue light. A patient with primarily rod dysfunction (nonrecordable scotopic electroretinogram) showed significantly reduced pupil responses to blue light at lower intensities. A patient with achromatopsia and an almost normal visual field showed selective reduction of the pupil response to red-light stimulation. A patient with ganglion cell dysfunction owing to anterior ischemic optic neuropathy demonstrated global loss of pupil responses to red and blue light in the affected eye. CONCLUSIONS: Pupil responses that differ as a function of light intensity and wavelength support the hypothesis that selected stimulus conditions can produce pupil responses that reflect phototransduction primarily mediated by rods, cones, or melanopsin. Use of chromatic pupil responses may be a novel way to diagnose and monitor diseases affecting either the outer or inner retina.

Keywords

Authors Karlsson B, Knutsson A, Lindahl B

Report Name Is there an association between shift work and having a metabolic syndrome? Results from a population based study of 27,485 people

Publication Occup Environ Med

Issue-page numbers 58:747–752 doi:10.1136/oem.58.11.747. PMID:11600731

URL http://www.jstor.org/pss/27731588

Abstract

OBJECTIVES:

To explore how metabolic risk factors for cardiovascular disease (CVD) differ between shift workers and day workers in a defined population. Shift work has been associated with an increased risk of CVD. Risk factors and causal pathways for this association are only partly known.
METHODS:

A working population of 27,485 people from the Västerbotten intervention program (VIP) has been analysed. Cross sectional data, including blood sampling and questionnaires were collected in a health survey.
RESULTS:

Obesity was more prevalent among shift workers in all age strata of women, but only in two out of four age groups in men. Increased triglycerides (>1.7 mmol/l) were more common among two age groups of shift working women but not among men. Low concentrations of high density lipoprotein (HDL) cholesterol (men<0.9 and women<1.0 mmol/l) were present in the youngest age group of shift workers in both men and women. Impaired glucose tolerance was more often found among 60 year old women shift workers. Obesity and high triglycerides persisted as risk factors in shift working men and women after adjusting for age and socioeconomic factors, with an OR of 1.4 for obesity and 1.1 for high triglyceride concentrations. The relative risks for women working shifts versus days with one, two, and three metabolic variables were 1.06, 1.20, and 1.71, respectively. The corresponding relative risks for men were 0.99, 1.30, and 1.63, respectively.
CONCLUSIONS:

In this study, obesity, high triglycerides, and low concentrations of HDL cholesterol seem to cluster together more often in shift workers than in day workers, which might indicate an association between shift work and the metabolic syndrome.

Keywords

Karmali RA, Lauder I, Horrobin DF

Year 1974

Authors Karmali RA, Lauder I, Horrobin DF

Report Name Letter: Prolactin and the immune response.

Publication Lancet

Issue-page numbers 304:106–107 doi:10.1016/S0140-6736(74)91670-5. PMID:4136979

URL http://www.ncbi.nlm.nih.gov/pubmed/4136979

Abstract N/A

Keywords

Karu TI, Pyatibrat LV, Afanasyeva NI

Year 2004

Authors Tiina I Karu, Ludmila V Pyatibrat, Natalia I Afanasyeva

Report Name A novel mitochondrial signaling pathway activated by visible-to-near infrared radiation

Publication Photochemistry and Photobiology

Issue-page numbers Volume: 80, Issue: 2, Pages: 366-72

URL http://www.mendeley.com/research/novel-mitochondrial-signaling-pathway-activated/

Abstract The number of cells attached to glass substratum increases if HeLa cell suspension is irradiated with monochromatic visible-to-near infrared radiation before plating (the action spectrum with maxima at 619, 657, 675, 700, 740, 760, 800, 820, 840 and 860 nm). Treating of cell suspension with sodium azide (2 x 10(-5) M), sodium nitroprusside (5 x 10(-5) M), ouabain (1 x 10(-6) M) or amiloride (1.7 x 10(-5) M) before irradiation significantly modifies the spectrum of cell attachment enhancement. A light-induced mitochondrial signaling pathway can be regulated by small ligands directly binding to the catalytic center of cytochrome c oxidase (N(3), NO) as well as by chemicals specifically binding to plasma membrane enzymes (ouabain, amiloride). The comparative analysis of action spectra allows the conclusions that first, Cu(A) and Cu(B) chromophores of cytochrome c oxidase could be involved as photoacceptors and second, various signaling pathways (reaction channels) between cytochrome c oxidase and cell attachment regulation are at work.

Keywords

Authors Nilesh N. Kate, M. Chandrasekhar, Ambareesha Kondam, E. Kayalvizhi, M.Suresh & U. Kavitha

Report Name A study on effect of altered circadian rhythm in the development of obesity

Publication International Journal of Biological & Medical Research

Issue-page numbers 3(2): 1595-1601

URL http://www.biomedscidirect.com/journalfiles/IJBMRF2012560/a_study_on_effect_of_altered_circadian_rhythm_in_the_development_of_obesity.pdf

Abstract

Background: Most living things have a daily cycle that reflects the rising and setting of the sun. A variety of studies have demonstrated that retinal light exposure can increase alertness at night. The global increase in the prevalence of obesity and metabolic disorders coincides with the increase of exposure to light at night (LAN) and shift work. The circadian clock prepares individuals for predictable events such as food availability and sleep, and disruption of clock function causes circadian and metabolic disturbances. Aim: To determine whether a causal relationship exists between night time light exposure behavioral changes and obesity. Methods: In this experiment 18 Swiss–albino male mice were divided into three groups i.e. Continuous light exposure (CL), light at night (LAN), standard (LD) light/dark cycle (control) and the effect of altered circadian rhythm on development of obesity and behavioral changes is seen. The body mass was assessed at the end of eight weeks to find out whether there was any correlation between the three variants. Results: Mice housed in continuous light (CL) or LAN have significantly increased body mass and increased prevalence of day time eating and altered behavioral pattern than mice in a standard (LD) light/dark cycle. Conclusion: These results suggest that light at night disrupt the timing of food intake and other metabolic signals, leading to excess weight gain. Melatonin is vital to this process, mediating the seasonal photoperiodic information through the clock system. Disrupting the melatonin signal or increasing the duration of light leads to changes in metabolism and adiposity consistent with fat storage and insulin resistance. These data are relevant to the coincidence between increasing use of light at night and obesity in humans (night shift worker).

Keywords Circadian rhythm, Open field behavior, Obesity, Light at night

Authors Tetsuo Katsuura, Yukifumi Ochiai, Toshihiro Senoo, Soomin Lee, Yoshika Takahashi, Yoshihiro Shimomura

Report Name Effects of blue pulsed light on human physiological functions and subjective

Publication Journal of Physiological Anthropology

Issue-page numbers 2012, 31:23 doi:10.1186/1880-6805-31-23

URL http://www.jphysiolanthropol.com/content/pdf/1880-6805-31-23.pdf

Abstract

Background
It has been assumed that light with a higher irradiance of pulsed blue light has a much greater influence than that of light with a lower irradiance of steady blue light, although they have the same multiplication value of irradiance and duration. We examined the non-visual physiological effects of blue pulsed light, and determined whether it is sensed visually as being blue.
Findings
Seven young male volunteers participated in the study. We placed a circular screen (diameter 500 mm) in front of the participants and irradiated it using blue and/or white light-emitting diodes (LEDs), and we used halogen lamps as a standard illuminant. We applied three steady light conditions of white LED (F0), blue LED + white LED (F10), and blue LED (F100), and a blue pulsed light condition of a 100-μs pulse width with a 10% duty ratio (P10). The irradiance of all four conditions at the participant's eye level was almost the same, at around 12 μW/cm2. We measured their pupil diameter, recorded electroencephalogram readings and Kwansei Gakuin Sleepiness Scale score, and collected subjective evaluations. The subjective bluish score under the F100 condition was significantly higher than those under other conditions. Even under the P10 condition with a 10% duty ratio of blue pulsed light and the F10 condition, the participant did not perceive the light as bluish. Pupillary light response under the P10 pulsed light condition was significantly greater than under the F10 condition, even though the two conditions had equal blue light components.
Conclusions
The pupil constricted under the blue pulsed light condition, indicating a non-visual effect of the lighting, even though the participants did not perceive the light as bluish.

Keywords

Katuguiri E

Year 1943

Authors Katuguiri E

Report Name Studies on the pineal gland. Tumor proliferation and the pineal gland

Publication Osaka Igakkai Zasshi

Issue-page numbers 42:935–938

URL N/A

Abstract N/A

Keywords

Katzenberg D, Young T, Finn L et al.

Year 1998

Authors Daniel Katzenberg, Terry Young, Laurel Finn, Ling Lin, David P. King, Joseph S. Takahashi, and Emmanuel Mignot

Report Name A CLOCK polymorphism associated with human diurnal preference

Publication Sleep

Issue-page numbers 21:569–576. PMID:9779516

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24035

Abstract Summary: A single nucleotide polymorphism located in the 3' flanking region of the human CLOCK gene was investigated as a predictor of diurnal preference in a population-based random sample of 410 normal adults. Morningness-eveningness preferences were determined using the 19-item Home-Ostberg questionnaire. Subjects carrying one of the two CLOCK alleles, 3111C, had a significantly lower mean Horne-Ostberg score. The distribution of scores was clearly shifted toward eveningness for these subjects. The score difference was independent of age, sex and ethnic heritage, thus making population stratification effects unlikely to explain this difference. These subjects had a substantial 10- to 44- minute delay in preferred timing for activity or sleep episodes. We suggest that the identified polymorphism or another tightly linked polymorphism within the CLOCK gene or its regulatory elements may be responsible for the finding.

Keywords

Year 1998

Authors Katznelson L, Riskind PN, Saxe VC, Klibanski A

Report Name Prolactin pulsatile characteristics in postmenopausal women

Publication J Clin Endocrinol Metab

Issue-page numbers 83:761–764 doi:10.1210/jc.83.3.761. PMID:9506722

URL http://jcem.endojournals.org/content/83/3/761.full.pdf

Abstract Pulsatile PRL secretion undergoes diurnal variation, with maximal PRL release in the evening during sleep in both women and men. However, the impact of the menopause on PRL pulsatile dynamics are largely unknown. To characterize diurnal PRL pulsatile secretion in postmenopausal women, we performed frequent venous sampling over 24 h every 10 min for serum PRL in 7 postmenopausal women (age, 56 +/- 4 yr) and in 2 control groups, 8 men (age, 25 +/- 8 yr) and 22 cycling women (age, 28 +/- 5 yr), at 3 phases of the menstrual cycle. Standard TRH tests (200 microg, i.v.) were administered at 0900 h after completion of the 24-h sampling, and PRL levels were then obtained at 0, 10, 20, 30, and 60 min in all subjects. PRL pulse characteristics were similar between the postmenopausal women and men. Mean serum PRL levels and PRL pulse frequency were significantly higher in the cycling women than in either postmenopausal women or men over 24 h and during either the day or night periods. Mean serum PRL levels and pulse frequency were significantly higher during the night compared to those during the day in all groups. Pulse amplitude was higher during the night vs. the day in all groups and was highest in the cycling women. PRL responses to TRH administration were greatest in cycling women. These data demonstrate that PRL pulse dynamics are significantly different between postmenopausal women and cycling women, and endogenous estrogen levels may have an important role in this difference. Pulsatile PRL secretion is similar between postmenopausal women and men, suggesting that estrogen levels modulate PRL dynamics across genders.

Keywords

Authors Kauppila A, Kivelä A, Pakarinen A, Vakkuri O

Report Name Inverse seasonal relationship between melatonin and ovarian activity in humans in a region with a strong seasonal contrast in luminosity

Publication J Clin Endocrinol Metab

Issue-page numbers 65:823–828 doi:10.1210/jcem-65-5-823. PMID:3667880

URL http://jcem.endojournals.org/content/65/5/823

Abstract

The effects of season on the activity of the pituitary-ovarian axis and the pineal gland were studied in 11 women by serum and urinary melatonin determinations and in 21 women by measurements of the serum concentrations of anterior pituitary and ovarian hormones during the dark and light seasons. A melatonin index was determined by integration of the area below the curve of serum melatonin concentrations during 24-h periods in both seasons.

During the dark season, the daytime 12-h melatonin index and daytime urinary melatonin excretion were significantly higher than during the light season. In addition, the duration of the nocturnal melatonin pulse (serum melatonin levels, >65 pmol/L) was lengthened during this season, whereas the mean serum estradiol concentration was significantly decreased at the time of ovulation and during the luteal phase of the cycle, indicating lowered ovarian activity. Luteal phase gonadotropin concentrations were increased during the dark season, which was also characterized by increased sex hormone-binding globulin (SHBG) and decreased free testosterone concentrations and free androgen indices (ratio of testosterone to SHBG ×700) throughout the menstrual cycle. The dark season was thus characterized by increased melatonin secretion and decreased ovarian and androgenic activities.

In summary, we characterized two season-dependent hormonal phenomena. Although we did not prove any cause and effect association between melatonin and anterior pituitaryovarian hormones, the inverse seasonal relationship in pineal gland and ovarian secretion suggests that melatonin is causally related to reproduction in humans.

Keywords

Kavčič P, Rojc B, Dolenc-Grošelj L, et al. **Year** 2011

Authors Pavel Kavčič, Bojan Rojc, Leja Dolenc-Grošelj, Bruno Claustrat, Kristina Fujs, and Mario Poljak

Report Name The impact of sleep deprivation and nighttime light exposure on clock gene expression in humans

Publication Croat Med J.

Issue-page numbers 2011 October; 52(5): 594–603.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3195968/

Abstract

Aim
To examine the effect of acute sleep deprivation under light conditions on the expression of two key clock genes, hPer2 and hBmal1, in peripheral blood mononuclear cells (PBMC) and on plasma melatonin and cortisol levels.
Methods
Blood samples were drawn from 6 healthy individuals at 4-hour intervals for three consecutive nights, including a night of total sleep deprivation (second night). The study was conducted in April-June 2006 at the University Medical Centre Ljubljana.
Results
We found a significant diurnal variation in hPer2 and hBmal1 expression levels under baseline ($P < 0.001$, $F = 19.7$, $df = 30$ for hPer2 and $P < 0.001$, $F = 17.6$, $df = 30$ for hBmal1) and sleep-deprived conditions ($P < 0.001$, $F = 9.2$, $df = 30$ for hPer2 and $P < 0.001$, $F = 13.2$, $df = 30$ for hBmal1). Statistical analysis with the single cosinor method revealed circadian variation of hPer2 under baseline and of hBmal1 under baseline and sleep-deprived conditions. The peak expression of hPer2 was at 13:55 ± 1:15 hours under baseline conditions and of hBmal1 at 16:08 ± 1:18 hours under baseline and at 17:13 ± 1:35 hours under sleep-deprived conditions. Individual cosinor analysis of hPer2 revealed a loss of circadian rhythm in 3 participants and a phase shift in 2 participants under sleep-deprived conditions. The plasma melatonin and cortisol rhythms confirmed a conventional alignment of the central circadian pacemaker to the habitual sleep/wake schedule.
Conclusion
Our results suggest that 40-hour acute sleep deprivation under light conditions may affect the expression of hPer2 in PBMCs.

Keywords

Kawara S, Mydlarski R, Mamelak AJ et al. **Year** 2002

Authors Kawara S, Mydlarski R, Mamelak AJ et al.

Report Name Low-dose ultraviolet B rays alter the mRNA expression of the circadian clock genes in cultured human keratinocytes.

Publication J Invest Dermatol

Issue-page numbers 119:1220–1223 doi:10.1046/j.1523-1747.2002.19619.x. PMID:12485420

URL http://www.nature.com/jid/journal/v119/n6/abs/5603326a.html

Abstract Current understanding of mammalian circadian rhythms suggests that they are regulated by light targeting signaling pathways in the hypothalamic suprachiasmatic nuclei. Recently, investigators have identified the existence of extraretinal photoreceptors and a potential role for the skin in this regulatory process has been implied. We demonstrated that mRNA of the circadian clock genes Per1, Clock, and bmal1/mop3 are expressed in normal human cultured keratinocytes. Low-dose ultraviolet B rays initially downregulate all circadian clock genes and then induce altered expression of the genes in keratinocyte cell cultures. Ultraviolet light targeting superficial layers of skin (keratinocytes) may therefore contribute to circadian rhythm modulation.

Keywords bmal1, mops, circadian rhythm, Clock, Per

Kayumov L, Casper RF, Hawa RJ et al. **Year** 2005

Authors Leonid Kayumov, Robert F. Casper, Raed J. Hawa, Boris Perelman, Sharon A. Chung, Steven Sokalsky and Colin M. Shapiro

Report Name Blocking low-wavelength light prevents nocturnal melatonin suppression with no adverse effect on performance during simulated shift work

Publication J Clin Endocrinol Metab

Issue-page numbers 90:2755–2761 doi:10.1210/jc.2004-2062. PMID:15713707

URL http://jcem.endojournals.org/content/90/5/2755.short

Abstract Decreases in melatonin production in human and animals are known to be caused by environmental lighting, especially short-wavelength lighting (between 470 and 525 nm). We investigated the novel hypothesis that the use of goggles with selective exclusion of all wavelengths less than 530 nm could prevent the suppression of melatonin in bright-light conditions during a simulated shift-work experiment. Salivary melatonin levels were measured under dim (<5 lux), bright (800 lux), and filtered (800 lux) light at hourly intervals between 2000 and 0800 h in 11 healthy young males and eight females (mean age, 24.7 ± 4.6 yr). The measurements were performed during three nonconsecutive nights over a 2-wk period. Subjective sleepiness was measured by self-report scales, whereas objective performance was assessed with the Continuous Performance Test. All subjects demonstrated preserved melatonin levels in filtered light similar to their dim-light secretion profile. Unfiltered bright light drastically suppressed melatonin production. Normalization of endogenous melatonin production while wearing goggles did not impair measures of performance, subjective sleepiness, or alertness.

Keywords

Kecklund G, Di Milia L, Axelsson J, et al. **Year** 2012

Authors Göran Kecklund, Lee Di Milia, John Axelsson, Arne Lowden, and Torbjörn Åkerstedt

Report Name 20th International Symposium on Shiftwork and Working Time: Biological Mechanisms, Recovery, and Risk Management in the 24-h Society

Publication

Issue-page numbers June 2012, Vol. 29, No. 5 , Pages 531-536 (doi:10.3109/07420528.2012.678673)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2012.678673

Abstract This dedicated issue of Chronobiology International is devoted to the selected proceedings of the 20th International Symposium on Shift Work and Working Time held in Stockholm, Sweden, 28 June to 1 July 2011. It constitutes the fifth such issue of the journal since 2004 dedicated to the selected proceedings to the meetings of the Working Time Society. The key theme of the 20th Symposium was “Biological Mechanisms, Recovery, and Risk Management in the 24-h Society.” The collection of papers of this dedicated issue represents the best of contemporary research on the effects of night and rotating shift schedules on worker health and safety. The contents cover such topics as sleep restriction, injuries, health, and performance of night work and rotating shiftwork, plus light treatment as a countermeasure against the circadian disruption of shiftwork. The majority of the papers are observational field studies, including some of large sample size, and three studies are well-designed laboratory experiments.

Keywords

Kelly JM, Lagarias JC **Year** 1985

Authors J M Kelly, J C Lagarias

Report Name Photochemistry of 124 Kilodalton Avena phytochrome under constant illumination in vitro

Publication Biochemistry

Issue-page numbers Volume: 24, Issue: 21, Pages: 6003-6010

URL http://www.mendeley.com/research/photochemistry-124-kilodalton-avena-phytochrome-under-constant-illumination-vitro-1/

Abstract

Keywords

Kenborg L, Jørgensen AD, Budtz-Jørgensen E, et al. ***Year*** 0

Authors Line Kenborg, Ane Dahl Jørgensen, Esben Budtz-Jørgensen, Lisbeth E. Knudsen and Johnni Hansen

Report Name Occupational exposure to the sun and risk of skin and lip cancer among male wage earners in Denmark: a population-based case-control study

Publication Cancer Causes and Control

Issue-page numbers Volume 21, Number 8, 1347-1355, DOI: 10.1007/s10552-010-9562-1

URL http://www.springerlink.com/content/23276j4008610nj1/

Abstract

Objective
We examined the association between outdoor work and the risks of non-melanoma skin cancer, cutaneous malignant melanoma, and lip cancer in a population-based case–control study.
Methods
Among all male wage earners in Denmark, 42,542 cases of non-melanoma skin cancer, 7,690 cases of cutaneous malignant melanoma, and 2,341 cases of lip cancer were identified in the nationwide Danish Cancer Registry. Population controls matched on sex and year of birth were selected at random among wage earners by incidence density sampling. Conditional logistic regression models were used to calculate odds ratios for risks of non-melanoma skin cancer, malignant melanoma, and lip cancer in relation to outdoor work after adjusting for covariates.
Results
For outdoor workers employed more than 10 years, the adjusted odds ratios were 0.83 (95% confidence interval (CI) 0.77–0.88) for non-melanoma skin cancer and 1.67 (95% CI 1.38–2.03) for lip cancer. Significantly reduced risk of basal cell cancers on the head, trunk, upper, or lower extremities were observed (range of odds ratios, 0.36 to 0.86).
Conclusions
The results support the hypothesis of a decreased risk of non-melanoma skin cancer and an increased risk of lip cancer among outdoor workers in the Northern Hemisphere.

Keywords Sunlight - Occupational exposure - Skin neoplasms - Melanoma - Lip cancer

Kennaway DJ, Lushington K, Dawson D et al. **Year** 1999

Authors Kennaway DJ, Lushington K, Dawson D et al.

Report Name Urinary 6-sulfatoxymelatonin excretion and aging: new results and a critical review of the literature

Publication J Pineal Res

Issue-page numbers 27:210–220 doi:10.1111/j.1600-079X.1999.tb00617.x. PMID:10551768

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1999.tb00617.x/pdf

Abstract The apparent age-related decline in melatonin production has been thought to continue in a secular manner across the lifespan. While it is clear that melatonin levels in children and adolescents are elevated compared to older individuals, the question of whether there is a sudden or gradual change has not been adequately addressed. In this study, we report the excretion of the melatonin metabolite, 6-sulfatoxymelatonin in 253 subjects aged between 21 and 82 yr. The correlation with age was significant ($r = -0.24$; $P < 0.05$). When the data was analysed by ANOVA using 5-yr age spans, there was a significant effect of age, but post hoc analysis indicated that after 25 yr of age there was no significant decline in excretion of the metabolite. Thus, although the oldest subjects excreted 36% less melatonin metabolite than the youngest, the decrease occurred at a very early age. In the second part of the study, we re-evaluated the data from seven previous studies that measured plasma melatonin levels or metabolite excretion across a wide range of ages and 11 studies comparing young versus older subjects. Statistical analysis by ANOVA again suggested that the changes in melatonin occurring with age were essentially complete before 30 yr of age. The youngest subjects produced at the most twice the amount of melatonin as the oldest subjects. Finally, we evaluated the mean plasma melatonin levels in 144 groups of normal subjects reported in 137 separate publications with respect to age. Again, whereas there was a significant correlation with age, ANOVA showed that there was no difference between groups after 35 yr of age, and the oldest groups had levels that were only 43% of the youngest groups. We conclude that melatonin production is lower in older people, but that the change occurs very early in life, around 20-30 yr of age.

Keywords

Kerenyi NA, Pandula E, Feuer G **Year** 1990

Authors N.A. Kerenyi, E. Pandula, G. Feuer

Report Name Why the incidence of cancer is increasing: the role of ‘light pollution’

Publication Medical Hypotheses

Issue-page numbers Volume 33, Issue 2, October 1990, Pages 75-78

URL http://www.sciencedirect.com/science/article/pii/030698779090182E

Abstract At present, cancer is responsible for almost half of all deaths among women 45–64 years of age, and about 30% of all deaths among men in the same age group (1). This high rate represents a marked increase from the end of the last century (2), and it probably has a multifactorial etiology. Air pollution, smoking, diet, alcohol, occupational exposures and stress are all considered as possible etiologic and risk factors (3). We put forward a hypothesis that one of the most important etiologic factors in the rapid growth rate of cancer is the change of light exposure that took place in the last 100 years, especially in the developed countries. Increased light exposure acting through the pineal gland reduces melatonin production, thereby diminishing the non-specific oncostatic effects of the pineal gland.

Keywords

Authors Line Kessel, Lars Eskildsen, Jesper HOLM Lundeman, Ole BJARLIN Jensen and Michael Larsen

Report Name Optical effects of exposing intact human lenses to ultraviolet radiation and visible light

Publication BMC Ophthalmology

Issue-page numbers Volume 11

URL http://www.biomedcentral.com/1471-2415/11/41/abstract

Abstract

Background

The human lens is continuously exposed to high levels of light. Ultraviolet radiation is believed to play a causative role in the development of cataract. In vivo, however, the lens is mainly exposed to visible light and the ageing lens absorbs a great part of the short wavelength region of incoming visible light. The aim of the present study was to examine the optical effects on human lenses of short wavelength visible light and ultraviolet radiation.
Methods

Naturally aged human donor lenses were irradiated with UVA (355 nm), violet (400 and 405 nm) and green (532 nm) lasers. The effect of irradiation was evaluated qualitatively by photography and quantitatively by measuring the direct transmission before and after irradiation. Furthermore, the effect of pulsed and continuous laser systems was compared as was the effect of short, intermediate and prolonged exposures.
Results

Irradiation with high intensity lasers caused scattering lesions in the human lenses. These effects were more likely to be seen when using pulsed lasers because of the high pulse intensity. Prolonged irradiation with UVA led to photodarkening whereas no detrimental effects were observed after irradiation with visible light.
Conclusions

Irradiation with visible light does not seem to be harmful to the human lens except if the lens is exposed to laser irradiances that are high enough to warrant thermal protein denaturation that is more readily seen using pulsed laser systems.

Keywords

Authors Kessel L, Siganos G, Jørgensen T, Larsen M.

Report Name Sleep disturbances are related to decreased transmission of blue light to the retina caused by lens yellowing.

Publication Sleep

Issue-page numbers 2011 Sep 1;34(9):1215-9.

URL http://www.ncbi.nlm.nih.gov/pubmed/21886359

Abstract

STUDY OBJECTIVES:

Sleep pattern and circadian rhythms are regulated via the retinohypothalamic tract in response to stimulation of a subset of retinal ganglion cells, predominantly by blue light (450 490 nm). With age, the transmission of blue light to the retina is reduced because of the aging process of the human lens, and this may impair the photoentrainment of circadian rhythm leading to sleep disorders. The aim of the study was to examine the association between lens aging and sleep disorders.
DESIGN:

Cross-sectional population based study.
SETTING:

The study was performed at the Research Center for Prevention and Health, Glostrup Hospital, Denmark and at the Department of Ophthalmology, Herlev Hospital, Denmark.
PARTICIPANTS:

An age- and sex-stratified sample of 970 persons aged 30 to 60 years of age drawn from a sample randomly selected from the background population.
INTERVENTIONS:

Not applicable.
MEASUREMENTS AND RESULTS:

Sleep disturbances were evaluated by a combination of questionnaire and the use of prescription sleeping medication. Lens aging (transmission and yellowing) was measured objectively by lens autofluorometry. The risk of sleep disturbances was significantly increased when the transmission of blue light to the retina was low, even after correction for the effect of age and other confounding factors such as smoking habits, diabetes mellitus, gender, and the risk of ischemic heart disease ($P < 0.0001$).
CONCLUSIONS:

Filtration of blue light by the aging lens was significantly associated with an increased risk of sleep disturbances. We propose that this is a result of disturbance of photoentrainment of circadian rhythms.

Keywords

Kessler RC, McGonagle KA, Swartz M, et al. **Year** 1993

Authors Kessler RC, McGonagle KA, Swartz M, Blazer DG, Nelson CB

Report Name Sex and depression in the National Comorbidity Survey. I: Lifetime prevalence, chronicity and recurrence

Publication J Affect Disord

Issue-page numbers 1993 Oct-Nov;29(2-3):85-96.

URL http://www.ncbi.nlm.nih.gov/pubmed/8300981

Abstract Basic epidemiologic prevalence data are presented on sex differences in DSM-III-R major depressive episodes (MDE). The data come from the National Comorbidity Survey (NCS), the first survey in the U.S. to administer a structured psychiatric interview to a nationally representative sample of the general population. Consistent with previous research, women are approximately 1.7 times as likely as men to report a lifetime history of MDE. Age of onset analysis shows that this sex difference begins in early adolescence and persists through the mid-50s. Women also have a much higher rate of 12-month depression than men. However, women with a history of depression do not differ from men with a history of depression in either the probability of being chronically depressed in the past year or in the probability of having an acute recurrence in the past year. This means that the higher prevalence of 12-month depression among women than men is largely due to women having a higher risk of first onset. The implications of these results for future research are discussed in a closing section of the paper.

Keywords

Khaetski IK **Year** 1965

Authors Khaetski IK.

Report Name Effect of hypothalamo-pituitary lesions induced by constant illumination on development of induced mammary tumors in rats

Publication Vopr Exp Oncol (Kiev)

Issue-page numbers 1965; 1: 87-93

URL N/A

Abstract N/A

Keywords

Khalsa SBS, Jewett ME, Cajochen C, Czeisler CA

Year 2003

Authors Khalsa SBS, Jewett ME, Cajochen C, Czeisler CA

Report Name A phase response curve to single bright light pulses in human subjects

Publication J Physiol

Issue-page numbers 549:945–952 doi:10.1113/jphysiol.2003.040477. PMID:12717008

URL http://jp.physoc.org/content/549/3/945.full

Abstract The circadian pacemaker is differentially sensitive to the resetting effects of retinal light exposure, depending upon the circadian phase at which the light exposure occurs. Previously reported human phase response curves (PRCs) to single bright light exposures have employed small sample sizes, and were often based on relatively imprecise estimates of circadian phase and phase resetting. In the present study, 21 healthy, entrained subjects underwent pre- and post-stimulus constant routines (CRs) in dim light (~2–7 lx) with maintained wakefulness in a semi-recumbent posture. The 6.7 h bright light exposure stimulus consisted of alternating 6 min fixed gaze (~10 000 lx) and free gaze (~5000–9000 lx) exposures. Light exposures were scheduled across the circadian cycle in different subjects so as to derive a PRC. Plasma melatonin was used to determine the phase of the onset, offset, and midpoint of the melatonin profiles during the CRs. Phase shifts were calculated as the difference in phase between the pre- and post-stimulus CRs. The resultant PRC of the midpoint of the melatonin rhythm revealed a characteristic type 1 PRC with a significant peak-to-trough amplitude of 5.02 h. Phase delays occurred when the light stimulus was centred prior to the critical phase at the core body temperature minimum, phase advances occurred when the light stimulus was centred after the critical phase, and no phase shift occurred at the critical phase. During the subjective day, no prolonged ‘dead zone’ of photic insensitivity was apparent. Phase shifts derived using the melatonin onsets showed larger magnitudes than those derived from the melatonin offsets. These data provide a comprehensive characterization of the human PRC under highly controlled laboratory conditions.

Keywords

Khazova M, O'Hagan JB

Year 2008

Authors M. Khazova and J. B. O'Hagan

Report Name Optical radiation emissions from compact fluorescent lamps

Publication Radiat Prot Dosimetry

Issue-page numbers 131 (4): 521-525. doi: 10.1093/rpd/ncn234

URL http://rpd.oxfordjournals.org/content/131/4/521

Abstract There is a drive to energy efficiency to mitigate climate change. To meet this challenge, the UK Government has proposed phasing out incandescent lamps by the end of 2011 and replacing them with energy efficient fluorescent lighting, including compact fluorescent lamps (CFLs) with integrated ballasts. This paper presents a summary of an assessment conducted by the Health Protection Agency in March 2008 to evaluate the optical radiation emissions of CFLs currently available in the UK consumer market. The study concluded that the UV emissions from a significant percentage of the tested CFLs with single envelopes may result in foreseeable overexposure of the skin when these lamps are used in desk or task lighting applications. The optical output of all tested CFLs, in addition to high-frequency modulation, had a 100-Hz envelope with modulation in excess of 15%. This degree of modulation may be linked to a number of adverse effects.

Keywords

Kheifets LI, Matkin CC

Year 1999

Authors Leeka 1. Kheifets and C. Chantal Matkin

Report Name Industrialization, Electromagnetic Fields, and Breast Cancer Risk

Publication Environmental Health Perspectives

Issue-page numbers Vol 107, Supplement 1, Feb 1999

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1566357/pdf/envhper00518-0148.pdf

Abstract The disparity between the rates of breast cancer in industrialized and less-industrialized regions has led to many hypotheses, including the theory that exposure to light-at-night and/or electromagnetic fields (EMF) may suppress melatonin and that reduced melatonin may increase the risk of breast cancer. In this comprehensive review we consider strengths and weaknesses of more than 35 residential and occupational epidemiologic studies that investigated the association between EMF and breast cancer. Although most of the epidemiologic data do not provide strong support for an association between EMF and breast cancer, because of the limited statistical power as well as the possibility of misclassification and bias present in much of the existing data, it is not possible to rule out a relationship between EMF and breast cancer. We make several specific recommendations for future studies carefully designed to test the melatonin-breast cancer and EMF-breast cancer hypotheses. Future study designs should have sufficient statistical power to detect small to moderate associations; include comprehensive exposure assessments that estimate residential and occupational exposures, including shift work; focus on a relevant time period; control for known breast cancer risks; and pay careful attention to menopausal and estrogen receptor status.

Keywords electromagnetic fields, breast cancer, melatonin, epidemiology

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Kiang JG, Poree L, Wei ET

Year 1987

Authors Kiang JG, Poree L, Wei ET

Report Name Anti-inflammatory activity of corticotropin releasing factor: II. Mechanisms of action

Publication Proc West Pharmacol Soc

Issue-page numbers 30:63–65. PMID:3498170

URL http://www.ncbi.nlm.nih.gov/pubmed/3498170

Abstract N/A

Keywords

Kiefer T, Ram PT, Yuan L, Hill SM **Year** 2002

Authors Kiefer T, Ram PT, Yuan L, Hill SM

Report Name Melatonin inhibits estrogen receptor transactivation and cAMP levels in breast cancer cells

Publication Breast Cancer Res Treat

Issue-page numbers 71:37–45 doi:10.1023/A:1013301408464. PMID:11859872

URL http://www.springerlink.com/content/w5lp803l257070t5/

Abstract We have previously demonstrated that the pineal hormone, melatonin, can inhibit the growth of estrogen receptor-alpha (ERagr)-positive breast cancer cells and suppress ERagr gene transcription. To investigate the relationship between the estrogen response pathway and melatonin's growth inhibition, ERagr-positive MCF-7 human breast cancer cells were transiently transfected with an estrogen response element (ERE) luciferase reporter construct and then treated with melatonin (10–9-10–6 M) for 30thinspmin followed by 10–9thinspM 17-beta-estradiol (E2) or treated with each compound alone. Melatonin pre-treatment significantly reduced E2-induced ERagr transactivation and ERagr-ERE binding activity. We also conducted experiments to determine if melatonin modulates cAMP levels in MCF-7 cells. Melatonin inhibited the forskolin-induced and E2-induced elevation of cAMP levels by 57 and 45%, respectively. These data indicate that melatonin can act as a biological modifier to affect ERagr transcriptional activity by regulating signal transduction pathways which impinge on the ERagr and by altering E2-mediated ERagr transactivation and ERagr DNA binding activity.

Keywords breast cancer - cAMP - estrogen receptor - melatonin

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King A, Gottlieb E, Brooks DG, et al. **Year** 2004

Authors Ayala King, Eyal Gottlieb, David G Brooks, Michael P Murphy, Joshua L Dunaief

Report Name Mitochondria-derived reactive oxygen species mediate blue light-induced death of retinal pigment epithelial cells

Publication Photochemistry and Photobiology

Issue-page numbers Volume: 79, Issue: 5, Pages: 470-475

URL http://www.mendeley.com/research/mitochondriaderived-reactive-oxygen-species-mediate-blue-lightinduced-death-retinal-pigment-epithelial-cells/

Abstract Throughout the lifetime of an individual, light is focused onto the retina. The resulting photooxidative stress can cause acute or chronic retinal damage. The pathogenesis of age-related macular degeneration (AMD), the leading cause of legal blindness in the developed world, involves oxidative stress and death of the retinal pigment epithelium (RPE) followed by death of the overlying photoreceptors. Evidence suggests that damage due to exposure to light plays a role in AMD and other age-related eye diseases. In this work a system for light-induced damage and death of the RPE, based on the human ARPE-19 cell line, was used. Induction of mitochondria-derived reactive oxygen species (ROS) is shown to play a critical role in the death of cells exposed to short-wavelength blue light (425 20 nm). ROS and cell death are blocked either by inhibiting the mitochondrial electron transport chain or by mitochondria-specific antioxidants. These results show that mitochondria are an important source of toxic oxygen radicals in blue light-exposed RPE cells and may indicate new approaches for treating AMD using mitochondria-targeted antioxidants.

Keywords

King DP, Zhao Y, Sangoram AM et al. **Year** 1997

Authors David P King, Yaliang Zhao, Ashvin M Sangoram, Lisa D Wilsbacher, Minoru Tanaka, Marina P Antoch, Thomas D.L Steeves, Martha Hotz Vitaterna, Jon M Kornhauser et al.

Report Name Positional cloning of the mouse circadian clock gene

Publication Cell

Issue-page numbers 89:641–653 doi:10.1016/S0092-8674(00)80245-7. PMID:9160755

URL http://www.cell.com/retrieve/pii/S0092867400802457

Abstract We used positional cloning to identify the circadian Clock gene in mice. Clock is a large transcription unit with 24 exons spanning ~100,000 bp of DNA from which transcript classes of 7.5 and ~10 kb arise. Clock encodes a novel member of the bHLH–PAS family of transcription factors. In the Clock mutant allele, an A→T nucleotide transversion in a splice donor site causes exon skipping and deletion of 51 amino acids in the CLOCK protein. Clock is a unique gene with known circadian function and with features predicting DNA binding, protein dimerization, and activation domains. CLOCK represents the second example of a PAS domain–containing clock protein (besides Drosophila PERIOD), which suggests that this motif may define an evolutionarily conserved feature of the circadian clock mechanism.

Keywords

Kitchel E **Year** 2000

Authors Kitchel, Elaine

Report Name The Effects of Blue Light on Ocular Health

Publication Journal of Visual Impairment & Blindness

Issue-page numbers v94 n6 p399-403 Jun 2000

URL http://www.naasln.org/documents/articles/kitchel_blue_light.pdf

Abstract This review of the literature examines the effects of blue light (or near UV - ultraviolet), especially that given off by black-light tubes, often used with children with visual impairments. It finds a long-term danger of retinal and lens damage and offers six practical suggestions which emphasize using proper filters and limiting exposure to black light.

Keywords

Kivelä A, Kauppila A, Ylöstalo P et al. **Year** 1988

Authors Kivelä A, Kauppila A, Ylöstalo P et al.

Report Name Seasonal, menstrual and circadian secretions of melatonin, gonadotropins and prolactin in women

Publication Acta Physiol Scand

Issue-page numbers 132:321–327 doi:10.1111/j.1748-1716.1988.tb08335.x. PMID:3147572

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1748-1716.1988.tb08335.x/abstract

Abstract In order to evaluate the role of the pineal gland in human reproduction, day- and nighttime concentrations of serum melatonin, FSH, LH and prolactin were measured by radioimmunoassays on various days of the menstrual cycle during summer (average daylight 22 h) and winter (daylight 5 h) in healthy females (n= 12) from northern Finland (65o N). A multifactorial analysis of variance showed that, in addition to the well-established increases of gonadotropins at midcycle and melatonin and prolactin at night, there was a significant effect of season on the serum levels of melatonin and LH. Night-time serum melatonin levels on cycle days 2 and 10 were 27% and 49% ($P < 0.05$ and < 0.01) higher in winter than in summer. Night-time serum LH levels at midcycle were 76% ($P < 0.05$) higher in summer than in winter. There were no significant effects of season on the serum levels of FSH, prolactin, day-time melatonin or LH outside the mid-cycle. Neither were there any significant effects of the day of the menstrual cycle on the serum melatonin levels. It is possible that in winter the high levels of melatonin in the follicular phase have an inhibitory effect on the serum LH levels. In summer the melatonin levels are lower and perhaps less inhibitory on the secretion of LH, resulting in the stimulation of the reproductive competence in human females.

Keywords annual rhythm; FSH; human; LH; light; serum

Klante G, Brinschwitz T, Secci K et al. **Year** 1997

Authors Klante G, Brinschwitz T, Secci K et al.

Report Name Creatinine is an appropriate reference for urinary sulphatoxymelatonin of laboratory animals and humans

Publication J Pineal Res

Issue-page numbers 23:191–197 doi:10.1111/j.1600-079X.1997.tb00354.x. PMID:9462851

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1997.tb00354.x/abstract

Abstract In our studies on diurnal 6-sulphatoxymelatonin (aMT6s) rhythms in various species, we have sometimes obtained fluctuating patterns. In most of these, the volume of individual urine fractions was not accurately measured because of methodological problems. Here, we report a simple method to overcome these problems by using urinary creatinine to estimate urine volume. The benefit of this method is demonstrated in two representative examples of the diurnal aMT6s rhythms of rats, domestic pigs and humans. Because the human urine fractions were collected accurately, the qualitative pattern of the aMT6s rhythm was not altered by using urinary creatinine as a substitute for urine volume. The total creatinine excretion (urine volume x creatinine concentration) was constant within a small range and showed no diurnal rhythm. In rats and pigs, the highly variable aMT6s concentrations relative to urine volume throughout the 24-hr period were changed drastically by referring to creatinine. All aMT6s patterns became stable and qualitatively similar to those of the rest of the group. From these results it can be concluded that creatinine is an adequate substitute for urine volume and a beneficial parameter with which to overcome technical problems with urine collection from laboratory animals or unknown urine volumes in human studies.

Keywords reatinine; sulphatoxymelatonin; urine collection; rats; pigs; humans

Klein D

Year 2006

Authors David C. Klein

Report Name Evolution of The Vertebrate Pineal Gland: The Aanat Hypothesis

Publication Chronobiology International

Issue-page numbers Vol. 23, No. 1-2 , Pages 5-20

URL http://informahealthcare.com/doi/abs/10.1080/07420520500545839

Abstract The defining feature of the pineal gland is the capacity to function as a melatonin factory that operates on a 24 h schedule, reflecting the unique synthetic capacities of the pinealocyte. Melatonin synthesis is typically elevated at night and serves to provide the organism with a signal of nighttime. Melatonin levels can be viewed as hands of the clock. Issues relating to the evolutionary events leading up to the immergence of this system have not received significant attention. When did melatonin synthesis appear in the evolutionary line leading to vertebrates? When did a distinct pineal gland first appear? What were the forces driving this evolutionary trend? As more knowledge has grown about the pinealocyte and the relationship it has to retinal photoreceptors, it has become possible to generate a plausible hypothesis to explain how the pineal gland and the melatonin rhythm evolved. At the heart of the hypothesis is the melatonin rhythm enzyme arylalkylamine N-acetyltransferase (AANAT). The advances supporting the hypothesis will be reviewed here and expanded beyond the original foundation; the hypothesis and its implications

Keywords Pineal, Evolution, Melatonin, Retina, AANAT, Vertebrates

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Klein DC

Year 2007

Authors Klein DC

Report Name Arylalkylamine N-acetyltransferase: “the Timezyme”

Publication J Biol Chem

Issue-page numbers 282:4233–4237 doi:10.1074/jbc.R600036200. PMID:17164235

URL http://www.jbc.org/content/282/7/4233.short

Abstract Arylalkylamine N-acetyltransferase controls daily changes in melatonin production by the pineal gland and thereby plays a unique role in biological timing in vertebrates. Arylalkylamine N-acetyltransferase is also expressed in the retina, where it may play other roles in addition to signaling, including neurotransmission and detoxification. Large changes in activity reflect cyclic 3′,5′-adenosine monophosphate-dependent phosphorylation of arylalkylamine N-acetyltransferase, leading to formation of a regulatory complex with 14-3-3 proteins. This activates the enzyme and prevents proteosomal proteolysis. The conserved features of regulatory systems that control arylalkylamine N-acetyltransferase are a circadian clock and environmental lighting.

Keywords

Klein DC, Weller JL, Moore RY

Year 1971

Authors David C. Klein, Joan L. Weller, and Robert Y. Moore

Report Name Melatonin Metabolism: Neural Regulation of Pineal Serotonin: Acetyl Coenzyme A N-Acetyltransferase Activity

Publication PNAS

Issue-page numbers December 1, 1971 vol. 68 no. 12 3107-3110

URL http://www.pnas.org/content/68/12/3107.short

Abstract There is a diurnal rhythm in the activity of serotonin N-acetyltransferase in the rat pineal gland. In the normal rat, the nocturnal enzyme activities are 15-to 30-fold greater than are daytime activities. This rhythm is abolished by decentralization or removal of the superior cervical ganglia, procedures that interrupt the only source of central neural input to the pineal gland. This effect of superior cervical sympathectomy on the N-acetyltransferase rhythm cannot be attributed to changes occurring in the denervated pineal parenchymal cells. When chronically denervated glands are placed in organ culture with norepinephrine, the neurotransmitter normally located in sympathetic terminals in the gland, N-acetyltransferase activity increases 10- to 20-fold. These data indicate that superior cervical sympathectomy abolishes the N-acetyltransferase rhythm by elimination of the input of central signals to the gland. These signals appear to regulate the N-acetyltransferase rhythm in the normal rat by regulation of the release of norepinephrine from the sympathetic terminals within the pineal gland.

Keywords rat, diurnal rhythm, melatonin, N-acetylserotonin, organ culture, circadian enzyme regulation

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Klerman EB

Year 2005

Authors Elizabeth B. Klerman

Report Name Clinical Aspects of Human Circadian Rhythms

Publication J Biol Rhythms

Issue-page numbers August 2005 vol. 20 no. 4 375-386

URL http://jbr.sagepub.com/content/20/4/375

Abstract Circadian rhythmicity can be important in the pathophysiology, diagnosis, and treatment of clinical disease. Due to the difficulties in conducting the necessary experimental work, it remains unknown whether ~24-h changes in pathophysiology or symptoms of many diseases are causally linked to endogenous circadian rhythms or to other diurnal factors that change across the day, such as changes in posture, activity, sleep or wake state, or metabolic changes associated with feeding or fasting. Until the physiology is accurately known, appropriate treatment cannot be designed. This review includes an overview of clinical disorders that are caused or affected by circadian or diurnal rhythms. The clinical side effects of disruption of circadian rhythmicity, such as in shiftwork, including the public health implications of the disrupted alertness and performance, are also discussed.

Keywords circadian rhythms, clinical disorders, clinical medicine, sleep disorders

Klerman EB, Gershengorn HB, Duffy JF, Kronauer RE **Year** 2002

Authors Klerman EB, Gershengorn HB, Duffy JF, Kronauer RE

Report Name Comparisons of the variability of three markers of the human circadian pacemaker

Publication J Biol Rhythms

Issue-page numbers 17:181–193 doi:10.1177/074873002129002474. PMID:12002165

URL http://jbr.sagepub.com/content/17/2/181.abstract

Abstract A circadian pacemaker within the central nervous system regulates the approximately 24-h physiologic rhythms in sleep cycles, hormone secretion, and other physiologic functions. Because the pacemaker cannot be examined directly in humans, markers of pacemaker function must be used to study the pacemaker and its response to environmental stimuli. Core body temperature (CBT), plasma cortisol, and plasma melatonin are three marker variables frequently used to estimate the phase of the human pacemaker. Measurements of circadian phase using markers can contain variability due to the circadian pacemaker itself, the intrinsic variability of the marker relative to the pacemaker, the method of analysis of the marker, and the marker assay. For this report, we compared the mathematical variability of a number of methods of identifying circadian phase from CBT, plasma cortisol, and plasma melatonin data collected in a protocol in which pacemaker variability was minimized using low light levels and regular timing of both the light pattern and the rest/activity schedule. We hoped to assess the relative variabilities of the different physiological markers and the analysis methods. Methods were based on the crossing of an absolute threshold, on the crossing of a relative threshold, or on fitting a curve to all data points. All methods of calculating circadian phase from plasma melatonin data were less variable than those calculated using CBT or cortisol data. The standard deviation for the phase estimates using CBT data was 0.78 h, using cortisol data was 0.65 h, and for the eight analysis methods using melatonin data was 0.23 to 0.35 h. While the variability for these markers might be different for other subject populations and/or less stringent study conditions, assessment of the intrinsic variability of the different calculations of circadian phase can be applied to allow inference of the statistical significance of phase and phase shift calculations, as well as estimation of sample size or statistical power for the number of subjects within an experimental protocol.

Keywords circadian rhythms, cortisol, temperature, melatonin, mathematical analysis, circadian phase

Klerman EB, Jayne GA, Smith KA, Czeisler CA **Year** 1997

Authors Klerman EB, Jayne GA, Smith KA, Czeisler CA

Report Name Apparent synchronization of the human circadian pacemaker to a scheduled (T-24 h) cycle of sleep in darkness and wake activity in very dim (20 lux) light in a sighted 22 year ol

Publication Sleep Res

Issue-page numbers 26:724

URL N.A

Abstract N/A

Keywords

	Klinkenborg V	***Year***	2008
Authors	Verlyn Klinkenborg		
Report Name	Our Vanishing Night		
Publication	National Geographic		
Issue-page numbers	November 2008		
URL	http://ngm.nationalgeographic.com/2008/11/light-pollution/klinkenborg-text		
Abstract	article		
Keywords			

	Kloog I, Haim A, Portnov BA	***Year***	0
Authors	Itai Kloog, Abraham Haim, Boris A. Portnov		
Report Name	Using kernel density function as an urban analysis tool: Investigating the association between nightlight exposure and the incidence of breast cancer in Haifa, Israel		
Publication	Computers, Environment and Urban Systems		
Issue-page numbers	Volume 33, Issue 1, January 2009, Pages 55-63		
URL	http://www.sciencedirect.com/science/article/pii/S0198971508000641		
Abstract	The kernel density (KD) function estimates the intensity of events across a surface by calculating the overall number of cases situated within a given search radius from a target point. To form a continuous surface from individual observations, the KD technique does not require the presence of a parameter's value in a given location (e.g., the incidence rate of a disease). This feature of KD smoothing is especially beneficial for empirical studies in which individual observations are represented by geographic coordinates only and have no other attributes, required by more commonly used smoothing techniques, such as spline and kriging. In the present study, we illustrate the use of KD technique for a study of association between the geographical distributions of breast cancer cases and exposure to artificial illumination during nighttime (light-at-night or LAN) in the city of Haifa, Israel.		
Keywords	Kernel density function; Light-at-night; Breast cancer; GIS		

Kloog I, Haim A, Stevens RG, et al. **Year** 2008

Authors Itai Kloog, Abraham Haim, Richard G. Stevens, Micha Barchana and Prof. Boris A. Portnov

Report Name Light at Night Co-distributes with Incident Breast but not Lung Cancer in the Female Population of Israel

Publication Chronobiology International

Issue-page numbers 2008 25:1, 65-81

URL http://informahealthcare.com/doi/abs/10.1080/07420520801921572

Abstract Recent studies of shift-working women have reported that excessive exposure to light at night (LAN) may be a risk factor for breast cancer. However, no studies have yet attempted to examine the co-distribution of LAN and breast cancer incidence on a population level with the goal to assess the coherence of these earlier findings with population trends. Coherence is one of Hill's “criteria” (actually, viewpoints) for an inference of causality. Nighttime satellite images were used to estimate LAN levels in 147 communities in Israel. Multiple regression analysis was performed to investigate the association between LAN and breast cancer incidence rates and, as a test of the specificity of our method, lung cancer incidence rates in women across localities under the prediction of a link with breast cancer but not lung cancer. After adjusting for several variables available on a population level, such as ethnic makeup, birth rate, population density, and local income level, a strong positive association between LAN intensity and breast cancer rate was revealed ($p<0.05$), and this association strengthened ($p<0.01$) when only statistically significant factors were filtered out by stepwise regression analysis. Concurrently, no association was found between LAN intensity and lung cancer rate. These results provide coherence of the previously reported case-control and cohort studies with the co-distribution of LAN and breast cancer on a population basis. The analysis yielded an estimated 73% higher breast cancer incidence in the highest LAN exposed communities compared to the lowest LAN exposed communities.

Keywords Breast cancer, Light at night, Melatonin Lung cancer

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Kloog I, Haim A, Stevens RG, Portnov BA **Year** 2009

Authors Itai Kloog, Abraham Haim, Richard G. Stevens and Prof. Boris A. Portnov

Report Name Global Co-Distribution of Light at Night (LAN) and Cancers of Prostate, Colon, and Lung in Men

Publication Chronobiology International

Issue-page numbers 26:1, 108-125

URL http://informahealthcare.com/doi/abs/10.1080/07420520802694020

Abstract The incidence rates of cancers in men differ by countries of the world. We compared the incidence rates of three of the most common cancers (prostate, lung, and colon) in men residing in 164 different countries with the population-weighted light at night (LAN) exposure and with several developmental and environmental indicators, including per capita income, percent urban population, and electricity consumption. The estimate of per capita LAN exposure was a novel aspect of this study. Both ordinary least squares (OLS) and spatial error (SE) regression models were used in the analysis. We found a significant positive association between population exposure to LAN and incidence rates of prostate cancer, but no such association with lung cancer or colon cancer. The prostate cancer result is consistent with a biological theory and a limited number of previous studies of circadian disruption and risk. The LAN-prostate cancer connection is postulated to be due to suppression of melatonin and/or disruption of clock gene function. An analysis holding other variables at average values across the 164 countries yielded a risk of prostate cancer in the highest LAN-exposed countries 110% higher than in the lowest LAN exposed countries. This observed association is a necessary condition for a potentially large effect of LAN on risk of prostate cancer. However, it is not sufficient due to potential confounding by factors that increase the risk of prostate cancer and are also associated with LAN among the studied countries.

Keywords Prostate cancer, Epidemiology, Geography, Incidence rates, LAN

Kloog I, Portnov BA, Rennert HS, Haim A

Year 2011

Authors Itai Kloog, Boris A. Portnov, Hedy S. Rennert, and Abraham Haim

Report Name Does the Modern Urbanized Sleeping Habitat Pose a Breast Cancer Risk?

Publication Chronobiology International

Issue-page numbers Feb., 2011, Vol. 28, No. 1 , Pages 76-80 (doi:10.3109/07420528.2010.531490)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2010.531490?journalCode=cbi

Abstract Due to its disruptive effects on circadian rhythms and sleep deprivation at night, shiftworking is currently recognized as a risk factor for breast cancer (BC). As revealed by the present analysis based on a comparative case-control study of 1679 women, exposure to light-at-night (LAN) in the “sleeping habitat” is significantly associated with BC risk (odds ratio [OR] = 1.220, 95% confidence interval [CI] = 1.118–1.311; p < .001), controlling for education, ethnicity, fertility, and alcohol consumption. The novelty of the present research is that, to the best of the authors' knowledge, it is the first study to have identified an unequivocal positive association between bedroom-light intensity and BC risk. Thus, according to the results of the present study, not only should artificial light exposure in the working environment be considered as a potential risk factor for BC, but also LAN in the “sleeping habitat.” (Author correspondence: ahaim@research.haifa.ac.il)

Read More: http://informahealthcare.com/doi/abs/10.3109/07420528.2010.531490?journalCode=cbi

Keywords Breast cancer, Circadian disruption, Light-at-night, Light pollution, Sleeping habitat

Kloog I, Portnov BA, Rennert HS, Haim A

Year 2011

Authors Itai Kloog, Boris A. Portnov, Hedy S. Rennert and Abraham Haim

Report Name Does the Modern Urbanized Sleeping Habitat Pose a Breast Cancer Risk?

Publication Chronobiology International

Issue-page numbers 28:1, 76-80

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2010.531490

Abstract Due to its disruptive effects on circadian rhythms and sleep deprivation at night, shiftworking is currently recognized as a risk factor for breast cancer (BC). As revealed by the present analysis based on a comparative case-control study of 1679 women, exposure to light-at-night (LAN) in the “sleeping habitat” is significantly associated with BC risk (odds ratio [OR] = 1.220, 95% confidence interval [CI] = 1.118–1.311; p < .001), controlling for education, ethnicity, fertility, and alcohol consumption. The novelty of the present research is that, to the best of the authors' knowledge, it is the first study to have identified an unequivocal positive association between bedroom-light intensity and BC risk. Thus, according to the results of the present study, not only should artificial light exposure in the working environment be considered as a potential risk factor for BC, but also LAN in the “sleeping habitat.”

Keywords Breast cancer, Circadian disruption, Light-at-night, Light pollution, Sleeping habitat

Kloog I, Stevens RG, Haim A, Portnov BA

Year 2010

Authors Itai Kloog, Stevens RG, Haim A, Portnov BA

Report Name Nighttime light level co-distributes with breast cancer incidence worldwide.

Publication Cancer Causes Control

Issue-page numbers 2010 Dec;21(12):2059-68. Epub 2010 Aug 3.

URL http://www.ncbi.nlm.nih.gov/pubmed/20680434

Abstract Breast cancer incidence varies widely among countries of the world for largely unknown reasons. We investigated whether country-level light at night (LAN) is associated with incidence. We compared incidence rates of five common cancers in women (breast, lung, colorectal, larynx, and liver), observed in 164 countries of the world from the GLOBOCAN database, with population-weighted country-level LAN, and with several developmental and environmental indicators, including fertility rate, per capita income, percent of urban population, and electricity consumption. Two types of regression models were used in the analysis: Ordinary Least Squares and Spatial Errors. We found a significant positive association between population LAN level and incidence rates of breast cancer. There was no such an association between LAN level and colorectal, larynx, liver, and lung cancers. A sensitivity test, holding other variables at their average values, yielded a 30-50% higher risk of breast cancer in the highest LAN exposed countries compared to the lowest LAN exposed countries. The possibility that under-reporting from the registries in the low-resource, and also low-LAN, countries created a spurious association was evaluated in several ways and shown not to account for the results. These findings provide coherence of the previously reported case-control and cohort studies with the co-distribution of LAN and breast cancer in entire populations.

Keywords

Knauth P

Year 1996

Authors Knauth P

Report Name Designing better shift systems

Publication Appl Ergon

Issue-page numbers 27:39–44 doi:10.1016/0003- 6870(95)00044-5. PMID:15676310

URL http://www.mendeley.com/research/designing-better-shift-systems/

Abstract The results of some intervention studies on the effects of the change from weekly rotating to quicker rotating shift systems are presented. Consequently, the following recommendations for the design of shift systems according to physiological, psychological and social criteria are discussed: (1) Nightwork should be reduced as much as possible. If this is not possible, quickly rotating shift systems are preferable to slowly rotating ones. Permanent nightwork does not seem to be recommendable for the majority of shiftworkers. (2) Extended workdays (9-12 hours) should only be contemplated when the nature of work and the workload are suitable for extended working hours, and the shift system is designed to minimize the accumulation of fatigue and toxic exposure is limited. (3) An early start for the morning shift should be avoided. Flexible working time arrangements can be achieved in all shift systems. The highest flexibility is possible in the so-called 'time autonomous groups'. (4) Quick changeovers (e.g. from night shift to afternoon shift on the same day) should be avoided. The number of consecutive working days should be limited to five-seven. Every shift system should include some free weekends with at least two consecutive days off. (5) The forward rotation (phase delay, clockwise rotation: morning/evening/night shift) would seem to be most preferred.

Keywords

Knauth P, Hornberger S

Year 2003

Authors Knauth P, Hornberger S

Report Name Preventive and compensatory measures for shift workers

Publication Occup Med (Lond)

Issue-page numbers 53:109–116 doi:10.1093/occmed/kqg049. PMID:12637595

URL http://occmed.oxfordjournals.org/content/53/2/109.abstract

Abstract Shift systems are known to be associated with a variety of psychosocial and physiological problems that can affect the health of workers. This review focuses on measures that can be taken to optimize the well-being of shift workers and to identify ill-health at an early stage. The discussion includes specific aspects of the design of shift systems, taking account of variation in the views and circumstances of employees, and strategies to combat sleepiness at work and elsewhere. Although an ideal shift system does not exist, a wholistic approach comprising education of managers, employees and their families can ameliorate some of the health consequences.

Keywords Alertness, coping strategies, ergonomic design of shift systems, health care, night work, participation, shift work, sleep

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Knels L, Valtink M, Roehlecke C, et al.

Year 2011

Authors Lilla Knels, Monika Valtink, Cora Roehlecke, Amelie Lupp, Jamlec de la Vega, Mirko Mehner, Richard H. W. Funk

Report Name Blue light stress in retinal neuronal (R28) cells is dependent on wavelength range and irradiance

Publication European Journal of Neuroscience

Issue-page numbers Volume 34, Issue 4, pages 548–558, August 2011

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1460-9568.2011.07790.x/full

Abstract The aim of our study was to elucidate the role of wavelength and irradiance in blue light retinal damage. We investigated the impact of blue light emitted from light-emitting diode (LED) modules with peaks at either 411 nm (half bandwidth 17 nm) or 470 nm (half bandwidth 25 nm) at defined irradiances of 0.6, 1.5 and 4.5 W/m2 for 411 nm and 4.5 W/m2 for 470 nm on retinal neuronal (R28) cells in vitro. We observed a reduction in metabolic activity and transmembrane potential of mitochondria when cells were irradiated at 411 nm at higher irradiances. Furthermore, production of mitochondrial superoxide radicals increased significantly when cells were irradiated with 411 nm light at 4.5 W/m2. In addition, such irradiation caused an activation of the antioxidative glutathion system. Using vital staining, flow cytometry and western blotting, we were able to show that apoptosis only took place when cells were exposed to 411 nm blue light at higher irradiances; necrosis was not observed. Enhanced caspase-3 cleavage product levels confirmed that this effect was dependent on light irradiance. Significant alterations of the above-mentioned parameters were not observed when cells were irradiated with 471 nm light despite a high irradiance of 4.5 W/m2, indicating that the cytotoxic effect of blue light is highly dependent on wavelength. The observed phenomena in R28 cells at 411 nm (4.5 W/m2) point to an apoptosis pathway elicited by direct mitochondrial damage and increased oxidative stress. Thus, light of 411 nm should act via impairment of mitochondrial function by compromising the metabolic situation of these retinal neuronal cells.

Keywords

Knower KC, To SQ, Takagi K, et al. **Year** 2011

Authors Kevin C. Knower, Sarah Q. To, Kiyoshi Takagi, Yasuhiro Miki, Hironobu Sasano, Evan R. Simpson and Colin D. Clyne

Report Name Melatonin suppresses aromatase expression and activity in breast cancer associated fibroblasts

Publication Breast Cancer Research and Treatment

Issue-page numbers DOI: 10.1007/s10549-012-1953-4

URL http://www.springerlink.com/content/e67024068703686h/

Abstract The main biological active substance secreted by the pineal gland, melatonin (MLT), counteracts the effects of estrogens in breast cancer via exerting a number of its own oncostatic properties. Recent studies of postmenopausal women have identified that the major metabolite of MLT is statistically significantly associated with a lower risk of developing breast cancer. While MLT production decreases with age, breast cancer risk, however, increases with age and obesity. We hypothesize that MLT inhibits estrogen production in breast adipose fibroblasts (BAFs), the main local source of estrogen in breast tumors of postmenopausal women, by inhibiting transcription of the CYP19A1 gene that encodes the key enzyme aromatase. Normal BAFs were cultured from women undergoing breast reduction surgery, while breast cancer-associated fibroblasts (CAFs) were isolated from three women with estrogen receptor (ER) positive invasive ductal carcinomas. MTNR1A and MTNR1B receptor expression and CYP19A1 mRNA expression following MLT treatments were determined by qRT-PCR. BAFs express the G-protein coupled MLT receptors MTNR1A and MTNR1B with elevated levels of MTNR1A found in CAFs. Treatment of BAFs and CAFs with MLT resulted in significant suppression of CYP19A1 transcription and aromatase activity at pharmacological, physiological and sub-physiological concentrations. MLT suppression occurred through promoter-specific PI.4-, PI.3- and PII-derived CYP19A1 mRNA. Stimulation of CYP19A1 PII-mRNA and aromatase activity by prostaglandin E2 (PGE2) were significantly attenuated by physiological doses of MLT. Lower levels of MLT in aging women may increase the risk of progressing ER-positive breast cancer through a decreased ability to suppress CYP19A1 expression and subsequent local estrogen production in BAFs/CAFs.

Keywords Melatonin – Aromatase – Postmenopause – Breast cancer – Epigenetic – Prostaglandin E2

Knutsson A **Year** 2003

Authors Knutsson A

Report Name Health disorders of shift workers

Publication Occup Med (Lond)

Issue-page numbers 53:103–108 doi:10.1093/occmed/kqg048. PMID:12637594

URL http://occmed.oxfordjournals.org/content/53/2/103.short

Abstract The effects of shift work on physiological function through disruption of circadian rhythms are well described. However, shift work can also be associated with specific pathological disorders. This article reviews the evidence for a relationship between specific medical disorders and working at night or on shift systems. The strongest evidence exists for an association with peptic ulcer disease, coronary heart disease and compromised pregnancy outcome.

Keywords Cardiovascular diseases, gastrointestinal diseases, health, medical surveillance, night work, pregnancy, shift work

Authors Knutsson A, Alfredsson L, Karlsson B, Akerstedt T, Fransson EI, Westerholm P, Westerlund H.

Report Name Breast cancer among shift workers: results of the WOLF longitudinal cohort study.

Publication Scand J Work Environ Health

Issue-page numbers 2013 Mar 1;39(2):170-7. doi: 10.5271/sjweh.3323. Epub 2012 Sep 24

URL http://www.ncbi.nlm.nih.gov/pubmed/23007867

Abstract

OBJECTIVE:

The aim of this study was to investigate whether shift work (with or without night work) is associated with increased risk of breast cancer.
METHODS:

The population consisted of 4036 women. Data were obtained from WOLF (Work, Lipids, and Fibrinogen), a longitudinal cohort study. Information about baseline characteristics was based on questionnaire responses and medical examination. Cancer incidence from baseline to follow-up was obtained from the national cancer registry. Two exposure groups were identified: shift work with and without night work. The group with day work only was used as the reference group in the analysis. Cox regression analysis was used to calculate relative risk.
RESULTS:

In total, 94 women developed breast cancer during follow-up. The average follow-up time was 12.4 years. The hazard ratio for breast cancer was 1.23 [95% confidence interval (95% CI) 0.70-2.17] for shifts without night work and 2.02 (95% CI 1.03-3.95) for shifts with night work. When including only women <60 years of age, the risk estimates were 1.18 (95% CI 0.67-2.07) for shifts without night work, and 2.15 (95% CI 1.10-4.21) for shifts with night work.
CONCLUSIONS:

Our results indicate an increased risk for breast cancer among women who work shifts that includes night work.

Keywords

Knutsson A, Andersson H, Berglund U **Year** 1990

Authors Knutsson A, Andersson H, Berglund U

Report Name Serum lipoproteins in day and shift workers: a prospective study

Publication Br J Ind Med

Issue-page numbers 47:132–134. PMID:2310717

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1035115/

Abstract This study was designed to assess changes in diet and serum lipoproteins in shift workers. Twelve shift workers and 13 day workers were examined before employment and after six months at work. Total cholesterol and serum triglycerides did not change significantly. In both groups a decrease in systolic blood pressure was observed. The ratio between apoB and apoA-1 lipoproteins increased by 18% in shift workers compared with 5% in day workers. The change in the ratio between apoB and apoA-1 lipoproteins showed a significant inverse correlation with the change in intake of dietary fibres.

Keywords

Koch S, Noble H **Year** 2011

Authors Susan Koch, Helen Noble

Report Name Use of sleep care guidelines in a surgical intensive care unit reduces noise levels and improves patient-reported sleep quality

Publication Evid Based Nurs

Issue-page numbers 2011;20: 396–407.

URL http://ebn.bmj.com/content/early/2011/06/14/ebn1172.extract

Abstract Implications for practice and research

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▪ Nurses need to be aware of the impact that care delivery has on sleep quality and the importance of sleep for recuperation.

*

▪ Changes to routine care may have a positive impact on sleep quality from the perception of the patient.

*

▪ Further studies to examine patients' perception of sleep quality throughout a hospital stay are required.

*

▪ Observational studies are needed to observe how staffs apply guidelines in practice to reduce noise and light to promote patients' sleep during a hospital stay.

Keywords

Kohyama J

Year 2011

Authors Jun Kohyama

Report Name Neurochemical and Neuropharmacological Aspects of Circadian Disruptions: An Introduction to Asynchronization

Publication Curr Neuropharmacol

Issue-page numbers 2011 June; 9(2): 330–341. doi: 10.2174/157015911795596522

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131723/

Abstract Circadian disruptions are common in modern society, and there is an urgent need for effective treatment strategies. According to standard diagnostic criteria, most adolescents showing both insomnia and daytime sleepiness are diagnosed as having behavioral-induced sleep efficiency syndrome resulting from insomnia due to inadequate sleep hygiene. However, a simple intervention of adequate sleep hygiene often fails to treat them. As a solution to this clinical problem, the present review first overviews the basic neurochemical and neuropharmachological aspects of sleep and circadian rhythm regulation, then explains several circadian disruptions from similar viewpoints, and finally introduces the clinical notion of asynchronization. Asynchronization is designated to explain the pathophysiology/pathogenesis of exhibition of both insomnia and hypersomnia in adolescents, which comprises disturbances in various aspects of biological rhythms. The major triggers for asynchronization are considered to be a combination of light exposure during the night, which disturbs the biological clock and decreases melatonin secretion, as well as a lack of light exposure in the morning, which prohibits normal synchronization of the biological clock to the 24-hour cycle of the earth and decreases the activity of serotonin. In the chronic phase of asynchronization, involvement of both wake- and sleep-promoting systems is suggested. Both conventional and alternative therapeutic approaches for potential treatment of asynchronization are suggested.

Keywords Melatonin, serotonin, circadian rhythm, social jet lag, singularity, sleep hygiene, desynchronization.

Authors Kojo K, Pukkala E, Auvinen A

Report Name Breast cancer risk among Finnish cabin attendants: a nested case-control study

Publication Occup Environ Med

Issue-page numbers 62:488–493.doi:10.1136/oem.2004.014738 PMID:15961626

URL http://oem.bmj.com/content/62/7/488.abstract

Abstract

Background: Earlier studies have found increased breast cancer risk among female cabin crew. This has been suggested to reflect lifestyle factors (for example, age at first birth), other confounding factors (for example, age at menarche), or occupational factors such as exposure to cosmic radiation and circadian rhythm alterations due to repeated jet lag.

Aims: To assess the contribution of occupational versus lifestyle and other factors to breast cancer risk among cabin attendants in Finland.

Methods: A standardised self-administered questionnaire on demographic, occupational, and lifestyle factors was given to 1041 cabin attendants. A total of 27 breast cancer cases and 517 non-cases completed the questionnaire. Breast cancer diagnoses were confirmed through the Finnish Cancer Registry. Exposure to cosmic radiation was estimated based on self-reported flight history and timetables. A conditional logistic regression model was used for analysis.

Results: In the univariate analysis, family history of breast cancer (OR=2.67, 95% CI: 1.00 to 7.08) was the strongest determinant of breast cancer. Of occupational exposures, sleep rhythm disruptions (OR=1.72, 95% CI: 0.70 to 4.27) were positively related and disruption of menstrual cycles (OR=0.71, 95% CI: 0.26 to 1.96) negatively related to breast cancer. However, both associations were statistically non-significant. Cumulative radiation dose (OR=0.99, 95% CI: 0.83 to 1.19) showed no effect on breast cancer.

Conclusions: Results suggest that breast cancer risk among Finnish cabin attendants is related to well established risk factors of breast cancer, such as family history of breast cancer. There was no clear evidence that the three occupational factors studied affected breast cancer risk among Finnish flight attendants.

Keywords

Authors Margit Koller, Mikko Härma, Jarmo T. Laitinen, Michael Kundi, Brigitte Piegler, Manfred Haider

Report Name Different patterns of light exposure in relation to melatonin and cortisol rhythms and sleep of night workers

Publication Journal of Pineal Research

Issue-page numbers Volume 16, Issue 3, pages 127–135, April 1994

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1994.tb00092.x/abstract

Abstract There is strong evidence to suggest that circadian psychophysiological adaptation processes are modified by light, depending on its intensity and timing. To characterize such modifications and determine whether they are associated with an alteration in the day/night pattern of melatonin excretion, measurements were obtained around the clock in 14 permanent night workers, each studied over a 48 hr period in the field. The light exposure behavior of these workers was studied with a newly developed light dosimetry by measuring light intensity at eye level. Physical activity was continuously registered and sleep indices were obtained by sleep logs and activity markings. Circadian rhythms of melatonin and Cortisol were analysed from salivary samples collected for 24 hr at 2 hr intervals. The inter individual variation of melatonin acrophase determined by cosinor analysis was greater than 180 degrees (from around midnight to noon) and that of Cortisol was about 135 degrees (from early morning to afternoon). Hormonal phase positions coincided significantly with light exposure: the more bright light pulses in the morning (maximum lux between 0600 and 0900), the less were the melatonin and Cortisol acrophases shifted into the day. There was also a negative correlation between melatonin acrophase shift and duration of the overall light exposure above 1500 lux. Morning light maximum and sleep onset correlated highly significantly. Night workers were divided into those with less than (‘non-shifters’, n = 9) and more than 6 hr deviation from midnight (‘shifters’, n = 5) of the melatonin acrophase. The group comparison revealed a marked difference of the mean melatonin concentrations at night, and at 0700. Shifters did not experience bright light exposure in the morning and showed a tendency towards shorter overall exposure of light above 1500 lux. In conclusion, light avoidance behavior during morning hours, as observed in 5 out of 14 night workers, coincided significantly with a phase delay of melatonin acrophase. Light avoidance also correlated with an earlier sleep onset and a tendency to longer sleep hours. Thus our data suggest that the interaction of a phase shifted activity cycle and the light/dark exposure leads in the field situation to different degrees of adaptation to the prevailing activity/rest requirements, depending on dose and phase position of bright light exposure.

Keywords Permanent night work—light; exposure—salivary; melatonin—salivary; Cortisol—sleep

Kooij JJS

Year 2011

Authors J.J.S. Kooij

Report Name S37-01 - Biological rhythms and ADHD

Publication European Psychiatry

Issue-page numbers Volume 26, Supplement 1, 2011, Pages 2141

URL http://www.sciencedirect.com/science/article/pii/S0924933811738445

Abstract The majority of the adults with ADHD have chronic difficulty to go to bed on time. This leads to a shorter sleep duration and daytime sleepiness that may aggravate the inattention problems of ADHD.

This sleep pattern is also known as a delayed sleepphase, and the patients as 'eveningtypes'. The other way round, eveningtypes have been associated with impulsiveness. The scope of this presentation is to study the impact of this sleep pattern in adults with ADHD on mood (i.e. seasonal affective disorder), eating habits (like timing of meals and binge eating), activity patterns (like nightshift work and light at night) and health in general, i.e. obesity and cancer.

Keywords

Korkmaz A, Manchester LC

Year 2011

Authors Ahmet Korkmaz, Lucien C. Manchester

Report Name Reactive nitrogen species; devastating intracellular players and melatonin as a defender

Publication Journal of Experimental and Integrative Medicine

Issue-page numbers 2011; 1(2):63-65

URL http://www.scopemed.org/mnstemps/4/4-1299704198.pdf

Abstract It is widely accepted that reactive oxygen species (ROS) readily cause cellular damage (i.e., oxidative stress) and play an important role in the pathogenesis of a variety of human diseases and sequelae [1-3]. Since the first seminal free radical studies by Harman in 1950's [4], oxidative stress has gained much attention and many studies have confirmed that free radicals especially those that are oxygen-based such as the superoxide anion (•O2–), hydroxyl radical (•OH), and non-radical hydrogen peroxide (H2O2) are harmful molecules intracellularly. However, H2O2 for example, functions as an important second messenger at physiological levels and involves a vast number of pathways within cells [5, 6]. Therefore, the general belief can be summarized as "oxygen-based free radicals are harmful when they are produced at high levels within a certain time period"

Keywords Melatonin; Nitric oxide; Peroxynitrite; Reactive nitrogen species

Korkmaz A, Rosales-Corral S, Reiter RJ

Year 2012

Authors Ahmet Korkmaz, Sergio Rosales-Corral, Russel J. Reiter

Report Name Gene regulation by melatonin linked to epigenetic phenomena

Publication Gene

Issue-page numbers Volume 503, Issue 1, 15 July 2012, Pages 1-11

URL http://www.sciencedirect.com/science/article/pii/S0378111912004660

Abstract Many exogenous (e.g., toxins, chemicals, ultraviolet, cigarette smoke) and endogenous (e.g., hyperglycemia, dyslipidemia, cytokines, chemokines) agents disrupt the intracellular environment and result in a massive production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). The molecular damage that ROS/RNS induce is referred to as nitrooxidative stress. The cellular consequences of nitrooxidative stress include lipid peroxidation, protein oxidation and DNA damage. Additionally, ROS and RNS deplete cellular defenses and initiate inflammation. It is widely accepted that nitrooxidative stress and inflammation play important roles in the pathogenesis of a variety of human diseases and sequelae. Several processes are crucial to overcome the damaging cellular events caused by nitrooxidative stress, e.g., scavenging both ROS and RNS, induction of defense mechanisms and alleviating/suppressing inflammation are essential. Both endogenous and pharmacological concentrations of melatonin have long been known to play role in the direct scavenging of ROS and RNS as well as inducing antioxidant defense mechanisms and ameliorating inflammation. The current review summarizes research related to two major transcription factors that participate in these processes and summarizes how melatonin regulates antioxidant and pro-inflammatory genes via epigenetic on/off mechanisms.

Keywords Melatonin; Free radicals; Oxidative stress; Transcription; Epigenetics; Cytokines

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Korkmaz A, Topal T, Tan E, Reiter RJ

Year 2009

Authors Ahmet Korkmaz, Turgut Topal, Dun-Xian Tan and Russel J. Reiter

Report Name Role of melatonin in metabolic regulation

Publication Reviews in Endocrine & Metabolic Disorders

Issue-page numbers Volume 10, Number 4, 261-270, DOI: 10.1007/s11154-009-9117-5

URL http://www.springerlink.com/content/95q47348w7810v51/

Abstract Although the human genome has remained unchanged over the last 10,000 years, our lifestyle has become progressively more divergent from those of our ancient ancestors. This maladaptive change became apparent with the Industrial Revolution and has been accelerating in recent decades. Socially, we are people of the 21st century, but genetically we remain similar to our early ancestors. In conjunction with this discordance between our ancient, genetically-determined biology and the nutritional, cultural and activity patterns in contemporary Western populations, many diseases have emerged. Only a century ago infectious disease was a major cause of mortality, whereas today non-infectious chronic diseases are the greatest cause of death in the world. Epidemics of metabolic diseases (e.g., cardiovascular diseases, type 2 diabetes, obesity, metabolic syndrome and certain cancers) have become major contributors to the burden of poor health and they are presently emerging or accelerating, in most developing countries. One major lifestyle consequence is light at night and subsequent disrupted circadian rhythms commonly referred to as circadian disruption or chronodisruption. Mounting evidence reveals that particularly melatonin rhythmicity has crucial roles in a variety of metabolic functions as an anti-oxidant, anti-inflammatory chronobiotic and possibly as an epigenetic regulator. This paper provides a brief outline about metabolic dysregulation in conjunction with a disrupted melatonin rhythm.

Keywords Syperglycemia - Hyperlipidemia - Dysmetabolism - Melatonin - Circadian rhythm

Kornmann B, Preitner N, Rifat D et al. **Year** 2001

Authors Kornmann B, Preitner N, Rifat D et al.

Report Name Analysis of circadian liver gene expression by ADDER, a highly sensitive method for the display of differentially expressed mRNAs

Publication Nucleic Acids Res

Issue-page numbers 29:E51–E1 doi:10.1093/nar/29.11.e51. PMID:11376163

URL http://nar.oxfordjournals.org/content/29/11/e51.abstract

Abstract We describe a novel and highly sensitive method for the differential display of mRNAs, called ADDER (Amplification of Double-stranded cDNA End Restriction fragments). The technique involves the construction and PCR amplification of double-stranded cDNA restriction fragments complementary to 3′-terminal mRNA sequences. Aliquots of these cDNA fragments are then amplified by touchdown PCR with 192 pairs of display primers (16 upstream primers and 12 downstream primers) that differ in their ultimate and penultimate nucleotides and the PCR products are compared by size-fractionation on urea–polyacrylamide sequencing gels. By using the ADDER technology for the comparison of liver RNAs harvested at different times around the clock we detected nearly 300 cDNA fragments complementary to mRNAs with circadian accumulation profiles and sequenced 51 of them. The majority of these cDNAs correspond to genes which were not previously known to be rhythmically expressed. A large fraction of the identified genes encoded factors involved in the processing and detoxification of nutrients. This suggests that a primary purpose of circadian transcription in the liver is the anticipation of food processing and detoxification. Several genes involved in human disease were also identified, including the one encoding presenilin II, a protein implicated in the development of Alzheimer's Disease.

Keywords

Køster B, Thorgaard C, Philip A, Clemmensen IH **Year** 2010

Authors Brian Køster, Camilla Thorgaard, Anja Philip, Inge H. Clemmensen

Report Name Prevalence of sunburn and sun-related behaviour in the Danish population: a cross-sectional study.

Publication Scand J Public Health

Issue-page numbers July 2010 vol. 38 no. 5 548-552

URL http://sjp.sagepub.com/content/38/5/548.abstract

Abstract Background: In Denmark, the incidence of melanoma has been increasing since the 1960s. Intermittent exposure to ultraviolet radiation and a history of sunburn and sunbed use are known risk factors. We describe the association between use of protective measures, sun-related behaviour and experience of sunburn in the Danish population three months after the start of the campaign. Method: A population-based sample of 3,499 persons aged 15—59 years completed a questionnaire that included items on exposure to ultraviolet radiation. We examined the relations between sunburn and sun-related behaviour by logistic regression analysis. Results: Within the previous 12 months, 35% of the study population had experienced sunburn. Sunburn became less frequent with age (odds ratio (OR) 4.44; 15—19 vs. 50—59) and skin type (OR 2.57; I vs. III). Sunburn was negatively associated with shade and clothing and positively with use of sunscreens. We found no significant difference in sunscreen use between intentional tanners who experienced sunburn and those who did not. A larger fraction of unintentional tanners with sunburn than those who were not sunburnt had used sunscreen. Sunscreen was used to prolong the time spent in the sun by 66% of sunburnt people; however, we found no association between duration of sun exposure and sunscreen use. Conclusions: Future campaigns to reduce the prevalence of sunburn in the Danish population must especially target young persons and intentional tanning, and they should emphasize that sunscreen cannot be used to extend the time spent in the sun and that shade and clothing provide the best protection against sunburn.

Keywords Cross-sectional, melanoma, prevention, questionnaire, sunburn, sunlight, sunscreen, ultraviolet radiation

Authors Kostoglou-Athanassiou I, Treacher DF, Wheeler MJ, Forsling ML

Report Name Melatonin administration and pituitary hormone secretion

Publication Clin Endocrinol (Oxf)

Issue-page numbers 48:31–37 doi:10.1046/j.1365-2265.1998.00341.x. PMID:9509065

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2265.1998.00341.x/abstract

Abstract

OBJECTIVE

The relationship between the pineal gland and pituitary function remains controversial, while the role of melatonin in the adaptation of the organism to the light-dark cycle of the environment is becoming increasingly recognized. The aim of this study was to investigate the effect of a manipulation of the melatonin rhythm on pituitary hormone secretion in man.
DESIGN

Double-blind controlled clinical study.
SUBJECTS

Ten adult healthy male volunteers, aged 21–33 years, were studied on two occasions: once after the administration of melatonin 5 mg orally for 4 days at 1700 hours and once after the administration of placebo, at similar times. On the day of each study the subjects undertook their normal duties but refrained from taking heavy exercise, from smoking and drinking alcohol.
MEASUREMENTS

Serum cortisol, growth hormone, prolactin and plasma vasopressin, oxytocin, melatonin, sodium, potassium, osmolality and packed cell volume were measured over the following 24 hours.
RESULTS

The cortisol peak was advanced and prolactin release increased after melatonin administration, while growth hormone was not affected. Vasopressin and oxytocin levels were found to increase during the night in the control study, but the period of the nocturnal increase in vasopressin concentrations was reduced after the administration of melatonin and the nocturnal increase of oxytocin was absent.
CONCLUSION

Altering the melatonin rhythm may affect neuroendocrine function, influencing the nocturnal pattern of neurohypophysial hormone secretion, augmenting prolactin release and advancing the peak of cortisol release.

Keywords

Kothari LS, Shah PN, Mhatre MC

Year 1982

Authors Lalita S. Kothari, Prabhaker N. Shah, Molina C. Mhatre

Report Name Effect of continuous light on the incidence of 9,10-dimethyl-1,2-benzanthracene induced mammary tumors in female Holtzman rats

Publication Cancer Letters

Issue-page numbers Volume 16, Issue 3, September 1982, Pages 313-317

URL http://www.sciencedirect.com/science/article/pii/030438358290012X

Abstract The pineal has been recently implicated in mammary tumorigenesis. Effect of physiological pinealectomy brought about by subjecting female Holtzman rats to permanent lighting (24 h/day) from birth was studied on the incidence of 9,10-dimethyl-1,2-benzanthracene (DMBA) induced mammary tumors. The incidence of adenocarcinoma was 95% in animals maintained in continuous photoperiod in contrast to that (60%) observed in control animals maintained on a light/dark (View the MathML source) schedule. Further, the latency period of tumor appearance (61.5 ± 9 days) in the former group was found to be significantly shorter than that seen in the latter group (93.7 ± 8.3 days). Explanations are offered for this difference in the observed incidence.

Keywords

Kothari LS, Shah PN, Mhatre MC

Year 1984

Authors Lalita S. Kothari, Prabhaker N. Shah, Molina C. Mhatre

Report Name Pineal ablation in varying photoperiods and the incidence of 9,10-dimethyl-1,2-benzanthracene induced mammary cancer in rats

Publication Cancer Letters

Issue-page numbers Volume 22, Issue 1, February 1984, Pages 99-102

URL http://www.sciencedirect.com/science/article/pii/0304383584900508

Abstract Our earlier observation of increased incidence of 9,10-dimethyl-1,2-benzanthracene (DMBA) induced mammary carcinoma in young, virgin ‘functionally pinealectomized Holtzman rats poses the question whether or not a comparable incidence would occur in surgically pinealectomized rats reared in varying photoperiods (e.g. light/dark (LD) View the MathML source or LD View the MathML source schedules). Results show that functionally or surgically pinealectomized rats in LD View the MathML source schedule have comparable mammary tumor incidence (95% and 83%, respectively) and latency period of tumor appearance (60 ± 3.1 and 69.2 ± 6.6 days, respectively). However, when surgically pinealectomized rats were kept in short photoperiods (LD View the MathML source), a significant difference was observed in both tumor incidence (60.9%) and latency period (91.8 ± 11.0 days). Our data suggest that the susceptibility of the mammary gland to carcinogenic insult may be modulated by the concentration of the pineal hormone, melatonin, in the CNS.

Keywords

Koyanagi M, Kubokawa K, Tsukamoto H, et al

Year 2005

Authors Mitsumasa Koyanagi, Kaoru Kubokawa, Hisao Tsukamoto, Yoshinori Shichida and Akihisa Terakita

Report Name Cephalochordate melanopsin: evolutionary linkage between invertebrate visual cells and vertebrate photosensitive retinal ganglion cells

Publication Current Biology

Issue-page numbers Volume 15, Issue 11, 1065-1069, 7 June 2005

URL http://www.cell.com/current-biology/abstract/S0960-9822%2805%2900512-9

Abstract Animal photoreceptor cells can be classified into two distinct types, depending on whether the photopigment is borne on the membrane of a modified cilium (ciliary type) or apical microvilli (rhabdomeric type) [1]. Ciliary photoreceptors are well known as vertebrate rods and cones and are also found in several invertebrates. The rhabdomeric photoreceptor, in contrast, is a predominant type of invertebrate visual cell, but morphologically identifiable rhabdomeric photoreceptors have never been found in vertebrates. It is hypothesized that the rhabdomeric photoreceptor cell had evolved to be the photosensitive retinal ganglion cell for the vertebrate circadian photoentrainment [2,3,4] owing to the fact that some molecules involved in cell differentiation are common among them [5]. We focused on the cephalochordate amphioxus because it is the closest living invertebrate to the vertebrates, and interestingly, it has rhabdomeric photoreceptor cells for putative nonvisual functions [6]. Here, we show that the amphioxus homolog of melanopsin [7,8,9], the circadian photopigment in the photosensitive retinal ganglion cells of vertebrates, is expressed in the rhabdomeric photoreceptor cells of the amphioxus and that its biochemical and photochemical properties, not just its primary structure, are considerably similar to those of the visual rhodopsins in the rhabdomeric photoreceptor cells of higher invertebrates. The cephalochordate rhabdomeric photoreceptor represents an evolutionary link between the invertebrate visual photoreceptor and the vertebrate circadian photoreceptor.

Keywords

Kramer A, Yang FC, Snodgrass P et al.

Year 2001

Authors Achim Kramer, Fu-Chia Yang, Pamela Snodgrass, Xiaodong Li, Thomas E. Scammell, Fred C. Davis and

Report Name Regulation of daily locomotor activity and sleep by hypothalamic EGF receptor signaling

Publication Science

Issue-page numbers 294:2511–2515 doi:10.1126/science.1067716. PMID:11752569

URL http://www.sciencemag.org/content/294/5551/2511.abstract

Abstract The circadian clock in the suprachiasmatic nucleus (SCN) is thought to drive daily rhythms of behavior by secreting factors that act locally within the hypothalamus. In a systematic screen, we identified transforming growth factor-α (TGF-α) as a likely SCN inhibitor of locomotion. TGF-α is expressed rhythmically in the SCN, and when infused into the third ventricle it reversibly inhibited locomotor activity and disrupted circadian sleep-wake cycles. These actions are mediated by epidermal growth factor (EGF) receptors on neurons in the hypothalamic subparaventricular zone. Mice with a hypomorphic EGF receptor mutation exhibited excessive daytime locomotor activity and failed to suppress activity when exposed to light. These results implicate EGF receptor signaling in the daily control of locomotor activity, and identify a neural circuit in the hypothalamus that likely mediates the regulation of behavior both by the SCN and the retina.

Keywords

Kräuchi K, Cajochen C, Werth E, Wirz-Justice A **Year** 2002

Authors Kräuchi K, Cajochen C, Werth E, Wirz-Justice A

Report Name Alteration of internal circadian phase relationships after morning versus evening carbohydrate-rich meals in humans

Publication J Biol Rhythms

Issue-page numbers 17:364–376. PMID:12164252

URL http://jbr.sagepub.com/content/17/4/364.abstract

Abstract The effects of a single morning and evening carbohydrate-rich meal for 3 consecutive days on circadian phase of core body temperature (CBT), heart rate, and salivary melatonin rhythms were compared under controlled constant routine conditions. In 10 healthy young men entrained to a natural light-dark cycle with regular sleep timing, CBT and heart rate were significantly elevated for approximately 8 h after the last evening carbohydrate-rich meal (EM), and nocturnal melatonin secretion (as measured by salivary melatonin and urinary 6-sulphatoxymelatonin levels) was reduced, compared to the morning carbohydraterich meal (MM) condition. Thus, circadian phase could not be measured until the following day due to this acute masking effect. The day after the last meal intervention, MM showed a significant advanced circadian phase position in CBT (+59 ± 12 min) and heart rate (+43 ± 18 min) compared to EM. However, dim-light melatonin onset was not significantly changed (+15 ± 13 min). The results are discussed with respect to central (light-entrainable) and peripheral (foodentrainable) oscillators. Food may be a zeitgeber in humans for the food-entrainable peripheral oscillators, but melatonin data do not support such a conclusion for the light-entrainable oscillator in the suprachiasmatic nucleus.

Keywords carbohydrate-rich food, nonphotic zeitgeber, constant routine, circadian phase shifts, core body temperature, heart rate, melatonin,

Kreslavskia VD, Fomina IR, Los DA, et al. **Year** 2012

Authors Vladimir D. Kreslavskia, Irina R. Fomina, Dmitry A. Los, Robert Carpentier, Vladimir V. Kuznetsov, Suleyman I. Allakhverdiev

Report Name Red and near infra-red signaling: Hypothesis and perspectives

Publication Journal of Photochemistry and Photobiology C: Photochemistry Reviews

Issue-page numbers Available online 2 February 2012

URL http://www.sciencedirect.com/science/article/pii/S1389556712000032

Abstract The review covers some of the proposed cellular photoreceptors responsible for the effect of red and near infra-red (NIR) light on mammalian cells, including cytochrome-c-oxidase, photoactive porphyrins, flavoproteins, and molecular oxygen. We do not discuss the clinical studies but consider animal models, especially fibroblasts. Several key hypotheses such as mitochondria signaling and free-radical conception of the effects of red light and NIR light based on the changes in redox properties of photoreceptor molecules as well as membrane conception are examined. Special attention is paid to common mechanisms of light signaling in mammalian and plant organisms.

Keywords

Krinsky NI, Landrum JT, Bone RA

Year 2003

Authors Norman I. Krinsky, John T. Landrum, and Richard A. Bone

Report Name Biologic mechanisms of the protective role of lutein and zeaxanthin in the eye

Publication Annual Review of Nutrition

Issue-page numbers Vol. 23: 171-201

URL http://www.annualreviews.org/doi/abs/10.1146/annurev.nutr.23.011702.073307

Abstract

The macular region of the primate retina is yellow in color due to the presence of the macular pigment, composed of two dietary xanthophylls, lutein and zeaxanthin, and another xanthophyll, meso-zeaxanthin. The latter is presumably formed from either lutein or zeaxanthin in the retina. By absorbing blue-light, the macular pigment protects the underlying photoreceptor cell layer from light damage, possibly initiated by the formation of reactive oxygen species during a photosensitized reaction. There is ample epidemiological evidence that the amount of macular pigment is inversely associated with the incidence of age-related macular degeneration, an irreversible process that is the major cause of blindness in the elderly. The macular pigment can be increased in primates by either increasing the intake of foods that are rich in lutein and zeaxanthin, such as dark-green leafy vegetables, or by supplementation with lutein or zeaxanthin. Although increasing the intake of lutein or zeaxanthin might prove to be protective against the development of age-related macular degeneration, a causative relationship has yet to be experimentally demonstrated.

Keywords

Kripke DF, Elliott JA, Youngstedt SD, et al. **Year** 2010

Authors Daniel F Kripke, Jeffrey A Elliott, Shawn D Youngstedt, Barbara L Parry, Richard L Hauger, and Katharine M Rex

Report Name Weak evidence of bright light effects on human LH and FSH

Publication J Circadian Rhythms

Issue-page numbers 2010; 8: 5

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2885316/

Abstract

Background
Most mammals are seasonal breeders whose gonads grow to anticipate reproduction in the spring and summer. As day length increases, secretion increases for two gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH). This response is largely controlled by light. Light effects on gonadotropins are mediated through effects on the suprachiasmatic nucleus and responses of the circadian system. There is some evidence that seasonal breeding in humans is regulated by similar mechanisms, and that light stimulates LH secretion, but primate responses seem complex.
Methods
To gain further information on effects of bright light on LH and FSH secretion in humans, we analyzed urine samples collected in three experiments conducted for other goals. First, volunteers ages 18-30 years and 60-75 commenced an ultra-short 90-min sleep-wake cycle, during which they were exposed to 3000 lux light for 3 hours at balanced times of day, repeated for 3 days. Urine samples were assayed to explore any LH phase response curve. Second, depressed participants 60-79 years of age were treated with bright light or dim placebo light for 28 days, with measurements of urinary LH and FSH before and after treatment. Third, women of ages 20-45 years with premenstrual dysphoric disorder (PMDD) were treated to one 3-hour exposure of morning light, measuring LH and FSH in urine before and after the treatments.
Results
Two of the three studies showed significant increases in LH after light treatment, and FSH also tended to increase, but there were no significant contrasts with parallel placebo treatments and no significant time-of-day treatment effects.
Conclusions
These results gave some support for the hypothesis that bright light may augment LH secretion. Longer-duration studies may be needed to clarify the effects of light on human LH and FSH.

Keywords

Krishnan N, Rakshit K, Chow ES, et al. **Year** 2011

Authors Natraj Krishnan, Kuntol Rakshit, Eileen S. Chow, Jill S. Wentzell, Doris Kretzschmar, Jadwiga M. Giebultowicz

Report Name Loss of circadian clock accelerates aging in neurodegeneration-prone mutants

Publication Neurobiology of Disease

Issue-page numbers 2011; DOI: 10.1016/j.nbd.2011.12.034

URL http://ir.library.oregonstate.edu/xmlui/bitstream/handle/1957/26511/RakshitKuntol.Zoology.LossCircadianClock.pdf?sequence=1

Abstract Circadian clocks generate rhythms in molecular, cellular, physiological, and behavioral processes. Recent studies suggest that disruption of the clock mechanism accelerates organismal senescence and age-related pathologies in mammals. Impaired circadian rhythms are observed in many neurological diseases; however, it is not clear whether loss of rhythms is the cause or result of neurodegeneration, or both. To address this important question, we examined the effects of circadian disruption in Drosophila melanogaster mutants that display clock-unrelated neurodegenerative phenotypes. We combined a null mutation in the clock gene period (per^{01}) that abolishes circadian rhythms, with a hypomorphic mutation in the carbonyl reductase gene sniffer (sni^{1}), which displays oxidative stress induced neurodegeneration. We report that disruption of circadian rhythms in sni^{1} mutants significantly reduces their lifespan compared to single mutants. Shortened lifespan in double mutants was coupled with accelerated neuronal degeneration evidenced by vacuolization in the adult brain. In addition, per^{01} sni^{1} flies showed drastically impaired vertical mobility and increased accumulation of carbonylated proteins compared to age-matched single mutant flies. Loss of per function does not affect sni mRNA expression, suggesting that these genes act via independent pathways producing additive effects. Finally, we show that per^{01} mutation accelerates the onset of brain pathologies when combined with neurodegeneration-prone mutation in another gene, swiss cheese (sws^{1}), which does not operate through the oxidative stress pathway. Taken together, our data suggest that the period gene may be causally involved in neuroprotective pathways in aging Drosophila.

Keywords biological clock, circadian rhythms, neuronal health, protein carbonyls, RING assay

Krueger JM, Obál F Jr **Year** 1993

Authors Krueger JM, Obál F Jr

Report Name Growth hormone-releasing hormone and interleukin-1 in sleep regulation

Publication FASEB J

Issue-page numbers 7:645–652. PMID:8500689

URL http://www.fasebj.org/content/7/8/645.short

Abstract Growth hormone-releasing hormone (GHRH) and interleukin-1 (IL-1) are putative endogenous sleep-promoting substances. Evidence is reviewed showing that, 1) GHRH and IL-1 promote non-rapid eye movement sleep (NREMS); 2) if their production is enhanced, sleep is enhanced; and 3) if they are inhibited using either specific antibodies or peptide antagonists, sleep is reduced. Both are in the brain and both are also indirectly linked to sleep/wake cycles by various other evidence, e.g., growth hormone release and IL-1 plasma levels vary in phase with sleep/wake cycles. Finally, their actions are directly linked to each other; e.g., IL-1-induced growth hormone release is mediated via GHRH. The evidence reviewed strongly implicates both GHRH and IL-1 as key components in humoral sleep regulation. Humoral theories of sleep regulation are complementary to neural theories; both mechanisms affect each other and undoubtedly continuously interact to regulate sleep/wake cycles.

Keywords

Krueger JM, Obal F Jr, Opp M et al. **Year** 1990

Authors Krueger JM, Obal F Jr, Opp M et al.

Report Name Somnogenic cytokines and models concerning their effects on sleep

Publication Yale J Biol Med

Issue-page numbers 63:157–172. PMID:2205056

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589298/

Abstract All the sleep-promoting substances currently identified also have other biological activities. Despite years of effort, a single specific central nervous system sleep center has not been described. These observations led us to propose a biochemical model of a sleep activational system in which the effects of several sleep factors are integrated into a regulatory scheme. These sleep factors interact by altering the metabolism, production, or activity of each other and thereby result in multiple feedback loops. This web of interactions leads to sleep stability in that minor challenges to the system will not greatly alter sleep. The system, however, is responsive to strong perturbations, such as sleep deprivation and infectious disease. The sleep-promoting effects of cytokines and their interactions with prostaglandins and the neuroendocrine system are used to illustrate the functioning of a part of the sleep activational system under normal conditions and during infectious disease. Although the actions of individuals sleep factors are not specific to sleep, their interactions at various levels of the neuraxis can mediate a specific sleep response. Such a system would also be responsive to the autonomic and environmental parameters that alter sleep.

Keywords

Krueger JM, Toth LA, Johannsen L, Opp MR **Year** 1990

Authors Krueger JM, Toth LA, Johannsen L, Opp MR

Report Name Infectious Disease and Sleep: Involvement of Neuroendocrine-Neuroimmune Mechanisms

Publication Int J Neurosci

Issue-page numbers 51:359–362 doi:10.3109/00207459008999744. PMID:2279902

URL http://informahealthcare.com/doi/abs/10.3109/00207459008999744

Abstract N/A

Keywords slow-wave sleep, sleep aclivational system, infection, somnogenic products

Authors Kubo T, Ozasa K, Mikami K et al.

Report Name Prospective cohort study of the risk of prostate cancer among rotating-shift workers: findings from the Japan collaborative cohort study

Publication Am J Epidemiol

Issue-page numbers 164:549–555.doi:10.1093/aje/kwj232 PMID:16829554

URL http://aje.oxfordjournals.org/content/164/6/549.short

Abstract Shift workers have been reported to have an increased risk of some cancers. However, the risk of prostate cancer in shift workers is not known to have been examined previously. This study prospectively examined the association between shift work and risk of prostate cancer incidence among 14,052 working men in Japan enrolled in a large-scale prospective cohort. A baseline survey was conducted between 1988 and 1990. Subjects were asked to indicate the most regular work schedule they had undertaken previously: day work, rotating-shift work, or fixed-night work. During 111,974 person-years, 31 cases of prostate cancer were recorded. The Cox proportional hazards model was used to estimate the risk, with adjustments for age, family history of prostate cancer, study area surveyed, body mass index, smoking, alcohol drinking, job type, physical activity at work, workplace, perceived stress, educational level, and marriage status. Compared with day workers, rotating-shift workers were significantly at risk for prostate cancer (relative risk = 3.0, 95% confidence interval: 1.2, 7.7), whereas fixed-night work was associated with a small and nonsignificant increase in risk. This report is the first known to reveal a significant relation between rotating-shift work and prostate cancer.

Keywords

Kuhn A, Krammer PH, Kolb-Bachofen V

Year 2006

Authors A. Kuhn, P. H. Krammer and V. Kolb-Bachofen

Report Name V. Pathophysiology of cutaneous lupus erythematosus--novel aspects. Rheumatology (Oxford).

Publication Rheumatology

Issue-page numbers (2006) 45 (suppl 3): iii14-iii16. doi: 10.1093/rheumatology/kel284

URL http://rheumatology.oxfordjournals.org/content/45/suppl_3/iii14.full

Abstract

The pathophysiology of cutaneous lupus erythematosus (CLE) has been investigated in numerous studies demonstrating that the combination of specific cellular and molecular events is leading to inflammation and tissue damage in this disease. However, a complete understanding of the diverse pathophysiological mechanisms and interactions does not exist. Various environmental factors influence the clinical expression of CLE and a striking relationship has emerged between sunlight exposure and the various subtypes of this disease. In the past years, photoprovocation tests with different ultraviolet (UV) wavelengths have been approved to be an optimal way to evaluate photosensitivity in patients with CLE. Furthermore, research on the pathogenetic mechanisms of UV-induced skin lesions has become an increasingly dynamic field and several new aspects of this disease could be identified. In this review, the impact of UV exposure that contributes to the manifestations of CLE is discussed and recently reported mechanisms in the pathophysiology of this disease are considered including the clearance of apoptotic cells, expression of inducible nitric oxide synthase, function of CD4+CD25+ regulatory T cells, and the role of chemokines for lymphocyte recruitment. Elucidation of the relevant factors might lead to future development of effective strategies to prevent abnormal reactivity in patients with CLE.

Cutaneous lupus erythematosus (CLE) is a disease with a wide spectrum of clinical manifestations with a variable evolution. Therefore, it has been difficult to develop a unifying concept of CLE and the similarities as well as the differences among the various subtypes have to be considered in discussing the pathophysiology of this disease. In 1977, a classification system has been established dividing the cutaneous manifestations into acute CLE (ACLE), subacute CLE (SCLE) and chronic CLE (CCLE). Recently, the intermittent subtype of CLE (ICLE) has been added to this classification system [1]; however, this classification system is not meant to rigidly define subtypes of this disease since overlapping features can occur. Furthermore, there are certain patterns of systemic disease activity that can also be seen in association with these subtypes resulting in limited patient quality of life and increased disability.

Keywords

Kütting B, Drexler H

Year 2010

Authors Birgitta Kütting, Hans Drexler

Report Name UV-induced skin cancer at workplace and evidence-based prevention

Publication nternational Archives of Occupational and Environmental Health

Issue-page numbers Volume: 83, Issue: 8, Pages: 843-854

URL http://www.mendeley.com/research/uvinduced-skin-cancer-workplace-evidencebased-prevention/

Abstract

The present review is aimed at providing an overview of skin cancer with particular focus on occupational concern and giving evidence-based recommendation for effective prevention at workplace.

Keywords

Year 2010

Authors Kvaskoff M, Weinstein P.

Report Name Are some melanomas caused by artificial light?

Publication Med Hypotheses

Issue-page numbers 2010 Sep;75(3):305-11. Epub 2010 Mar 29.

URL http://www.ncbi.nlm.nih.gov/pubmed/20347530

Abstract The incidence rate of cutaneous melanoma has been increasing faster than that of any other cancer in white-skinned populations over the past decades. The main risk factors for melanoma (i.e. exposure to sunlight, naevus count, phototype, and family history of melanoma) may not wholly explain the epidemiological trends observed for this cancer. The light-at-night theory postulates that increasing use of artificial light-at-night may contribute to the increasing breast cancer incidence through suppressed secretion of melatonin (a hormone produced in the dark and inhibited by light, which regulates circadian rhythms). Here, we postulate that this theory may also apply to melanoma and that it may explain a part of this cancer burden. Consistent with our hypothesis is evidence from experimental studies suggesting a lightening effect of melatonin on frog skin and mammal hair during seasonal changes, its antioxidant and anti-carcinogenic effects in skin melanocytes, as well as the expression of melatonin receptors in melanocytes. Also, epidemiological data suggest lower melatonin concentrations in melanoma patients compared with controls; a potential therapeutic effect of melatonin in patients with metastatic disease; a higher prevalence of melanoma in pilots and aircrews, with increased risks with higher time zones travelled; and increased melanoma risks in office workers exposed to fluorescent lighting. Moreover, melanoma incidence and seasonal patterns are consistent with a reduction of melatonin secretion with intensity of exposure to light, although it remains difficult to distinguish the effect of melatonin disruption from that of sun exposure on the basis of ecological studies. Finally, the reported associations between hormonal factors and melanoma are consistent with melatonin inhibition increasing the risk of melanoma by increasing circulating oestrogen levels. Despite the existing suggestive evidence, the light-at-night hypothesis has never been directly tested for melanoma. Very few studies examined the potential associations between melanoma risk and shift work or melatonin concentrations, and we found no studies reporting on the relationship between melanoma and number of sleeping hours, use of melatonin supplements, blindness, night-time city light levels, bedroom light levels, or clock genes polymorphisms. Therefore, since several observations support our hypothesis and very little research has been undertaken on this subject, we strongly encourage analytic epidemiological studies to test the light-at-night theory for melanoma causation.

Keywords

Kwon KJ, Kim JN, Kim MK, et al. **Year** 2011

Authors Kyoung Ja Kwon, Jung Nam Kim, Min Kyeong Kim, Jongmin Lee, Louis J. Ignarro, Hee-Jin Kim, Chan Young Shin, Seol-Heui Han

Report Name Melatonin synergistically increases resveratrol-induced heme oxygenase-1 expression through the inhibition of ubiquitin-dependent proteasome pathway: a possible role in neuro

Publication Journal of Pineal Research

Issue-page numbers Volume 50, Issue 2, pages 110–123, March 2011

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2010.00820.x/abstract?

Abstract Melatonin is an indoleamine secreted by the pineal gland as well as a plant-derived product, and resveratrol (RSV) is a naturally occurring polyphenol synthesized by a variety of plant species; both molecules act as a neuroprotector and antioxidant. Recent studies have demonstrated that RSV reduced the incidence of Alzheimer's disease and stroke, while melatonin supplementation was found to reduce the progression of the cognitive impairment in AD. The heme oxygenase-1 (HO-1) is an inducible and redox-regulated enzyme that provides tissue-specific antioxidant effects. We assessed whether the co-administration of melatonin and RSV shows synergistic effects in terms of their neuroprotective properties through HO-1. RSV significantly increased the expression levels of HO-1 protein in a concentration-dependent manner both in primary cortical neurons and in astrocytes, while melatonin per se did not. Melatonin + RSV showed a synergistic increase in the expression levels of HO-1 protein but not in the HO-1 mRNA level compared to either melatonin or RSV alone, which is mediated by the activation of PI3K-Akt pathway. Treatment of melatonin + RSV significantly attenuated the neurotoxicity induced by H2O2 in primary cortical neurons and also in organotypic hippocampal slice culture. The blockade of HO-1 induction by shRNA attenuated HO-1 induction by melatonin + RSV and hindered the neuroprotective effects against oxidative stress induced by H2O2. The treatment of MG132 + RSV mimicked the effects of melatonin + RSV, and melatonin + RSV inhibited ubiquitination of HO-1. These data suggest that melatonin potentiates the neuroprotective effect of RSV against oxidative injury, by enhancing HO-1 induction through inhibiting ubiquitination-dependent proteasome pathway, which may provide an effective means to treat neurodegenerative disorders.

Keywords heme oxygenase-1; melatonin; neuroprotection; resveratrol; ubiquitination

Laakso ML, Alila A, Hätönen T, Mustanoja SM **Year** 1996

Authors M L Laakso, A Alila, T Hätönen, S M Mustanoja

Report Name Ontogeny of pineal melatonin rhythm in rats under 12:12-hr and 14:14-hr light:dark conditions.

Publication Journal of Pineal Research

Issue-page numbers Volume: 21, Issue: 3, Pages: 155-164 PubMed: 8981260

URL http://www.mendeley.com/research/ontogeny-pineal-melatonin-rhythm-rats-under-1212hr-1414hr-lightdark-conditions/

Abstract The aim of the study was to determine whether a discrepancy between the genetically determined endogenous circadian period and an abnormally long Zeitgeber period disturbs the development of melatonin synthesis. Breeding pairs of rats were kept under 12:12- or 14:14-hr light:dark (LD) conditions. Pineal melatonin contents in the offspring were measured by radioimmunoassay. At 2 weeks of age high melatonin contents were found from lights-off to lights-on in both conditions suggesting dominance of the photic regulation. At 3 weeks of age the signs of the circadian regulation in the melatonin profiles were evident: a lag period after the light offset in control conditions and a significant decline before the light onset in both conditions. However, in 14:14-hr LD conditions the melatonin content did not decrease to daytime levels until the lights were on. This could suggest incomplete maturation of the circadian system. The phase relationships between the melatonin peak and LD cycle were different in the two conditions. A statistically significant LD difference was first found at the age of 8-10 days in male pups and at 14 days in female pups under both lighting. The results suggest that the abnormally long LD cycle did not cause any major disorders in the development of photic or circadian regulation of the melatonin synthesis.

Keywords

Laakso ML, Porkka-Heiskanen T, Alila A et al. ***Year*** 1990

Authors Laakso ML, Porkka-Heiskanen T, Alila A et al.

Report Name Correlation between salivary and serum melatonin: dependence on serum melatonin levels

Publication J Pineal Res

Issue-page numbers 9:39–50. PMID:2231272 doi:10.1111/j.1600-079X.1990.tb00692.x

URL http://www.ncbi.nlm.nih.gov/pubmed/2231272

Abstract Saliva and serum samples were collected from eight healthy volunteers every two hours during a 26-hour period. Melatonin concentrations were measured by radioimmunoassay after chloroform extraction using radioiodinated melatonin as a tracer. Five of the subjects had high serum melatonin levels at night (peak levels higher than 75 pg/ml); in three subjects the highest serum melatonin concentration was 20-40 pg/ml. All subjects had low levels (less than 10 pg/ml) during the day. The correlations between salivary and serum levels were calculated. The regression line y = 0.33x + 3.7 pg/ml, r = 0.95, P less than 0.001, was obtained for all detectable value pairs (n = 73). The regression and correlation coefficients were almost equal for the peak values of melatonin and during the rising and descending phases of the secretion patterns. However, no significant correlation was found between low daytime salivary and serum concentrations when calculated separately. In the five high-secretors the melatonin levels in saliva reflected reliably the changes in serum, but in the three low-secretors the correlation between salivary and serum melatonin was not significant. The proportion of melatonin found in saliva decreased with increasing serum melatonin levels. Circadian rhythm parameters were estimated by single cosinor analysis. The acrophases did not differ significantly within a subject in the concomitant measurements of serum and salivary melatonin. The measurements of salivary melatonin levels seem valid for studies on melatonin rhythms, but the melatonin concentrations measured in saliva do not always consistently reflect the absolute concentrations in blood.

Keywords

Lacassagne A, Chamorro A, Hurst L, Nguyen-Ba-Giao ***Year*** 1969

Authors Lacassagne A, Chamorro A, Hurst L, Nguyen-Ba-Giao

Report Name [Effect of epiphysectomy on chemical hepatocancerogenesis in rats]

Publication C R Acad Sci Hebd Seances Acad Sci D

Issue-page numbers 269:1043–1046.PMID:4981428

URL http://www.biomedsearch.com/nih/Effect-epiphysectomy-chemical-hepatocancerogenesis-in/4981428.html

Abstract N/A

Keywords

Lahti T, Merikanto I, Partonen T

Year 2012

Authors Tuuli Lahti, Ilona Merikanto, Timo Partonen

Report Name Circadian clock disruptions and the risk of cancer

Publication Annals of Medicine

Issue-page numbers December 2012, Vol. 44, No. 8 , Pages 847-853 (doi:10.3109/07853890.2012.727018)

URL http://informahealthcare.com/doi/abs/10.3109/07853890.2012.727018

Abstract Disrupted circadian rhythms may lead to failures in the control of the cell division cycle and the subsequent malignant cell growth. In order to understand the pathogenesis of cancer more in detail, it is crucial to identify those mechanisms of action which contribute to the loss of control of the cell division cycle. This mini-review focuses on the recent findings concerning the links between the human circadian clock and cancer. Clinical implications concern not only feasible methods for the assessment of the circadian time of an individual or for the determination of the best time for administration of a drug of treatment, but also in the future genetic tests for screening and for planning treatment.

Keywords Carcinogen, diurnal, epidemiology, exposure assessment, gene variant, occupational

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Lahti TA, Partonen T, Kyyr€onen P, et al.

Year 2008

Authors Tuuli A. Lahti, Timo Partonen, Pentti Kyyr€onen, Timo Kauppinen and Eero Pukkala

Report Name Night-time work predisposes to non-Hodgkin lymphoma

Publication Int. J. Cancer

Issue-page numbers 123, 2148-2151 (2008)

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.23566/pdf

Abstract Our aim was to find out whether non-Hodgkin lymphoma (NHL) was more common than expected among night-time shift workers. The Finnish job-exposure matrix (FINJEM) provided estimates of
the proportion of exposed persons and the mean level of exposure among the exposed in each occupation. The probability of nighttime work in each occupation was assessed, the observed and expected numbers of cancer cases in a cohort of persons born in 1906–1945 during the years of 1971–1995 were calculated, and the cumulative index of night time work was scored. The cohort compromised of 1,669,272 persons of whom 6,307 (3,813 men and 2,494 women) had NHL during the follow-up. Night-time work increased significantly (p 5 0.01) the risk of NHL in men, the overall relative risk being 1.10 (95% confidence interval of 1.03–1.19). Using the lag period of 10 years, the risk ratio was 1.28 (1.03–1.59) for men who worked in night-time shifts to a high degree as compared with those who had not been exposed to night-time work.
Night-time workers are cancer prone and have a greater risk of NHL than population on average.

Keywords circadian clock; night-time shift work; non-Hodgkin lymphoma

Lakatua DJ, Haus E, Swoyer JK et al. ***Year*** 1975

Authors Lakatua DJ, Haus E, Swoyer JK et al.

Report Name Meal timing shifts circadian rhythms in serum iron and insulin but not in plasma cortisol in human volunteers

Publication Chronobiologia

Issue-page numbers 2 Suppl 1;39–40.

URL N/A

Abstract N/A

Keywords

Lakatua DJ, Haus M, Berge C et al. ***Year*** 1988

Authors Lakatua DJ, Haus M, Berge C et al.

Report Name Diet and mealtiming as circadian synchronizers

Publication Annu Rev Chronopharm

Issue-page numbers 5:303–306

URL N/A

Abstract N/A

Keywords

Lakatua DJ, White M, Sackett-Lundeen LL, Haus E **Year** 1983

Authors Lakatua DJ, White M, Sackett-Lundeen LL, Haus E

Report Name Change in phase relations of circadian rhythms in cell proliferation induced by time-limited feeding in BALB/c X DBA/2F1 mice bearing a transplantable Harding-Passey tumor

Publication Cancer Res

Issue-page numbers 43:4068–4072. PMID:6871848

URL http://www.ncbi.nlm.nih.gov/pubmed/6871848

Abstract The synchronization of the circadian rhythms of [3H]thymidine uptake (as gauge of DNA synthesis and presumably of cell proliferation) in colon, thymus, and Harding-Passey melanoma were studied in 456 male BALB/c X DBA/2F1 mice under a 12-hr-light, 12-hr-dark regimen. In two groups of animals, the feeding time was restricted to 4 hr/day (either at the beginning of the light span or at the beginning of the dark span). The circadian rhythms in body temperature and [3H]thymidine uptake in the colon were determined in their timing primarily by the time of food intake. In contrast, the circadian rhythm of [3H]thymidine uptake in the thymus and in the transplanted melanoma remained synchronized with the lighting regimen, and under the conditions of this study, was not altered in its timing by the change in feeding time. It thus appears feasible to alter the phase relations between certain circadian rhythms of host and tumor. If applicable to the human situation, this observation might be of interest for the scheduling of chemo- and radiotherapy, in an attempt to obtain maximal effects upon the tumor with minimal undesired side effects upon vital functions of the host.

Keywords

Lall GS, Revell VL, Momiji H, et al. ***Year*** 2010

Authors Gurprit S. Lall, Victoria L. Revell, Hiroshi Momiji, Jazi Al Enezi, Cara M. Altimus, Ali D. Güler, Carlos Aguilar, Morven A. Cameron, Susan Allender, Mark W. Hankins, Robert J. Li

Report Name Distinct Contributions of Rod, Cone, and Melanopsin Photoreceptors to Encoding Irradiance

Publication Neuron

Issue-page numbers Volume 66, Issue 3, 417-428, 13 May 2010

URL http://www.cell.com/neuron/abstract/S0896-6273%2810%2900330-2

Abstract

* Highlights
* Red cone knockin (Opn1mwR) mice reveal rod, cone, and melanopsin phases to NIF vision
* Rods drive circadian responses to very low irradiances (scotopic threshold)
* Circadian responses to light in the photopic range can be rod driven
* Light adaptation limits the influence of cones on NIF vision

Summary

Photoreceptive, melanopsin-expressing retinal ganglion cells (mRGCs) encode ambient light (irradiance) for the circadian clock, the pupillomotor system, and other influential behavioral/physiological responses. mRGCs are activated both by their intrinsic phototransduction cascade and by the rods and cones. However, the individual contribution of each photoreceptor class to irradiance responses remains unclear. We address this deficit using mice expressing human red cone opsin, in which rod-, cone-, and melanopsin-dependent responses can be identified by their distinct spectral sensitivity. Our data reveal an unexpectedly important role for rods. These photoreceptors define circadian responses at very dim “scotopic” light levels but also at irradiances at which pattern vision relies heavily on cones. By contrast, cone input to irradiance responses dissipates following light adaptation to the extent that these receptors make a very limited contribution to circadian and pupillary light responses under these conditions. Our data provide new insight into retinal circuitry upstream of mRGCs and optimal stimuli for eliciting irradiance responses.

Keywords

Lang D

Year 2012

Authors Dieter Lang

Report Name Blue enhanced light sources: opportunities and risks

Publication Proc. SPIE

Issue-page numbers 8278, 827803 (2012); doi:10.1117/12.906170

URL http://spiedigitallibrary.org/proceedings/resource/2/psisdg/8278/1/827803_1?isAuthorized=no

Abstract

Natural daylight is characterized by high proportions of blue light. By proof of a third type of photoreceptor in the human eye which is only sensitive in this spectral region and by subsequent studies it has become obvious that these blue proportions are essential for human health and well being. In various studies beneficial effects of indoor lighting with higher blue spectral proportions have been proven. On the other hand with increasing use of light sources having enhanced blue light for indoor illumination questions are arising about potential health risks attributed to blue light. Especially LED are showing distinct emission characteristics in the blue. Recently the French agency for food, environmental and occupational health & safety ANSES have raised the question on health issues related to LED light sources and have claimed to avoid use of LED for lighting in schools. In this paper parameters which are relevant for potential health risks will be shown and their contribution to risk factors will quantitatively be discussed. It will be shown how to differentiate between photometric parameters for assessment of beneficial as well as hazardous effects. Guidelines will be discussed how blue enhanced light sources can be used in applications to optimally support human health and well being and simultaneously avoid any risks attributed to blue light by a proper design of lighting parameters. In the conclusion it will be shown that no inherent health risks are related to LED lighting with a proper lighting design.

Keywords

Authors Lange T, Dimitrov S, Fehm H-L et al.

Report Name Shift of monocyte function toward cellular immunity during sleep

Publication Arch Intern Med

Issue-page numbers 166:1695–1700 doi:10.1001/archinte.166.16.1695. PMID:16983046

URL http://archinte.ama-assn.org/cgi/reprint/166/16/1695.pdf

Abstract

Background: Sleep is considered to strengthen immune defense. We hypothesized that sleep achieves this effect by shifting the balance between types 1 and 2 cytokine activity toward increased type 1 activity, thereby supporting adaptive cellular immune responses.

Methods: We analyzed monocyte-derived type 1 (interleukin 12 [IL-12]) and type 2 (IL-10) cytokines by means of multiparametric flow cytometry in healthy human subjects (n=11) during a regular sleep-wake cycle and 24 hours of wakefulness.

Results: Sleep increased the number of IL-12– producing monocytes and concurrently decreased the number of IL-10–producing monocytes, thereby inducing clear rhythms in these cells, with maximum numbers at 2:20 and 11:30 AM, respectively. The rhythms were completely absent during continuous wakefulness. Correlation analyses and supplementary in vitro studies suggest that high prolactin and low cortisol levels are factors contributing to the shift in the IL-12/IL-10 ratio toward increased IL-12 activity during sleep.

Conclusions: Monocyte-derived IL-12 and IL-10 play a critical role for tuning the synapse between antigenpresenting cells and lymphocytes. By preferentially supporting type 1 IL 12 activity, sleep induces a 24-hour oscillation between predominant types 1 and 2 cytokines and, in this way, acts to globally increase the efficacy of adaptive immune responses. Improving sleep could represent a therapeutic option to enhance the success of vaccinations and success in the treatment of diseases (eg, atopic dermatitis and human immunodeficiency virus infection) that are characterized by type 2 cytokine overactivity.

Keywords

Langley AR, Graham CH, Grundy AL, et al. **Year** 2012

Authors Annie R Langley, Charles H Graham, Anne L Grundy, Joan E Tranmer, Harriet Richardson, Kristan J Aronson

Report Name A cross-sectional study of breast cancer biomarkers among shift working nurses

Publication BMJ Open

Issue-page numbers 2012;2:e000532 doi:10.1136/bmjopen-2011-000532

URL http://bmjopen.bmj.com/content/2/1/e000532.full

Abstract

Objectives In 2007, the International Agency for Research on Cancer classified long-term shift work as a probable carcinogen, with the strongest evidence for breast cancer. One proposed mechanism involves night-time light exposure and decreases in melatonin, a circadian rhythmic hormone. It is hypothesised that melatonin influences patterns of sex hormone production that in turn influence breast cancer risk. This study sought to investigate the relationships of shift work history, 6-sulfatoxymelatonin (aMTs-6, the primary melatonin metabolite) and sex hormone levels among shift working nurses.

Design This is a cross-sectional biomarker study.

Setting 94 premenopausal nurses who work a full-time rotating shift schedule at one Ontario hospital were recruited for this study; 82 completed follow-up.

Primary and secondary outcome measures Study participants provided morning void urine and fasting blood samples for the assessment of aMTs-6 and sex hormone (oestradiol, oestrone, progesterone, prolactin) levels, respectively. These data were collected at two time points (summer and winter) such that relationships between melatonin and sex hormones could be assessed with respect to two time frames of interest (acute and cross-seasonal).

Results An inverse relationship between aMTs-6 and oestradiol was suggested in the winter ($\beta=-0.18$, $p=0.04$), but this result was not statistically significant in multivariate modelling that adjusted for age, body mass index and menstrual cycle. Likewise, while oestradiol, oestrone and progesterone levels increased with greater years of shift work history (all $p<0.05$), these associations were attenuated after confounder adjustment.

Conclusions These results do not support the proposed relationship between melatonin and sex hormone levels as biomarkers on the pathway of shift work and breast cancer but emphasise the importance of adjusting for confounders in modelling.

Keywords

Lapin V **Year** 1978

Authors Lapin V

Report Name Effects of reserpine on the incidence of 9,10-dimethyl-1,2-benzanthracene-induced tumors in pinealectomised and thymectomised rats

Publication Oncology

Issue-page numbers 35:132–135 doi:10.1159/000225271. PMID:97606

URL http://www.mendeley.com/research/effects-of-reserpine-on-the-incidence-of-910dimethyl12benzanthraceneinduced-tumors-in-pinealectomised-and-thymectomised-rats/

Abstract After reserpine treatment the incidence of dimethyl-benzathrance-induced tumors was found to be significantly higher in pinealectomised rats than in intact or thymectomised ones. A very high rate of DMBA-leukemia was observed in immune deficient pinealectomised rats after reserpine administration. It is therefore suggested that the neuro-endocrine disturbances, due to removal of the pineal gland in the new-born animals, are latent and become evident after reserpine administration, as reflected in an increased tumor incidence.

Keywords

Lapin V **Year** 1974

Authors Lapin V

Report Name Influence of simultaneous pinealectomy and thymectomy on the growth and formation of metastases of the Yoshida sarcoma in rats

Publication Exp Pathol (Jena)

Issue-page numbers 9:108–112. PMID:4452369

URL http://www.ncbi.nlm.nih.gov/pubmed/4452369

Abstract N/A

Keywords

Authors Laughlin GA, Loucks AB, Yen SS

Report Name Marked augmentation of nocturnal melatonin secretion in amenorrheic athletes, but not in cycling athletes: unaltered by opioidergic or dopaminergic blockade

Publication J Clin Endocrinol Metab

Issue-page numbers 73:1321–1326 doi:10.1210/jcem-73-6-1321. PMID:1955514

URL http://jcem.endojournals.org/content/73/6/1321.abstract

Abstract

Exercise of sufficient intensity during daylight hours has been demonstrated to result in an acute elevation of circulating melatonin levels. The possibility that repeated elevations of daytime melatonin secretion may result in alterations of the nocturnal maxima of the circadian rhythm in highly trained athletic women with and without amenorrhea was investigated. Twenty-four-hour melatonin profiles in matched cyclic sedentary (CS; n = 10) women, cyclic athletic (CA; n = 10) women, and amenorrheic athletic (AA; n = 8) women were compared. The roles of endogenous opioids and dopamine as potential modulators of melatonin secretion were also evaluated by comparing the melatonin profiles during sequential 24-h infusions of saline, followed by either naloxone or metoclopramide (both at30/μg/kg–h).

Elevated (P < 0.05) mean daytime (1000–1700 h) melatonin levels were observed in both groups of athletic women compared to sedentary women. In contrast, nocturnal melatonin levels in sedentary and athletic cycling women were indistinguishable, while amenorrheic athletic women displayed a marked increase in nocturnal peak amplitude (P < 0.001 vs. CS and CA) and a 2-h delay in offset (P < 0.001 vs. CS and CA), which yielded a 2–fold amplification of the integrated nocturnal melatonin secretion (P < 0.001 vs. CS and CA). The onset of the nocturnal rise did not differ among the three groups. Opioidergic and dopaminergic blockade with naloxone and metoclopramide at the doses used did not alter any parameter of melatonin secretion in any of the three groups of women.

In conclusion, athleticism in women is associated with an elevation of daytime melatonin levels independent of menstrual status. AA women, but not CA women, display a 2-fold amplification of nocturnal melatonin secretion with a 2-h delay of offset, which does not seem to be linked to athleticism per se. The significance and neuroendocrine basis for the expanded melatonin secretion in athletic amenorrheic women remains to be elucidated.

Keywords

Lavalle C, Loyo E, Paniagua R et al. **Year** 1987

Authors Lavalle C, Loyo E, Paniagua R et al.

Report Name Correlation study between prolactin and androgens in male patients with systemic lupus erythematosus

Publication J Rheumatol

Issue-page numbers 14:268–272. PMID:3298648

URL http://www.ncbi.nlm.nih.gov/pubmed/3298648

Abstract The hypothalamic-pituitary-gonadal axis was studied in 8 male patients with systemic lupus erythematosus (SLE), both before and after intravenous administration of luteinizing hormone-releasing hormone (LH-RH). We provide evidence herein that resting serum levels of estrone are increased and that resting serum testosterone (T) and dihydrotestosterone (DHT) levels are decreased in male patients with SLE. The decreased serum T levels were observed even after the IV administration of 25 micrograms of LH-RH. The high basal serum prolactin (PRL) levels observed in these patients with SLE is a novel finding not previously reported that could explain why serum T and DHT levels are low in this syndrome. We observed a decrease in the pituitary response to LH-RH stimulation; this low response could also be a hormonal manifestation of hyperprolactinemia. Furthermore, it has been suggested that PRL plays a role in immunocompetence, and therefore it could have influence either directly or indirectly in the altered immunoregulation observed in SLE.

Keywords

Lavie P, Weler B **Year** 1989

Authors Lavie P, Weler B

Report Name Timing of naps: effects of post-nap sleepiness levels

Publication Electroencephalogr Clin Neurophysiol

Issue-page numbers 72:218–224 doi:10.1016/0013-4694(89)90246-0. PMID: 2465124

URL http://www.sciencedirect.com/science/article/pii/0013469489902460

Abstract The present study investigated the effects of timing of naps on nap content and sleep inertia, and the relationship between pre- and post-nap sleepiness level and nap content. Nine subjects were tested twice on the 13 min waking-7 min resisting sleep paradigm after one night of total sleep deprivation for 24 h. The ultrashort sleep-wake paradigms started at 07.00 h and were interrupted at 15.00 and 19.00 h for 2 naps. The 2 experimental conditions were counterbalanced across subjects and separated by a 7 day rest period.

The results showed that the early nap was significantly more efficient, contained more stage 3/4, and produced less sleep inertia than the late nap. The late nap was more efficient in reducing sleepiness during the last 5 h of the experiments (23.00–04.00). Only the early nap was significantly related to pre- and post-nap sleepiness levels. Overall sleepiness level and the timing of the nocturnal sleepiness gates were significantly correlated between the two parts of the study.

The results were interpreted to support the priority of the ultradian phase on prior wakefulness with respect to sleep structure.

Keywords Timing of naps; Post-nap sleepiness; Sleep levels; Nap content

Lawson NO, Wee BE, Blask DE et al. *Year* 1992

Authors Lawson NO, Wee BE, Blask DE et al.

Report Name Melatonin decreases estrogen receptor expression in the medial preoptic area of inbred (LSH/SsLak) golden hamsters

Publication Biol Reprod

Issue-page numbers 47:1082–1090 doi:10.1095/biolreprod47.6.1082. PMID:1493172

URL http://www.biolreprod.org/content/47/6/1082.full.pdf

Abstract Daily late afternoon injections of melatonin (25 pg/day s.c.) were found to reduce the number of cells expressing estrogen receptor immunoreactivity in the medial preoptic area of ovariectomized inbred (LSH/SsLak) golden hamsters. Employing immunocytochemical analysis with the H222 monoclonal antibody to the human estrogen receptor, we examined the effects of melatonin on estrogen receptor expression in the hypothalamus, particularly the medial preoptic area, of ovariectomized virgin female hamsters. Analysis of the results showed that melatonin administration induced a 50-70% decrease in numbers of estrogen receptor-immunoreactive neurons in the medial preoptic area of ovariectomized female hamsters. Furthermore, an overall qualitative decrease in the intensity of estrogen receptor immunoreactivity was observed. In intact regularly cycling female hamsters used to monitor the efficacy of melatonin treatment, there were significant reductions in the serum levels of FSH, LH, and prolactin as measured by radioimmunoassay and in uterine and pituitary weights after 8 wk of melatonin treatment. These results suggest that melatonin may exert its anti-reproductive effects in hamsters by modulating estrogen receptor levels in medial preoptic area neurons, thus influencing steroid feedback mechanisms.

Keywords

Le Minh N, Damiola F, Tronche F et al. *Year* 2001

Authors Le Minh N, Damiola F, Tronche F et al.

Report Name Glucocorticoid hormones inhibit food-induced phase-shifting of peripheral circadian oscillators

Publication EMBO J

Issue-page numbers 20:7128–7136 doi:10.1093/emboj/20.24.7128. PMID:11742989

URL http://www.nature.com/emboj/journal/v20/n24/full/7594200a.html

Abstract The circadian timing system in mammals is composed of a master pacemaker in the suprachiasmatic nucleus (SCN) of the hypothalamus and slave clocks in most peripheral cell types. The phase of peripheral clocks can be completely uncoupled from the SCN pacemaker by restricted feeding. Thus, feeding time, while not affecting the phase of the SCN pacemaker, is a dominant Zeitgeber for peripheral circadian oscillators. Here we show that the phase resetting in peripheral clocks of nocturnal mice is slow when feeding time is changed from night to day and rapid when switched back from day to night. Unexpectedly, the inertia in daytime feeding-induced phase resetting of circadian gene expression in liver and kidney is not an intrinsic property of peripheral oscillators, but is caused by glucocorticoid signaling. Thus, glucocorticoid hormones inhibit the uncoupling of peripheral and central circadian oscillators by altered feeding time.

Keywords adrenalectomy, circadian gene expression, clock, corticosterone, GR knockout

Authors Leake RD, Waters CB, Rubin RT et al.

Report Name Oxytocin and prolactin responses in long-term breastfeeding

Publication Obstet Gynecol

Issue-page numbers 62:565–568. PMID:6684741

URL http://www.hopkinsguides.com/hopkins/ub/citation/6684741/Oxytocin_and_prolactin_responses_in_long_term_breast_feeding_

Abstract Plasma levels of oxytocin and prolactin were measured before and during 12 minutes of breast pump stimulation in five healthy, lactating, amenorrheic women on three occasions: ten to 90 days post partum, 90 to 180 days post partum, and 180 days to one year post partum. Baseline mean (+/- SEM) plasma oxytocin levels were similar in the three study periods. Mean stimulated plasma oxytocin levels increased in the three study periods (each P less than .001; mean baseline versus stimulated). Stimulated plasma oxytocin values were significantly greater at ten to 90 than at 90 to 180 days (P less than .05; analysis of variance). Baseline serum prolactin levels were 61 +/- 9.5, 36 +/- 8.6, and 33 +/- 10.8 ng/ml, respectively (not significant; one-way analysis of variance). Mean stimulated prolactin levels were 71 +/- 8.1, 43 +/- 4.5, and 43 +/- 2.8 ng/ml, respectively (not significant). Thus, the oxytocin secretory reflex continues in long-term lactation for the first year post partum. In addition, breast stimulation in long-term lactating women continues to produce a slight increase in serum prolactin levels.

Keywords

Lee C, Smith MR, Eastman CI

Year 2006

Authors Clara Lee, Mark R. Smith and Charmane I. Eastman

Report Name A Compromise Phase Position for Permanent Night Shift Workers: Circadian Phase after Two Night Shifts with Scheduled Sleep and Light/Dark Exposure

Publication Chronobiology International

Issue-page numbers 23:4, 859-875

URL http://informahealthcare.com/doi/abs/10.1080/07420520600827160

Abstract

Night shift work is associated with a myriad of health and safety risks. Phase-shifting the circadian clock such that it is more aligned with night work and day sleep is one way to attenuate these risks. However, workers will not be satisfied with complete adaptation to night work if it leaves them misaligned during days off. Therefore, the goal of this set of studies is to produce a compromise phase position in which individuals working night shifts delay their circadian clocks to a position that is more compatible with nighttime work and daytime sleep yet is not incompatible with late nighttime sleep on days off. This is the first in the set of studies describing the magnitude of circadian phase delays that occurs on progressively later days within a series of night shifts interspersed with days off. The series will be ended on various days in order to take a “snapshot” of circadian phase. In this set of studies, subjects sleep from 23:00 to 7:00 h for three weeks. Following this baseline period, there is a series of night shifts (23:00 to 07:00 h) and days off. Experimental subjects receive five 15 min intermittent bright light pulses (3500 lux; 1100 μW/cm2) once per hour during the night shifts, wear sunglasses that attenuate all visible wavelengths—especially short wavelengths (“blue-blockers”)—while traveling home after the shifts, and sleep in the dark (08:30–15:30 h) after each night shift. Control subjects remain in typical dim room light (<50 lux) throughout the night shift, wear sunglasses that do not attenuate as much light, and sleep whenever they want after the night shifts. Circadian phase is determined from the circadian rhythm of melatonin collected during a dim light phase assessment at the beginning and end of each study. The sleepiest time of day, approximated by the body temperature minimum (Tmin), is estimated by adding 7 h to the dim light melatonin onset. In this first study, circadian phase was measured after two night shifts and day sleep periods. The Tmin of the experimental subjects (n=11) was 04:24±0.8 h (mean±SD) at baseline and 7:36±1.4 h after the night shifts. Thus, after two night shifts, the Tmin had not yet delayed into the daytime sleep period, which began at 08:30 h. The Tmin of the control subjects (n=12) was 04:00±1.2 h at baseline and drifted to 4:36±1.4 h after the night shifts. Thus, two night shifts with a practical pattern of intermittent bright light, the wearing of sunglasses on the way home from night shifts, and a regular sleep period early in the daytime, phase delayed the circadian clock toward the desired compromise phase position for permanent night shift workers. Additional night shifts with bright light pulses and daytime sleep in the dark are expected to displace the sleepiest time of day into the daytime sleep period, improving both nighttime alertness and daytime sleep but not precluding adequate sleep on days off.

Keywords Night shift work, Light, Sleep, Human, Circadian rhythms, Melatonin

Lee CC **Year** 2005

Authors Lee CC

Report Name The circadian clock and tumor suppression by mammalian period genes

Publication Methods Enzymol

Issue-page numbers 393:852–861 doi:10.1016/S0076-6879(05)93045-0. PMID:15817328

URL http://www.sciencedirect.com/science/article/pii/S0076687905930450

Abstract Period (Per) genes are key circadian rhythm regulators in mammals. Expression of mouse Per (mPer) genes has a diurnal pattern in the suprachiasmatic nucleus and in peripheral tissues. Genetic ablation mPER1 and mPER2 function results in a complete loss of circadian rhythm control based on wheel-running activity in mice. In addition, these animals also display apparent premature aging and a significant increase in neoplastic and hyperplastic phenotypes. When challenged by γ radiation, mPer2-deficient mice respond by rapid hair graying, are deficient in p53-mediated apoptosis in thymocytes, and have robust tumor occurrences. Studies have demonstrated that the circadian clock function is very important for cell cycle, DNA damage response, and tumor suppression in vivo. The temporal expression of genes involved in cell cycle regulation and tumor suppression, such as c-Myc, Cyclin D1, Cyclin A, Mdm-2, and Gadd45α, is deregulated in mPer2 mutant mice. Genetic studies have demonstrated that many key regulators of cell cycle and growth control are also important circadian clock regulators, confirming the critical role of circadian function in organismal homeostasis.

Keywords

Lee E, Salic A, Kirschner MW **Year** 2001

Authors Lee E, Salic A, Kirschner MW

Report Name Physiological regulation of [beta]-catenin stability by Tcf3 and CK1epsilon

Publication J Cell Biol

Issue-page numbers 154:983–993 doi:10.1083/jcb.200102074. PMID:11524435

URL http://www.mendeley.com/research/physiological-regulation-betacatenin-stability-tcf3-ck1epsilon-1/

Abstract The wnt pathway regulates the steady state level of -catenin, a transcriptional coactivator for the Tcf3/Lef1 family of DNA binding proteins. We demonstrate that Tcf3 can inhibit -catenin turnover via its competition with axin and adenomatous polyposis for -catenin binding. A mutant of -catenin that cannot bind Tcf3 is degraded faster than the wild-type protein in Xenopus embryos and extracts. A fragment of -catenin and a peptide encoding the NH2 terminus of Tcf4 that block the interaction between -catenin and Tcf3 stimulate -catenin degradation, indicating this interaction normally plays an important role in regulating -catenin turnover. Tcf3 is a substrate for both glycogen synthase kinase (GSK) 3 and casein kinase (CK) 1 , and phosphorylation of Tcf3 by CKI stimulates its binding to -catenin, an effect reversed by GSK3. Tcf3 synergizes with CK1 to inhibit -catenin degradation, whereas CKI-7, an inhibitor of CK1 , reduces the inhibitory effect of Tcf3. Finally, we provide evidence that CK1 stimulates the binding of dishevelled (dsh) to GSk3 binding protein (GBP) in extracts. Along with evidence that a significant amount of Tcf protein is nonnuclear, these findings suggest that CK1 can modulate wnt signaling in vivo by regulating both the -catenin-Tcf3 and the GBP-dsh interfaces.

Keywords

Authors Susie Lee, Lawrence A. Donehower, Alan J. Herron, David D. Moore, and Loning Fu

Report Name Disrupting Circadian Homeostasis of Sympathetic Signaling Promotes Tumor Development in Mice

Publication PloS One

Issue-page numbers 5:e10995. doi: 10.1371/journal.pone.0010995

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2881876/

Abstract

Background
Cell proliferation in all rapidly renewing mammalian tissues follows a circadian rhythm that is often disrupted in advanced-stage tumors. Epidemiologic studies have revealed a clear link between disruption of circadian rhythms and cancer development in humans. Mice lacking the circadian genes Period1 and 2 (Per) or Cryptochrome1 and 2 (Cry) are deficient in cell cycle regulation and Per2 mutant mice are cancer-prone. However, it remains unclear how circadian rhythm in cell proliferation is generated in vivo and why disruption of circadian rhythm may lead to tumorigenesis.
Methodology/Principal Findings
Mice lacking Per1 and 2, Cry1 and 2, or one copy of Bmal1, all show increased spontaneous and radiation-induced tumor development. The neoplastic growth of Per-mutant somatic cells is not controlled cell-autonomously but is dependent upon extracellular mitogenic signals. Among the circadian output pathways, the rhythmic sympathetic signaling plays a key role in the central-peripheral timing mechanism that simultaneously activates the cell cycle clock via AP1-controlled Myc induction and p53 via peripheral clock-controlled ATM activation. Jet-lag promptly desynchronizes the central clock-SNS-peripheral clock axis, abolishes the peripheral clock-dependent ATM activation, and activates myc oncogenic potential, leading to tumor development in the same organ systems in wild-type and circadian gene-mutant mice.
Conclusions/Significance
Tumor suppression in vivo is a clock-controlled physiological function. The central circadian clock paces extracellular mitogenic signals that drive peripheral clock-controlled expression of key cell cycle and tumor suppressor genes to generate a circadian rhythm in cell proliferation. Frequent disruption of circadian rhythm is an important tumor promoting factor.

Keywords

Authors Lee SE, Kim SJ, Youn JP, Hwang SY, Park CS, Park YS.

Report Name MicroRNA and gene expression analysis of melatonin-exposed human breast cancer cell lines indicating involvement of the anticancer effect

Publication J Pineal Res

Issue-page numbers Oct;51(3):345-52. doi: 10.1111/j.1600-079X.2011.00896.x. Epub 2011 May 26.

URL http://www.ncbi.nlm.nih.gov/pubmed/21615491

Abstract MicroRNAs (miRNAs) are small, noncoding RNAs that play a crucial role in regulation of gene expression. Recent studies have shown that miRNAs implicated in initiation and progression of various human cancers, including breast cancer and also analysis of miRNA expression profiles in cancer provide new insights into potential mechanisms of carcinogenesis. Melatonin, N-acetyl-5-methoxytryptamine, is synthesized by the pineal gland in response to the dark/light cycle and has been known to act as a synchronizer of the biological clock. Melatonin has a variety of therapeutic effects, such as immunomodulatory actions, anti-inflammatory effects, and antioxidant actions. Furthermore, melatonin is reported to have an anticancer function including suppression of the metabolism of tumor cells and induction of tumor suppressor genes in cancer cells, including breast cancer cells. In this study, we determined whether miRNAs play a role in regulation of various gene expression responses to melatonin in MCF-7 human breast cancer cells. We examined whole-genome miRNA and mRNA expression and found that 22 miRNAs were differentially expressed in melatonin-treated MCF-7 cells. We further identified a number of mRNAs whose expression level shows a high inverse correlation with miRNA expression. The Gene Ontology (GO) enrichment analysis and pathways analysis were performed for identification of the signaling pathways and biological processes affected by differential expression of miRNA and miRNA-related genes. Our findings suggested that melatonin may modulate miRNA and gene expression as an anticancer mechanism in human breast cancer cells.

Keywords

Legan SJ, Donoghue KM, Franklin KM, Duncan MJ **Year** 2009

Authors Sandra J. Legan,1 Kathleen M. Donoghue,2 Kathleen M. Franklin,2 and Marilyn J. Duncan

Report Name Phenobarbital blockade of the preovulatory luteinizing hormone surge: association with phase-advanced circadian clock and altered suprachiasmatic nucleus Period1 gene expre

Publication Am J Physiol Regul Integr Comp Physiol

Issue-page numbers May; 296(5): R1620–R1630.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2689824/

Abstract The suprachiasmatic nucleus (SCN) controls the timing of the preovulatory luteinizing hormone (LH) surge in laboratory rodents. Barbiturate administration during a critical period on proestrus delays the surge and prolongs the estrous cycle 1 day. Because a nonphotic timing signal (zeitgeber) during the critical period that phase advances activity rhythms can also induce the latter effect, we hypothesized that barbiturates delay the LH surge by phase-advancing its circadian timing signal beyond the critical period. In experiment 1, locomotor rhythms and estrous cycles were monitored in hamsters for 2–3 wk preinjection and postinjection of vehicle or phenobarbital and after transfer to darkness at zeitgeber time (ZT) 6 on proestrus. Phenobarbital delayed estrous cycles in five of seven hamsters, which exhibited phase shifts that averaged twofold greater than those exhibited by vehicle controls or phenobarbital-injected hamsters with normal cycles. Experiment 2 used a similar protocol, but injections were at ZT 5, and blood samples for LH determination were collected from 1200 to 1800 on proestrus and the next day via jugular cannulae inserted the day before proestrus. Phenobarbital delayed the LH surge 1 day in all six hamsters, but it occurred at an earlier circadian time, supporting the above hypothesis. Experiment 3 investigated whether phenobarbital, like other nonphotic zeitgebers, suppresses SCN Period1 and Period2 transcription. Two hours postinjection, phenobarbital decreased SCN expression of only Period1 mRNA, as determined by in situ hybridization. These results suggest that phenobarbital advances the SCN pacemaker, governing activity rhythms and hormone release in part by decreasing its Period1 gene expression.

Keywords critical period, activity rhythm, estrous cycle, barbiturate, Per1, Per2

Authors Lennernäs M, Akerstedt T, Hambraeus L

Report Name Nocturnal eating and serum cholesterol of threeshift workers

Publication Scand J Work Environ Health

Issue-page numbers 20:401–406. PMID:7701285

URL http://www.sjweh.fi/download.php?abstract_id=1381&file_nro=1

Abstract

OBJECTIVES:

The goal of this study was to examine the effect of rotating three-shift work on the circadian distribution of dietary intake and to investigate the relationships between displaced eating and nutritional status variables [blood lipids, blood glucose, body mass index (BMI)].
METHODS:

Dietary data were collected by 147 replicate 24-h dietary recalls from 22 male industrial workers in rotating three-shift work. The intakes of energy and nutrients were estimated by the use of a nutrient data base. The BMI was calculated, and blood glucose, serum triglycerides, high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol were measured once.
RESULTS:

The dietary intakes of energy, protein, total fat, saturated fat, total carbohydrates, sucrose, and dietary fiber did not differ between 24-h periods but did differ between work shifts and were lowest during the night. Correlation analyses between dietary intakes and nutritional status parameters showed that those who redistributed their eating most to the night shift had higher levels of serum total cholesterol and LDL and a higher LDL:HDL ratio; 63% of the LDL cholesterol level was explained by carbohydrate intake during night shifts. In contrast, the total intake for whole 24-h periods or across entire shift cycles was not related to serum variables or BMI.
CONCLUSIONS:

Dietary intake is lower during night shifts (34-37% of 24-h intake of various nutrients) than during morning shifts (43-47%) and afternoon shifts (47-59%). The redistribution of food intake to the night may be associated with metabolic disturbances in lipid metabolism.

Keywords

Lennernäs MA, Hambraeus L, Akerstedt T *Year* 1993

Authors Lennernäs MA, Hambraeus L, Akerstedt T

Report Name Nutrition and shiftwork: the use of meal classification as a new tool for qualitative/quantitative evaluation of dietary intake in shiftworkers

Publication Ergonomics

Issue-page numbers 36:247–254 doi:10.1080/00140139308967879. PMID:8440220

URL http://www.tandfonline.com/doi/abs/10.1080/00140139308967879

Abstract Established nutritional science methods and a new concept for meal–classification were applied to shiftworker (rotating 3-shift) data. The frequency of meals and snacks of different nutritional quality as a function of work schedule was evaluated, as well as the content of selected nutrients (energy, fat, sucrose, dietary fibres, ascorbic acid) in these meals and snacks. The results do not indicate that rotating 3-shift work affects the nutritional quality of the diet or the frequency of different types of meals and snacks. A qualitative classification of meals and snacks might be a cost–effective strategy for data–evaluation in field studies of shift workers' eating habits when quantitative estimations of the dietary intake are to be complicated.

Keywords

Leonardi GC, Rapisarda V, Marconi A, et al. *Year* 2012

Authors Leonardi GC, Rapisarda V, Marconi A, Scalisi A, Catalano F, Proietti L, Travali S, Libra M, Fenga C.

Report Name Correlation of the risk of breast cancer and disruption of the circadian rhythm (Review).

Publication Oncol Rep

Issue-page numbers 2012 Aug;28(2):418-28. doi: 10.3892/or.2012.1839. Epub 2012 May 29.

URL http://www.ncbi.nlm.nih.gov/pubmed/22664950

Abstract Breast cancer is the worldwide leading cause of cancer incidence among women. Night shift work exposure has been recently considered one of the significant breast cancer risk factors in industrialized countries. The mechanisms by which this work exposure may be responsible for cancer development is still discussed. In the last 15 years, many authors have paid attention to the relationship between night shift work and breast cancer risk. In the current study, eight case-control studies and four prospective epidemiological studies describing such relationship are discussed. A positive correlation between night shift work and breast cancer risk was described in 8 out of 12 studies. However, different reasons suggest that some of these studies have an Achilles heel according to the International Agency of Cancer (IARC) indications. Both the circadian system alteration and the melatonin output reduction, related to the exposure to light-at-night during night shift work, remain the most valid hypotheses on the causal relation of shift work and breast cancer. Overall, the results of the present study suggest that there is an association between night shift work and breast cancer development in western countries. However, further studies are needed to confirm such association and to understand which biomolecular mechanisms may be involved in the pathogenesis of cancer diagnosed in patients with night shift work exposure.

Keywords

Leon-Blanco MM, Guerrero JM, Reiter RJ et al. **Year** 2003

Authors Leon-Blanco MM, Guerrero JM, Reiter RJ et al.

Report Name Melatonin inhibits telomerase activity in the MCF-7 tumor cell line both in vivo and in vitro

Publication J Pineal Res

Issue-page numbers 35:204–211 doi:10.1034/j.1600- 079X.2003.00077.x. PMID:12932205

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079X.2003.00077.x/abstract?

Abstract In this study for the first time the relationship between melatonin and telomerase activity was investigated. Melatonin exhibits oncostatic properties, but the actual mechanism of action by which the indole reduces tumor cell activity is not clear. Telomerase is an enzyme responsible of telomere elongation and is activated in most human cancers. In the current in vivo study, eight nude mice received a MCF-7 xenograft and thereafter they were treated for 5 weeks with 0.1 mg/mL of melatonin in the drinking water. Melatonin treatment caused a significant reduction in the weight of tumors and reduced metastases when compared with the control group. As indicated by the Telomerase Repeats Amplification Protocol (TRAP) assay, a significant decrease in telomerase activity was observed in the group treated with melatonin. In related in vitro studies, cultured MCF-7 cells were treated with three different concentrations of melatonin and a control without indole treatment. A significant dose-dependent decrease in Telomerase reverse transcriptase (TERT), the catalytic subunit of telomerase, mRNA expression was observed in the melatonin-treated cells. We also observed a significant reduction in TR, the RNA telomerase subunit, mRNA expression at physiological concentrations of melatonin (1 nm). Significant differences in TEP1, an associated telomerase protein, mRNA expression were also observed. In conclusion, melatonin influences telomerase both in vivo and in vitro, decreasing its activity in the tumors of nude mice and the mRNA expression of the TERT and TR subunits, essential factors for the proper function of the telomerase enzyme.

Keywords MCF-7 cells; melatonin; nude mice; oncostatic; telomerase

Leon-Blanco MM, Guerrero JM, Reiter RJ, Pozo D **Year** 2004

Authors Leon-Blanco MM, Guerrero JM, Reiter RJ, Pozo D

Report Name RNA expression of human telomerase subunits TR and TERT is differentially affected by melatonin receptor agonists in the MCF-7 tumor cell line

Publication Cancer Lett

Issue-page numbers 216:73–80 doi:10.1016/j.canlet.2004.05.003. PMID:15500950

URL http://www.cancerletters.info/article/S0304-3835%2804%2900350-7/abstract

Abstract The RNA expression levels of human catalytic subunit (TERT) and the RNA subunit (TR) of telomerase were analysed after treatment with the agonists of the membrane receptor (S 20098) and the nuclear receptor (CGP 52608) for melatonin in the MCF-7 human breast tumor cell line. Neither membrane nor nuclear signalling affected the RNA steady-state levels of the TR subunit of telomerase. On the contrary, we observed a significant decreased in the RNA levels of TERT after treatment with CGP 52608 while S 20098 produced a significant increase in the RNA levels of TERT. These results support a cross-talk between membrane and nuclear melatonin signalling and provide new data on the hormonal regulation of telomerase function.

Keywords Telomerase, Telomerase reverse transcriptase (TERT), Telomerase RNA (TR), Melatonin, Tumorogenesis, Breast cancer

Léone J, Pennaforte JL, Delhinger V, et al. **Year** 1997

Authors J Léone, J L Pennaforte, V Delhinger, J Detour, K Lefondre, J P Eschard, J C Etienne

Report Name Influence of seasons on risk of flare-up of systemic lupus retrospective study of 66 patients.

Publication La Revue de medecine interne fondee par la Societe nationale francaise de medecine interne

Issue-page numbers Volume: 18, Issue: 4, Pages: 286-291

URL http://www.mendeley.com/research/influence-seasons-risk-flareup-systemic-lupus-retrospective-study-66-patients-1/

Abstract PURPOSE: To establish the possible connection between visceral, arthro-cutaneous and biological spreading of systemic lupus (SL) and hours of sunlight. MATERIAL AND METHODS: Retrospective study of 66 SL patients, consisting of 52 visceral and 14 arthro-cutaneous cases taking into account the chronological pattern of each new aggravation, based on 480 clinical records. RESULTS: Increased frequency in visceral aggravation was observed in the post-summer period (August-January) (n = 57), as compared with the pre-summer period (February-July) (n = 25) (RR = 1.75, P = 0.006). This post-summer visceral aggravation was correlated with cutaneous affection (RR = 4.18) and absence of previous corticotherapy (RR = 3.97). Visceral and arthro-cutaneous aggravations taken together revealed a more disturbed immune balance pattern in the post-summer period (anti-dsDNA: 30 versus 25.1 IU/L P = 0.07; C3: 0.83 vs 0.921 IU/L P = 0.05; C4: 0.146 vs 0.183 P = 0.05), providing evidence of greater severity. Moderate thrombopenia (50-120 10(9)/L) accompanying visceral SL with antiphospholipids (n = 33) was more frequent during the post-summer period, even in the absence of aggravation (P = 0.03). The quarterly distribution of visceral aggravations was correlated with average hours of sunlight in the preceding quarter (P = 0.01). CONCLUSION: There is a post-summer increase in the frequency and severity of visceral SL spreading correlated to cutaneous exacerbation and sunlight.

Keywords

Leproult R, Copinschi G, Buxton O, Van Cauter E **Year** 1997

Authors Leproult R, Copinschi G, Buxton O, Van Cauter E

Report Name Sleep loss results in an elevation of cortisol levels the next evening

Publication Sleep

Issue-page numbers 20:865–870. PMID:9415946

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24246

Abstract Sleep curtailment constitutes an increasingly common condition in industrialized societies and is thought to affect mood and performance rather than physiological functions. There is no evidence for prolonged or delayed effects of sleep loss on the hypothalamo-pituitary-adrenal (HPA) axis. We evaluated the effects of acute partial or total sleep deprivation on the nighttime and daytime profile of cortisol levels. Plasma cortisol profiles were determined during a 32-hour period (from 1800 hours on day 1 until 0200 hours on day 3) in normal young men submitted to three different protocols: normal sleep schedule (2300- 0700 hours), partial sleep deprivation (0400-0800 hours), and total sleep deprivation. Alterations in cortisol levels could only be demonstrated in the evening following the night of sleep deprivation. After normal sleep, plasma cortisol levels over the 1800-2300-hour period were similar on days 1 and 2. After partial and total sleep deprivation, plasma cortisol levels over the 1800-2300-hour period were higher on day 2 than on day 1 (37 and 45% increases, p = 0.03 and 0.003, respectively), and the onset of the quiescent period of cortisol secretion was delayed by at least 1 hour. We conclude that even partial acute sleep loss delays the recovery of the HPA from early morning circadian stimulation and is thus likely to involve an alteration in negative glucocorticoid feedback regulation. Sleep loss could thus affect the resiliency of the stress response and may accelerate the development of metabolic and cognitive consequences of glucocorticoid excess.

Keywords

Lerchl A

Year 2002

Authors Alexander Lerchl

Report Name Biological rhythms in the context of light at night (LAN)

Publication Neuro endocrinology letters (2002)

Issue-page numbers Volume: 23 Suppl 2, Pages: 23-27

URL http://www.mendeley.com/research/biological-rhythms-context-light-night-lan/

Abstract In mammals including man, the most important zeitgeber for endogenous rhythms is the environmental light/dark cycle. Mammals perceive light through the eyes and that perception is relayed to the suprachiasmatic nucleus (SCN) by means of neuronal signals. The SCN, in turn, innervates the pineal gland, resulting in the production and release of melatonin almost exclusively during night-time hours. Thus, besides object recognition, eyes serve as the sensory organ for detecting the presence or absence of light. The way that light entrains the SCN is still a matter of intense research. It has been shown, for example, that the light intensities required for affecting melatonin rhythms are much higher than the intensities needed for object identification. On the other hand, even in rodents who completely lack the "classical" photoreceptors of the retina, their endogenous rhythms still can be synchronized by normal light/dark cycles. These two observations led to the hypothesis that there must be photoreceptors, apart from the known (object-identifying) retinal photoreceptors, which are responsible for the entrainment of internal rhythms. Very recently, a number of reports showed that in fact a completely new type of retinal photoreceptor, located in ganglion cells, may be responsible for entraining the SCN. It contains a photopigment, melanopsin, which shares homologies with rhodopsin, but also is evolutionarily older. Compared to rods or cones, the melanopsin-containing neurons are rare, but evenly distributed within the retina, indicating that they serve as a global, integrating light sensor. These ganglion cells apparently project directly into the SCN. Taken together, these new developments in photo-chronobiology open new areas of research. It will be of special interest, for example, to determine how the photosensitive ganglion cells and their dendrites integrate the environmental light stimuli.

Keywords

Lerner AB, Case JD, Takahashi Y et al.

Year 1958

Authors Lerner AB, Case JD, Takahashi Y et al.

Report Name Isolation of melatonin, the pineal gland factor that lightens melanocytes

Publication J Am Chem Soc

Issue-page numbers 80:2587 doi:10.1021/ja01543a060

URL http://pubs.acs.org/doi/abs/10.1021/ja01543a060

Abstract N/A

Keywords

Levallois P, Dumont M, Touitou Y et al. **Year** 2001

Authors Levallois P, Dumont M, Touitou Y et al.

Report Name Effects of electric and magnetic fields from highpower lines on female urinary excretion of 6-sulfatoxymelatonin

Publication Am J Epidemiol

Issue-page numbers 154:601–609 doi:10.1093/aje/154.7.601. PMID:11581093

URL http://aje.oxfordjournals.org/content/154/7/601.abstract

Abstract In 1998, the authors studied the effect of residential exposure to electric and magnetic fields from high-power lines on female urinary excretion of 6-sulfatoxymelatonin (6-OHMS) in the Quebec city, Canada, metropolitan area. A sample of 221 women living near a 735-kV line was compared with 195 women the same age living away from any power lines. Participants provided morning urine samples on 2 consecutive days and wore a magnetic dosimeter for 36 consecutive hours to measure personal magnetic exposure. The indoor electric field was assessed by spot measurements. After adjustment for other factors associated with low melatonin secretion, such as medication use or light exposure, nighttime concentration of 6-OHMS was similar in the two groups. When either 24-hour or sleep-time exposure to magnetic field or electric field measurements was used, no exposure-effect relation was evident. However, the trend of decreasing 6-OHMS concentration with age was more pronounced for women living near the lines, as was a lower 6-OHMS concentration in women with high body mass index. Chronic residential exposure to magnetic fields from high-power lines may accentuate the decrease in melatonin secretion observed in some vulnerable subgroups of the population.
Key words

Keywords age factors, body mass index, electromagnetic fields, melatonin, urinalysis

Levi F, Schibler U **Year** 2007

Authors Levi F, Schibler U

Report Name Circadian rhythms: mechanisms and therapeutic implications

Publication Annu Rev Pharmacol Toxicol

Issue-page numbers 47:593–628 doi:10.1146/annurev.pharmtox.47.120505.105208. PMID:17209800

URL http://www.annualreviews.org/doi/abs/10.1146/annurev.pharmtox.47.120505.105208

Abstract The mammalian circadian system is organized in a hierarchical manner in that a central pacemaker in the suprachiasmatic nucleus (SCN) of the brain's hypothalamus synchronizes cellular circadian oscillators in most peripheral body cells. Fasting-feeding cycles accompanying rest-activity rhythms are the major timing cues in the synchronization of many, if not most, peripheral clocks, suggesting that the temporal coordination of metabolism and proliferation is a major task of the mammalian timing system. The inactivation of noxious food components by hepatic, intestinal, and renal detoxification systems is among the metabolic processes regulated in a circadian manner, with the understanding of the involved clock output pathways emerging. The rhythmic control of xenobiotic detoxification provides the molecular basis for the dosing time-dependence of drug toxicities and efficacy. This knowledge can in turn be used in improving or designing chronotherapeutics for the patients who suffer from many of the major human diseases.

Keywords

Levine ME, Milliron AN, Duffy LK | ***Year*** 1994

Authors Levine ME, Milliron AN, Duffy LK

Report Name Diurnal and seasonal rhythms of melatonin, cortisol and testosterone in interior Alaska

Publication Arctic Med Res

Issue-page numbers 53:25–34. PMID:8048998

URL http://www.mendeley.com/research/diurnal-seasonal-rhythms-melatonin-cortisol-testosterone-interior-alaska/

Abstract The diurnal variations in the secretory patterns of melatonin, cortisol and testosterone were studied in a Fairbanks, Alaska population who were unadapted to the extreme light variations of the North. Statistically significant variations in hormonal levels were found in both diurnal and seasonal rhythms. Prominent findings included unusually high levels of cortisol at 0200 and 0800 in the fall and elevated daytime levels (1030) of melatonin in the winter. These results indicate a delayed phase secretory pattern when compared to the normal pattern at lower latitudes. These findings imply possible underlying physiological causes for the high incidence of behavior disorders such as depression and alcoholism in Alaska and circumpolar environments in general.

Keywords

Lewiński A, Sewerynek E, Wajs E et al. | ***Year*** 1993

Authors Lewiński A, Sewerynek E, Wajs E et al.

Report Name Effects of the pineal gland on the growth processes of Guerin epithelioma in male Wistar rats

Publication Cytobios

Issue-page numbers 73:89–94. PMID:8319500

URL http://www.ncbi.nlm.nih.gov/pubmed/8319500

Abstract The effects of pinealectomy (PX) and melatonin (Mel) administration on the growth processes of Guerin epithelioma, a malignant tumour derived from spontaneous cancer in Wistar rat uterus, was investigated in five groups of male rats. The mean life span of the rats bearing Guerin tumours (GT) and subjected to PX was shorter than in animals with an intact pineal gland. Mel did not affect the lifespan in rats with intact pineals or in those subjected to PX. Mel decreased the mitotic activity of GT cells in rats with and without the pineal gland. Pathomorphological examination revealed high malignancy of the primary tumour but no metastases. The results confirmed the important role of the pineal gland in 'oncostasis'.

Keywords

Lewy AJ **Year** 1999

Authors Lewy AJ

Report Name The dim light melatonin onset, melatonin assays and biological rhythm research in humans

Publication Biol Signals Recept

Issue-page numbers 8:79–83 doi:10.1159/000014573. PMID:10085467

URL http://www.mendeley.com/research/dim-light-melatonin-onset-melatonin-assays-biological-rhythm-research-humans/

Abstract The most useful marker for human circadian phase position is the dim light melatonin onset (DLMO). This is optimally obtained by sampling blood or saliva in the evening at intervals of 30 min or less. Ambient light intensity should not exceed 30-50 lx. For many years, the DLMO was determined mainly with the 'gold standard' GCMS technique for measuring melatonin in human plasma. However, new and improved RIAs now provide the requisite sensitivity and accuracy (specificity) for detecting the time that low daytime levels begin to increase in the evening: the lower the operational threshold for the DLMO, the more reliable it is as a phase marker.

Keywords

Lewy AJ , Wehr TA, Goodwin FK, et al. **Year** 1980

Authors AJ Lewy, TA Wehr, FK Goodwin, DA Newsome and SP Markey

Report Name Light suppresses melatonin secretion in humans

Publication Science

Issue-page numbers 12 December 1980: Vol. 210 no. 4475 pp. 1267-1269

URL http://www.sciencemag.org/content/210/4475/1267.abstract

Abstract Bright artificial light suppressed nocturnal secretion of melatonin in six normal human subjects. Room light of less intensity, which is sufficient to suppress melatonin secretion in other mammals, failed to do so in humans. In contrast to the results of previous experiments in which ordinary room light was used, these findings establish that the human response to light is qualitatively similar to that of other mammals.

Keywords

Lewy AJ, Ahmed S, Jackson JML, Sack RL | *Year* 1992

Authors Lewy AJ, Ahmed S, Jackson JML, Sack RL

Report Name Melatonin shifts human circadian rhythms according to a phase-response curve

Publication Chronobiol Int,

Issue-page numbers 9:380–392 doi:10.3109/07420529209064550. PMID:1394610

URL http://www.ncbi.nlm.nih.gov/pubmed/1394610

Abstract A physiological dose of orally administered melatonin shifts circadian rhythms in humans according to a phase-response curve (PRC) that is nearly opposite in phase with the PRCs for light exposure: melatonin delays circadian rhythms when administered in the morning and advances them when administered in the afternoon or early evening. The human melatonin PRC provides critical information for using melatonin to treat circadian phase sleep and mood disorders, as well as maladaptation to shift work and transmeridional air travel. The human melatonin PRC also provides the strongest evidence to date for a function of endogenous melatonin and its suppression by light in augmenting entrainment of circadian rhythms by the light-dark cycle.

Keywords

Lewy AJ, Bauer VK, Ahmed S et al. | *Year* 1998

Authors Lewy AJ, Bauer VK, Ahmed S et al.

Report Name The human phase response curve (PRC) to melatonin is about 12 hours out of phase with the PRC to light

Publication Chronobiol Int

Issue-page numbers 15:71–83 doi:10.3109/07420529808998671. PMID:9493716

URL http://informahealthcare.com/doi/abs/10.3109/07420529808998671

Abstract Melatonin's timekeeping function is undoubtedly related to the fact that it is primarily produced during nighttime darkness; that is, melatonin and light occur at opposite times. The human phase response curve (PRC) to melatonin appears to be about 12h out of phase with the PRC to light. These striking complementarities, together with light's acute suppressant effect on melatonin production, suggest that a function for endogenous melatonin is to augment entrainment of the circadian pacemaker by the light-dark cycle. The melatonin PRC also indicates correct administration times for using exogenous melatonin to treat circadian phase disorders.

Keywords Melatonin administration, Melatonin phase response curve, Light phase response curve, Circadian phase disorders, Dim light melatonin onset

Lewy AJ, Cutler NL, Sack RL **Year** 1999

Authors Lewy AJ, Cutler NL, Sack RL

Report Name The endogenous melatonin profile as a marker for circadian phase position

Publication J Biol Rhythms

Issue-page numbers 14:227–236 doi:10.1177/074873099129000641. PMID:10452335

URL http://jbr.sagepub.com/content/14/3/227.abstract

Abstract Several circadian rhythms have been used to assess the phase of the endogenous circadian pacemaker (ECP). However, when more than one marker rhythm is measured, results do not always agree. Questions then inevitably arise. Are there multiple oscillators? Are some markers more reliable than others? Masking is a problem for all marker rhythms. Masking of melatonin is minimized by sampling under dim light. The dim-light melatonin onset (DLMO) is particularly convenient since it can usually be obtained before sleep. However, assessing the DLMO in low melatonin producers may be problematic, particularly with the commonly used operationally defined threshold of 10 pg/ml. This study evaluates various circadian phase markers provided by the plasma melatonin profile in 14 individuals, several of whom are low melatonin producers. The amount (amplitude) of melatonin production appears to influence the phase of many points on the melatonin profile. Accordingly, when low producers are in a data set, we now prefer a lower DLMO threshold than the one previously recommended (10 pg/ml). Indeed, there are some low producers who never exceed this threshold at any time. Radioimmunoassays are now available that have the requisite sensitivity and specificity to support the use of a lower threshold. Nevertheless, the dim-light melatonin offset (DLMOff), even when operationally defined at thresholds less than 10 pg/ml, appears to be confounded by amplitude in this study; in such cases, it may be preferable to use the melatonin synthesis offset (SynOff) because it is not confounded by amplitude and because, theoretically, it is temporally closer to the endogenous mechanism signaling the offset of production. The question of whether the termination mechanism of melatonin synthesis is related to an interval timer or to a second oscillator loosely coupled to the onset oscillator is probably best answered using the SynOff rather than the DLMOff. It is hoped that these findings will make a useful contribution to the debate on the best ways to use points on the melatonin profile to assess circadian phase position in humans.

Keywords melatonin, dim-light melatonin onset (DLMO), dim-light melatonin offset (DLMOff), melatonin synthesis offset (SynOff), circadian phase,

Lewy AJ, Sack RL, Miller LS, Hoban TM **Year** 1987

Authors AJ Lewy, RL Sack, LS Miller and TM Hoban

Report Name Antidepressant and circadian phase-shifting effects of light

Publication Science

Issue-page numbers 16 January 1987: Vol. 235 no. 4786 pp. 352-354

URL http://www.sciencemag.org/content/235/4786/352.abstract

Abstract Bright light can suppress nighttime melatonin production in humans, but ordinary indoor light does not have this effect. This finding suggested that bright light may have other chronobiologic effects in humans as well. Eight patients who regularly became depressed in the winter (as day length shortens) significantly improved after 1 week of exposure to bright light in the morning (but not after 1 week of bright light in the evening). The antidepressant response to morning light was accompanied by an advance (shift to an earlier time) in the onset of nighttime melatonin production. These results suggest that timing may be critical for the antidepressant effects of bright light.

Keywords

Lewy H, Haus E, Ashkenazi IE **Year** 2007

Authors Lewy H, Haus E, Ashkenazi IE

Report Name Possible linkage between the ability to change the period (tau) of the prolactin and cortisol rhythms in women and breast cancer risk

Publication Chronobiol Int

Issue-page numbers 24:365–381 doi:10.1080/07420520701282349. PMID:17453854

URL http://informahealthcare.com/doi/abs/10.1080/07420520701282349

Abstract The 24 h profiles of plasma hormone concentrations are rhythmic. The circadian period (τ) changes in development, with seasons, and in women with different stages of the menstrual cycle. It is known that the rhythms of prolactin and cortisol are sensitive to environmental time cues, such as changes in day length and phase; however, the importance of these changes is not yet understood. This study investigates whether there is a relation between the ability of a subject to respond to external cues that are associated with seasonal changes causing alteration of the rhythm's periods in cortisol and prolactin and the epidemiologically determined susceptibility to breast cancer. It is shown that the rhythmic output pattern of prolactin and cortisol in vivo is generated by more than one oscillator and structured by more than one rhythmic component. Each cohort of American women, classified on an epidemiologic basis as high risk (HR) or low risk (LR) to develop breast cancer, expresses different rhythmic output patterns of both variables, suggesting that the genetic background as defined by the risk state is related to differences in the circadian time structure, including the ability of the subject to change the rhythm's τ. The LR cohort exhibited a statistically significant change between seasons in the rhythm's τ of both the prolactin and cortisol patterns. In contrast, the HR cohort showed no change in the rhythm's τ between seasons for prolactin and cortisol patterns. These results show that in human beings, the presence of a circannual rhythm in the circadian time structure or the ability to adapt the circadian rhythmic pattern of these variables to external cues, such as seasons, is related to the partly genetically determined risk state to develop breast cancer and may be of importance for human health.

Keywords Rhythm's period, Breast cancer risk, Prolactin, Cortisol, Biological rhythm

Li B, Ahmed F, Bernstein PS **Year** 2010

Authors Binxing Li, Faisal Ahmed, Paul S. Bernstein

Report Name Studies on the singlet oxygen scavenging mechanism of human macular pigment

Publication Archives of Biochemistry and Biophysics

Issue-page numbers Volume 504, Issue 1, 1 December 2010, Pages 56-60

URL http://www.sciencedirect.com/science/article/pii/S0003986110003036

Abstract It is thought that direct quenching of singlet oxygen and scavenging free radicals by macular pigment carotenoids is a major mechanism for their beneficial effects against light-induced oxidative stress. Corresponding data from human tissue remains unavailable, however. In the studies reported here, electron paramagnetic resonance (EPR) spectroscopy was used to measure light-induced singlet oxygen generation in post-mortem human macula and retinal pigment epithelium/choroid (RPE/choroid). Under white-light illumination, production of singlet oxygen was detected in RPE/choroid but not in macular tissue, and we show that exogenously added macular carotenoids can quench RPE/choroid singlet oxygen. When the singlet oxygen quenching ability of the macular carotenoids was investigated in solution, it was shown that a mixture of meso-zeaxanthin, zeaxanthin, and lutein in a ratio of 1:1:1 can quench more singlet oxygen than the individual carotenoids at the same total concentration.

Keywords

Li Q, Zheng T, Holford TR, et al. **Year** 2010

Authors Qian Li, Tongzhang Zheng, Theodore R. Holford, Peter Boyle, Yawei Zhang and Min Dai

Report Name Light at night and breast cancer risk: results from a population-based case–control study in Connecticut, USA

Publication Cancer Causes and Control

Issue-page numbers Volume 21, Number 12, 2281-2285

URL http://www.springerlink.com/content/u0l131j8160t2145/

Abstract

Objective
To investigate the potential association between domestic exposure to light at night (LAN) and the risk of human breast cancer.
Methods
A case–control study of female breast cancer was conducted in Connecticut. A total of 363 incident breast cancer cases and 356 age frequency-matched controls were interviewed using a standardized, structured questionnaire to obtain information on sleeping patterns and bedroom light environment. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by unconditional multivariate logistic regression.
Results
A non-significantly increased risk of breast cancer was observed among postmenopausal women for those keeping lights on while sleeping (OR = 1.4, 95% CI 0.7, 2.7), those who reported mainly sleeping in the daytime (OR = 1.4, 95% CI 0.5, 4.3), and those not drawing the curtains/window shades while sleeping at night (OR = 1.2, 95% CI 0.8, 1.9).
Conclusion
The results from this study suggest a potential increased risk of breast cancer associated with domestic exposure to LAN. Further studies with larger sample size are needed to confirm the results.

Keywords Light at night - Breast cancer - Case-control study

Lie JA, Roessink J, Kjaerheim K **Year** 2006

Authors Lie JA, Roessink J, Kjaerheim K

Report Name Breast cancer and night work among Norwegian nurses

Publication Cancer Causes Control

Issue-page numbers 17:39–44.doi:10.1007/s10552-005-3639-2 PMID:16411051

URL http://www.springerlink.com/content/y3t72mt72878647r/

Abstract Objective Previous studies have suggested an association between breast cancer and night work. We evaluated the relationship among Norwegian nurses.
Methods A case–control study, nested within a cohort of 44,835 nurses educated between 1914 and 1980 was performed, based on a registry of all Norwegian nurses. Four controls were individually matched by year of birth to each of 537 breast cancer cases that occurred during the period 1960–1982. The reconstruction of work history and number of years with night work for each nurse was based on information from the nurse registry, and data from three censuses. We used conditional logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for total duration of work as a nurse and parity. All statistical tests were two-sided.
Results The adjusted OR of breast cancer among nurses who worked nights for 30 or more years was 2.21 (CI 1.10–4.45) compared with those who did not work nights after graduation from nursing school (ptrend = 0.01).
Conclusion Our results are in accordance with previous studies that find an association between night work and breast cancer risk among women.

Keywords Nurses - Occupation - Night work - Breast cancer - Melatonin

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Lie JS, Kjuus H, Zienolddiny S, et al. **Year** 2011

Authors Jenny-Anne S. Lie, Helge Kjuus, Shan Zienolddiny, Aage Haugen, Richard G. Stevens and Kristina Kjærheim

Report Name Night Work and Breast Cancer Risk Among Norwegian Nurses: Assessment by Different Exposure Metrics

Publication American Journal of Epidemiology

Issue-page numbers Volume173, Issue11 Pp. 1272-1279

URL http://aje.oxfordjournals.org/content/173/11/1272.short

Abstract Associations between night work and breast cancer risk were investigated in a nested case-control study within a cohort of 49,402 Norwegian nurses. A total of 699 (74%) of the live cases diagnosed in 1990–2007 and 895 (65%) controls, cancer free at the time of sampling, were interviewed about work history and potential risk factors. The odds ratios for risk of breast cancer in relation to different exposure metrics were estimated by multivariate unconditional logistic regression models. No increase of risk was found after long duration of work by nurses working ≥3 night shifts per month. Small, nonsignificantly increased risks were observed for exposure to ≥30 years in hospitals or other institutions (odds ratio (OR) = 1.1), ≥12 years in schedules including night work (OR = 1.3), ≥1,007 night shifts during the lifetime (OR = 1.2), and lifetime average number of ≥4 night shifts per month (OR = 1.2). Nonsignificantly increased risks of breast cancer were observed in nurses who worked ≥5 years with ≥4 (OR = 1.4) and ≥5 (OR = 1.6) consecutive night shifts. Significantly increased risks were seen in nurses who worked ≥5 years with ≥6 consecutive night shifts (OR = 1.8, 95% confidence interval: 1.1, 2.8). The results suggest that risk may be related to number of consecutive night shifts.

Keywords breast neoplasms, case-control studies, chronobiology phenomena, Norway, nurses, risk

Lie JS, Kjuus H, Zienolddiny S, et al. **Year** 2013

Authors Jenny-Anne S. Lie, Helge Kjuus, Shan Zienolddiny, Aage Haugen and Kristina Kjærheim

Report Name Breast Cancer Among Nurses: Is the Intensity of Night Work Related to Hormone Receptor Status?

Publication Am. J. Epidemiol.

Issue-page numbers doi: 10.1093/aje/kws428 First published online: June 20, 2013

URL http://aje.oxfordjournals.org/content/early/2013/06/20/aje.kws428.abstract

Abstract The aim of this study was to investigate whether night work is related to breast cancer receptor status. The effect of night work on the risk of estrogen receptor– and progesterone receptor–defined breast cancers was evaluated in 513 nurses diagnosed with breast cancer between 1996 and 2007 and in 757 frequency-matched controls, all of whom were selected from a cohort of Norwegian nurses. Odds ratios for the exposure “duration of work with a minimum of 6 consecutive night shifts” were compared for tumor subgroups with respect to the common control group through the use of polytomous logistic regression. Statistically significant associations were observed between breast cancer and work durations of ≥5 years with ≥6 consecutive night shifts, with the highest risk observed for progesterone receptor–positive tumors (odds ratio = 2.4, 95% confidence interval: 1.3, 4.3; P-trend = 0.01). When the exposure variable was dichotomized (ever/never worked ≥6 consecutive night shifts), a borderline statistically significant heterogeneity (P = 0.05) was seen between progesterone receptor–positive and progesterone receptor–negative tumors in postmenopausal women. The association observed between consecutive night shifts and progesterone receptor–positive cancers suggests that progesterone could play an important role in the detrimental effects of night work.

Keywords breast cancer, case-control studies, chronobiology phenomenon, estrogen, Norway, nurses, progesterone,

Liebmann PM, Hofer D, Felsner P et al. **Year** 1996

Authors Liebmann PM, Hofer D, Felsner P et al.

Report Name Beta-blockade enhances adrenergic immunosuppression in rats via inhibition of melatonin release

Publication J Neuroimmunol

Issue-page numbers 137–142 doi:10.1016/0165-5728(96)00050-1. PMID:8765337

URL http://www.sciencedirect.com/science/article/pii/0165572896000501

Abstract We have recently shown in rats that an in vivo treatment with catecholamines via α2,-receptors leads to a pronounced suppression of T-and B-cell mitogen responses of peripheral blood lymphocytes (PBL), provided that a β-blocker is administered concomitantly. Since melatonin (MEL) reportedly has stress-protective effects on several immune functions, and since the release of MEL from the pineal gland is inhibited by β-blockade, we tested the effect of MEL substitution on T-and B-cell mitogen responses of PBL in rats treated with two s.c. implanted retard tablets containing noradrenaline (NA) and propranolol. It was found that an oral treatment with MEL (about 40 /j,g/animal) abolished the adrenergic immunosuppression. Furthermore, functional pinealectomy induced by constant light had a similar enhancing effect on the α2adrenergic immunosuppression as observed with β-blockers, whereas PBL from animals kept at the regular light/dark interval were resistant to the treatment with the selective α2agonist clonidine. It is concluded that endogenous MEL effectively protects rat PBL from adrenergic immunosuppression, and that β-blockers enhance the immunosuppressive property of os-adrenergic agents via blocking the night-time release of MEL.

Keywords Melatonin; Mitogen response; Adrenergic immunosuppression; Noradrenaline; β-blocker

Authors Lin MC, Kripke DF, Parry BL, Berga SL

Report Name Night light alters menstrual cycles

Publication Psychiatry Res

Issue-page numbers 33:135–138 doi:10.1016/0165-1781(90)90067-F. PMID:2243890

URL http://www.sciencedirect.com/science/article/pii/016517819090067F

Abstract Dewan asserted 20 years ago that a bedside light could shorten and regularize the menstrual cycle among women with long and irregular menstrual patterns. To replicate this, seven volunteers slept with a 100-watt bulb by the bedside from days 13–17 of their menstrual cycles, while nine controls similarly used a dim red placebo (photographic safe light). Indeed, the 100-watt bulbs shortened menstrual cycles from a mean of 45.7 days to 33.1 days and reduced variability, but the placebo had no effect. These results sugges that light may have promise for treatment of infertility, for contraception, and for other endocrine interventions.

Keywords Light; menstruation; phototherapy

Authors Yingsong Lin, Junko Ueda, Kiyoko Yagyu, Michiko Kurosawa, Akiko Tamakoshi, Shogo Kikuchi

Report Name A prospective cohort study of shift work and the risk of death from pancreatic cancer in Japanese men

Publication Cancer Causes & Control

Issue-page numbers July 2013, Volume 24, Issue 7, pp 1357-1361

URL http://link.springer.com/article/10.1007/s10552-013-0214-0

Abstract

Purpose
There is mounting evidence that shift work involving night work increases cancer risk. We examined the relationship between working rotating shifts and the risk of death from pancreatic cancer on the basis of data from the Japanese Collaborative Cohort Study (JACC Study).
Methods

The present analysis was restricted to 22,224 men who were 40–65 years of age at baseline (1988–1990) and who reported working full time or were self-employed in the JACC Study. The subjects were followed through 31 December 2009. Information on occupation and lifestyle factors was collected using a self-administered questionnaire. The Cox proportional hazards model was used to estimate the relative risk (RR) and 95 % confidence interval (CI) for the risk of death from pancreatic cancer in relation to shift work.
Results

During the follow-up period, 127 pancreatic cancer deaths were observed. Overall, we found no statistically significant increase in the risk of death from pancreatic cancer associated with rotating shift work. As compared to day-shift workers, the RRs were 0.83 (95 % CI 0.43–1.60) for rotating shift workers and 0.61 (95 % CI 0.22–1.60) for fixed night-shift workers, after adjustment for potential confounding factors. The multivariable-adjusted RR was 1.34 (95 % CI 0.66–2.75) among rotating shift workers in the analysis restricted to men who reported working full time at baseline.
Conclusions

Our data did not support the hypothesis that shift work is significantly associated with the risk of death from pancreatic cancer in this cohort of Japanese men.

Keywords

Lincoln G, Messenger S, Andersson H, Hazlerigg D **Year** 2002

Authors Lincoln G, Messenger S, Andersson H, Hazlerigg D

Report Name Temporal expression of seven clock genes in the suprachiasmatic nucleus and the pars tuberalis of the sheep: evidence for an internal coincidence timer

Publication Proc Natl Acad Sci USA

Issue-page numbers 99:13890–13895 doi:10.1073/pnas.212517599. PMID: 12374857

URL http://www.pnas.org/content/99/21/13890.full

Abstract The 24-h expression of seven clock genes (Bmal1, Clock, Per1, Per2, Cry1, Cry2, and CK1ε) was assayed by in situ hybridization in the suprachiasmatic nucleus (SCN) and the pars tuberalis (PT) of the pituitary gland, collected every 4 h throughout 24 h, from female Soay sheep kept under long (16-h light/8-h dark) or short (8-h light/16-h dark) photoperiods. Locomotor activity was diurnal, inversely related to melatonin secretion, and prolactin levels were increased under long days. All clock genes were expressed in the ovine SCN and PT. In the SCN, there was a 24-h rhythm in Clock expression, in parallel with Bmal1, in antiphase with cycles in Per1 and Per2; there was low-amplitude oscillation of Cry1 and Cry2. The waveform of only Per1 and Per2 expression was affected by photoperiod, with extended elevated expression under long days. In the PT, the high-amplitude 24-h cycles in the expression of Bmal1, Clock, Per1, Per2, Cry1, and Cry2, but not CK1ε, were influenced by photoperiod. Per1 and Per2 peaked during the day, whereas Cry1 and Cry2 peaked early in the night. Hence, photoperiod via melatonin had a marked effect on the phase relationship between Per/Cry genes in the PT. This supports the conclusion that an ”external coincidence model“ best explains the way photoperiod affects the waveform of clock gene expression in the SCN, the central pacemaker, whereas an ”internal coincidence model“ best explains the way melatonin affects the phasing of clock gene expression in the PT to mediate the photoperiodic control of a summer or winter physiology.

Keywords

Lincoln GA **Year** 2002

Authors Lincoln GA

Report Name Neuroendocrine regulation of seasonal gonadotrophin and prolactin rhythms: lessons from the Soay ram model

Publication Reprod Suppl

Issue-page numbers 59:131–147. PMID:12698978

URL http://www.ncbi.nlm.nih.gov/pubmed/12698978

Abstract Marked seasonality, responsiveness to photoperiod, diurnal behaviour, large body size, long lifespan and adaptability in captivity are characteristics that make the Soay ram a useful model for neuroendocrine research. Adult rams are routinely housed indoors under artificial lighting of alternating 16 week periods of long and short days to entrain the seasonal cycles in reproduction, growth and metabolism. The long-term cycles in individuals are monitored directly (measurements of testis diameter, androgen-dependent skin coloration, food intake, pelage moult, locomotor activity) and retrospectively (measurements of reproductive and metabolic hormone concentrations in peripheral blood). A wide spectrum of experimental procedures, including serial blood and cerebrospinal fluid (CSF) sampling with hormone or drug treatments, tissue biopsy, stereotaxic cerebral implantation and surgical lesions, not feasible in smaller species, are used to investigate the multiple interactive neuroendocrine systems regulating seasonality. The results from a recent experiment in which rams received a lesion of the caudal arcuate nucleus (caudal ARCX) or hypothalamo-pituitary disconnection (HPD) are presented to demonstrate the fidelity of long-term data derived from the Soay ram model. The results support the view that the melatonin signal that encodes photoperiod acts within the mediobasal hypothalamus to time the gonadotrophin/gonadal cycle, but acts directly within the pituitary gland to time the prolactin/pelage cycle.

Keywords

Lincoln GA

Year 2006

Authors Lincoln GA

Report Name Decoding the nightly melatonin signal through circadian clockwork

Publication Mol Cell Endocrinol

Issue-page numbers 252:69–73 doi:10.1016/j.mce.2006.03.006. PMID:16647195

URL http://www.sciencedirect.com/science/article/pii/S0303720706001134

Abstract Photoperiod regulates the timing of seasonal cycles in reproduction, energy metabolism, moult and other seasonal characteristics, and the effects are transduced through changes in the duration of nocturnal melatonin secretion from the pineal gland. Short daily melatonin signals (4–8 h/day) activate a summer physiology, while long signals (>10 h/day) produce a winter phenotype. Decoding signal duration occurs in specific target cells in the brain and pituitary gland, each governing a different component of the seasonal adaptation. The pars tuberalis (PT) of the pituitary regulates prolactin release and provides a tractable model system to investigate the molecular decoding mechanism. In the PT, melatonin onset at dusk activates cryptochrone (Cry1) gene expression and melatonin offset at dawn activates period (Per1) gene expression, thus the Cry/Per interval varies directly with nightlength, and inverse to daylength. It is proposed that photoperiod-induced changes in this phase-relationship dictates the level of CRY/PER protein heterodimer formation, and in turn, the level of transcriptional drive to the genes that control PT output – up-regulated under long days stimulating prolactin secretion and a summer physiology, and – down-regulated by short days in winter. The melatonin signal is thus decoded through circadian clock genes.

Keywords Circadian; Melatonin; Pars tuberalis; Photoperiod time measurement; Prolactin

Lincoln GA

Year 2006

Authors Lincoln GA

Report Name Melatonin entrainment of circannual rhythms

Publication Chronobiol Int

Issue-page numbers 23:301–306 doi:10.1080/07420520500464452. PMID:16687303

URL http://informahealthcare.com/doi/abs/10.1080/07420520500464452

Abstract A melatonin-based photoperiod timing mechanism and a circannual rhythm-generating system interact to govern seasonal cycles in physiology and behavior in many vertebrates. This paper focuses on the pars tuberalis (PT) of the mammalian pituitary gland as a model melatonin-responsive tissue to investigate the molecular basis of these two basic long-term timing processes.

Keywords Circadian, Circannual, Pars Tuberalis, Photoperiod, Prolactin

Authors Lincoln GA, Andersson H, Hazlerigg D

Report Name Clock genes and the long-term regulation of prolactin secretion: evidence for a photoperiod/circannual timer in the pars tuberalis

Publication J Neuroendocrinol

Issue-page numbers 15:390–397 doi:10.1046/j.1365-2826.2003.00990.x. PMID:12622839

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2826.2003.00990.x/pdf

Abstract Prolactin secretion is regulated by photoperiod through changes in the 24-h melatonin profile and displays circannual rhythmicity under constant photoperiod. These two processes appear to occur principally within the pituitary gland, controlled by the pars tuberalis. This is evident because: (i) hypothalamic-pituitary disconnected (HPD) sheep show marked changes in prolactin secretion in response to switches in photoperiod and manipulations of melatonin, similar to brain-intact controls; (ii) HPD sheep also show photoperiod-specific, long-term cycles in prolactin secretion under constant long or short days, with the timing maintained even when prolactin secretion is blocked for 2-3 months; and (iii) pars tuberalis cells, but not lactotrophs, express high concentrations of melatonin (MT1) receptor, and exhibit a duration-sensitive, cAMP-dependant, inhibitory response to physiological concentrations of melatonin. This suggests the existence of an intrinsic, reversible photoperiod-circannual timer in pars tuberalis cells. A full complement of clock genes (Bmal1, Clock, Per1, Per2, Cry1 and Cry2) are expressed in the ovine pars tuberalis, and undergo 24-h cyclical expression as observed in a cell autonomous, circadian clock. Activation of Per genes occurs in the early day (melatonin off-set), while activation of Cry genes occurs in the early night (melatonin on-set). This temporal association is evident under both long and short days, thus the Per-Cry interval varies directly with photoperiod. Because, PER : CRY, protein : protein interactions affect stability, nuclear entry and gene transcription based on rodent data, the change in phasing of Per/Cry expression provides a potential mechanism for decoding the long day/short day melatonin signal. A speculative, but testable, extension of this hypothesis is that intrinsically regulated changes in the phase of Per/Cry rhythms, regulates both photorefractoriness and the generation of circannual rhythms in prolactin secretion.

Keywords

Authors Lincoln GA, Clarke IJ

Report Name Photoperiodically-induced cycles in the secretion of prolactin in hypothalamo-pituitary disconnected rams: evidence for translation of the melatonin signal in the pituitary gland

Publication J Neuroendocrinol

Issue-page numbers 6:251–260 doi:10.1111/j.1365-2826.1994.tb00580.x. PMID:7920591

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2826.1994.tb00580.x/abstract?

Abstract Long term changes in the secretion of prolactin were monitored in groups of hypothalamo-pituitary disconnected rams (HPD rams, n = 8) and control rams (HPD sham-operated and unoperated, n = 8) while exposed to an artificial lighting regimen of alternating 16-weekly periods of long days (16L : 8D) and short days (8L : 16D) for 72 weeks, and during a treatment with subcutaneous constant-release implants of melatonin under long days. The HPD rams showed all the clinical characteristics of complete pituitary disconnection (diabetes insipidus, gonadal regression and slight obesity), and were unresponsive to a range of provocation tests (exposure to a barking sheep dog, cannulation of the jugular vein, injection of serotonin and NMDA) which caused acute changes in the blood plasma concentrations of prolactin in the controls. Nevertheless, there was a clearly defined cycle in the blood concentrations of prolactin in the HPD rams related to the imposed lighting regimen with values 10-fold higher under long days compared to short days (HPD mean ± SEM: 90.1 ± 24.7 vs 9.4 ± 2.0 μl, long vs short day respectively, P < 0.001). The temporal pattern was very similar to that observed in the controls, although the concentrations of prolactin were higher in the HPD rams and more variable (control mean ± SEM: 55.6 ± 3.6 vs 3.0±0.5 μl, long vs short day, P < 0.001). There was a corresponding cycle in the growth and moulting of the wool in the HPD rams consistent with a biological response to the photoperiodically-induced changes in the secretion of prolactin. The diurnal rhythm in the blood concentrations of prolactin was absent in the HPD rams, but there was a normal rhythm in the secretion of melatonin. The treatment of the animals with constant-release implants of melatonin under long days caused a marked decrease in the blood concentrations of prolactin in both the HPD and control rams. The overall conclusion is that the endogenously generated daily melatonin signal which encodes daylength acts directly in the pituitary gland to mediate the effects of photo-period on the secretion of prolactin. The photo-period transduction pathway thus by-passes the hypothalamus.

Keywords prolactin; daylength; melatonin; pars tuberalis; pars distalis; sheep; seasonal cycles

Authors Lindmaier A, Neumann R

Report Name The patient with polymorphous light dermatosis. Skin type, hardening and other light-associated markers

Publication Hautarzt

Issue-page numbers 1991 Jul; 42(7) :430-3.

URL http://www.unboundmedicine.com/5minute/ub/citation/1938396/%5BThe_patient_with_polymorphous_light_dermatosis__Skin_type_hardening_and_other_light_associated_mar

Abstract

From 1985 to 1989 we interviewed 312 patients suffering from polymorphous light eruption (PLE). The interviews were based on a questionnaire dealing with the various light-dependent factors that exacerbate the disease. Of 90 patients who were tested with artificial UV-A and UV-B irradiation sources, 60 reacted with typical PLE lesions: (a) 27 patients to UV-A alone, (b) 12 to UV-B alone, and (c) 21 to both UV-A and UV-B. Using UV-A provocation tests we were able to determine the anamnestic criteria indicating a possible UV-A induction of PLE, e.g. occurrence in the shade, no protection from window glass, no benefit from conventional sunscreens, and occurrence in solaria. The period from experimental irradiation to induction of skin lesions was shorter in skin types I and II than in skin type III and IV. Hardening phenomenon was reported by 37% of our patients. Of the UV-A-positive patients, 38% showed the first presentation of PLE lesions at the height of summer, as against 64% of the total number of patients questioned. Additional lesions at non-irradiated skin sites occurred in 25% of our patients, the frequency rising with increasing duration of the tendency to PLE.

Keywords

Authors A Linnersjö, N Hammar, B-G Dammström, M Johansson, H Eliasch

Report Name Cancer incidence in airline cabin crew: experience from Sweden

Publication Occup Environ Med

Issue-page numbers 60:810–814.doi:10.1136/oem.60.11.810 PMID:14573710

URL http://oem.bmj.com/content/60/11/810.abstract

Abstract

Aims: To determine the cancer incidence in Swedish cabin crew.

Methods: Cancer incidence of cabin crew at the Swedish Scandinavian Airline System (SAS) (2324 women and 632 men) employed from 1957 to 1994 was determined during 1961–96 from the Swedish National Cancer Register. The cancer incidence in cabin crew was compared with that of the general Swedish population by comparing observed and expected number of cases through standardised incidence ratios (SIR). A nested case-control study was performed, including cancer cases diagnosed after 1979 and four controls per case matched by gender, age, and calendar year.

Results: The SIR for cancer overall was 1.01 (95% CI 0.78 to 1.24) for women and 1.16 (95% CI 0.76 to 1.55) for men. Both men and women had an increased incidence of malignant melanoma of the skin (SIR 2.18 and 3.66 respectively) and men of non-melanoma skin cancer (SIR 4.42). Female cabin attendants had a non-significant increase of breast cancer (SIR 1.30; 95% CI 0.85 to 1.74). No clear associations were found between length of employment or cumulative block hours and cancer incidence.

Conclusions: Swedish cabin crew had an overall cancer incidence similar to that of the general population. An increased incidence of malignant melanoma and non-melanoma skin cancer may be associated with exposure to UV radiation, either at work or outside work. An increased risk of breast cancer in female cabin crew is consistent with our results and may in part be due to differences in reproductive history.

Keywords

Authors Linthorst AC, Flachskamm C, Hopkins SJ et al.

Report Name Long-term intracerebroventricular infusion of corticotropin-releasing hormone alters neuroendocrine, neurochemical, autonomic, behavioral, and cytokine responses to a systemic

Publication J Neurosci

Issue-page numbers 17:4448–4460. PMID:9151762

URL http://www.jneurosci.org/content/17/11/4448.full.pdf

Abstract

Corticotropin-releasing hormone (CRH) was infused intracerebroventricularly into rats for 7 d via a miniosmotic pump (1 mg z ml21 z hr21). Body temperature and locomotor activity were recorded during the treatment using biotelemetry, whereas hippocampal serotonergic neurotransmission and free corticosterone levels were monitored using in vivo microdialysis on day 7 of CRH treatment. During the microdialysis experiment, behavioral activity was scored by assessing the time during which rats were active (locomotion, grooming, eating, drinking). Continuous intracerebroventricular infusion of CRH produced a transient increase in body temperature and locomotion. Moreover, intracerebroventricularly CRH-treated rats showed elevated free corticosterone levels with no apparent diurnal rhythm.

Intraperitoneal administration of bacterial endotoxin [lipopolysaccharide (LPS); 100 mg/kg body weight] on day 7 of CRH/vehicle treatment produced a marked fever response in control animals, which was significantly blunted in intracerebroventricularly CRH-treated rats. Although free corticosterone levels reached similar peak concentrations in both intracerebroventricularly vehicle- and CRH-infused groups after LPS, this response was delayed significantly by ;1 hr in the intracerebroventricularly CRH-treated animals. Microdialysis experiments showed no changes in basal extracellular levels of serotonin and 5-hydroxyindoleacetic acid in intracerebroventricularly CRHinfused animals. Injection of LPS in intracerebroventricularly CRHtreated rats produced a blunted 5-HT response and a delayed onset of behavioral inhibition and other signs of sickness behavior. Assessment of the endotoxin-induced cytokine responses showed significantly enhanced plasma interleukin-1 (IL-1) and IL-6 bioactivities in the intracerebroventricularly CRH-infused animals 3 hr after injection of LPS, whereas tumor necrosis factor bioactivity responses were not different.

Our data demonstrate that chronically elevated brain CRH levels produce marked changes in basal (largely CRH regulated) physiological and behavioral processes accompanied by aberrant responses to an acute challenge. The present study provides evidence that chronic CRH hypersecretion is an important factor in the etiology of stress-related disorders.

Keywords corticotropin-releasing hormone; endotoxin; hypothalamic-pituitary-adrenocortical axis; corticosterone; body temperature; sickness behavior

Lissoni P, Barni S, Tancini G et al ***Year*** 1994

Authors Lissoni P, Barni S, Tancini G et al

Report Name Role of the pineal gland in the control of macrophage functions and its possible implication in cancer: a study of interactions between tumor necrosis factor-alpha and the pineal h

Publication J Biol Regul Homeost Agents

Issue-page numbers 8:126–129. PMID:7660855

URL http://www.ncbi.nlm.nih.gov/pubmed/7660855

Abstract Recent studies have shown the existence of reciprocal links between cytokine activity and immunomodulating neurohormones or neuropeptides. In particular, the pineal hormone melatonin (MLT) appears to influence IL-2 activity in cancer. The present study was performed to evaluate which interaction exists between MLT and another important cytokine, tumor necrosis factor-alpha (TNF), which is responsible for both antitumor cytolytic activity and cancer-related cachexia. In a first study, we analyzed MLT circadian rhythm under TNF administration (0.75 mg/day i.v. for 5 days) in 10 metastatic solid tumor patients. In a second study, we evaluated TNF serum levels in 10 metastatic solid tumor patients under therapy with MLT alone (20 mg/day orally in the evening for at least 1 month). In a third study, we have measured concomitantly daily serum levels of MLT and TNF in 30 patients with metastatic solid neoplasms. Nocturnal mean serum concentrations significantly increased in response to TNF injection. MLT therapy induced a significant decline in TNF mean values. Finally, patients with abnormally high MLT diurnal levels showed significantly lower TNF mean concentrations with respect to those with normal levels of the pineal hormone. This study, by showing the stimulatory effect of TNF on MLT secretion and the inhibitory action of MLT on TNF release, would suggest the existence of feed-back mechanisms operating between the pineal gland and TNF released from macrophages in human neoplasms.

Keywords

Authors Lissoni P, Barni S, Tancini G et al.

Report Name Pineal-opioid system interactions in the control of immunoinflammatory responses

Publication Ann N Y Acad Sci

Issue-page numbers 741 1 Neuroimmunomo;191–196 doi:10.1111/j.1749-6632.1994.tb39659.x. PMID:7825805

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1994.tb39659.x/abstract

Abstract

Several studies have demonstrated involvement of the pineal gland in the regulation of neuropeptide secretion and activity. In particular, the existence of links between the pineal gland and the brain opioid system has been documented. Both opioid peptides and melatonin (MLT), the most investigated pineal hormone, play an important role in neuromodulation of the immunity. Moreover, the immune effects of MLT are mediated by endogenous opioid peptides, which may be produced by both the endocrine system and the immune cells. In addition, the immune dysfunctions that characterize some human diseases, such as cancer, depend not only on the immune system per se, but also at least in part, on altered secretion of immunomodulating neurohormones, including MLT and opioid peptides. Therefore, the exogenous administration of neurohormones could potentially improve the immune status in humans. The present study evaluates the effects of MLT on changes in the number of T lymphocytes, natural killer cells, and eosinophils induced by exogenous administration of interleukin-2 (IL-2). Macrophage activity was also evaluated by determining serum levels of its specific marker, neopterin. The study was performed in 90 patients with advanced solid neoplasms, who received IL-2 at a dose of 3 million IU/day subcutaneously for 6 days a week for 4 weeks plus MLT at a daily dose of 40 mg. Both drugs were given in the evening. The results were compared to those in 40 cancer patients treated with IL-2 alone. The mean increase in T lymphocytes, natural killer cells, and eosinophils was significantly higher in patients treated with IL-2 plus MLT than in those who received IL-2 alone.(ABSTRACT TRUNCATED AT 250 WORDS)

Keywords

Lissoni P, Chilelli M, Villa S et al. **Year** 2003

Authors P. Lissoni, M. Chilelli, S. Villa, L. Cerizza, G. Tancini

Report Name Five years survival in metastatic non-small cell lung cancer patients treated with chemotherapy alone or chemotherapy and melatonin: a randomized trial

Publication J Pineal Res

Issue-page numbers 35:12–15 doi:10.1034/j.1600-079X.2003.00032.x. PMID:12823608

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079X.2003.00032.x/abstract?

Abstract Numerous experimental data have documented the oncostatic properties of melatonin. In addition to its potential direct antitumor activity, melatonin has proved to modulate the effects of cancer chemotherapy, by enhancing its therapeutic efficacy and reducing its toxicity. The increase in chemotherapeutic efficacy by melatonin may depend on two main mechanisms, namely prevention of chemotherapy-induced lymphocyte damage and its antioxidant effect, which has been proved to amplify cytotoxic actions of the chemotherapeutic agents against cancer cells. However, the clinical results available at present with melatonin and chemotherapy in the treatment of human neoplasms are generally limited to the evaluation of 1-year survival in patients with very advanced disease. Thus, the present study was performed to assess the 5-year survival results in metastatic non-small cell lung cancer patients obtained with a chemotherapeutic regimen consisting of cisplatin and etoposide, with or without the concomitant administration of melatonin (20 mg/day orally in the evening). The study included 100 consecutive patients who were randomized to receive chemotherapy alone or chemotherapy and melatonin. Both the overall tumor regression rate and the 5-year survival results were significantly higher in patients concomitantly treated with melatonin. In particular, no patient treated with chemotherapy alone was alive after 2 years, whereas a 5-year survival was achieved in three of 49 (6%) patients treated with chemotherapy and melatonin. Moreover, chemotherapy was better tolerated in patients treated with melatonin. This study confirms, in a considerable number of patients and for a long follow-up period, the possibility to improve the efficacy of chemotherapy in terms of both survival and quality of life by a concomitant administration of melatonin. This suggests a new biochemotherapeutic strateg in the treatment of human neoplasms.

Keywords lung cancer; melatonin; pineal gland

Lissoni P, Marelli O, Mauri R et al. **Year** 1986

Authors Lissoni P, Marelli O, Mauri R et al.

Report Name Ultradian chronomodulation by melatonin of a Placebo effect upon human killer cell activity

Publication Chronobiologia

Issue-page numbers 13:339–343. PMID:3816407

URL http://www.ncbi.nlm.nih.gov/pubmed/3816407

Abstract The effect of melatonin injection evaluated earlier with respect to placebo-treated controls is reevaluated, also with reference to spontaneous changes in natural killer cell activity. This effect consists, first, of stimulation of natural killer cell activity over and above any changes brought about by placebo (saline). After 6 h, the melatonin effect appears to be an inhibition as compared to values from placebo-treated subjects, or no effect as compared to values from untreated subjects. In this case, amplification and attenuation of the placebo effect by melatonin are found within the relatively short span of 1/4 of a day, rather than within a day or a week. An ultradian 'feed-sideward' by melatonin may be aligned with the corresponding previously reported circadian and infradian chronomodulation.

Keywords

Liu B, Zuo Z, Liu H, et al. **Year** 2011

Authors Bin Liu, Zecheng Zuo, Hongtao Liu, Xuanming Liu, Chentao Lin

Report Name Arabidopsis cryptochrome 1 interacts with SPA1 to suppress COP1 activity in response to blue light

Publication Genes & Dev.

Issue-page numbers 2011. 25: 1029-1034 doi: 10.1101/gad.2025011

URL http://genesdev.cshlp.org/content/25/10/1029.short

Abstract Plant photoreceptors mediate light suppression of the E3 ubiquitin ligase COP1 (CONSTITUTIVE PHOTOMORPHOGENIC 1) to affect gene expression and photomorphogenesis. However, how photoreceptors mediate light regulation of COP1 activity remains unknown. We report here that Arabidopsis blue-light receptor cryptochrome 1 (CRY1) undergoes blue-light-dependent interaction with the COP1-interacting protein SPA1 (SUPPRESSOR OF PHYTOCHROME A). We further show that the CRY1–SPA1 interaction suppresses the SPA1–COP1 interaction and COP1-dependent degradation of the transcription factor HY5. These results are consistent with a hypothesis that photoexcited CRY1 interacts with SPA1 to modulate COP1 activity and plant development.

Keywords blue-light receptor, cryptochrome, E3 ubiquitin ligase, protein degradation, photomorphogenesis

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Liu C, Weaver DR, Strogatz SH, Reppert SM **Year** 1997

Authors Liu C, Weaver DR, Strogatz SH, Reppert SM

Report Name Cellular construction of a circadian clock: period determination in the suprachiasmatic nuclei

Publication Cell

Issue-page numbers 91:855–860 doi:10.1016/S0092-8674(00)80473-0. PMID:9413994

URL http://www.sciencedirect.com/science/article/pii/S0092867400804730

Abstract The circadian clock in the suprachiasmatic nuclei is composed of multiple, single-cell circadian oscillators (clock cells). We now test the hypothesis that the circadian period in behavior is determined by the mean period that arises from the coupling of clock cells with diverse circadian periods. For these studies, we monitored firing rate rhythms of individual suprachiasmatic nuclei neurons on fixed multielectrode plates and exploited the altered circadian periods expressed by heterozygous and homozygous tau mutant hamsters. The results show that circadian period in the whole animal is determined by averaging widely dispersed periods of individual clock cells. The data also demonstrate that the tau mutation affects circadian function in a cell-autonomous manner.

Keywords

Authors Liu F, Ng TB, Fung MC

Report Name Pineal indoles stimulate the gene expression of immunomodulating cytokines

Publication J Neural Transm

Issue-page numbers 108:397–405 doi:10.1007/s007020170061. PMID:11475007

URL http://www.springerlink.com/content/au68wr43yqutvkjf/

Abstract Male C57 mice received 10 consecutive daily intraperitoneal injections of melatonin, 5-methoxytryptamine or 5-methoxytryptophol (5 mg/kg body weight). Control mice received the alcoholic saline vehicle. All mice were sacrificed 24 hours after the last injection. Following extraction of RNA from peritoneal exudate cells (PEC) and splenocytes, the level of gene expression was analyzed with the reverse transcription-polymerase chain reaction (RT-PCR). The results revealed that melatonin up-regulated the level of gene expression of transforming growth factor-β (TGF-β), macrophage-colony stimulating factor (M-CSF), tumor necrosis factor-α (TNF-α) and stem cell factor (SCF) in PEC, and the level of gene expression of interleukin-1β (IL-1β), M-CSF, TNF-α, interferon-γ (IFN-γ) and SCF in splenocytes. 5-Methoxytryptamine augmented the level of gene expression of TGF-β, M-CSF and SCF in PEC, and the level of gene expression of IL-1β, TNF-α, IFN-γ, M-CSF and SCF in splenocytes. 5-Methoxytryptophol elevated the level of gene expression of TNF-α, IL-1β, TGF-β and M-CSF in PEC, and the level of gene expression of inducible nitric oxide synthase (iNOS), IL-1β, M-CSF, TNF-α, IFN-γ and SCF in splenocytes.

Keywords Cytokine - pineal indoles - gene expression

Liu JHK, Kripke DF, Hoffman Re, et al. **Year** 1999

Authors John H. K. Liu, Daniel F. Kripke, Rivak E. Hoffman, Michael D. Twa, Richard T. Loving, Katharine M. Rex, Brian L. Lee, Steven L. Mansberger, Robert N. Weinreb

Report Name Elevation of Human Intraocular Pressure at Night under Moderate Illumination

Publication Invest. Ophthalmol. Vis. Sci

Issue-page numbers September 1999 vol. 40 no. 10 2439-2442

URL http://www.iovs.org/content/40/10/2439.short

Abstract

purpose. An endogenous elevation of intraocular pressure (IOP) occurs at night in healthy young adults. The authors studied whether or not this IOP elevation can be detected under moderate illumination.

methods. Twenty-five healthy volunteers, ages 18 to 25 years, were housed overnight in a sleep laboratory under a strictly controlled light–dark environment. Intraocular pressure was measured in the supine position every 2 hours, using a pneumatonometer. An 8-hour sleep period was assigned to each volunteer according to individual's accustomed sleep cycle. In the early part of this assigned period, sleep was encouraged with room lights off. Researchers performed IOP measurements at two time points with the aid of night vision goggles. In the middle to the late part of the assigned period, lights were turned on twice for a 1-hour interval. The light intensity was the same as before the bedtime. At the ending of each light period, IOP was measured under illumination.

results. Average IOP was significantly higher in the assigned sleep period versus outside the period. The trough of mean IOP occurred just before the bedtime, and then IOP gradually increased and peaked at the end of the 8-hour assigned sleep period. The difference between the trough and peak IOP was 3.5 ± 0.7 mm Hg (mean ± SEM, n = 25). Within the assigned sleep period, the average IOP determined under illumination was significantly higher than the average IOP preceding the illumination.

conclusions. Elevation of IOP occurred during the assigned sleep period with two 1-hour light exposures of moderate intensity. Environmental light at night had no significant effect on the nocturnal IOP elevation in healthy young adults.

Keywords

Year 2011

Authors Liu JS, Passaglia CL.

Report Name Spike firing pattern of output neurons of the Limulus circadian clock.

Publication J Biol Rhythms

Issue-page numbers Aug;26(4):335-44.

URL http://www.ncbi.nlm.nih.gov/pubmed/21775292

Abstract

The lateral eyes of the horseshoe crab (Limulus polyphemus) show a daily rhythm in visual sensitivity that is mediated by efferent nerve signals from a circadian clock in the crab's brain. How these signals communicate circadian messages is not known for this or other animals. Here the authors describe in quantitative detail the spike firing pattern of clock output neurons in living horseshoe crabs and discuss its possible significance to clock organization and function. Efferent fiber spike trains were recorded extracellularly for several hours to days, and in some cases, the electroretinogram was simultaneously acquired to monitor eye sensitivity. Statistical features of single- and multifiber recordings were characterized via interval distribution, serial correlation, and power spectral analysis. The authors report that efferent feedback to the eyes has several scales of temporal structure, consisting of multicellular bursts of spikes that group into clusters and packets of clusters that repeat throughout the night and disappear during the day. Except near dusk and dawn, the bursts occur every 1 to 2 sec in clusters of 10 to 30 bursts separated by a minute or two of silence. Within a burst, each output neuron typically fires a single spike with a preferred order, and intervals between bursts and clusters are positively correlated in length. The authors also report that efferent activity is strongly modulated by light at night and that just a brief flash has lasting impact on clock output. The multilayered firing pattern is likely important for driving circadian rhythms in the eye and other targe organs.

Keywords

Liu R, Fu A, Hoffman AE, et al. **Year** 2013

Authors Ran Liu, Alan Fu, Aaron E Hoffman, Tongzhang Zheng and Yong Zhu

Report Name Melatonin enhances DNA repair capacity possibly by affecting genes involved in DNA damage

Publication BMC Cell Biology

Issue-page numbers 2013, 14:1

URL http://www.biomedcentral.com/content/pdf/1471-2121-14-1.pdf

Abstract Background: Melatonin, a hormone-like substance involved in the regulation of the circadian rhythm, has been demonstrated to protect cells against oxidative DNA damage and to inhibit tumorigenesis.
Results: In the current study, we investigated the effect of melatonin on DNA strand breaks using the alkaline DNA comet assay in breast cancer (MCF-7) and colon cancer (HCT-15) cell lines. Our results demonstrated that cells pretreated with melatonin had significantly shorter Olive tail moments compared to non-melatonin treated cells upon mutagen (methyl methanesulfonate, MMS) exposure, indicating an increased DNA repair capacity after melatonin treatment. We further examined the genome-wide gene expression in melatonin pretreated MCF-7 cells upon carcinogen exposure and detected altered expression of many genes involved in multiple DNA damage responsive pathways. Genes exhibiting altered expression were further analyzed for functional interrelatedness using network- and pathway-based bioinformatics analysis. The top functional network was defined as having relevance for “DNA Replication, Recombination, and Repair, Gene Expression, [and] Cancer”.
Conclusions: These findings suggest that melatonin may enhance DNA repair capacity by affecting several key genes involved in DNA damage responsive pathways.

Keywords Melatonin, DNA repair, Comet assay, Genome-wide expression, Network analysis

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Liu X, Uchiyama M, Shibui K et al. **Year** 2000

Authors Liu X, Uchiyama M, Shibui K et al.

Report Name Diurnal preference, sleep habits, circadian sleep propensity and melatonin rhythm in healthy human subjects

Publication Neurosci Lett

Issue-page numbers 280:199–202 doi:10.1016/S0304-3940(00)00793-X. PMID:10675795

URL http://www.sciencedirect.com/science/article/pii/S030439400000793X

Abstract After 24-h sleep deprivation, 33 healthy young subjects entered the 10/20 min ultra-short sleep–wake schedule for 26 h. Melatonin rhythm was hourly assessed simultaneously. Results indicated that morning preference was significantly correlated with habitual sleep onset ($r=-0.41$, $P=0.04$), habitual sleep offset ($r=-0.52$, $P=0.002$), melatonin peak time ($r=-0.36$, $P=0.04$), and sleep propensity onset time ($r=-0.36$, $P=0.04$). The intervals between habitual sleep mid-point and melatonin peak time and between habitual sleep mid-point and sleep propensity onset time were significantly longer in morning-preference subjects than in evening-preference subjects ($P<0.05$). These findings suggest that the variance of diurnal preference may be related to differences in phase relations between habitual sleep timing and the circadian pacemaker.

Keywords Circadian rhythm; Melatonin; Sleep propensity; Morningness; Habitual sleep; Ultra-short sleep–wake schedule

Loane E, Nolan JM, O'Donovan O, et al. ***Year*** 2008

Authors Loane E, Nolan JM, O'Donovan O, Bhosale P, Bernstein PS, Beatty S.

Report Name Transport and retinal capture of lutein and zeaxanthin with reference to age-related macular degeneration

Publication Survey of Ophthalmology

Issue-page numbers Volume 53, Issue 1 , Pages 68-81, January 2008

URL http://www.surveyophthalmol.com/article/S0039-6257%2807%2900255-X/abstract

Abstract Age-related macular degeneration (AMD) is the most common cause of irreversible blindness in the elderly population in the western world. The etiology and pathogenesis of this disease remain unclear. However, there is an increasing body of evidence supporting the hypothesis that the macular pigment carotenoids, lutein and zeaxanthin, play an important role in protection against AMD, by filtering out blue light at a pre-receptoral level, or by quenching free radicals. Lutein and zeaxanthin are dietary xanthophyll carotenoids, which are delivered to the retina via plasma lipoproteins. The biological mechanisms governing retinal capture and accumulation of lutein and zeaxanthin, to the exclusion of other carotenoids, are still poorly understood. Although these mechanisms remain unclear, it is possible that selective capture of these carotenoids is related to lipoprotein, or apolipoprotein, function and profile. Xanthophyll-binding proteins appear to play an important role in the retinal capture of the xanthophyll carotenoids. The Pi isoform of GSTP1 has been isolated as a specific binding protein for zeaxanthin. The binding protein responsible for retinal uptake of lutein remains elusive. This article reviews the literature germane to the mechanisms involved in the capture, accumulation and stabilization of lutein and zeaxanthin by the retina, and the processes involved in their transport in serum.

Keywords

Lockley SW, Arendt J, Skene DJ ***Year*** 2007

Authors Lockley SW, Arendt J, Skene DJ.

Report Name Visual impairment and circadian rhythm disorders

Publication Dialogues Clin Neurosci

Issue-page numbers 2007;9(3):301-14.

URL http://www.ncbi.nlm.nih.gov/pubmed/17969867

Abstract Many aspects of human physiology and behavior are dominated by 24-hour circadian rhythms that have a major impact on our health and well-being, including the sleep-wake cycle, alertness and performance patterns, and many daily hormone profiles. These rhythms are spontaneously generated by an internal "pacemaker" in the hypothalamus, and daily light exposure to the eyes is required to keep these circadian rhythms synchronized both internally and with the external environment. Sighted individuals take this daily synchronization process for granted, although they experience some of the consequences of circadian desynchrony when "jetlagged" or working night shifts. Most blind people with no perception of light, however, experience continual circadian desynchrony through a failure of light information to reach the hypothalamic circadian clock, resulting in cyclical episodes of poor sleep and daytime dysfunction. Daily melatonin administration, which provides a replacement synchronizing daily "time cue, " is a promising therapeutic strategy, although optimal treatment dose and timing remain to be determined.

Keywords

Authors Lockley SW, Brainard GC, Czeisler CA.

Report Name High sensitivity of the human circadian melatonin rhythm to resetting by short wavelength light

Publication J Clin Endocrinol Metab

Issue-page numbers 2003 Sep;88(9):4502-5

URL http://www.ncbi.nlm.nih.gov/pubmed/12970330

Abstract

The endogenous circadian oscillator in mammals, situated in the suprachiasmatic nuclei, receives environmental photic input from specialized subsets of photoreceptive retinal ganglion cells. The human circadian pacemaker is exquisitely sensitive to ocular light exposure, even in some people who are otherwise totally blind. The magnitude of the resetting response to white light depends on the timing, intensity, duration, number and pattern of exposures. We report here that the circadian resetting response in humans, as measured by the pineal melatonin rhythm, is also wavelength dependent. Exposure to 6.5 h of monochromatic light at 460 nm induces a two-fold greater circadian phase delay than 6.5 h of 555 nm monochromatic light of equal photon density. Similarly, 460 nm monochromatic light causes twice the amount of melatonin suppression compared to 555 nm monochromatic light, and is dependent on the duration of exposure in addition to wavelength. These studies demonstrate that the peak of sensitivity of the human circadian pacemaker to light is blue-shifted relative to the three-cone visual photopic system, the sensitivity of which peaks at approximately 555 nm. Thus photopic lux, the standard unit of illuminance, is inappropriate when quantifying the photic drive required to reset the human circadian pacemaker.

Keywords

Authors Steven W. Lockley, Erin E. Evans, Frank A.J.L. Scheer, George C. Brainard, Charles A. Czeisler, Daniel Aeschbach

Report Name Short-Wavelength Sensitivity for the Direct Effects of Light on Alertness, Vigilance, and the Waking Electroencephalogram in Humans

Publication Sleep

Issue-page numbers VOLUME 29, ISSUE 02, 161-8

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=26455

Abstract

Study Objectives:

To assess the wavelength-dependent sensitivity of the acute effects of ocular light exposure on alertness, performance, waking electroencephalogram (EEG), and cortisol.

Design:

A between-subjects design was employed to compare the effects of exposure to 460-nm or 555-nm light for 6.5 hours during the biological night.

Setting:

Intensive Physiological Monitoring Unit, Brigham and Women's Hospital, Boston, MA.

Patients and Participants:

Sixteen healthy adults (8 women; mean age ± SD = 23.3 ± 2.4 years).

Interventions:

Subjects were exposed to equal photon densities (2.8 x 1013 photons• cm-2• s-1) of either 460-nm (n = 8) or 555-nm (n = 8) monochromatic light for 6.5 hours, 15 minutes after mydriasis.

Measurements and Results:

Subjects underwent continuous EEG/electrooculogram recordings and completed a performance battery every 30 to 60 minutes. As compared with those exposed to 555-nm light, subjects exposed to 460-nm light had significantly lower subjective sleepiness ratings, decreased auditory reaction time, fewer attentional failures, decreased EEG power density in the delta-theta range (0.5-5.5 Hz), and increased EEG power density in the high-alpha range (9.5-10.5 Hz). Light had no direct effect on cortisol.

Conclusions:

Short-wavelength sensitivity to the acute alerting effects of light indicates that the visual photopic system is not the primary photoreceptor system mediating these responses to light. The frequency-specific changes in the waking EEG indicate that short-wavelength light is a powerful agent that immediately attenuates the negative effects of both homeostatic sleep pressure and the circadian drive for sleep on alertness, performance, and the ability to sustain attention.

Keywords

Lockley SW, Skene DJ, Arendt J et al. **Year** 1997

Authors Lockley SW, Skene DJ, Arendt J et al.

Report Name Relationship between melatonin rhythms and visual loss in the blind

Publication J Clin Endocrinol Metab

Issue-page numbers 82:3763–3770 doi:10.1210/jc.82.11.3763. PMID:9360538

URL http://jcem.endojournals.org/content/82/11/3763

Abstract Melatonin rhythms were assessed in 49 registered blind individuals by measurement of the urinary metabolite of melatonin, 6-sulfatoxymelatonin (aMT6s). Subjects had different causes of visual loss and were classified as having light perception or better (LP; n = 19) or having no perception of light (NPL; n = 30). Subjects collected four-hourly urine samples (eight-hourly overnight) for 48 h at weekly intervals for 3–5 weeks. The majority of LP subjects (14 of 19) had normally entrained aMT6s rhythms (mean acrophase range, 2.4–6.2 h), 4 were abnormally entrained to 24 h (mean acrophase range, 8.9–1.0 h), and 1 was unclassified. Conversely, most NPL subjects had abnormal rhythms (23 of 30), the incidence of which was greater in uni- and bilaterally enucleated subjects. The majority of NPL subjects (17 of 30) had free-running aMT6s rhythms (period range, 24.13–24.79 h), 5 were abnormally entrained to 24 h (acrophase range, 7.2–20.6 h), and 1 was unclassified. Output (micrograms of aMT6s per 24 h) and amplitude (micrograms per h) of aMT6s production did not vary between LP and NPL subjects (mean 24-h output ± sd, 12.7 ± 7.5 and 9.4 ± 6.4μ g aMT6s/24 h, respectively; mean amplitude ± sd, 0.6 ± 0.4 and 0.5 ± 0.3 μg/h, respectively). These results indicate that a higher proportion of NPL subjects have abnormal melatonin rhythms compared to those with LP.

Keywords

Lockley SW, Skene DJ, James K et al. **Year** 2000

Authors SW Lockley, DJ Skene, K James, K Thapan, J Wright and J Arendt

Report Name Melatonin administration can entrain the free-running circadian system of blind subjects

Publication J Endocrinol

Issue-page numbers 164:R1–R6 doi:10.1677/joe.0.164R001. PMID:10607943

URL http://joe.endocrinology-journals.org/content/164/1/R1.abstract

Abstract Although melatonin treatment has been shown to phase shift human circadian rhythms, it still remains ambiguous as to whether exogenous melatonin can entrain a free-running circadian system. We have studied seven blind male subjects with no light perception who exhibited free-running urinary 6-sulphatoxymelatonin (aMT6s) and cortisol rhythms. In a single-blind design, five subjects received placebo or 5 mg melatonin p.o. daily at 2100 h for a full circadian cycle (35-71 days). The remaining two subjects also received melatonin (35-62 days) but not placebo. Urinary aMT6s and cortisol (n=7) and core body temperature (n=1) were used as phase markers to assess the effects of melatonin on the During melatonin treatment, four of the seven free-running subjects exhibited a shortening of their cortisol circadian period (tau). Three of these had taus which were statistically indistinguishable from entrainment. In contrast, the remaining three subjects continued to free-run during the melatonin treatment at a similar tau as prior to and following treatment. The efficacy of melatonin to entrain the free-running cortisol rhythms appeared to be dependent on the circadian phase at which the melatonin treatment commenced. These results show for the first time that daily melatonin administration can entrain free-running circadian rhythms in some blind subjects assessed using reliable physiological markers of the circadian system.

Keywords

Longcore T, Rich C

Year 2006

Authors Travis Longcore and Catherine Rich

Report Name Ecological Consequences of Artificial Night Lighting

Publication Island Press, Washington DC

Issue-page numbers 458 pp

URL http://www.urbanwildlands.org/ecanlbook.html

Abstract N/A

Keywords

Longcore T, Rich C

Year 2004

Authors Travis Longcore and Catherine Rich

Report Name Ecological light pollution

Publication Front Ecol Environ

Issue-page numbers 2004; 2(4): 191–198

URL http://www.urbanwildlands.org/Resources/LongcoreRich2004.pdf

Abstract In a nutshell:
• Ecological light pollution includes chronic or periodically increased illumination, unexpected changes in illumination, and direct glare
• Animals can experience increased orientation or disorientation from additional illumination and are attracted to or repulsed by glare, which affects foraging, reproduction, communication, and other critical behaviors
• Artificial light disrupts interspecific interactions evolved in natural patterns of light and dark, with serious implications for community ecology

Keywords

Authors Lopez-Gonzalez MA, Calvo JR, Osuna C, Guerrero JM

Report Name Interaction of melatonin with human lymphocytes: evidence for binding sites coupled to potentiation of cyclic AMP stimulated by vasoactive intestinal peptide and activation of cyc

Publication J Pineal Res

Issue-page numbers 12:97–104 doi:10.1111/j.1600-079X.1992.tb00034.x. PMID:1324307

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1992.tb00034.x/abstract

Abstract

Melatonin binding sites were characterized in human blood lymphocytes. The specific binding 2-[125I]iodomelatonin ([125I]MEL) to human lymphocytes was dependent on time and temperature, stability, saturation, and reversibility. Moreover, guanine nucleotides decreased the specific binding of [125I]MEL to crude membranes of human lymphocytes, suggesting the coupling of these binding sites to a guanosine nucleotide binding regulatory protein(s). In competition studies, the specific binding of [125I]MEL to lymphocytes was inhibited by increasing concentrations of native melatonin. Scatchard analysis showed that data were compatible with the existence of two classes of binding sites: a high-affinity site with a Kd of 5.20 ± 0.79 nM and a binding capacity of 50.6 ± 11.0 fmol/107 cells, and a low-affinity site with a Kd of 208.5 ± 50.2 nM and a binding capacity of 2691 ± 265 fmol/107 cells. However, concentration-dependent binding of [125I]MEL to lymphocytes was saturable and resulted in a linear Scatchard plot, suggesting binding to a single class of binding sites. The Kd for the single site was 1.02 ± 0.34 nM with a binding capacity of 10.1 ± 1.6 fmol/107 cells. Their affinities closely correlated with the production of cyclic nucleotides, suggesting a physiological role for the melatonin binding sites. Thus, melatonin potentiated the effect of vasoactive intestinal peptide (VIP) on cyclic AMP production (ED50= 1.9 nM) and stimulated cyclic GMP accumulation (ED50= 125 nM). Results demonstrate the existence of two binding sites for [125I]MEL in human blood lymphocytes, with a high-affinity binding site coupled to the potentiation of the effect of VIP on cyclic AMP production and a low-affinity binding site coupled to activation of cyclic GMP production.

Keywords

Authors Loucks AB, Mortola JF, Girton L, Yen SS

Report Name Alterations in the hypothalamic-pituitary-ovarian and the hypothalamic-pituitary-adrenal axes in athletic women

Publication J Clin Endocrinol Metab

Issue-page numbers 68:402–411 doi:10.1210/jcem-68-2-402. PMID:2537332

URL http://jcem.endojournals.org/content/68/2/402?related-urls=yes&legid=jcem;68/2/402

Abstract

The functional integrity of the hypothalamicpituitary-ovarian and hypothalamic-pituitary-adrenal axes was assessed by determining pulsatile LH, ACTH, and cortisol secretion during the early follicular phase in athletic women with regular menstrual cycles (CA; n = 9), athletic women with amenorrhea (AA; n = 9), and regularly cyclic sedentary women (CS; n = 8). The CA and AA women were not significantly different in body composition, exercise training, psychometric tests, or dietary consumption. The CA women had shorter luteal phases ($P < 0.05$) and lower urinary excretion of pregnanediol glucuronide than the CS women. In the AA women, urinary estrone glucuronide, pregnanediol glucuronide, and LH excretion were low throughout a 30-day period.

The CA women had a 24-h pattern of pulsatile LH secretion characterized by reduced frequency ($P < 0.05$) and increased amplitude ($P < 0.05$), yielding an overall increased 24-h mean level ($P < 0.05$), but interpulse intervals similar to those in the CS women. During sleep, LH pulse frequency slowed in the CS and CA women, while pulse amplitude increased and the mean serum LH level decreased in both groups. The AA women had even fewer pulses ($P < 0.05$) of normal amplitude occurring at much more variable ($P < 0.01$) interpulse intervals. Sleepassociated changes in LH pulsatility were absent. Responses to a 10-μg bolus GnRH dose revealed blunted ($P < 0.05$) FSH release in CA and augmented ($P < 0.05$) LH release in AA women.

The groups did not differ in any 24-h ACTH pulse pattern parameter or in cortisol pulse frequencies. Yet, early morning (0200–0800 h) serum cortisol levels were higher ($P < 0.05$) in both groups of athletes, and this elevation was extended through the day (0800–2000 h; $P < 0.001$) and evening (2000–0200 h; $P < 0.05$) in the AA women. The plasma ACTH and serum cortisol responses to bolus human CRH administration were blunted in the CA and AA women [change from baseline (Δ) in ACTH, $P < 0.05$ and $P < 0.01$; Δ cortisol, $P < 0.01$ and $P < 0.01$, respectively], but adrenal sensitivity (Δ cortisol/Δ ACTH ratio) was increased ($P < 0.05$). The plasma ACTH and serum cortisol responses to meals also were blunted in the athletic groups ($P < 0.05$).

These results indicate that the degree to which the hypothalamic-pituitary-adrenal axis is disturbed in cyclic and amenorrheic athletes is associated, perhaps causally, with their hypothalamic-pituitary-ovarian axis abnormalities.

Keywords

Lovenberg W, Jequier E, Sjoerdsma A **Year** 1967

Authors Lovenberg W, Jequier E, Sjoerdsma A

Report Name Tryptophan hydroxylation: measurement in pineal gland, brainstem, and carcinoid tumor

Publication Science

Issue-page numbers 155:217–219 doi:10.1126/science.155.3759.217. PMID:6015530

URL http://www.sciencemag.org/content/155/3759/217.short

Abstract Development of a rapid and sensitive radioassay has permitted study of the conversion of tryptophan to 5-hydroxytryptophan in mammalian tissues. Of normal tissues examined, beef and rat pineal gland contained the highest activity. This is the first direct demonstration of tryptophan hydroxylase in this hydroxyindole-rich tissue. Rat and rabbit brainstem and human carcinoid tumor also had quantities of enzyme that could be measured easily. The reaction requires a reduced pteridine and oxygen and is inhibired by Para-Chorophenylalanine.

Keywords

Lowden A, Åkerstedt T **Year** 2012

Authors Arne Lowden and Torbjörn Åkerstedt

Report Name Assessment of a New Dynamic Light Regimen in a Nuclear Power Control Room Without Windows on Quickly Rotating Shiftworkers—Effects on Health, Wakefulness, and Circa

Publication

Issue-page numbers Vol. 29, No. 5 , Pages 641-649 (doi:10.3109/07420528.2012.675850)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2012.675850

Abstract The aim of the study was to test whether a new dynamic light regime would improve alertness, sleep, and adaptation to rotating shiftwork. The illumination level in a control room without windows at a nuclear power station was 200 lux (straight-forward horizontal gaze) using a weak yellow light of 200 lux, 3000 K (Philips Master TLD 36 W 830). New lighting equipment was installed in one area of the control room above the positions of the reactor operators. The new lights were shielded from the control group by a distance of >6 m, and the other operators worked at desks turned away from the new light. The new lights were designed to give three different light exposures: (i) white/blue strong light of 745 lux, 6000 K; (ii) weak yellow light of 650 lux, 4000 K; and (iii) yellow moderate light of 700 lux, 4000 K. In a crossover design, the normal and new light exposures were given during a sequence of three night shifts, two free days, two morning shifts, and one afternoon shift (NNN + MMA), with 7 wks between sessions. The operators consisted of two groups; seven reactor operators from seven work teams were at one time exposed to the new equipment and 16 other operators were used as controls. The study was conducted during winter with reduced opportunities of daylight exposure during work, after night work, or before morning work. Operators wore actigraphs, filled in a sleep/wake diary, including ratings of sleepiness on the Karolinska Sleepiness Scale (KSS) every 2 h, and provided saliva samples for analysis of melatonin at work (every 2nd h during one night shift and first 3 h during one morning shift). Results from the wake/sleep diary showed the new light treatment increased alertness during the 2nd night shift (interaction group × light × time, $p < .01$). Time of waking was delayed in the light condition after the 3rd night shift (group × light, $p < .05$), but the amount of wake time during the sleep span increased after the 2nd night shift ($p < .05$), also showing a tendency to affect sleep efficiency ($p < .10$). Effects on circadian phase were difficult to establish given the small sample size and infrequent sampling of saliva melatonin. Nonetheless, it seems that appropriate dynamic light in rooms without windows during the dark Nordic season may promote alertness, sleep, and better adaptation to quickly rotating shiftwork.

Keywords Circadian rhythms, Melatonin, Night work, Sleep, Sleepiness, Work light condition

Authors Luboshitzky R, Lavi S, Thuma I, Lavie P

Report Name Testosterone treatment alters melatonin concentrations in male patients with gonadotropin-releasing hormone deficiency

Publication J Clin Endocrinol Metab

Issue-page numbers 81:770–774 doi:10.1210/jc.81.2.770. PMID:8636302

URL http://jcem.endojournals.org/content/81/2/770.short

Abstract

Recently, we demonstrated that melatonin secretion is increased in untreated male patients with GnRH deficiency. As testosterone (T) can be aromatized to estradiol (E2), and both T and E2 increase during T enanthate treatment, we were interested in determining whether T treatment (when T and E2 levels were well matched with pubertal control values) has an effect on melatonin levels in these patients. We measured nocturnal serum melatonin levels during the administration of 250 mg testosterone enantale/month for 4 months in 12 male patients with idiopathic hypogonadotropic hypogonadism (IGD; n = 6) and delayed puberty (DP; n = 6). Serum samples for melatonin and LH determinations were obtained every 15 min from 1900-0700 h in a controlled light-dark environment. The results of melatonin profiles were compared with the pretreatment values in each group and with values obtained in six normal pubertal male controls. After 4 months of testosterone treatment, all patients attained normal serum testosterone (19.5 +/- 3.7 in IGD vs. 20.8 +/- 4.1 nmol/L in DP) and E2 levels (83 +/- 12 in IGD vs. 84 +/- 9 pmol/L in DP). Serum LH levels were suppressed in all patients during T treatment (0.12 +/- 0.1 in IGD vs. 0.12 +/- 0.2 IU/L in DP). Before T treatment, patient melatonin levels were greater than those in age-matched pubertal controls. Melatonin levels were equal in patients and controls when T and E2 levels were well matched. Mean (+/- SD) dark-time melatonin levels decreased from 286 +/- 23 to 157 +/- 36 pmol/L in IGD and from 217 +/- 32 to 133 +/- 47 pmol/L in DP (vs. 183 +/- 64 pmol/L in controls). The integrated melatonin values decreased to normal (from 184 +/- 16 to 102 +/- 21 in IGD and from 142 +/- 19 to 90 +/- 26 pmol/min.L x 10(3) in DP vs. 119 +/- 61 pmol/min.L x 10(3) in controls). The intraindividual variations in melatonin levels ranged from 7.2-14.5%. These data indicate that male patients with GnRH deficiency have increased nocturnal melatonin secretion. T treatment decreased melatonin secretion to normal levels. The results suggest that in GnRH-deficient male patients, sex steroids, rather than LH, modulate pineal melatonin in a reverse fashion.

Keywords

Luboshitzky R, Lavi S, Thuma I, Lavie P **Year** 1995

Authors Luboshitzky R, Lavi S, Thuma I, Lavie P

Report Name Increased nocturnal melatonin secretion in male patients with hypogonadotropic hypogonadism and delayed puberty

Publication J Clin Endocrinol Metab

Issue-page numbers 80:2144–2148 doi:10.1210/jc.80.7.2144. PMID:7608268

URL http://jcem.endojournals.org/content/80/7/2144.short

Abstract Hypogonadotropic hypogonadism (IGD) and constitutional delayed puberty (DP) share a common pathophysiologic process, i.e. GnRH deficiency. Both conditions are heterogenous and exhibit different grades of GnRH deficiency. To discern whether these disorders of GnRH deficiency are associated with altered melatonin secretion profiles, we compared untreated young males IGD (n = 7) and DP (n = 7) to normal pubertal male controls (n = 6). Serum samples for melatonin, LH, and prolactin concentrations were obtained every 15 min from 1900 h to 0700 h in a controlled light-dark environment with simultaneous sleep recordings. Mean (+/- SD) darktime nocturnal melatonin levels were significantly higher in IGD (259 +/- 73 pmol/L) and DP (217 +/- 29 pmol/L) compared with 182 +/- 69 pmol/L in controls ($P < 0.02$). So were the mean (+/- SD) peak melatonin levels (410 +/- 117, 327 +/- 97 and 298 +/- 95 pmol/L in IGD, DP, and controls, respectively ($P < 0.05$). Integrated nocturnal melatonin secretion values (AUC) were also higher in IGD and DP (168 +/- 45 and 134 +/- 28) compared with 119 +/- 45 pmol/min.1 x 10(3) in controls ($P < 0.02$). The time of melatonin peak and the time of onset of the nocturnal melatonin rise were observed earlier in IGD and DP. Light-time mean (+/- SD) serum melatonin levels were similar in all three groups. No correlations were found between melatonin and LH levels, nor between melatonin and prolactin levels. These data indicate that melatonin secretion is increased in male patients with GnRH deficiency. The lack of correlations between melatonin and LH suggest that circulating sex steroids, rather than LH, modulate melatonin secretion in a reverse fashion.

Keywords

Luboshitzky R, Levi M, Shen-Orr Z et al. **Year** 2000

Authors Luboshitzky R, Levi M, Shen-Orr Z et al.

Report Name Long-term melatonin administration does not alter pituitary-gonadal hormone secretion in normal men

Publication Hum Reprod

Issue-page numbers 15:60–65 doi:10.1093/humrep/15.1.60. PMID:10611189

URL http://humrep.oxfordjournals.org/content/15/1/60.full

Abstract The role of melatonin in the regulation of reproduction in humans is still controversial. In the present study the effects of melatonin were examined, 6 mg given orally every day at 1700 h for 1 month in a double-blind, placebo controlled fashion, on the nocturnal secretory profiles of luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone and inhibin β in six healthy adult men. Serum concentrations of LH, FSH, testosterone and inhibin β were determined before and after treatment every 15 min from 1900 to 0700 h over 3 nights in a controlled dark-light environment with simultaneous polysomnographic sleep recordings. The following sleep parameters were determined: total recording time, sleep latency, actual sleep time, sleep efficiency, rapid eye movement (REM) sleep latency and percentages of sleep stages 2, 3/4 and REM. There were no statistically significant differences in all sleep parameters between baseline and placebo or between baseline and melatonin except for longer REM latency and lower percentage REM at baseline than under melatonin treatment. These are explained as reflecting first-night effect at baseline. The mean nocturnal LH, FSH, testosterone and inhibin β integrated nocturnal secretion values did not change during the treatment period. Likewise, their pulsatile characteristics during melatonin treatment were not different from baseline values. Taken together, these data suggest that long-term melatonin administration does not alter the secretory patterns of reproductive hormones in normal men.

Keywords follicle-stimulating hormone, β inhibin, luteinizing hormone, melatonin, testosterone

Authors Luboshitzky R, Wagner O, Lavi S et al.

Report Name Decreased nocturnal melatonin secretion in patients with Klinefelter's syndrome

Publication Clin Endocrinol (Oxf)

Issue-page numbers 45:749–754 doi:10.1046/j.1365-2265.1996.8710881.x. PMID:9039342

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2265.1996.8710881.x/abstract?

Abstract

OBJECTIVE We have recently demonstrated that GnRH deficient male patients have increased nocturnal melatonin secretion which decreases to normal levels during testosterone treatment. The results suggested that sex steroids, rather than LH, modulate pineal melatonin in an inverse fashion. The purpose of this study was to characterize circulating melatonin levels in untreated males with hypergonadotrophic hypogonadism due to Klinefelter's syndrome (KS).

DESIGNS Prospective, controlled.

SUBJECTS Eleven patients with Klinefelter's syndrome and seven controls. Patients were subdivided into two groups: (1) with low testosterone, and (2) with normal testosterone levels.

MEASUREMENTS Serum samples for melatonin concentrations were obtained every 15 minutes from 1900 to 0700 h in a controlled light–dark environment.

RESULTS All patients had elevated FSH, LH and oestradiol (E2) levels. Mean (±SD) dark time nocturnal melatonin levels were significantly lower in low testosterone KS (92±19 pmol/l) compared with 146±42 pmol/l in normal testosterone KS and 179±59 pmol/l in controls ($P<0.02$). A similar pattern was observed for the mean (±SD) peak melatonin levels (165±41, 236±59 and 293±89 pmol/l) in low testosterone KS, normal testosterone KS and controls, respectively ($P<0.01$). Integrated nocturnal melatonin secretion values (AUC) were also lower in low testosterone KS (64±13) compared with 96±26 in normal testosterone KS and 116±39 pmol/min l×103 in controls ($P<0.02$).

The time of melatonin peak and the time of the nocturnal melatonin rise as well as the light-time mean (±SD) serum melatonin levels were similar in all three groups.

No correlations were found between melatonin and LH, FSH, or E2 levels.

CONCLUSIONS Melatonin secretion is decreased in male patients with low testosterone hypergonadotrophic hypogonadism whereas in normal testosterone Klinefelter's syndrome patients, melatonin secretory profiles are normal.

The results suggest that the suppression of melatonin secretion in these patients is mediated by GnRH (either directly or indirectly) and/or oestradiol.

Keywords

Lucas RJ, Douglas RH, Foster RG

Year 2001

Authors Robert J. Lucas, Ronald H. Douglas & Russell G. Foster

Report Name Characterization of an ocular photopigment capable of driving pupillary constriction in mice

Publication Nature Neuroscience

Issue-page numbers 4, 621 - 626 (2001) doi:10.1038/88443

URL http://www.nature.com/neuro/journal/v4/n6/full/nn0601_621.html

Abstract This work demonstrates that transgenic mice lacking both rod and cone photoreceptors (rd/rd cl) retain a pupillary light reflex (PLR) that does not rely on local iris photoreceptors. These data, combined with previous reports that rodless and coneless mice show circadian and pineal responses to light, suggest that multiple non-image-forming light responses use non-rod, non-cone ocular photoreceptors in mice. An action spectrum for the PLR in rd/rd cl mice demonstrates that over the range 420–625 nm, this response is driven by a single opsin/vitamin A-based photopigment with peak sensitivity around 479 nm (opsin photopigment/OP479). These data represent the first functional characterization of a non-rod, non-cone photoreceptive system in the mammalian CNS.

Keywords

Lucas RJ, Freedman MS, Lupi D et al.

Year 2001

Authors Lucas RJ, Freedman MS, Lupi D et al.

Report Name Identifying the photoreceptive inputs to the mammalian circadian system using transgenic and retinally degenerate mice

Publication Behav Brain Res

Issue-page numbers 125:97–102 doi:10.1016/S0166-4328(01)00274-1. PMID:11682100

URL http://www.sciencedirect.com/science/article/pii/S0166432801002741

Abstract The endogenous circadian clock of mammals retains synchrony with the external light:dark cycle through ocular photoreceptors. To date the identity of the photoreceptors responsible for mediating this response is unknown. This review outlines attempts using transgenic mouse models to address this deficit. Mice bearing specific inherited lesions of both rod and cone photoreceptors retain circadian photosensitivity as assessed by photoentrainment of behavioural rhythms and the light-induced suppression of pineal melatonin. These findings indicate that as yet unidentified non-rod, non-cone ocular photoreceptors are capable of contributing to circadian light responses. Nevertheless, the possibility that circadian photosensitivity is the responsibility of multiple photoreceptor classes including both rod/cone and novel photopigments remains. There is some indirect evidence in favour of this hypothesis. A definitive resolution of this issue is likely to employ comparisons of circadian action spectra in wild type and retinally degenerate mice.

Keywords Mice; Circadian rhythms; Photoentrainment; Retina; Photoreceptors; Light; Pineal

Lucas RJ, Freedman MS, Muñoz M et al. **Year** 1999

Authors Robert J. Lucas, Melanie S. Freedman, Marta Muñoz, José-M. Garcia-Fernández and Russell G. Foster

Report Name Regulation of the mammalian pineal by non-rod, non-cone, ocular photoreceptors

Publication Science

Issue-page numbers 284:505–507 doi:10.1126/science.284.5413.505. PMID:10205062

URL http://www.sciencemag.org/content/284/5413/505.abstract

Abstract In mammals, ocular photoreceptors mediate an acute inhibition of pineal melatonin by light. The effect of rod and cone loss on this response was assessed by combining the rd mutation with a transgenic ablation of cones (cl) to produce mice lacking both photoreceptor classes. Despite the loss of all known retinal photoreceptors, rd/rd cl mice showed normal suppression of pineal melatonin in response to monochromatic light of wavelength 509 nanometers. These data indicate that mammals have additional ocular photoreceptors that they use in the regulation of temporal physiology.

Keywords

Lucey DR, Clerici M, Shearer GM **Year** 1996

Authors Lucey DR, Clerici M, Shearer GM

Report Name Type 1 and type 2 cytokine dysregulation in human infectious, neoplastic, and inflammatory diseases

Publication Clin Microbiol Rev

Issue-page numbers 9:532–562. PMID:8894351

URL http://cmr.asm.org/cgi/content/short/9/4/532

Abstract In the mid-1980s, Mosmann, Coffman, and their colleagues discovered that murine CD4+ helper T-cell clones could be distinguished by the cytokines they synthesized. The isolation of human Th1 and Th2 clones by Romagnani and coworkers in the early 1990s has led to a large number of reports on the effects of Th1 and Th2 on the human immune system. More recently, cells other than CD4+ T cells, including CD8+ T cells, monocytes, NK cells, B cells, eosinophils, mast cells, basophils, and other cells, have beer shown to be capable of producing "Th1" and "Th2" cytokines. In this review, we examine the literature on human diseases, using the nomenclature of type 1 (Th1-like) and type 2 (Th2-like) cytokines, which includes all cell types producing these cytokines rather than only CD4+ T cells. Type 1 cytokines include interleukin-2 (IL-2), gamma interferon, IL-12 and tumor necrosis factor beta, while type 2 cytokines include IL-4, IL-5, IL-6, IL-10, and IL-13. In general, type 1 cytokines favor the development of a strong cellular immune response whereas type 2 cytokines favor a strong humoral immune response. Some of these type 1 and type 2 cytokines are cross- regulatory. For example, gamma interferon and IL-12 decrease the levels of type 2 cytokines whereas IL-4 and IL-10 decrease the levels of type 1 cytokines. We use this cytokine perspective to examine human diseases including infections due to viruses, bacteria, parasites, and fungi, as well as selected neoplastic, atopic, rheumatologic, autoimmune, and idiopathic-inflammatory conditions. Clinically, type 1 cytokine- predominant responses should be suspected in any delayed-type hypersensitivity-like granulomatous reactions and in infections with intracellular pathogens, whereas conditions involving hypergammaglobulinemia, increased immunoglobulin E levels, and/or eosinophilia are suggestive of type 2 cytokine-predominant conditions. If this immunologic concept is relevant to human diseases, the potential exists for novel cytokine-based therapies and novel cytokine- directed preventive vaccines for such diseases.

Keywords

Authors Lurie SJ, Gawinski B, Pierce D, Rousseau SJ.

Report Name Seasonal affective disorder

Publication Am Fam Physician

Issue-page numbers 2006 Nov 1;74(9):1521-4.

URL http://www.ncbi.nlm.nih.gov/pubmed/17111890

Abstract Patients with seasonal affective disorder have episodes of major depression that tend to recur during specific times of the year, usually in winter. Like major depression, seasonal affective disorder probably is underdiagnosed in primary care settings. Although several screening instruments are available, such screening is unlikely to lead to improved outcomes without personalized and detailed attention to individual symptoms. Physicians should be aware of comorbid factors that could signal a need for further assessment. Specifically, some emerging evidence suggests that seasonal affective disorder may be associated with alcoholism and attention-deficit/hyperactivity disorder. Seasonal affective disorder often can be treated with light therapy, which appears to have a low risk of adverse effects. Light therapy is more effective if administered in the morning. It remains unclear whether light is equivalent to drug therapy, whether drug therapy can augment the effects of light therapy, or whether cognitive behavior therapy is a better treatment choice.

Keywords

Authors Luthra R, Nemesure BB, Wu SY, Xie SH, Leske MC;

Report Name Frequency and risk factors for pterygium in the Barbados Eye Study

Publication Arch Ophthalmol

Issue-page numbers 2001;119:1827-1832.

URL http://archopht.ama-assn.org/cgi/content/abstract/119/12/1827

Abstract

Objective To describe the distribution and risk factors for pterygium in the predominantly black population of the Barbados Eye Study, which was based on a random sample of Barbadian-born citizens between the ages of 40 and 84 years.

Methods The standardized protocol included ophthalmic and other measurements, automated perimetry, lens gradings, fundus photography, and a detailed interview. A 10% systematic sample of participants and those meeting specific criteria also received a comprehensive ophthalmologic evaluation.

Results The Barbados Eye Study included 4709 participants, of whom 2978 were referred for an ophthalmologic evaluation and 2781 (93%) completed the examination. Cases of pterygium were found among 23.4% of 2617 black, 23.7% of 97 mixed (black and white), and 10.2% of 59 white participants examined. In addition to African ancestry, logistic regression analyses indicated a positive association between pterygium and age (odds ratio [OR], 1.01; 95% confidence interval [CI], 1.00-1.02), fewer years of education (OR, 1.43; 95% CI, 1.01-2.03), and an outdoor job location (OR, 1.87; 95% CI, 1.52-2.29). Having a darker skin complexion (OR, 0.66; 95% CI, 0.52-0.83), always using sunglasses outdoors (OR, 0.18; 95% CI, 0.06-0.59), and the use of prescription glasses (OR, 0.75; 95% CI, 0.60-0.93) were protective factors.

Conclusions Approximately one quarter of the black participants examined had pterygia, a frequency that was 2.5 to 3 times higher than among whites in the Barbados Eye Study and elsewhere. Pterygium was almost twice as frequent among persons who worked outdoors but was only one fifth as likely among those who always used sunglasses outdoors. Educational interventions to modify these potential exposures may assist in preventing pterygium.

Keywords

Authors Lynch HJ, Ho M, Wurtman RJ

Report Name The adrenal medulla may mediate the increase in pineal melatonin synthesis induced by stress, but not that caused by exposure to darkness

Publication J Neural Transm

Issue-page numbers 40:87–97 doi:10.1007/BF01250561. PMID:192851

URL http://www.springerlink.com/content/v2461364056652k1/

Abstract

As previously shown (Lynch et al.: Proc. Nat. Acad. Sci. [U.S.A.]70, 1704–1707 [1973]), the activity of the enzyme serotonin-N-acetyltransferase (NAT) in the rat pineal increases when the animal is placed in darkness or is subjected to the stress of physical immobilization; partial sympathetic denervation (i.e., pretreatment of the animal with intravenous 6-hydroxydopamine [6-OHDA]) does not block either response. The present studies explored the roles of the pineal sympathetic nerves and the adrenal medullas in mediating these responses. The stress-induced increase in pineal NAT activity was blocked by bilateral adrenalectomy, but not by bilateral superior cervical ganglionectomy or by treatment with 6-OHDA (both of which potentiate the NAT response in normal rats and restore it in adrenalectomized ones). The increase in pineal melatonin content caused by immobilization was also blocked by adrenalectomy, but potentiated by pineal sympathetic denervation. In contrast, bilateral adrenalectomy did not affect the darkness-induced rise in pineal NAT activity, although pineal sympathetic denervation (by bilateral superior cervical ganglionectomy) did block this response. 6-OHDA pretreatment neither blocked the response to darkness nor restored it in ganglionectomized animals; thus, this treatment apparently fails to produce a complete pineal denervation. The pineal response to stress has previously been shown to be blocked bybeta-adrenergic blocking agents. The present studies demonstrate thatagr-adrenergic blockade (with phenoxybenzamine) potentiates this response in intact animals and restores it in adrenalectomized rats (possibly by acting presynaptically on receptors on pineal sympathetic terminals and thereby augmenting norepinephrine release). These observations show that the rat pineal organ normally receives information from two ldquochannelsrdquo,i.e., trans-synaptically (from pineal sympathetic nerves) and via the circulation (from the adrenal medullas and, perhaps, from distant sympathetic nerves).

Keywords

Lynge E

Year 1996

Authors Lynge E

Report Name Risk of breast cancer is also increased among Danish female airline cabin attendants

Publication BMJ

Issue-page numbers 312:253. PMID:8563615

URL http://www.bmj.com/content/312/7025/253.1.full

Abstract EDITOR,—Eero Pukkala and colleagues report the incidence of cancer among a cohort of Finnish airline cabin attendants.1 Women made up the overwhelming majority of the cohort, and they were found to have an excess risk of cancer of the breast (number of cases observed, 20; standardised incidence ratio 1.87 (95% confidence interval 1.15 to 2.23)). Excess risks were also found for cancer of the bone and leukaemia, on the basis of only two cases of each of these diseases.

In Denmark the incidence of cancer has been monitored for 17 years for the cohort of participants in the 1970 census.2 The standardised incidence ratio was calculated for each occupational group on the basis of the incidence for all economically active people. In 1970, 915 women were registered as airline cabin attendants in Denmark, while 362 men were registered as cabin attendants and 620 men as pilots. Table I shows the Danish data for the three types of cancer found in excess among the Finnish workers. The standardised incidence ratio for breast cancer in the Danish female cabin attendants is 1.61 (0.9 to 2.7), while that in all women in social class I is 1.40. The Danish data thus support the Finnish observation that the risk of breast cancer in female airline cabin attendants is higher than that for their social class.

Keywords

Lytle CD, Cyr WH, Beer JZ, et al.

Year 1993

Authors Lytle CD, Cyr WH, Beer JZ, Miller SA, James RH, Landry RJ, Jacobs ME, Kaczmarek RG, Sharkness CM, Gaylor D, et al.

Report Name An estimation of squamous cell carcinoma risk from ultraviolet radiation emitted by fluorescent lamps

Publication Photodermatol Photoimmunol Photomed

Issue-page numbers 1992-1993 Dec;9(6):268-74.

URL http://www.ncbi.nlm.nih.gov/pubmed/1343229

Abstract The risk of squamous cell carcinoma (SCC) from ultraviolet radiation (UV) emitted by unfiltered fluorescent lamps was assessed. The assessment employed a mathematical power model based on human epidemiological data, which relates the SCC incidence in the United States white population to ambient solar UV. The annual numbers of new SCC on anatomical sites chronically exposed to solar UV (head/face/neck and hands) were estimated for indoor workers. Then the number of SCC that may be caused by additional UV exposure from indoor fluorescent lighting was estimated: the lifetime exposure of indoor workers to typical fluorescent lighting (if unfiltered) may add 3.9% (1.6-12%) to the risk from solar UV, resulting in the induction of an additional 1500 (600-4500) SCC per annum in the United States. This calculated projection must be compared with the 110,000 SCC caused by solar exposure. Thus, this analysis suggests there may be a small increased risk of SCC from exposure to UV-emitting fluorescent lamps.

Keywords

Lyytimäkia J, Tapiob P, Assmuth T

Year 2011

Authors Jari Lyytimäkia, Petri Tapiob, Timo Assmuth

Report Name Unawareness in environmental protection: The case of light pollution from traffic

Publication Land Use Policy

Issue-page numbers In Press, Corrected Proof - Note to users doi:10.1016/j.landusepol.2011.10.002 |

URL http://www.sciencedirect.com/science/article/pii/S0264837711001165

Abstract New information is often emphasized as a basis of effective and scientifically sound environmental policy and management. However, outdated or incorrect information is not automatically nor instantly replaced by new insights. This article focuses on the various ways environmental information can be unintentionally left with insufficient attention or purposefully neglected. Energy-related emissions caused by road traffic in Finland are used as an illustrative example and light pollution caused by artificial lighting is identified as an emerging issue that has gained especially low recognition in the environmental agenda. Four different reasons for this lack of recognition are discussed: recognized unawareness, false awareness, deliberate unawareness and concealed awareness. Paying attention to light pollution is important because of various ecological, socio-cultural and economic effects but also because implementing measures aimed for reducing light pollution create possibilities for alleviating other social and environmental problems in transport and land use policies.
Highlights

► Light pollution from artificial lighting is a widespread environmental change affecting most areas of industrialized world. ► It can have serious ecological, health and economic consequences. ► Light pollution has not been recognized as a key environmental problem. ► Acknowledging the problem is required in order to decrease the extent and intensity of harmful light pollution.

Keywords Energy; Environment; Recognition; Risk; Road traffic; Light pollution

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Ma D, Li S, Molusky MM, Lin JD

Year 2012

Authors Di Ma, Siming Li, Matthew M. Molusky, Jiandie D. Lin

Report Name Circadian autophagy rhythm: a link between clock and metabolism?

Publication Trends in Endocrinology & Metabolism

Issue-page numbers Available online 18 April 2012

URL http://www.sciencedirect.com/science/article/pii/S1043276012000483

Abstract Nutrient and energy metabolism in mammals exhibits a strong diurnal rhythm that aligns with the body clock. Circadian regulation of metabolism is mediated through reciprocal signaling between the clock and metabolic regulatory networks. Recent work has demonstrated that autophagy is rhythmically activated in a clock-dependent manner. Because autophagy is a conserved biological process that contributes to nutrient and cellular homeostasis, its cyclic induction may provide a novel link between clock and metabolism. This review discusses the mechanisms underlying circadian autophagy regulation, the role of rhythmic autophagy in nutrient and energy metabolism, and its implications in physiology and metabolic disease.

Keywords

Maaskanta M, van de Wouwa E, van Wijckb R, et al. ***Year*** 2013

Authors Marijke Maaskanta, Ellen van de Wouwa, Ruud van Wijckb, Heleen M. Evenhuisa, Michael A. Echtelda

Report Name Circadian sleep–wake rhythm of older adults with intellectual disabilities

Publication Research in Developmental Disabilities

Issue-page numbers Volume 34, Issue 4, April 2013, Pages 1144–1151

URL http://www.sciencedirect.com/science/article/pii/S0891422212003290

Abstract

The circadian sleep–wake rhythm changes with aging, resulting in a more fragmented sleep–wake pattern. In individuals with intellectual disabilities (ID), brain structures regulating the sleep–wake rhythm might be affected. The aims of this study were to compare the sleep–wake rhythm of older adults with ID to that of older adults in the general population, and to investigate which factors are associated with the sleep–wake rhythm in older adults with ID.

This study is part of the 'Healthy Aging and Intellectual Disabilities' study (HA-ID). We applied actigraphy in 551 persons with ID and 58 persons in the general population, aged 50 years and over. Outcome measures were stability (interdaily stability), fragmentation (intradaily variability) and amplitude (relative amplitude) of the sleep–wake rhythm.

Compared to older adults in the general population, the sleep–wake rhythm of older adults with ID was significantly less stable ($p = 0.03$), more fragmented ($p < 0.001$) and had a lower relative amplitude ($p < 0.001$). Multivariate regression analysis revealed that higher age, dementia, depression, visual impairment, severe hearing impairment, epilepsy and spasticity are independently associated with a more disturbed sleep–wake rhythm in this group. The sleep–wake rhythm is more stable in females and those living at a setting for more intensive care. Higher physical activity levels are strongly associated with both a less fragmented ($p < 0.001$) and a more stable ($p < 0.001$) sleep–wake rhythm. Higher age, dementia and depression are also associated with the sleep–wake rhythm in the general population. Neurological and sensory impairments that were associated with the sleep–wake rhythm in older adults with ID, are frequent known conditions in the ID population. Further research should focus on which factors specifically influence the sleep–wake rhythm in older adults with ID, and on the effects of more physical daytime activity on the sleep–wake rhythm in this population.

Keywords

MacMahon B, Cole P, Brown J ***Year*** 1973

Authors MacMahon B, Cole P, Brown J

Report Name Etiology of human breast cancer: a review

Publication Natl Cancer Inst

Issue-page numbers 50:21–42. PMID:4571238

URL http://ukpmc.ac.uk/abstract/MED/4571238

Abstract N/A

Keywords

MacMahon B, Cole P, Lin TM et al. **Year** 1970

Authors MacMahon B, Cole P, Lin TM et al.

Report Name Age at first birth and breast cancer risk

Publication Bull World Health Organ

Issue-page numbers 43:209–221. PMID:5312521

URL http://www.ncbi.nlm.nih.gov/pubmed/5312521

Abstract An international collaborative study of breast cancer and reproductive experience has been carried out in 7 areas of the world. In all areas studied, a striking relation between age at first birth and breast cancer risk was observed. It is estimated that women having their first child when aged under 18 years have only about one-third the breast cancer risk of those whose first birth is delayed until the age of 35 years or more. Births after the first, even if they occur at an early age, have no, or very little, protective effect. The reduced risk of breast cancer in women having their first child at an early age explains the previously observed inverse relationship between total parity and breast cancer risk, since women having their first birth early tend to become ultimately of high parity. The association with age at first birth requires different kinds of etiological hypotheses from those that have been invoked in the past to explain the association between breast cancer risk and reproductive experience.

Keywords

Madokoro S, Nakagawa H, Misaki K et al. **Year** 1997

Authors Madokoro S, Nakagawa H, Misaki K et al.

Report Name Nocturnal melatonin profiles before and one year after beginning shift-work

Publication Psychiatry Clin Neurosci

Issue-page numbers 51:17–22 doi:10.1111/j.1440-1819.1997.tb02360.x. PMID:9076855

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1440-1819.1997.tb02360.x/pdf

Abstract Nocturnal serum melatonin profiles were determined twice for seven single women, during their time of employment as nurses (baseline), and after one year (follow up), in order to investigate the effects of shift-work on. nocturnal melatonin secretion. All subjects were working in the same hospital under an irregularly rotating three-shift system. Five (5) mL blood samples were drawn six times at 2 h intervals between 2O:OO-06:OO hours under dim light conditions (< 50 lux). The same sampling procedures were repeated the following year. The results showed pronounced inter-individual differences in melatonin concentrations. There was a trend towards increasing maximum melatonin concentration (MAX melatonin) at follow up, with a similar tendency seen in summed melatonin (the sum of six measured melatonin concentrations). A trend was also seen towards increasing melatonin ratio at 06:OO hours (the percentage of melatonin concentration at 06:OO hours by summed melatonin) at follow up. Melatonin concentration at 06:OO hours was significantly higher at follow up, and a significant correlation between Morningness-Eveningness score (M-E score) at baseline and increased summed melatonin at follow up was also seen. These results suggest that: nocturnal melatonin secretion does not significantly increase after beginning shift-work; and that greater increases in melatonin secretion at follow up are found in subjects with higher M-E scones (increased morning type). With more subjects, however, there may be significant increase in MAX melatonin and/or summed melatonin in the follow-up study.

Keywords

Madronich S, de Gruijl FR **Year** 199

Authors Madronich S, de Gruijl FR.

Report Name Skin cancer and UV radiation

Publication Nature

Issue-page numbers 366, 23 (04 November 1993); doi:10.1038/366023a0

URL http://www.nature.com/nature/journal/v366/n6450/abs/366023a0.html

Abstract N/A

Keywords

Authors Akiko Maeda, Tadao Maeda, Marcin Golczak, Steven Chou, Amar Desai, Charles L. Hoppel, Shigemi Matsuyama and Krzysztof Palczewski

Report Name Involvement of all-trans-retinal in acute light-induced retinopathy of mice

Publication The Journal of Biological Chemistry

Issue-page numbers 284, 15173-15183.

URL http://www.jbc.org/content/284/22/15173.abstract

Abstract

Exposure to bright light can cause visual dysfunction and retinal photoreceptor damage in humans and experimental animals, but the mechanism(s) remain unclear. We investigated whether the retinoid cycle (i.e. the series of biochemical reactions required for vision through continuous generation of 11-cis-retinal and clearance of all-trans-retinal, respectively) might be involved. Previously, we reported that mice lacking two enzymes responsible for clearing all-trans-retinal, namely photoreceptor-specific ABCA4 (ATP-binding cassette transporter 4) and RDH8 (retinol dehydrogenase 8), manifested retinal abnormalities exacerbated by light and associated with accumulation of diretinoid-pyridinium-ethanolamine (A2E), a condensation product of all-trans-retinal and a surrogate marker for toxic retinoids. Now we show that these mice develop an acute, light-induced retinopathy. However, cross-breeding these animals with lecithin:retinol acyltransferase knock-out mice lacking retinoids within the eye produced progeny that did not exhibit such light-induced retinopathy until gavaged with the artificial chromophore, 9-cis-retinal. No significant ocular accumulation of A2E occurred under these conditions. These results indicate that this acute light-induced retinopathy requires the presence of free all-trans-retinal and not, as generally believed, A2E or other retinoid condensation products. Evidence is presented that the mechanism of toxicity may include plasma membrane permeability and mitochondrial poisoning that lead to caspase activation and mitochondria-associated cell death. These findings further understanding of the mechanisms involved in light-induced retinal degeneration.

Keywords

Maestroni GJ

Year 2001

Authors Maestroni GJ

Report Name The immunotherapeutic potential of melatonin

Publication Expert Opin Investig Drugs

Issue-page numbers 10:467–476 doi:10.1517/13543784.10.3.467. PMID:11227046

URL http://informahealthcare.com/doi/abs/10.1517/13543784.10.3.467

Abstract

The interaction between the brain and the immune system is essential for the adaptive response of an organism against environmental challenges. In this context, the pineal neurohormone melatonin (MEL) plays an important role. T-helper cells express G-protein coupled cell membrane MEL receptors and, perhaps, MEL nuclear receptors. Activation of MEL receptors enhances the release of T-helper cell Type 1 (Th1) cytokines, such as γ-interferon (γ-IFN) and IL-2, as well as of novel opioid cytokines. MEL has been reported also to enhance the production of IL-1, IL-6 and IL-12 in human monocytes. These mediators may counteract stress-induced immunodepression and other secondary immunodeficiences and protect mice against lethal viral encephalitis, bacterial diseases and septic shock. Therefore, MEL has interesting immunotherapeutic potential in both viral and bacterial infections. MEL may also influence haemopoiesis either by stimulating haemopoietic cytokines, including opioids, or by directly affecting specific progenitor cells such as pre-B cells, monocytes and NK cells. MEL may thus be used to stimulate the immune response during viral and bacterial infections as well as to strengthen the immune reactivity as a prophylactic procedure. In both mice and cancer patients, the haemopoietic effect of MEL may diminish the toxicity associated with common chemotherapeutic protocols. Through its pro-inflammatory action, MEL may play an adverse role in autoimmune diseases. Rheumatoid arthritis patients have increased nocturnal plasma levels of MEL and their synovial macrophages respond to MEL with an increased production of IL-12 and nitric oxide (NO). In these patients, inhibition of MEL synthesis or use of MEL antagonists might have a therapeutic effect. In other diseases such as multiple sclerosis the role of MEL is controversial. However, the correct therapeutic use of MEL or MEL antagonists should be based on a complete understanding of their mechanism of action. It is not yet clear whether MEL acts only on Th1 cells or also on T-helper Type 2 cells (Th2). This is an important point as the Th1/Th2 balance is of crucial importance in the immune system homeostasis. Furthermore, MEL being the endocrine messenger of darkness, its endogenous synthesis depends on the photoperiod and shows seasonal variations. Similarly, the pharmacological effects of MEL might also be season-dependent. No information is available concerning this point. Therefore, studies are needed to investigate whether the immunotherapeutic effect of MEL changes with the alternating seasons.

Keywords

Maestroni GJ, Conti A **Year** 1996

Authors Maestroni GJ, Conti A

Report Name Melatonin and the immune-hematopoietic system therapeutic and adverse pharmacological correlates

Publication Neuroimmunomodulation

Issue-page numbers 3:325–332 doi:10.1159/000097292. PMID:9266542

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=97292

Abstract The pineal neurohormone melatonin functionally synchronizes the photoper-iod in the organism. In the last decade, it has become increasingly clear that the pineal gland and melatonin also play an important immunoregulatory role. T helper (Th) cells bear G-protein-coupled melatonin receptors. Activation of melatonin receptors enhances the release of Th cell cytokines, such as γ-interferon and interleukin-2, as well as novel opioid cytokines which cross-react immunologically with both interleukin-4 and dynorphin B. These mediators may counteract secondary immunodeficiencies, protect mice against lethal viral and bacterial diseases, synergize with interleukin-2 in cancer patients and affect hematopoiesis. Hematopoiesis is apparently influenced by the action of melatonin-induced opioids on κ-opioid receptors present on stromal bone marrow cells. Most interestingly, γ-interferon and colony-stimulating factors may modulate the production of melatonin in the pineal gland. A hypothetical pineal-immune-hematopoietic network is, therefore, taking shape. From the immunopharmacological point of view, there is a need for clinical studies on the effect of melatonin in human immunodeficiency-viruis-infected patients and cancer patients. In conclusion, melatonin seems to be an important immunomodulatory hormone which deserves to be further studied to identify its relevance in immune-based diseases, its therapeutic indications and its adverse effects.

Keywords Melatonin, Melatonin receptors, T helper cells, Immunopharmacology, Viral diseases, Secondary immunodeficiency

Maestroni GJ, Conti A, Pierpaoli W **Year** 1986

Authors Maestroni GJ, Conti A, Pierpaoli W

Report Name Role of the pineal gland in immunity. Circadian synthesis and release of melatonin modulates the antibody response and antagonizes the immunosuppressive effect of corticoste

Publication J Neuroimmunol

Issue-page numbers 13:19–30 doi:10.1016/0165-5728(86)90047-0. PMID:2944914

URL http://www.sciencedirect.com/science/article/pii/0165572886900470

Abstract Inhibition of synthesis of the pineal neurohormone melatonin (MEL) in mice, by administration of propranolol (PRO) in the evening, and daily injections of p-chlorophenylalanine (PCPA), resulted in a significant depression of the primary antibody response to sheep red blood cells (SRBC). Spleen cells from these mice showed a reduced reactivity against antigens in the autologous mixed lymphocyte reaction (AMLR). In contrast, alloreactivity remained normal. Reconstitution of the night-time peak of plasma MEL by evening injections to the mice completely reversed the suppression of the humoral response and the AMLR. MEL administration was able to antagonize the depression of antibody production induced by corticosterone in vivo. These results suggest that the pineal gland has important immunomodulatory functions through its cyclic, circadian release of MEL.

Keywords Antibody production; Corticosterone antagonism; Melatonin; Pharmacologic pinealectomy; Pineal gland

Maestroni GJ, Conti A, Pierpaoli W **Year** 1988

Authors Maestroni GJ, Conti A, Pierpaoli W

Report Name Role of the pineal gland in immunity. III. Melatonin antagonizes the immunosuppressive effect of acute stress via an opiatergic mechanism

Publication Immunology

Issue-page numbers 63:465–469. PMID:3350581

URL http://www.ncbi.nlm.nih.gov/pubmed/3350581

Abstract We have recently demonstrated that the pineal neurohormone melatonin exerts important immunoregulatory functions. We now report that exogenous melatonin counteracts completely the effect of acute anxiety-restraint stress on thymus weight and antibody response to sheep red blood cells (SRBC). In addition, administration of melatonin in the evening prevented paralysis and death of mice infected with sublethal doses of encephalomyocarditis virus (EMCV) after acute stress. The anti-stress activity of melatonin was present in mice injected with T-dependent antigens, and it was abolished by the contemporary administration of the specific opioid-antagonist naltrexone. This suggests that melatonin exerts its remarkable anti-stress effect on antigen-activated cells via an opiatergic mechanism. These findings have important implications at both basic and clinical levels. They provide a new approach to a possible physiological 'up-regulation' of the immune response under virus- and/or stress-related immunosuppression.

Keywords

Maestroni GJ, Conti A, Pierpaoli W **Year** 1988

Authors Maestroni GJ, Conti A, Pierpaoli W

Report Name Pineal melatonin, its fundamental immunoregulatory role in aging and cancer

Publication Ann N Y Acad Sci

Issue-page numbers 521 1 Neuroimmunomo;140–148 doi:10.1111/j.1749-6632.1988.tb35272.x. PMID:3377360

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1988.tb35272.x/abstract

Abstract N/A

Keywords

Magri F, Locatelli M, Balza G et al. **Year** 1997

Authors Magri F, Locatelli M, Balza G et al.

Report Name Changes in endocrine circadian rhythms as markers of physiological and pathological brain aging

Publication Chronobiol Int

Issue-page numbers 14:385–396 doi:10.3109/07420529709001459. PMID:9262874

URL http://informahealthcare.com/doi/abs/10.3109/07420529709001459

Abstract We studied the circadian rhythm of plasma melatonin, growth hormone (GH), prolactin (PRL), adrenocorticotropic hormone (ACTH), and Cortisol in 52 mentally healthy old subjects, 35 old demented patients, and 22 clinically healthy young controls. When compared to young controls, the circadian profile of plasma melatonin of old subjects, both demented or not, was clearly flattened, particularly during the night. The selective impairment of nocturnal melatonin secretion was significantly related to both the age and the severity of mental impairment (Mini Mental State Examination [MMSE] score). The PRL and GH circadian profiles were similar in the three groups during the day, but a significant lowering of the values recorded during the night occurred with aging. The impairment of the nocturnal secretion was related to the subjects' age and, for the GH secretory pattern only, also to the MMSE score. The ACTH circadian profile was similar in the three groups studied, even when old subjects exhibited higher ACTH levels throughout the 24h cycle, compared to young controls. Significantly higher Cortisol values at evening- and nighttime occurred in elderly subjects and particularly in the demented group. Both the mean levels and the nadir values of plasma Cortisol were positively related to age and negatively to MMSE score. In order to verify the sensitivity of the hypothalamo-pituitary-adrenal (HPA) axis to the steroid feedback, the circadian profile of plasma Cortisol was evaluated also after dexamethasone (DXM) administration (1 mg at 23:00h); the sensitivity of the HPA axis was significantly impaired in old subjects and particularly in the demented ones. These findings suggest that the neuroendocrine alterations already present in physiological aging, due to both anatomical damages and unbalanced central neurotransmitters, are enhanced in senile dementia.

Keywords

Mahoney MM. **Year** 2010

Authors Mahoney MM.

Report Name Shift work, jet lag, and female reproduction

Publication International Journal of Endocrinology

Issue-page numbers Volume 2010, Article ID 813764, 9 pages doi:10.1155/2010/813764

URL http://downloads.hindawi.com/journals/ije/2010/813764.pdf

Abstract Circadian rhythms and “clock gene” expression are involved in successful reproductive cycles, mating, and pregnancy. Alterations or disruptions of biological rhythms, as commonly occurs in shift work, jet lag, sleep deprivation, or clock gene knock out models, are linked to significant disruptions in reproductive function. These impairments include altered hormonal secretion patterns, reduced conception rates, increased miscarriage rates and an increased risk of breast cancer. Female health may be particularly susceptible to the impact of desynchronizing work schedules as perturbed hormonal rhythms can further influence the expression patterns of clock genes. Estrogen modifies clock gene expression in the uterus, ovaries, and suprachiasmatic nucleus, the site of the primary circadian clock mechanism. Further work investigating clock genes, light exposure, ovarian hormones, and reproductive function will be critical for indentifying how these factors interact to impact health and susceptibility to disease.

Keywords

Mainster MA, Turner PL

Year 2009

Authors Martin A. Mainster, Patricia L. Turner

Report Name Blue-blocking IOLs decrease photoreception without providing significant photoprotection

Publication Survey of Ophthalmology

Issue-page numbers Volume 55, Issue 3 , Pages 272-283, May 2010

URL http://www.surveyophthalmol.com/article/S0039-6257%2809%2900205-7/abstract

Abstract Violet and blue light are responsible for 45% of scotopic, 67% of melanopsin, 83% of human circadian (melatonin suppression) and 94% of S-cone photoreception in pseudophakic eyes (isoilluminance source). Yellow chromophores in blue-blocking intraocular lenses (IOLs) eliminate between 43 and 57% of violet and blue light between 400 and 500 nm, depending on their dioptric power. This restriction adversely affects pseudophakic photopic luminance contrast, photopic S-cone foveal threshold, mesopic contrast acuity, scotopic short-wavelength sensitivity and circadian photoreception. Yellow IOL chromophores provide no tangible clinical benefits in exchange for the photoreception losses they cause. They fail to decrease disability glare or improve contrast sensitivity. Most epidemiological evidence shows that environmental light exposure and cataract surgery are not significant risk factors for the progression of age-related macular degeneration (AMD). Thus, the use of blue-blocking IOLs is not evidence-based medicine. Most AMD occurs in phakic adults over 60 years of age, despite crystalline lens photoprotection far greater than that of blue-blocking IOLs. Therefore, if light does play some role in the pathogenesis of AMD, then 1) senescent crystalline lenses do not prevent it, so neither can blue-blocking IOLs that offer far less photoprotection, and 2) all pseudophakes should wear sunglasses in bright environments. Pseudophakes have the freedom to remove their sunglasses for optimal photoreception whenever they choose to do so, provided that they are not encumbered permanently by yellow IOL chromophores. In essence, yellow chromophores are placebos for prevention of AMD that permanently restrict a pseudophake's dim light and circadian photoreception at ages when they are needed most. If yellow IOLs had been the standard of care, then colorless UV-blocking IOLs could be advocated now as “premium” IOLs because they offer dim light and circadian photoreception roughly 15–20 years more youthful than blue-blocking IOLs.

Keywords blue light, cell culture, circadian photoreception, intraocular lens, macular degeneration, melanoma, melanopsin, melatonin,

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Makkison I, Arendt J

Year 1991

Authors Makkison I, Arendt J

Report Name Melatonin secretion in humans on two different antarctic bases (68° and 75°S)

Publication J Interdiscipl Cycle Res

Issue-page numbers 22:149–150

URL N/A

Abstract N/A

Keywords

Malpaux B, Migaud M, Tricoire H, Chemineau P **Year** 2001

Authors Malpaux B, Migaud M, Tricoire H, Chemineau P

Report Name Biology of mammalian photoperiodism and the critical role of the pineal gland and melatonin

Publication J Biol Rhythms

Issue-page numbers 16:336–347 doi:10.1177/074873001129002051. PMID:11506379

URL http://jbr.sagepub.com/content/16/4/336.short

Abstract In mammals, photoperiodic information is transformed into a melatonin secretory rhythm in the pineal gland (high levels at night, low levels during the day). Melatonin exerts its effects in discrete hypothalamic areas, most likely through MT1 melatonin receptors. Whether melatonin is brought to the hypothalamus from the cerebrospinal fluid or the blood is still unclear. The final action of this indoleamine at the level of the central nervous system is a modulation of GnRH secretion but it does not act directly on GnRH neurones; rather, its action involves a complex neural circuit of interneurones that includes at least dopaminergic, serotoninergic and aminoacidergic neurones. In addition, this network appears to undergo morphological changes between seasons.

Keywords melatonin, photoperiod, mammals, rhythm, reproduction

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Mansfield CM, Carabasi RA, Wells W, Borman K **Year** 1973

Authors Mansfield CM, Carabasi RA, Wells W, Borman K

Report Name Circadian rhythm in the skin temperature of normal and cancerous breasts

Publication Int J Chronobiol

Issue-page numbers 1:235–243. PMID:4776534

URL http://www.ncbi.nlm.nih.gov/pubmed/4776534

Abstract N/A

Keywords

Authors Marcheva B, Ramsey KM, Buhr ED, Kobayashi Y, Su H, Ko CH, Ivanova G, Omura C, Mo S, Vitaterna MH, Lopez JP, Philipson LH, Bradfield CA, Crosby SD, JeBailey L, Wang

Report Name Disruption of the clock components CLOCK and BMAL1 leads to hypoinsulinaemia and diabetes

Publication Nature

Issue-page numbers 466:627–31. doi: 10.1038/nature09253

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2920067/

Abstract

The molecular clock maintains energy constancy by producing circadian oscillations of rate-limiting enzymes involved in tissue metabolism across the day and night1–3. During periods of feeding, pancreatic islets secrete insulin to maintain glucose homeostasis, and while rhythmic control of insulin release is recognized to be dysregulated in humans with diabetes4, it is not known how the circadian clock may affect this process. Here we show that pancreatic islets possess self-sustained circadian gene and protein oscillations of the transcription factors CLOCK and BMAL1. The phase of oscillation of islet genes involved in growth, glucose metabolism, and insulin signaling is delayed in circadian mutant mice, and both Clock5,6 and Bmal17 mutants exhibit impaired glucose tolerance, reduced insulin secretion, and defects in size and proliferation of pancreatic islets that worsen with age. Clock disruption leads to transcriptome-wide alterations in the expression of islet genes involved in growth, survival, and synaptic vesicle assembly. Remarkably, conditional ablation of the pancreatic clock causes diabetes mellitus due to defective β-cell function at the very latest stage of stimulus-secretion coupling. These results demonstrate a role for the β-cell clock in coordinating insulin secretion with the sleep-wake cycle, and reveal that ablation of the pancreatic clock can trigger onset of diabetes mellitus.

Keywords diabetes, hypoinsulinemia

Margrain TH, Boulton M, Marshall J, Sliney DH

Year 2004

Authors Margrain TH, Boulton M, Marshall J, Sliney DH.

Report Name Do blue light filters confer protection against age related macular degeneration?

Publication Prog Retin Eye Res

Issue-page numbers 2004 Sep;23(5):523-31.

URL http://www.ncbi.nlm.nih.gov/pubmed/15302349

Abstract Age-related macular degeneration (AMD) is a major health problem in the developed world accounting for approximately half of all blind registrations. Current treatment options are unsuitable for the majority of patients and therefore the identification of modifiable risk factors that may inform disease prevention programmes is a priority. This review evaluates the long-held belief that blue light exposure has a role in the pathogenesis of AMD. Laboratory evidence has demonstrated that photochemical reactions in the oxygen-rich environment of the outer retina lead to the liberation of cytotoxic reactive oxygen species (ROS). These ROS cause oxidative stress which is known to contribute to the development of AMD. The precise chromopore that may be involved in the pathogenesis of AMD is unclear but the age pigment lipofuscin is a likely candidate. Its aerobic photoreactivity and adverse effects on antioxidant activity combined with its gradual accumulation over time suggests that its in vivo phototoxicity increases with age despite changes in the absorption characteristics of the crystalline lens. Evidence from animal studies confirms blue light's damaging potential but the results are not directly applicable to macular degeneration in humans. Studies of human macular pigment density and the risk of AMD progression following cataract surgery lend further weight to the hypothesis that blue light exposure has a role in the pathogenesis of AMD but the epidemiological evidence is equivocal. On balance the evidences suggests but does not yet confirm that blue light is a risk factor for AMD. Given the socio-economic impact of this disease and urgent need to identify modifiable risk factors, future work should include a large-scale clinical trial to evaluate the effect of blue blocking filters on AMD progression rates.

Keywords

Markey SP, Higa S, Shih M et al.

Year 1985

Authors Markey SP, Higa S, Shih M et al.

Report Name The correlation between human plasma melatonin levels and urinary 6-hydroxymelatonin excretion

Publication Clin Chim Acta

Issue-page numbers 150:221–225 doi:10.1016/0009-8981(85)90247-5. PMID:4064329

URL http://www.mendeley.com/research/the-correlation-between-human-plasma-melatonin-levels-and-urinary-6hydroxymelatonin-excretion/

Abstract A significant correlation (0.76) has been found between nighttime peak plasma melatonin levels and the 24-h urinary excretion totals for conjugated 6-hydroxymelatonin for a group of 22 women. This study validates the comparison of plasma levels of the hormone or urinary levels of its metabolite to assess pineal gland production of melatonin in humans.

Keywords

Marko PB, Miljković J, Gorenjak M, et al.

Year 2007

Authors P B Marko, J Miljković, M Gorenjak, P Povalej, A Kansky

Report Name Erythropoietic protophorphyria patients in Slovenia

Publication Acta Dermatovenerologica Alpina Panonica Et Adriatica

Issue-page numbers Volume: 16, Issue: 3, Pages: 99-102, 104

URL http://www.mendeley.com/research/erythropoietic-protoporphyria-patients-slovenia/

Abstract BACKGROUND: There are only scarce epidemiological data on the prevalence of erythropoietic protoporphyria (EPP) in a given population. The aim of this study was to assess the prevalence of EPP within the Slovenian population. MATERIALS AND METHODS: The patients were selected by routine examination of photosensitive patients and by studying hospital records. A quantitative spectrophotometric method was used to assess protoporphyrin, with values larger than 530 nm/l considered elevated. RESULTS: 32 EPP patients were detected, which allows us to estimate the prevalence of EPP in Slovenia at 1.75 per 100,000 inhabitants.

Keywords

Marshall WJ, Sliney DH

Year 1997

Authors Wesley J Marshall and David H Sliney

Report Name Transient visual effects and laser safety standards

Publication J. Radiol. Prot.

Issue-page numbers 17 229 doi:10.1088/0952-4746/17/4/001

URL http://iopscience.iop.org/0952-4746/17/4/001

Abstract

Laser Maximum Permissible Exposure (MPE) limits for the human eye are designed to protect against biological damage and permanent visual impairment [1 - 3]. However, in some instances transient visual impairment may result from viewing visible laser light, and these temporary visual effects may pose potential secondary safety hazards. This potential problem has long been recognized [3]; however, only in recent years has there been a wide recognition that it must be addressed with new types of laser safety standards [4]. Incidents of both accidental and intentional direct exposure of persons by laser pointers, the exposure of audiences at laser light shows (Corder et al, this issue, page 231), and even the accidental exposures of airline pilots at night by laser light-show beams have produced not only complaints, but allegations of eye injuries [5, 6]. Because individuals exposed to a bright light are frequently concerned about potential eye injury, they self-examine their vision and may detect a pre-existing visual deficit that may be misinterpreted by an eye-care practitioner to be laser-related [7].

Partly because of these growing concerns, the American National Standards Institute Accredited Committee Z136 on the Safe Use of Lasers was prompted to form a new subgroup (W Marshall, Chair) to draft a standard on the `Safe Use of Lasers in the Outdoors'. A draft standard (ANSI Z136.6) is currently in preparation [4].

Transient visual effects are quite subjective and difficult to quantify. These effects may have more dramatic results if experienced by the observer under totally unexpected conditions. Generally, there are about four effects of concern: disability (dazzle or `veiling') glare, discomfort glare, startle (distraction), and after-images (flash blindness). Discomfort and disability glare are the visual effects familiar to anyone who drives at night and encounters the high-beam headlights of an oncoming vehicle; it is difficult or even discomforting to see near the light source. Startle is difficult to quantify, but if one is performing a task requiring great concentration, e.g. landing an aeroplane, a sudden flash of a coloured light can pose a severe distraction. After-images produced by a flash of light can be most disconcerting at night as the after-image can last for a number of seconds and make it difficult to see clearly through the after-image. Because of the importance of these phenomena to pilots, the US Federal Aviation Administration (FAA) updated its laser safety guidance (FAA Order 7400.2D) two years ago to reduce pilots' exposure to laser light-show beams.

These beams were previously limited to the MPE in the airspace. Now, the permitted nighttime exposure has been lowered, with the level depending upon how close to an airport (a flight zone), the laser light show would be. The flight zone very close to the actual runway was labelled `laser free.' Other flight zones near an airport were labeled `critical', the zone further away, the `sensitive flight zone', and the general airspace, the `normal flight zone'. Working in consonance with the FAA, the US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH), which regulates laser light-show operators, placed a moratorium on casino laser light shows in Las Vegas, NV, where interference with aviation had been a particular problem.

The light levels which produce transient effects such as glare and dazzle are strongly dependent upon the ambient light level. In the dark a very weak beam can be quite dazzling, whereas in daylight the same light level can be totally inconsequential. For example, the MPE for momentary, unintentional, 0.25 s intrabeam viewing of a CW visible laser (e.g. argon, krypton or He - Ne) is 2.5 mW cm-2; however, a level of only 0.1% of this irradiance can appear quite bright and even somewhat dazzling in daylight, and very disturbing at night. Light levels less than even 1 μW cm-2 can be very dazzling at night.

The emphasis in laser eye safety has recently shifted from being solely concerned about permanent effects to a more balanced approach in the US. Complaints of visual disturbances have prompted the development of specialized standards for outdoor laser use. One can anticipate that this approach will find its way into the international arena as well.

Keywords

Marte B

Year 2005

Authors Marte B

Report Name Cell division and cancer

Publication Nature

Issue-page numbers 432:293–295 doi:10.1038/432293a

URL http://www.nature.com/nature/insights/7015.html

Abstract

The development of cancer can be viewed as an evolutionary process. Cells are constantly subject to mutations in their DNA which are usually detrimental to the cell. But occasionally these changes produce cells that can escape the normal constraints and flourish as pathological tumours.

Cancer cells are selected for their ability to divide when they shouldn't, trigger their own blood supply to support unlimited expansion, and invade the bloodstream and other tissues to form fatal metastases. Changes in the cell-cycle and apoptotic machineries, or in the signalling pathways that control them allow cancer cells to escape the normal control of cell proliferation and cell death.

There is also a growing recognition that changes in the microenvironment of cancer cells can promote their proliferation. Moreover, genomic instability caused by faulty cell division or defective DNA repair may increase the rate of potentially tumorigenic mutations and so contribute to cancer evolution.

Cancer is a complex disease. Enormous heterogeneity in the genetic changes and the context in which they affect cancer development and progression makes it difficult to design effective treatments. Understanding and exploiting these complexities holds promise for more effective therapies in the future. Moreover, the notion that tumour maintenance critically depends on a small subset of cells with stem-cell-like behaviour may mean that a cancer cure ultimately has to target these cells.

Paradoxically, the altered cellular networks of molecular pathways that sustain cancer cell growth and make them resistant to certain therapies may offer new targets for therapy. Critical signalling junctions may exist that are more important for the survival of cancerous than normal cells.

We hope the articles in this Insight capture the excitement and promise of this rapidly advancing field. We are grateful to the authors for their contributions and to the reviewers for their valuable input.

Keywords

Martikainen H, Tapanainen J, Vakkuri O et al. ***Year*** 1985

Authors Martikainen H, Tapanainen J, Vakkuri O et al.

Report Name Circannual concentrations of melatonin, gonadotrophins, prolactin and gonadal steroids in males in a geographical area with a large annual variation in daylight

Publication Acta Endocrinol (Copenh)

Issue-page numbers 109:446–450. PMID:3929512

URL http://www.eje.org/content/109/4/446.short

Abstract Abstract. This study was aimed at elucidating the possible effects of a large annual variation in photoperiodicity on the secretory activities of the pineal gland, pituitary and testes. Serum daytime melatonin, FSH, LH, prolactin (Prl), testosterone and oestradiol concentrations were determined monthly over a year in 24 healthy young adult men (except for melatonin which was analysed only in 11 subjects) in northern Finland, where the day length is 22 h in mid-summer and 3.5 h in midwinter.

Serum daytime melatonin levels showed two annual peak values, in December and May, and a nadir was observed in August. The absolute values of the other hormones measured did not show significant month to month variation over the observation period. When hormone levels were calculated as percentages of the individual annual means, several significant differences were found between monthly levels. The melatonin peak in May (133 ±20%, se, of the annual mean) was associated with significant increases in LH (110 ±4%) and FSH (107 ± 3%). Prl levels (115 ± 9%) reached a maximum in January. The nadirs of melatonin and the pituitary hormones measured were seen in August. Oestradiol showed the highest values in April-June, but no significant variation was found in serum testosterone levels. Positive correlations were observed between FSH and LH ($r = 0.41$, $P < 0.01$), and Prl and LH ($r = 0.26$, $P < 0.01$), whereas Prl and testosterone ($r = -0.17$, $P < 0.01$) were inversely correlated.

This study indicates circannual rhythmicity of peripheral serum daytime melatonin, gonadotrophin, Prl and oestradiol levels, but this variation was not related to extremes in daylight and therefore seasonal factors other than light may regulate this circannual variation.

Keywords

Martin JE, Klein DC ***Year*** 1976

Authors Martin JE, Klein DC

Report Name Melatonin inhibition of the neonatal pituitary response to luteinizing hormone-releasing factor

Publication Science

Issue-page numbers 191:301–302 doi:10.1126/science.1108199. PMID:1108199

URL http://www.sciencemag.org/content/191/4224/301.short

Abstract Neonatal rat anterior pituitary glands treated in organ culture with 1 nanomolar luteinzing hormone-releasing factor (LRF) showed a tenfold increase in medium luteinizing hormone (LH) concentrations over control values. Simultaneous treatment of the glands with 1 nanomolar melatonin significantly reduced the stimulatory effect of LRF on release of LH. This finding indicates that melatonin can act directly on the neonatal pituitary to inhibit the LH response to LRF.

Keywords

Authors Martin JE, McKellar S, Klein DC

Report Name Melatonin inhibition of the in vivo pituitary response to luteinizing hormone-releasing hormone in the neonatal rat

Publication Neuroendocrinology

Issue-page numbers 31:13–17 doi:10.1159/000123044. PMID:6993981

URL http://www.ncbi.nlm.nih.gov/pubmed/6993981

Abstract

The effects of melatonin on the in vivo pituitary LH response to LH-releasing hormone (LHRH) were examined in neonatal male and female rats, in 35- to 44-day-old male rats, and in 35- to 44-day-old male animals which had been either pinealectomized or maintained in constant light for at least 3 weeks before use. Animals were given saline or melatonin (1--100 micrograms/rat) followed within 30 sec by saline or LHRH (10--1,000 ng/rat) at separate subcutaneous sites. Blood was collected following decapitation either without prior injection or 15, 30, 45, or 60 min afterwards. Serum LH concentrations were determined by double antibody radioimmunoassay. In neonatal male and female rats, melatonin (1 microgram) significantly (p less than 0.01) suppressed by approximately 65% serum LH at 15 min after LHRH. Suppression was maintained for at least 60 min, a finding which indicates that melatonin blocks rather than delays the response to LHRH. By contrast, in normal, pinealectomized, and constant light older male rats, melatonin (100 micrograms) had no detectable effect on either the magnitude or the time course of LH release by LHRH. These data extend our previous in vitro findings by demonstrating that melatonin is a potent inhibitor of the in vivo pituitary response to LHRH in neonatal rats but not in older animals. Neither pinealectomy nor constant light, both of which are assumed to reduce pineal melatonin production, for at least 3 weeks before use restores neonatal pituitary responsiveness to the pineal indole in the older animals.

Keywords

Martin JE, Sattler C **Year** 1982

Authors Martin JE, Sattler C

Report Name Selectivity of melatonin pituitary inhibition for luteinizing hormone-releasing hormone

Publication Neuroendocrinology

Issue-page numbers 34:112–116 doi:10.1159/000123287. PMID:6122168

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=123287

Abstract The pineal indole melatonin suppresses the neonatal rat luteinizing hormone (LH) and follicle-stimulating hormone (FSH) responses to LH-releasing hormone (LHRH), as shown in previous studies from this laboratory. We show in this study that the melatonin inhibition is a selective effect and is not due to general inhibition of pituitary function. The effects of the indole on the responses to thyrotropin-releasing hormone (TRH) and somatostatin (SRIF) and on basal pituitary hormone secretion were examined with cells in culture. Neonatal rat anterior pituitary cells dissociated with collage-nase and hyaluronidase were cultured overnight and distributed to 35-mm dishes at the time of use. For examination of melatonin effects on the response to releasing hormones, the cells were incubated for 3 h in control medium or medium containing LHRH (10–9-10–6M), TRH (10–10-10–6M), or SRIF (10–9-10–6M), either alone or in the presence of melatonin (10–8 or 10–6M). For examination of basal hormone secretion, the cells were incubated for 1.5, 3, 6, 15, or 24 h in either medium alone or medium containing melatonin (10–6M). Medium and cell lysate concentrations of LH, FSH, thyroid-stimulating hormone (TSH), prolactin (PRL) and growth hormone (GH) were determined by double antibody RIA. As previously, melatonin (10–8M) significantly suppressed LH and FSH release by all concentrations of LHRH. This concentration of the indole produced maximal suppression of both LH and FSH responses to LHRH.By contrast, melatonin at a 100-fold greater concentration (10–6M) had no effect on TRH stimulation of TSH or PRL release or on SRIF inhibition of GH release. Similarly, melatonin had no effect on basal release of TSH, PRL, or GH at the times examined. These findings show that melatonin inhibition of the gonadotroph response to LHRH is a selective effect.

Keywords Melatonin, Luteinizing hormone-releasing hormone, Luteinizing hormone, Follicle-stimulating hormone, Pituitary, Pineal, Thyrotropin-releasing hormone

Martin-Cacao A, Lopez-Gonzalez MA, Calvo JR, et al. **Year** 1995

Authors Alejandro Martin-Cacao, M. A. Lopez-Gonzalez, Juan R. Calvo, Mirta Giordano and Juan M. Guerrero

Report Name Diurnal Variations in [125I]Melatonin Binding by Rat Thymus Membranes: Effects of Continuous Light Exposure and Pinealectomy

Publication Chronobiology International

Issue-page numbers 12:6, 382-388

URL http://informahealthcare.com/doi/abs/10.3109/07420529509057287

Abstract Binding of melatonin by rat thymus membranes exhibited diurnal changes. Binding increased during the daytime and reached maximal values before entering the dark period. Then, binding decreased rapidly during the dark phase. In rats kept in light at night, binding of [125I]melatonin by membranes was significantly higher than in animals that entered the normal dark period. Neonatal pinealectomy, which suppresses the circadian rhythm of melatonin, led to an increase in melatonin binding of 106%. Moreover, in animals maintained under continuous light exposure, which corresponds to functional pinealectomy, binding of melatonin by thymus membranes also increased in a time-dependent manner. The results support the hypothesis of a regulatory role of melatonin in the thymus in which melatonin downregulates its own binding sites.

Keywords Melatonin, Pineal gland, Immune system, Thymus

Martinez-Nicolas A, Ortiz-Tudela E, Madrid JA, Rol MA

Year 2011

Authors Antonio Martinez-Nicolas, Elisabet Ortiz-Tudela, Juan Antonio Madrid and Maria Angeles Rol

Report Name Crosstalk Between Environmental Light and Internal Time in Humans

Publication Chronobiology International

Issue-page numbers 28:7, 617-629

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.593278

Abstract Daily exposure to environmental light is the most important zeitgeber in humans, and all studied characteristics of light pattern (timing, intensity, rate of change, duration, and spectrum) influence the circadian system. However, and due to lack of current studies on environmental light exposure and its influence on the circadian system, the aim of this work is to determine the characteristics of a naturalistic regimen of light exposure and its relationship with the functioning of the human circadian system. Eighty-eight undergraduate students (18–23 yrs) were recruited in Murcia, Spain (latitude 38°01′N) to record wrist temperature (WT), light exposure, and sleep for 1 wk under free-living conditions. Light-exposure timing, rate of change, regularity, intensity, and contrast were calculated, and their effects on the sleep pattern and WT rhythm were then analyzed. In general, higher values for interdaily stability, relative amplitude, mean morning light, and light quality index (LQI) correlated with higher interdaily stability and relative amplitude, and phase advance in sleep plus greater stability in WT and phase advance of the WT circadian rhythm. On the other hand, a higher fragmentation of the light-exposure rhythm was associated with more fragmented sleep. Naturalistic studies using 24-h ambulatory light monitoring provide essential information about the main circadian system input, necessary for maintaining healthy circadian tuning. Correcting light-exposure patterns accordingly may help prevent or even reverse health problems associated with circadian disruption.

Keywords Free-living conditions, Human circadian system, Light exposure, Light quality index, Sleep-wake cycle, Wrist temperature, 24-h ambulatory monitoring

Martins E Jr, Fernandes LC, Bartol I et al.

Year 1998

Authors Martins E Jr, Fernandes LC, Bartol I et al.

Report Name The effect of melatonin chronic treatment upon macrophage and lymphocyte metabolism and function in Walker-256 tumour-bearing rats

Publication J Neuroimmunol

Issue-page numbers 82:81–89 doi:10.1016/S0165-5728(97)00191-4. PMID:9526849

URL http://www.mendeley.com/research/effect-melatonin-chronic-treatment-upon-macrophage-lymphocyte-metabolism-function-walker256-tumourbearing-rats/

Abstract Melatonin is the main hormone involved in the neuroendocrine-immune axis. It also presents antitumour activity. To evaluate the role of melatonin on the progression of Walker-256 tumour in rats we determined the effect of the hormone on some biochemical and functional aspects of macrophage and lymphocytes from cachectic rats. An important finding observed in immune cells from tumour-bearing (TB) rats is the impairment on glutamine and glucose metabolism in such cells. These changes are very similar to those observed in pinealectomized rats (PNX). The increased production of lactate and the flux of glucose through the Krebs cycle and the reduction in glutamine consumption seems to be involved in the immunosuppression presented in the TB and PNX animals. Melatonin treatment restored the changes observed in the metabolism of glucose and glutamine and stimulated the proliferation of lymphocytes from tumour-bearing rats. The results indicate that the effect of melatonin upon tumour growth involves the stimulation of the immune system by the hormone.

Keywords

Marzec S

Year 2011

Authors Stanisław Marzec

Report Name Exposure of workers to optical radiation and electromagnetic fields of welding equipment

Publication Welding International

Issue-page numbers iFirst, Available online: 03 Nov 2011

URL http://www.tandfonline.com/doi/abs/10.1080/09507116.2011.606129

Abstract

Keywords Blue Light, Ultraviolet Light, retina damage

Masson-Pévet M, George D, Kalsbeek A et al.

Year 1994

Authors Masson-Pévet M, George D, Kalsbeek A et al.

Report Name An attempt to correlate brain areas containing melatonin-binding sites with rhythmic functions: a study in five hibernator species

Publication Cell Tissue Res

Issue-page numbers 278:97–106. PMID:7954706 doi:10.1007/BF00305781

URL http://www.mendeley.com/research/attempt-correlate-brain-areas-containing-melatoninbinding-sites-rhythmic-functions-study-five-hibernator-species-1/

Abstract High affinity melatonin-binding sites have been described, by means of autoradiography with 2-125I-melatonin as the ligand, in more than 60 brain areas of about 20 mammalian species, with dramatic variations in the nature and number of labelled structures among the different species studied. As melatonin is involved in the synchronization of biological rhythms, we have tried to correlate the brain areas containing melatonin-binding sites with some rhythmic functions typical of given species. Therefore, we have studied the location of melatonin-binding sites in the complete brain of five long-day breeders with hibernation cycles, viz. one insectivore and four rodents. With the exception of the suprachiasmatic nuclei and the pars tuberalis of the pituitary, both of which contain binding sites in all five species, few reactive structures are common, even among species from the same family, e.g. the edible dormouse and the garden dormouse.

Keywords

Masumoto K, Ukai-Tadenuma M, Kasukawa T, et al. **Year** 2010

Authors Koh-Hei Masumoto, Maki Ukai-Tadenuma, Takeya Kasukawa, Mamoru Nagano, Kenichiro D Uno, Kaori Tsujino, Kazumasa Horikawa, Yasufumi Shigeyoshi, Hiroki R Ueda

Report Name Acute induction of Eya3 by late-night light stimulation triggers TSHβ expression in photoperiodism.

Publication Current Biology (2010)

Issue-page numbers Volume: 20, Issue: 24, Publisher: Elsevier Ltd, Pages: 2199-2206

URL http://www.mendeley.com/research/acute-induction-eya3-latenight-light-stimulation-triggers-tsh-expression-photoperiodism/

Abstract Living organisms detect seasonal changes in day length (photoperiod) 1-3 and alter their physiological functions accordingly to fit seasonal environmental changes. TSH , induced in the pars tuberalis (PT), plays a key role in the pathway that regulates vertebrate photoperiodism 4, 5. However, the upstream inducers of TSH expression remain unknown. Here we performed genome-wide expression analysis of the PT under chronic short-day and long-day conditions in melatonin-proficient CBA/N mice, in which the photoperiodic TSH expression response is preserved 6. This analysis identified "short-day" and "long-day" genes, including TSH , and further predicted the acute induction of long-day genes by late-night light stimulation. We verified this by advancing and extending the light period by 8hr, which induced TSH expression within one day. In the following genome-wide expression analysis under this acute long-day condition, we searched for candidate upstream genes by looking for expression that preceded TSH 's, and we identified the Eya3 gene. We demonstrated that Eya3 and its partner Six1 synergistically activate TSH expression and that this activation is further enhanced by Tef and Hlf. These results elucidate the comprehensive transcriptional photoperiodic response in the PT, revealing the complex regulation of TSH expression and unexpectedly rapid response to light changes in the mammalian photoperiodic system.

Keywords

Mata NL, Tzekov RT, Liu X, et al. **Year** 2001

Authors N L Mata, R T Tzekov, X Liu, J Weng, D G Birch, G H Travis

Report Name Delayed dark-adaptation and lipofuscin accumulation in abcr+/- mice: implications for involvement of ABCR in age related macular degeneration

Publication Investigative Ophthalmology & Visual Science

Issue-page numbers Volume: 42, Issue: 8, Pages: 1685-1690

URL http://www.mendeley.com/research/delayed-darkadaptation-lipofuscin-accumulation-abcr-mice-implications-involvement-abcr-agerelated-macular-degeneration/

Abstract PURPOSE: To examine the ocular phenotype in mice heterozygous for a null mutation in the abcr gene. METHODS: Retinas and retinal pigment epithelia (RPE) were prepared from wild-type, abcr+/-, and abcr-/- mice. Fresh tissues were homogenized and analyzed by normal phase high-performance liquid chromatography (HPLC) for the presence of retinoids and phospholipids. In another study, fixed tissues were sectioned and analyzed by light and electron microscopy. Finally, anesthetized mice were studied by electroretinography (ERG) at different times after exposure to strong light. RESULTS: A2E, the major fluorophore of lipofuscin, and its precursors, A2PE-H(2) and A2PE, were approximately fourfold more abundant in 8-month-old abcr+/- than in the wild-type retina and RPE. The levels of these substances in abcr+/- mice were approximately 40% those in abcr-/- mice. Lipofuscin pigment-granules were also visible in abcr+/- RPE cells by electron microscopy. Accumulation of A2PE-H(2) and A2E in abcr+/- retina and RPE, respectively, was strongly dependent on light exposure. Heterozygous mutants also exhibited delayed recovery of rod sensitivity by ERG. This delay was correlated with elevated levels of all-trans-retinaldehyde (all-trans-RAL) in retina after a photobleach and was not caused by a reduction in quantum-catch due to depletion of 11-cis-retinaldehyde (11-cis-RAL). CONCLUSIONS: Partial loss of the ABCR or rim protein is sufficient to cause a phenotype in mice similar to recessive Stargardt's disease (STGD) and age-related macular degeneration (AMD) in humans. These data are consistent with the suggestion that the STGD carrier-state may predispose to the development of AMD.

Keywords

Matsui DH, Machado-Santelli GM | ***Year*** 1997

Authors Matsui DH, Machado-Santelli GM

Report Name Alterations in F-actin distribution in cells treated with melatonin

Publication Pineal Res

Issue-page numbers 23:169–175 doi:10.1111/j.1600-079X.1997.tb00351.x. PMID:9462848

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1997.tb00351.x/abstract?

Abstract One of the possible pathways of action of melatonin is its effect on the cytoskeleton. In this work we looked for alterations in the cytoskeleton of cells treated with melatonin at physiological concentrations. T-47D, Hs-578T (human breast carcinoma cell lines), and MDCK (normal dog kidney) cells were maintained in MCDB 153 supplemented with 1% fetal bovine serum (FBS), or in Dulbecco's modified Eagle's medium (DMEM) supplemented with 5% FBS and treated with melatonin (10--9M or 10--10M) for 2 and 5 days, with or without 10--8 M estradiol. F-actin was stained with phalloidin-fluorescein isothiocyanate (FITC). Cytokeratin 19 and β-tubulin filaments were detected with specific monoclonal antibodies and secondary antibodies bound to FITC. Melatonin-treated T-47D cells observed in a transmission electronic microscope (TEM) showed an irregular nuclear shape and intermediate filaments disposed around the nucleus, which was not observed in control cells. Immunofluorescence analysis of cytokeratin filaments did not show significant differences between their distribution in control and treated cells. Melatonin did not induce significant alterations in cytokeratin filaments of T-47D, Hs578T or MDCK cells in DMEM and MCDB 153, or T-47D cells in DMEM. Melatonin induced the derangement of F-actin both in T-47D and MDCK cells kept in MCDB 153. The same was not observed when estradiol was also present. We did not observe significant alterations in the distribution of F-actin in T-47D or Hs-578T cells grown in DMEM. In DMEM, melatonin-treated MDCK cells were more elongated, with a slight concentration of F-actin on the cell boundary. Melatonin induced very slight alterations in microtubule organization of all cell lines studied.

Keywords melatonin; cytoskeleton; ultrastructure; F-actin; cell culture

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Matsuo T, Yamaguchi S, Mitsui S et al | ***Year*** 2003

Authors Matsuo T, Yamaguchi S, Mitsui S et al

Report Name Control mechanism of the circadian clock for timing of cell division in vivo

Publication Science

Issue-page numbers 302:255–259 doi:10.1126/science.1086271. PMID:12934012

URL http://stke.sciencemag.org/cgi/content/abstract/sci;302/5643/255

Abstract Cell division in many mammalian tissues is associated with specific times of day, but just how the circadian clock controls this timing has not been clear. Here, we show in the regenerating liver (of mice) that the circadian clock controls the expression of cell cycle–related genes that in turn modulate the expression of active Cyclin B1-Cdc2 kinase, a key regulator of mitosis. Among these genes, expression of wee1 was directly regulated by the molecular components of the circadian clockwork. In contrast, the circadian clockwork oscillated independently of the cell cycle in single cells. Thus, the intracellular circadian clockwork can control the cell-division cycle directly and unidirectionally in proliferating cells.

Keywords

Authors Matthews CD, Guerin MV, Wang X

Report Name Human plasma melatonin and urinary 6-sulphatoxy melatonin: studies in natural annual photoperiod and in extended darkness

Publication Clin Endocrinol (Oxf)

Issue-page numbers 35:21–27 doi:10.1111/j.1365-2265.1991.tb03491.x. PMID:1889136

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1991.tb03491.x/abstract?

Abstract

Objectives The alms of the study were (1) to examine the human plasma melatonin rhythm at the equinoxes and the solstices in the natural photoperlod (35.S); (2) to examine melatonin rhythms in the same subjects under extended darkness conditions to expose any suppressive (gating) effects of light at any time of the year; (3) to undertake a rigorous examination of the relationship between plasma melatonin and the urinary metabolite 6-suiphatoxy melatonin at varying times of the year.

Design At the equinoxes and solstices, unrestricted subjects had hourly urine collections followed by venous blood sampling taken under natural light conditions for 24 hours. Following a 24 hour Interval, a similar collection regime was performed with subjects held under conditions of extended darkness (5 hours darkness prior to natural sunset and following natural sunrise) for a further 24 hours.

Subjects Groups of four (minimum) to six female volunteers (age range 18–35 years) were studied, who had a normal lifestyle, no history of depression, and were not taking any medication or recently engaged in shiftwork.

measurements The plasma was assayed for melatonin and the urine samples for 6-suiphatoxy melatonin by radioimmunoassay.

results The onset of natural melatonin secretion was delayed until after sunset at all seasons but was earlier In summer, and not different from the time of sunset in extended darkness. The offset of melatonin secretion under natural conditions occurred at sunrise in autumn and winter but was delayed until after sunrise during spring and summer, particularly in extended darkness.

No significant changes in the duration of melatonin secretion were observed between seasons nor between the duration of melatonin secretion under natural photoperiod or extended darkness.

The measurement of 6-suiphatoxy melatonin proved to be a close Indicator of the phase and amplitude of secretion of plasma melatonin. Both onset and offset times of 6-sulphatoxy melatonin were delayed compared to the times when plasma melatonin was detectable/undetectable. A good correlation exists between the total plasma melatonin secretion and that of 6-sulphatoxy melatonin.

conclusions The results suggest evidence for a suppressive

(gating) effect of light at dawn only during summer which was associated with a phase advance of the onset of melatonin secretion at this time of year. The lack of a major gating effect of environment light on melatonin secretion, and the unchanging duration of secretion through the year In the normally entrained human, highlight differences between the human and those photoperiodic animal species which breed seasonally.

Urinary 6-suiphatoxy melatonin proved to be a good Indicator of plasma melatonin levels under rigorous examination and Is confirmed as a useful clinical measure.

Keywords

Mavroudis PD, Scheff JD, Calvano SE, Androulakis IP

Year 2012

Authors P.D. Mavroudis, J.D. Scheff, S.E. Calvano, I.P. Androulakis

Report Name Systems Biology of Circadian-Immune Interactions

Publication J Innate Immun

Issue-page numbers (DOI: 10.1159/000342427), PubMed ID 23006670

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=342427

Abstract There is increasing evidence that the immune system is regulated by circadian rhythms. A wide range of immune parameters, such as the number of red blood cells and peripheral blood mononuclear cells as well as the level of critical immune mediators, such as cytokines, undergo daily fluctuations. Current experimental data indicate that circadian information reaches immune tissues mainly through diurnal patterns of autonomic and endocrine rhythms. In addition, immune factors such as cytokines can also influence the phase of the circadian clock, providing bidirectional flow of circadian information between the neuroendocrine and immune systems. This network of neuroendocrine-immune interactions consists of complexly integrated molecular feedback and feedforward loops that function in synchrony in order to optimize immune response. Chronic stress can disrupt this intrinsic orchestration, as several endocrine signals of chronically stressed patients present blunted rhythmic characteristics. Reprogramming of biological rhythms has recently gained much attention as a potent method to leverage homeostatic circadian controls to ultimately improve clinical outcomes. Elucidation of the intrinsic properties of such complex systems and optimization of intervention strategies require not only an accurate identification of the signaling pathways that mediate host responses, but also a system-level description and evaluation.

Keywords

Mawson AR

Year 1998

Authors Mawson AR

Report Name Breast cancer in female flight attendants

Publication Lancet

Issue-page numbers 626.doi:10.1016/S0140-6736(05)79582-9 PMID:9746034

URL http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2979582-9/fulltext

Abstract A high rate of breast cancer is present among Finnish female flight attendants after a mean of 13·9 years at work (standard incidence ratio 1·87 [95% CI 1·15—2·23]). The risk is most prominent 15 years after recruitment. 1 This increase may be due to melatonin deficiency, resulting from work-associated interruptions in sleep-waking cycles (jetlag). Chronic disturbances in circadian rhythm are thought to lead to many of the health problems reported by shift workers, and because flight attendants co …

Keywords

Maywood ES, Bittman EL, Hastings MH **Year** 1996

Authors Maywood ES, Bittman EL, Hastings MH

Report Name Lesions of the melatonin- and androgen-responsive tissue of the dorsomedial nucleus of the hypothalamus block the gonadal response of male Syrian hamsters to programmed

Publication Biol Reprod

Issue-page numbers 54:470–477 doi:10.1095/biolreprod54.2.470. PMID:8788201

URL http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.119.5324&rep=rep1&type=pdf

Abstract The objective of this study was to characterize a site at which it is likely that melatonin mediates photoperiodic control of reproduction in the male Syrian hamster. The first experiment was a comparison of the distributions of iodomelatonin (IMEL)-binding sites and cells immunoreactive to androgen receptors (AR-ir) in the medio-basal hypothalamus (MBH). AR-ir cells extended throughout the MBH, whereas IMEL binding was restricted to the dorsomedial nucleus (DMN). Comparisons between IMEL binding and AR-ir on adjacent cryostat sections revealed a clear overlap between the IMEL-binding sites and a distinct subpopulation of AR-ir cells within the DMN. The second experiment examined whether lesions of these IMEL- and androgen-responsive cells affected the response of the hamsters to short-day (SD)-like infusions of melatonin. Animals received sham or bilateral electrolytic lesions of the IMEL-binding sites within the DMN of the hypothalamus (MBH-X). Animals were pinealectomized and 4 wk later fitted with an s.c. cannula for the daily infusion of either melatonin (50 ng/h) or saline (500 microliters/10 h). After 6 wk the animals with sham lesions showed gonadal atrophy and lower serum concentrations of LH and prolactin (PRL) after infusions with melatonin. In contrast, MBH-X animals given melatonin had large testes and long-day (LD)-like serum LH concentrations. Infusions of melatonin did, however, cause a significant decline in serum PRL level. This study shows that an intact MBH is essential for the expression of gonadotrophic but not lactotrophic responses to melatonin and/or photoperiod. It also suggests that cells responsive to both gondal steroids and melatonin may be involved in the seasonal variation in GnRH release, and indicates a site at which melatonin might influence sensitivity to steroid feedback, a hypothalamic function known to be regulated by photoperiod.

Keywords

McArthur AJ, Hunt AE, Gillette MU **Year** 1997

Authors McArthur AJ, Hunt AE, Gillette MU

Report Name Melatonin action and signal transduction in the rat suprachiasmatic circadian clock: activation of protein kinase C at dusk and dawn

Publication Endocrinology

Issue-page numbers 138:627–634 doi:10.1210/en.138.2.627. PMID:9002996

URL http://endo.endojournals.org/content/138/2/627.full

Abstract Nocturnal synthesis of the pineal hormone melatonin (MEL) is regulated by the circadian clock in the suprachiasmatic nucleus (SCN) of the hypothalamus. We examined the hypothesis that MEL can feed back to regulate the SCN using a brain slice preparation from rat. We monitored the SCN ensemble firing rate and found that MEL advanced the time of peak firing rate by more than 3 h at restricted circadian times (CTs) near subjective dusk [CT 10–14 (10–14 h after lights on)] and dawn (CT 23–0) on days 2 and 3 after treatment. The effect of MEL at CT 10 was blocked by pertussis toxin. The protein kinase C (PKC) activator, 12-O-tetradecanoylphorbol 13-acetate, reset the SCN firing rate rhythm with a profile of temporal sensitivity congruent with that of MEL. Two specific PKC inhibitors, calphostin C and chelerythrine chloride, independently blocked MEL-induced phase advances at each sensitive period. Furthermore, MEL administration increased PKC phosphotransferase activity transiently to 200% at CT 10 and CT 23, but not at CT 6. These data demonstrate that 1) MEL can directly modulate the circadian timing of the SCN within two windows of sensitivity corresponding to dusk and dawn; and 2) MEL alters SCN cellular function via a pertussis toxin-sensitive G protein pathway that activates PKC.

Keywords

McClung CR

Year 2006

Authors C. Robertson McClung

Report Name Plant Circadian Rhythms

Publication The Plant Cell

Issue-page numbers 18:792-803 (2006)

URL http://www.plantcell.org/content/18/4/792.full

Abstract The earth rotates on its axis every 24 h, with the result that any position on the earth's surface alternately faces toward or away from the sun—day and night. That the metabolism, physiology, and behavior of most organisms changes profoundly between day and night is obvious to even the most casual observer. These biological oscillations are apparent as diurnal rhythms. It is less obvious that most organisms have the innate ability to measure time. Indeed, most organisms do not simply respond to sunrise but, rather, anticipate the dawn and adjust their biology accordingly. When deprived of exogenous time cues, many of these diurnal rhythms persist, indicating their generation by an endogenous biological circadian clock. Until recently, the molecular mechanisms by which organisms functioned in this fourth dimension, time, remained mysterious. However, over the last 30 or so years, the powerful approaches of molecular genetics have revealed the molecular underpinnings of a cellular circadian clockwork as complicated and as beautiful as the wonderful chronometers developed in the 18th century. Then, the need to accurately measure time to precisely determine longitude sparked an international competition to claim a prize, the princely sum of 20,000 pounds sterling, offered by the British Crown

Keywords

McColl SL, Veitch JA

Year 2001

Authors McColl, S.L.; Veitch, J.A.

Report Name Full-spectrum fluorescent lighting: a review of its effects on physiology and and health

Publication Psychological Medicine

Issue-page numbers v. 31, no. 6, August 2001, pp. 949-964

URL http://www.nrc-cnrc.gc.ca/obj/irc/doc/pubs/nrcc43097/nrcc43097.pdf

Abstract Background. Full-spectrum fluorescent lighting (FSFL) has been credited with causing dramatic beneficial effects on a wide variety of behaviours, mental health outcomes, and physical health effects, as compared to other fluorescent lamp types. These effects are hypothesized to occur because of similarity between FSFL emissions and daylight, which is said to have evolutionary superiority over other light sources.
Method. This review, covering the period 1941-1999, critically considers the evidence for direct effects of FSFL through skin absorption as well as indirect effects on hormonal and neural processes.
Conclusions . Overall, the evidence does not show dramatic effects of fluorescent lamp type on behaviour or health, nor does it support the evolutionary hypothesis.

Keywords

McEwen BS **Year** 1998

Authors McEwen BS

Report Name Protective and damaging effects of stress mediators

Publication N Engl J Med

Issue-page numbers 338:171–179 doi:10.1056/NEJM199801153380307. PMID:9428819

URL http://www.nejm.org/doi/full/10.1056/NEJM199801153380307

Abstract N/A

Keywords

McIntyre IM, Norman TR, Burrows GD, Armstrong SM **Year** 1989

Authors Ian M. McIntyre, Trevor R. Norman, Graham D. Burrows, Stuart M. Armstrong

Report Name Human melatonin response to light at different times of the night

Publication Psychoneuroendocrinology

Issue-page numbers Volume 14, Issue 3, 1989, Pages 187-193

URL http://www.sciencedirect.com/science/article/pii/0306453089900164

Abstract Normal control subjects were examined on three separate occasions with light of sufficient intensity to suppress nocturnal plasma melatonin concentrations. One hour of light was given at each of the following times: (a) 2100–2200h; (b) midnight to 0100h; (c) 0400–0500h. Melatonin synthesis was just becoming apparent at 2100h. There was significant suppression of melatonin by light when given at midnight-0100h and 0400–0500h, but not when light was given at 2100–2200h. In each case following light, melatonin synthesis was shown to resume, even after light applied in the second half of the dark period (0400–0500h). A second experiment was undertaken to examine a possible “rebound” in melatonin levels following light given at 2100–2200h. Six further control subjects were exposed to light at this time, and plasma melatonin levels were measured until 0400h. No rebound in melatonin concentrations was observed. These results are compared with other studies of melatonin response to evening light exposure.

Keywords

Mcintyre IM, Norman TR, Burrows GD, Armstrong SM

Year 1990

Authors Iain M Mcintyre , Trevor R Norman , Graham D Burrows , Stuart M Armstrong

Report Name Melatonin supersensitivity to dim light in seasonal affective disorder

Publication Lancet

Issue-page numbers 1990 Feb 24;335(8687):488.

URL http://thelancet.it/journals/lancet/article/PII0140-6736%2890%2990732-K/fulltext

Abstract N/A

Keywords

Mclntyre IM, Norman TR, Burrows GD, Armstrong SM

Year 1989

Authors Iain M. Mclntyre, Trevor R. Norman, Graham D. Burrows, Stuart M. Armstrong

Report Name Human Melatonin Suppression by Light is Intensity Dependent

Publication Journal of Pineal Research

Issue-page numbers Volume 6, Issue 2, pages 149-156, April 1989

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1989.tb00412.x/abstract

Abstract Five intensities of artificial light were examined for the effect on nocturnal melatonin concentrations. Maximum suppression of melatonin following 1 hr of light at midnight was 71%, 67%, 44%, 38%, and 16% with intensities of 3,000, 1,000, 500, 350, and 200 lux (lx), respectively. In contrast to some previous reports, light of 1,000 lx intensity was sufficient to suppress melatonin to near daytime levels, and intensities down to 350 lx were shown to significantly suppress nocturnal melatonin levels below prelight values. On the basis of these data, it is suggested that when examining the melatonin sensitivity of patient groups (such as bipolar affective disorders) to artificial light, an appropriate light intensity should be established in each laboratory. Light of less intensity (e.g., 200–350 lx) may be more suitable to dichotomize patient groups from control subjects.

Keywords low light intensity; melatonin

McMurray R, Keisler D, Kanuckel K et al. **Year** 1991

Authors R McMurray, D Keisler, K Kanuckel, S Izui and SE Walker

Report Name Prolactin influences autoimmune disease activity in the female B/W mouse

Publication J Immunol

Issue-page numbers 147:3780–3787. PMID:1940367

URL http://www.jimmunol.org/content/147/11/3780.abstract

Abstract Prolactin, an anterior pituitary hormone, stimulates humoral and cell- mediated immunity. This study investigated effects of manipulating prolactin levels in the autoimmune B/W mouse model of SLE. A group of B/W females was treated with daily injections of the prolactin- suppressing drug, bromocriptine. These mice had delayed elevation of anti-DNA antibodies and serum IgG; longevity was increased compared to control mice. Functioning syngeneic pituitary glands, implanted under the renal capsule, produced prolonged hyperprolactinemia in a separate group of female B/W mice. Hyperprolactinemic animals were characterized by premature albuminuria, elevated circulating gp70IC and IgG, and accelerated mortality. Analyses of thymic and splenic lymphocytes revealed no differences in lymphocyte subpopulations in mice with altered prolactin levels. This is the first report to substantiate an immunomodulatory role for prolactin in B/W mice. Further evaluation of this model may identify specific means of intervening clinically with immunosuppressive hormone-modulating therapy in SLE.

Keywords

McNamara P, Seo SB, Rudic RD et al. **Year** 2001

Authors McNamara P, Seo SB, Rudic RD et al.

Report Name Regulation of CLOCK and MOP4 by nuclear hormone receptors in the vasculature: a humoral mechanism to reset a peripheral clock

Publication Cell

Issue-page numbers 105:877–889 doi:10.1016/S0092-8674(01)00401-9. PMID:11439184

URL http://www.sciencedirect.com/science/article/pii/S0092867401004019

Abstract Circadian clock genes are expressed in the suprachiasmatic nucleus and in peripheral tissues to regulate cyclically physiological processes. Synchronization of peripheral oscillators is thought to involve humoral signals, but the mechanisms by which these are mediated and integrated are poorly understood. We report a hormone-dependent interaction of the nuclear receptors, RARα and RXRα, with CLOCK and MOP4. These interactions negatively regulate CLOCK/MOP4:BMAL1-mediated transcriptional activation of clock gene expression in vascular cells. MOP4 exhibits a robust rhythm in the vasculature, and retinoic acid can phase shift Per2 mRNA rhythmicity in vivo and in serum-induced smooth muscle cells in vitro, providing a molecular mechanism for hormonal control of clock gene expression. We propose that circadian or periodic availability of nuclear hormones may play a critical role in resetting a peripheral vascular clock.

Keywords

	Mead MN	***Year***	2008
Authors	Mead MN		
Report Name	Benefits of Sunlight: A Bright Spot for Human Health		
Publication	Environ Health Perspect		
Issue-page numbers	116:A160-A167		
URL	http://dx.doi.org/10.1289/ehp.116-a160		
Abstract	Article		
Keywords	sunlight, melatonin, night		

	Meerman L, Verwer R, Slooff MJ, et al.	***Year***	1994
Authors	Meerman L, Verwer R, Slooff MJ, van Hattum J, Beukeveld GJ, Kleibeuker JH, Haagsma EB.		
Report Name	Perioperative measures during liver transplantation for erythropoietic protoporphyria		
Publication	Transplantation		
Issue-page numbers	1994 Jan;57(1):155-8.		
URL	http://www.ncbi.nlm.nih.gov/pubmed/8291103		
Abstract	N/A		
Keywords			

Meermeier N, Krishnan N

Year 2012

Authors N. Meermeier, N. Krishnan

Report Name Circadian regulation of cellular homeostasis – Implications for cell metabolism and clinical diseases

Publication Medical Hypotheses

Issue-page numbers Volume 79, Issue 1, July 2012, Pages 17–24

URL http://www.sciencedirect.com/science/article/pii/S0306987712001429

Abstract The major pathways involving nutrient and energy metabolism including cellular homeostasis are profoundly impacted by the circadian clock, which orchestrates diurnal rhythms in physiology and behavior. While the links between circadian and metabolic rhythms are unclear, recent studies imply a close link between the two with one feeding back on the other. In this discussion, we present the hypothesis that circadian clocks likely contribute to cellular homeostasis, especially proteostasis, through regulation of metabolic rhythms, which in turn feed-back on circadian oscillators. The disruption of circadian clocks leads to altered metabolic rhythms and metabolic disease states as a result of altered cellular homeostasis.

Keywords

Megdal SP, Kroenke CH, Laden F et al.

Year 2005

Authors Megdal SP, Kroenke CH, Laden F et al.

Report Name Night work and breast cancer risk: a systematic review and meta-analysis

Publication Eur J Cancer

Issue-page numbers 41:2023–2032.doi:10.1016/j.ejca.2005.05.010 PMID:16084719

URL http://www.sciencedirect.com/science/article/pii/S0959804905004910

Abstract The association between occupations that involve night shift work (a surrogate for exposure to light at night with subsequent melatonin suppression) and breast cancer risk is uncertain. We therefore conducted a systematic review and meta-analysis of observational studies to assess the effects of night work on breast cancer risk.

Data sources were MEDLINE from January 1960 to January 2005, experts in the field, bibliographies, and abstracts. Search terms included night work terms, flight personnel terms, cancer terms, and risk terms. Independent data extraction by two authors using standardised forms was performed. The method of DerSimonian and Laird was used to derive combined estimates and Egger's; and Begg and Mazumdar's tests for publication bias were conducted.

Based on 13 studies, including seven studies of airline cabin crew and six studies of other night shift workers, the aggregate estimate for all studies combined was 1.48 (95% CI, 1.36–1.61), with a similar significant elevation of breast cancer risk among female airline cabin crew (standardised incidence ratio (SIR), 1.44; 95% CI, 1.26–1.65), and female night workers (relative risk (RR), 1.51; 95% CI, 1.36–1.68) separately. We found some evidence suggesting confounding due to incomplete adjustment for breast cancer risk factors, with smaller effects in the studies that more completely adjusted for reproductive history and other confounding factors. Egger's and Begg and Mazumdar's tests for publication bias showed no significant asymmetry ($P > 0.05$).

Studies on night shift work and breast cancer risk collectively show an increased breast cancer risk among women. Publication bias is unlikely to have influenced the results.

Keywords Breast cancer; Night work; Flight attendants

Mehta R, Zhu RJ

Year 2009

Authors Ravi Mehta and Rui (Juliet) Zhu

Report Name Blue or red? Exploring the effect of color on cognitive task performances

Publication Science

Issue-page numbers Vol. 323 no. 5918 pp. 1226-1229

URL http://www.sciencemag.org/content/323/5918/1226.short

Abstract Existing research reports inconsistent findings with regard to the effect of color on cognitive task performances. Some research suggests that blue or green leads to better performances than red; other studies record the opposite. Current work reconciles this discrepancy. We demonstrate that red (versus blue) color induces primarily an avoidance (versus approach) motivation (study 1, n = 69) and that red enhances performance on a detail-oriented task, whereas blue enhances performance on a creative task (studies 2 and 3, n = 208 and 118). Further, we replicate these results in the domains of product design (study 4, n = 42) and persuasive message evaluation (study 5, n = 161) and show that these effects occur outside of individuals' consciousness (study 6, n = 68). We also provide process evidence suggesting that the activation of alternative motivations mediates the effect of color on cognitive task performances.

Keywords

Mendez N, Abarzua-Catalan L, Vilches N, et al.

Year 2012

Authors Natalia Mendez, Lorena Abarzua-Catalan, Nelson Vilches, Hugo A. Galdames, Carlos Spichiger, Hans G. Richter, Guillermo J. Valenzuela, Maria Seron-Ferre, Claudia Torres-Fa

Report Name Timed Maternal Melatonin Treatment Reverses Circadian Disruption of the Fetal Adrenal Clock Imposed by Exposure to Constant Light

Publication PLoS ONE

Issue-page numbers 7(8): e42713. doi:10.1371/journal.pone.0042713

URL http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0042713

Abstract Surprisingly, in our modern 24/7 society, there is scant information on the impact of developmental chronodisruption like the one experienced by shift worker pregnant women on fetal and postnatal physiology. There are important differences between the maternal and fetal circadian systems; for instance, the suprachiasmatic nucleus is the master clock in the mother but not in the fetus. Despite this, several tissues/organs display circadian oscillations in the fetus. Our hypothesis is that the maternal plasma melatonin rhythm drives the fetal circadian system, which in turn relies this information to other fetal tissues through corticosterone rhythmic signaling. The present data show that suppression of the maternal plasma melatonin circadian rhythm, secondary to exposure of pregnant rats to constant light along the second half of gestation, had several effects on fetal development. First, it induced intrauterine growth retardation. Second, in the fetal adrenal in vivo it markedly affected the mRNA expression level of clock genes and clock-controlled genes as well as it lowered the content and precluded the rhythm of corticosterone. Third, an altered in vitro fetal adrenal response to ACTH of both, corticosterone production and relative expression of clock genes and steroidogenic genes was observed. All these changes were reversed when the mother received a daily dose of melatonin during the subjective night; supporting a role of melatonin on overall fetal development and pointing to it as a ‘time giver’ for the fetal adrenal gland. Thus, the present results collectively support that the maternal circadian rhythm of melatonin is a key signal for the generation and/or synchronization of the circadian rhythms in the fetal adrenal gland. In turn, low levels and lack of a circadian rhythm of fetal corticosterone may be responsible of fetal growth restriction; potentially inducing long term effects in the offspring, possibility that warrants further research.

Keywords

Menegaux F, Truong T, Anger A, et al. **Year** 2012

Authors Florence Menegaux, Thérèse Truong, Antoinette Anger, Emilie Cordina-Duverger, Farida Lamkarkach, Patrick Arveux, Pierre Kerbrat, Joëlle Févotte, Pascal Guénel

Report Name Night work and breast cancer: A population-based case–control study in France (the CECILE study)

Publication International Journal of Cancer

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.27669/abstract

Abstract Night work involving disruption of circadian rhythm was suggested as a possible cause of breast cancer. We examined the role of night work in a large population-based case-control study carried out in France between 2005 and 2008. Lifetime occupational history including work schedules of each night work period was elicited in 1,232 cases of breast cancer and 1,317 population controls. Thirteen percent of the cases and 11% of the controls had ever worked on night shifts (OR = 1.27 [95% confidence interval = 0.99–1.64]). Odds ratios were 1.35 [1.01–1.80] in women who worked on overnight shifts, 1.40 [1.01–1.92] in women who had worked at night for 4.5 or more years, and 1.43 [1.01–2.03] in those who worked less than three nights per week on average. The odds ratio was 1.95 [1.13–3.35] in women employed in night work for >4 years before their first full-term pregnancy, a period where mammary gland cells are incompletely differentiated and possibly more susceptible to circadian disruption effects. Our results support the hypothesis that night work plays a role in breast cancer, particularly in women who started working at night before first full-term pregnancy.

Keywords case-control study; breast cancer; circadian disruption

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Meng Y, He Z, Yin J, Zhang Y, Zhang T. **Year** 2011

Authors Meng Y, He Z, Yin J, Zhang Y, Zhang T.

Report Name Quantitative calculation of human melatonin suppression induced by inappropriate light at night

Publication Med Biol Eng Comput

Issue-page numbers 2011 Sep;49(9):1083-8. Epub 2011 Jun 30.

URL http://www.springerlink.com/content/rm445lq237555102/

Abstract Melatonin ($C_{13}H_{16}N_2O_2$) has a wide range of functions in the body. When is inappropriately exposed to light at night, human circadian rhythm will be interfered and then melatonin secretion will become abnormal. For nearly three decades great progresses have been achieved in analytic action spectra and melatonin suppression by various light conditions. However, so far few articles focused on the quantitative calculation of melatonin suppression induced by light. In this article, an algorithm is established, in which all the contributions of rods, cones, and intrinsically photosensitive retinal ganglion cells are considered. Calculation results accords with the experimental data in references very well, which indicate the validity of this algorithm. This algorithm can also interpret the rule of melatonin suppression varying with light correlated color temperature very well.

Keywords

Mergler S, Valtink M, Coulson-Thomas VJ, et al. **Year** 2010

Authors Stefan Mergler, Monika Valtink, Vivien Jane Coulson-Thomas, Dirk Lindemann, Peter S Reinach, Katrin Engelmann, Uwe Pleyer

Report Name TRPV channels mediate temperature-sensing in human corneal endothelial cells

Publication Experimental Eye Research

Issue-page numbers Volume: 90, Issue: 6, Publisher: Elsevier Ltd, Pages: 758-770

URL http://www.mendeley.com/research/trpv-channels-mediate-temperaturesensing-human-corneal-endothelial-cells-5/

Abstract The physiology and transparency of the cornea are dependent on corneal endothelial function. The role of temperature sensitive ion channels in maintaining such activity is unknown. This study was undertaken to probe for the functional expression of such pathways in human corneal endothelial cells (HCEC). We used HCEC-12, an immortalized population derived from whole corneal endothelium, and two morphologically distinct clonal cell lines derived from HCEC-12 (HCEC-H9C1, HCEC-B4G12) to probe for gene expression and function of transient receptor potential (TRP) channels of the vanilloid (V) isoform subfamily (i.e. TRPV1-3) in these cell types. Expression of TRPV isotypes 1, 2 and 3 were detected by RT-PCR. Protein expression of TRPV1 in situ was confirmed by immunostaining of corneoscleral remnants after keratoplasty. TRPV1-3 functional activity was evident based on capsaicin-induced Ca(2+) transients and induction of these responses through rises in ambient temperature from 25 degrees C to over 40 degrees C. The currents underlying Ca(2+) transients were characterized with a novel high throughput patch-clamp system. The TRPV1 selective agonist, capsaicin (CAP) (10-20 microM) increased non-selective cation whole-cell currents resulting in calcium increases that were fully blocked by either the TRPV1 antagonist capsazepine (CPZ) or removal of extracellular calcium. Similarly, heating from room temperature to over 40 degrees C increased the same currents resulting in calcium increases that were significantly reduced by the TRP channel blockers lanthanum chloride (La(3+)) (100 microM) and ruthenium-red (RuR) (10 microM), respectively. Moreover, application of the TRPV channel opener 2-aminoethoxydiphenyl borate (2-APB) (400 microM) led to a reversible increase in intracellular Ca(2+) indicating putative TRPV1-3 channel activity. Taken together, TRPV activity modulation by temperature underlies essential homeostatic mechanisms contributing to the support of corneal endothelial function under different ambient conditions.

Keywords

Metcalf G, Jackson IMD, editors **Year** 1989

Authors Metcalf G, Jackson IMD, editors

Report Name Thyrotropin releasing hormone: Biomedical significance

Publication Ann N Y Acad Sci

Issue-page numbers 553:1–631. PMID: 2497668

URL http://www.lib.muohio.edu/multifacet/record/mu3ugb1499447

Abstract N/A

Keywords

Métivier R, Penot G, Hübner MR et al. **Year** 2003

Authors Métivier R, Penot G, Hübner MR et al.

Report Name Estrogen receptor-alpha directs ordered, cyclical, and combinatorial recruitment of cofactors on a natural target promoter

Publication Cell

Issue-page numbers 115:751–763 doi:10.1016/S0092-8674(03)00934-6. PMID:14675539

URL http://www.cell.com/abstract/S0092-8674%2803%2900934-6

Abstract Transcriptional activation of a gene involves an orchestrated recruitment of components of the basal transcription machinery and intermediate factors, concomitant with an alteration in local chromatin structure generated by posttranslational modifications of histone tails and nucleosome remodeling. We provide here a comprehensive picture of events resulting in transcriptional activation of a gene, through evaluating the estrogen receptor-α (NR3A1) target pS2 gene promoter in MCF-7 cells. This description integrates chromatin remodeling with a kinetic evaluation of cyclical networks of association of 46 transcription factors with the promoter, as determined by chromatin immunoprecipitation assays. We define the concept of a “transcriptional clock” that directs and achieves the sequential and combinatorial assembly of a transcriptionally productive complex on a promoter. Furthermore, the unanticipated findings of key roles for histone deacetylases and nucleosome-remodeling complexes in limiting transcription implies that transcriptional activation is a cyclical process that requires both activating and repressive epigenetic processes.

Keywords

Mhatre MC, Shah PN, Juneja HS **Year** 1984

Authors Mhatre MC, Shah PN, Juneja HS.

Report Name Effect of varying photoperiods on mammary morphology, DNA synthesis, and hormone profile in female rats.

Publication J Natl Cancer Inst

Issue-page numbers 1984 Jun;72(6):1411-6.

URL http://www.ncbi.nlm.nih.gov/pubmed/6427503

Abstract A clear positive correlation between circulating levels of prolactin (Prl) and morphologic development as well as DNA synthetic index in the mammary gland was established in young virgin Holtzman rats exposed to constant light from birth. The observed elevated level of circulating Prl by virtue of its morphogenic and mitogenic properties induced changes in mammary epithelium [numerous actively differentiating terminal end buds into alveolar buds (AB)] highly susceptible for the action of 7,12-dimethylbenz[a]anthracene [(DMBA) CAS: 57-97-6]. Conversely, substitution treatment with melatonin in such a model caused a significant decrease in both Prl and 17 beta-estradiol (E2) levels as well as in the morphologic and DNA synthetic pattern of the mammary gland. Administration of 2-bromo-alpha- ergocryptin in these animals caused a significant decrease in the plasma level of Prl (without affecting the level of E2) and a decrease in the density of AB and in DNA synthesis. These changes impaired the mammary gland responsiveness to DMBA as seen from the significant decrease in the incidence of mammary carcinoma.

Keywords

Middleton B, Stone BM, Arendt J | ***Year*** 2002

Authors Middleton B, Stone BM, Arendt J

Report Name Human circadian phase in 12:12 h, 200: <8 lux and 1000: <8 lux light-dark cycles, without scheduled sleep or activity

Publication Neurosci Lett

Issue-page numbers 329:41–44 doi:10.1016/S0304-3940(02)00574-8. PMID:12161258

URL http://www.sciencedirect.com/science/article/pii/S0304394002005748

Abstract The light levels required to maintain human circadian phase in the absence of other strong time cues are not defined. We investigated circadian phase in two groups of men, living in partial temporal isolation, exposed to 12 h:12 h light:dark cycles of: (A) 200:<8 lux, broad spectrum white light for 14 days; and (B) 1000:<8lux for 14 days. The rhythm variables measured were urinary 6-sulphatoxymelatonin, rectal temperature, activity and rest (actigraphy and sleep logs). In 200:<8 lux four/six individuals showed phase delays. Exposure to 1000:<8 lux appeared to maintain synchronisation of rest-activity to 24 h, but with a significant overall phase advance of 0.81 h in temperature. These observations suggest that domestic intensity light does not maintain phase without scheduled sleep/activity, possibly due to indirect effects on behaviour influencing light exposure.

Keywords Light; Circadian rhythms; Melatonin; Entrainment; Phase relationship; Core body temperature; Rest-activity cycle; Human

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Midwinter MJ, Arendt J | ***Year*** 1991

Authors Midwinter MJ, Arendt J

Report Name Adaptation of the melatonin rhythm in human subjects following night-shift work in Antarctica

Publication Neurosci Lett

Issue-page numbers 122:195–198 doi:10.1016/0304-3940(91)90856-O. PMID:2027519

URL http://www.ncbi.nlm.nih.gov/pubmed/2027519

Abstract Different environmental conditions, particularly daylength and intensity of natural light, may influence the ability of shiftworkers to adapt to the abrupt phase-shifts of 24 h time cues imposed by the nature of their work. We have investigated this problem in terms of the circadian rhythm of the pineal hormone melatonin in nightshift workers on the British Antarctic Survey Base at Halley (75 degrees South). Melatonin production was assessed by measurement of its major urinary metabolite 6-sulphatoxymelatonin (aMT6s) by radio-immunoassay in sequential urine samples collected for 48 h at weekly intervals. The acrophase of the melatonin rhythm was significantly delayed from 5.22 h. min to 14.54 h. min (summer) and 8.73 h.min to 13.23 h.min (winter) during a week of night-shift work. Readaptation of the rhythm following night-shift work was markedly slower during the Antarctic winter taking 3 weeks compared to summer where the baseline phase position was re-established after 1 week. Morning and evening treatment (08.00-09.00 h, 16.00-17.00 h) with bright (greater than 2500 lux) full spectrum white light did not significantly modify this phenomenon in summer, but a trend to faster adaptation with light treatment was seen in winter. These observations are likely to be of importance to shift-workers in temperate zones. Further investigations of phase-shifting techniques, such as appropriately timed bright light and administration of melatonin itself, are indicated, particularly in relation to performance at work.

Keywords

Authors Migaud M, Daveau A, Malpaux B

Report Name MTNR1A melatonin receptors in the ovine premammillary hypothalamus: day-night variation in the expression of the transcripts

Publication Biol Reprod

Issue-page numbers 72:393–398 doi:10.1095/biolreprod.104.030064. PMID:15470001

URL http://www.biolreprod.org/content/72/2/393.full.pdf

Abstract Melatonin regulation of reproductive functions in sheep is mediated by action in the premammillary hypothalamus (PMH). The aim of this study was to identify the high-affinity melatoninreceptor
subtypes expressed in this structure. To achieve this, we used reverse transcription-polymerase chain reaction (RTPCR) and developed in situ hybridization techniques (ISH). By using RT-PCR, we detected a band corresponding to the MTNR1A melatonin-receptor cDNA in the PMH as well as in the pars tuberalis (PT). On the opposite, MTNR1B melatoninreceptor transcripts were not detected using degenerate primers
in any of the structures considered, confirming the lack of expression of this receptor subtype in sheep. The expression of MTNR1A mRNA was further confirmed in the PMH by ISH with a 35S-labeled ovine MTNR1A riboprobe. We next investigated the variation in the expression of MTNR1A mRNA between the
end of the day and the end of the night (absence and presence of melatonin, respectively). MTNR1A transcript expression was greater at the end of the night than at the end of the day in the PMH. In contrast, MTNR1A mRNA expression was lower at the end of the night than at the end of the day in the PT. No significant variation in the MTNR1A mRNA expression was observed in a more dorsal hypothalamic area. Overall, these results show that MTNR1A transcripts are expressed in the ovine PMH and that their expression follows a diurnal rhythm, which is different from the pattern of expression observed in the PT.

Keywords hypothalamus, melatonin, neuroendocrinology, receptors, seasonal

Millard TP, Hawk JLM, Mcgregor JM

Year 2000

Authors T P Millard, J L M Hawk, J M Mcgregor

Report Name Photosensitivity in lupus

Publication Lupus

Issue-page numbers January 2000 vol. 9 no. 1 3-10

URL http://lup.sagepub.com/content/9/1/3

Abstract

A wide variety of skin conditions may present in patients with lupus erythematosus (LE). These can be broadly divided into three main groups: cutaneous forms of LE (`LE-specific skin disease'), nonspecific cutaneous manifestations of SLE (`LE non-specific skin disease') and cutaneous complications of drug treatments for LE. This review examines clinical photosensitivity in LE, a trait most commonly associated with cutaneous forms of LE but which may also manifest in SLE. All humans are photosensitive, developing reddening of the skin if exposed to sufficient ultraviolet radiation (UVR). Therefore we define photosensitivity in clinical practice as an abnormal cutaneous response to UVR.

Abnormal photosensitivity in LE may manifest in a number of different forms. The lesions of LE-specific skin disease may be induced or exacerbated by UVR. Patients with LE who are prescribed photosensitizing medications such as thiazide diuretics, neuroleptics and tetracyclines may also develop phototoxic reactions which usually present as easy sunburn. Photosensitivity may also, rarely, manifest as fragile skin and blistering in patients with both LE and porphyria cutanea tarda. Several other photosensitive disorders have been reported in association with LE, including solar urticaria and erythropoetic protoporphyria (EPP), but these appear to be chance associations.

Assessment of patients with LE and photosensitivity requires a careful history and examination. Phototesting and photoprovocation tests may be used to demonstrate photosensitivity in some cases, but these are rarely required for diagnosis. Photosensitive patients should be advised about sun avoidance, photoprotection and sunscreen use as a first line treatment.

Keywords cutaneous lupus, photosensitivity, polymorphic light eruption, photoprotection, lupus

Mitchell CS, Zhang J, Sigsgaard T, et al. **Year** 2007

Authors Mitchell CS, Zhang J, Sigsgaard T, Jantunen M, Lioy PJ, Samson R, et al.

Report Name Current State of the Science: Health Effects and Indoor Environmental Quality

Publication Environ Health Perspect

Issue-page numbers 115:958-964

URL http://dx.doi.org/10.1289/ehp.8987

Abstract Our understanding of the relationship between human health and the indoor environment continues to evolve. Previous research on health and indoor environments has tended to concentrate on discrete pollutant sources and exposures and on specific disease processes. Recently, efforts have been made to characterize more fully the complex interactions between the health of occupants and the interior spaces they inhabit. In this article we review recent advances in source characterization, exposure assessment, health effects associated with indoor exposures, and intervention research related to indoor environments. Advances in source characterization include a better understanding of how chemicals are transported and processed within spaces and the role that other factors such as lighting and building design may play in determining health. Efforts are under way to improve our ability to measure exposures, but this remains a challenge, particularly for biological agents. Researchers are also examining the effects of multiple exposures as well as the effects of exposures on vulnerable populations such as children and the elderly. In addition, a number of investigators are also studying the effects of modifying building design, materials, and operations on occupant health. Identification of research priorities should include input from building designers, operators, and the public health community.

Keywords allergens, chemistry, exposure, fungi, humans, indoor air pollution, intervention, review

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Miyauchi F, Nanjo K, Otsuka K **Year** 1991

Authors Miyauchi F, Nanjo K, Otsuka K

Report Name [Effects of continuous lighting on secretion of melatonin and pituitary hormones in women]

Publication Nippon Sanka Fujinka Gakkai Zasshi

Issue-page numbers 43:529–534. PMID:1905333

URL Effects of light exposure on the serum concentrations of melatonin, prolactin, LH and FSH were studied in 53 women during their follicular phases. Twenty seven women were ex

Abstract http://www.ncbi.nlm.nih.gov/pubmed/1905333

Keywords

Miyauchi F, Nanjo K, Otsuka K **Year** 1992

Authors Miyauchi F, Nanjo K, Otsuka K

Report Name [Effects of night shift on plasma concentrations of melatonin, LH, FSH and prolactin, and menstrual irregularity].

Publication Sangyo Igaku

Issue-page numbers 34:545–550. PMID:1460786

URL http://www.ncbi.nlm.nih.gov/pubmed/1460786

Abstract To examine the effect of night shift on the ovarian function, 122 teachers, 67 office workers, 377 nurses, 133 factory workers and 67 barmaids were surveyed. The incidence of irregular menstrual cycle was 13.1% in teachers, 14.9% in office workers, 24.9% in nurses, 36.8% in factory workers and 40.3% in barmaids. The incidence was significantly higher in women working at night than women working during the day. Plasma concentrations of melatonin, LH, FSH and prolactin were determined at 2200 h and 0200 h in 5 nurses working at night and in 6 nurses resting in their quarters. Plasma concentrations of melatonin and prolactin at 0200 h were significantly lower in nurses of the working group than others of the resting group, but plasma concentrations of LH and FSH did not differ between the two groups. These results indicate that night shift suppresses the ovarian function by affecting the circadian rhythm of melatonin and prolactin.

Keywords

Mocchegiani E, Bulian D, Santarelli L et al. **Year** 1996

Authors Mocchegiani E, Bulian D, Santarelli L et al.

Report Name The zinc pool is involved in the immunereconstituting effect of melatonin in pinealectomized mice

Publication J Pharmacol Exp Ther

Issue-page numbers 277:1200–1208. PMID:8667179

URL http://jpet.aspetjournals.org/content/277/3/1200.short

Abstract Melatonin (MEL) affects the immune system by direct or indirect mechanisms. An involvement of the zinc pool in the immune-reconstituting effect of MEL in old mice has recentl been documented. An altered zinc turnover and impaired immune functions are also evident in pinealectomized (px) mice. The present work investigates further the effect of "physiological" doses of MEL on the zinc pool and on thymic and peripheral immune functions in px mice. Daily injections of MEL (100 micrograms/mouse) for 1 month in px mice restored the crude zinc balance from negative to positive values. Thymic and peripheral immune functions, including plasma levels of interleukin-2, also recovered. The nontoxic effect of MEL on immune functions was observed in sham-operated mice. Because the half-life of MEL is very short (12 min), interruption of MEL treatment in px mice resulted, after 1 month, in a renewed negative crude zinc balance and a regression of immune functions. Both the zinc pool and immunological parameters were restored by 30 further days of MEL treatment. The existence of a significant correlation between zinc and thymic hormone after both cycles of MEL treatment clearly shows an involvement of the zinc pool in the immunoenhancing effects of MEL and thus suggests an inter-relationship between zinc and MEL in px mice. Moreover, the existence of significant positive correlations between zinc or thymulin and interleukin-2 suggests that interleukin-2 may participate in the action of MEL, via zinc, on thymic functions in px MEL-treated mice.

Keywords

Moldofsky H **Year** 1994

Authors Moldofsky H

Report Name Central nervous system and peripheral immune functions and the sleep-wake system

Publication J Psychiatry Neurosci

Issue-page numbers 19:368–374. PMID:7803370

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1188626/

Abstract This paper reviews the relationship of aspects of the immune system to the sleep-wake system in animals and humans. In addition to the influence of certain cytokines such as interleukin-1 (IL-1) on the sleeping-waking brain, circadian measures of plasma IL-1 and peripheral immune cellular functions, for example, natural killer cell activities and cortisol are related to the sleep-wake system in humans. Changes in the circadian patterns of immune functions over the menstrual cycle are associated with the amount of progesterone and slow wave sleep. The harmonious inter-relationship of the circadian pattern of the immune, endocrine and sleep-wake systems may be important in the cause and functions of sleep.

Keywords

Molinero P, Soutto M, Benot S et al. **Year** 2000

Authors Molinero P, Soutto M, Benot S et al.

Report Name Melatonin is responsible for the nocturnal increase observed in serum and thymus of thymosin alpha1 and thymulin concentrations: observations in rats and humans

Publication J Neuroimmunol

Issue-page numbers 103:180–188 doi:10.1016/S0165-5728(99)00237-4. PMID:10696913

URL http://www.biomedexperts.com/Abstract.bme/10696913/Melatonin_is_responsible_for_the_nocturnal_increase_observed_in_serum_and_thymus_of_thymosin_alpha1_and_thym

Abstract This paper shows that melatonin regulates both thymosin alpha1 and thymulin production as well as the expression of the prothymosin alpha gene. The results revealed the following facts: (a) The concentrations of thymosin alpha1 in both serum and thymus of rat showed a nyctohemeral profile with peak values late at night and basal values during the day. The concentrations of thymulin in rat serum also showed a 24-h rhythm with an increase in their values at night. This rhythmical character for thymosin alpha1, and thymulin was also found in the human serum. (b) Rats injected with melatonin during the day exhibited a significant increase in the concentrations of both peptides. Moreover, continuous light exposure on the animals at daytime and pinealectomy cause a decrease in thymosin a1 and thymulin concentrations with regards to those found in control rats. (c) Melatonin regulates the expression of the prothymosin alpha gene, analyzed by Northern blot. These results suggest that melatonin may be involved in the regulation of immune functions by increasing the thymic peptides production.

Keywords

Authors Molis TM, Spriggs LL, Hill SM

Report Name Modulation of estrogen receptor mRNA expression by melatonin in MCF-7 human breast cancer cells

Publication Mol Endocrinol

Issue-page numbers 8:1681–1690 doi:10.1210/me.8.12.1681. PMID:7708056

URL http://mend.endojournals.org/content/8/12/1681.short

Abstract Melatonin, the hormonal product of the pineal gland, has been shown to inhibit the development of mammary tumors in vivo and the proliferation of MCF-7 human breast cancer cells in vitro by mechanisms not yet identified. However, previous studies have demonstrated that melatonin significantly decreased estrogen-binding activity and the expression of immunoreactive estrogen receptor (ER) in MCF-7 breast cancer cells. To determine the mechanism(s) by which melatonin regulates ER expression in MCF-7 cells, the relationship between the level of steady state ER mRNA and the rate of ER gene transcription were examined in response to melatonin. Physiological concentrations of melatonin decreased steady state levels of ER mRNA expression in a dose- and time-specific manner. This decrease was not dependent upon the presence of estrogen since similar decreases in steady state ER mRNA levels were seen in MCF-7 cells cultured in both complete and estrogen-depleted media. The decreased expression of ER mRNA in response to melatonin appears to be directly related to the suppression of transcription of the ER gene. This regulation is independent of the synthesis of new proteins, as cycloheximide was unable to block the melatonin-induced decrease of steady-state ER mRNA levels. The down-regulation of ER by melatonin appears to not be mediated via a direct interaction with the ER and subsequent feedback on its own expression, since melatonin treatment did not alter the transcriptional regulatory ability of the fully activated wild type ER or a constitutively active hormone-binding domain-deleted ER variant. In addition, the stability of the ER transcript was unaffected by melatonin. Thus, it appears that the antiproliferative actions of this pineal indoleamine are mediated, at least in part, through the suppression of the transcription of the ER gene in MCF-7 human breast cancer cells.

Keywords

Møller M, Baeres FMM

Year 2002

Authors Møller M, Baeres FMM

Report Name The anatomy and innervation of the mammalian pineal gland

Publication Cell Tissue Res

Issue-page numbers 309:139–150 doi:10.1007/s00441-002-0580-5. PMID:12111544

URL http://www.springerlink.com/content/u3f3cr7gwpl9r61r/

Abstract The parenchymal cells of the mammalian pineal gland are the hormone-producing pinealocytes and the interstitial cells. In addition, perivascular phagocytes are present. The phagocytes share antigenic properties with microglial and antigen-presenting cells. In certain species, the pineal gland also contains neurons and/or neuron-like peptidergic cells. The peptidergic cells might influence the pinealocyte by a paracrine secretion of the peptide. Nerve fibers innervating the mammalian pineal gland originate from perikarya located in the sympathetic superior cervical ganglion and the parasympathetic sphenopalatine and otic ganglia. The sympathetic nerve fibers contain norepinephrine and neuropeptide Y as neurotransmitters. The parasympathetic nerve fibers contain vasoactive intestinal peptide and peptide histidine isoleucine. Recently, neurons in the trigeminal ganglion, containing substance P, calcitonin gene-related peptide, and pituitary adenylate cyclase-activating peptide, have been shown to project to the mammalian pineal gland. Finally, nerve fibers originating from perikarya located in the brain containing, for example, GABA, orexin, serotonin, histamine, oxytocin, and vasopressin innervate the pineal gland directly via the pineal stalk. Biochemical studies have demonstrated numerous receptors on the pinealocyte cell membrane, which are able to bind the neurotransmitters located in the pinealopetal nerve fibers. These findings indicate that the mammalian pinealocyte can be influenced by a plethora of neurotransmitters.

Keywords

Monk TH

Year 1992

Authors Monk TH

Report Name Chronobiology of mental performance

Publication In: Touitou Y & Haus E, Eds. Biologic Rhythms in Clinical and Laboratory Medicine

Issue-page numbers Berlin, Heidelberg, Paris: Springer-Verlag. pp. 208–213

URL N/A

Abstract N/A

Keywords

Monsees GM, Kraft P, Hankinson SE, et al. **Year** 2012

Authors Genevieve M. Monsees, Peter Kraft, Susan E. Hankinson, David J. Hunter, Eva S. Schernhammer

Report Name Circadian genes and breast cancer susceptibility in rotating shift workers

Publication International Journal of Cancer

Issue-page numbers Accepted Article (Accepted, unedited articles published online for future issues)

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.27564/abstract

Abstract

Rotating night shift work is associated with increased risk of breast cancer, likely via circadian disruption. We hypothesized that circadian pathway genes influence breast cancer risk, particularly in rotating night shift workers. We selected 178 common variants across 15 genes pertinent to the circadian system. Using a mixed candidate- and tag-single nucleotide polymorphism approach, we tested for associations between these variants and breast cancer risk in 1,825 women within the Nurses' Health Study II cohort and investigated potential interactions between genotype and rotating shift-work in a subset of 1,318 women. Multiple-testing-adjusted p-values were obtained by permutation (n=10,000). None of the selected variants was significantly associated with breast cancer risk. However, when accounting for potential effect modification, rs23051560 (Ala394Thr) in the largest circadian gene, Neuronal PAS domain protein 2 (NPAS2) was most strongly associated with breast cancer risk (nominal test for interaction p-value=0.0005; 10,000-permutation-based main-effects p-value among women with <24 months of shift-work=0.003). The observed multiplicative association with breast cancer risk per minor allele (A) was 0.65 (95%CI=0.51-0.82) among women with <24 months of shift-work, and 1.19 (95%CI=0.93-1.54) with ≥24 months of shift-work. Women homozygous for the minor allele (AA) with ≥24 months of shift-work had a 2.83-times higher breast cancer risk compared to homozygous AA women with <24 months of shift-work (95%CI=1.47-5.56).

In summary, common variation in circadian genes plays at most a small role in breast cancer risk among women of European ancestry. The impact of NPAS2 Ala394Thr in the presence of rotating shift-work requires further investigation.

Keywords circadian genes;

Monteleone P, Esposito G, La Rocca A, Maj M **Year** 1995

Authors P. Monteleone, G. Esposito, A. La Rocca and M. Maj

Report Name Does bright light suppress nocturnal melatonin secretion more in women than men?

Publication Journal of Neural Transmission

Issue-page numbers Volume 102, Number 1, 75-80

URL http://www.springerlink.com/content/l1723530037282q1/

Abstract

Sex differences in the sensitivity of the human pineal gland to the suppressant effect of bright light on melatonin synthesis were studied in 6 healthy men and women. Blood samples were collected in two randomly ordered sessions: in one, subjects rested supine in bed, in the dark, from 21.00 to 7.00h; in the other session, they were exposed to bright light (2,000 lux) from 2.00 to 4.00 h. In the dark condition, no significant differences were observed between men and women in either the timing or the absolute values of melatonin plasma levels, whereas after bright light exposure, the suppression of plasma melatonin was a 40% greater in women than in men. These findings suggest that, in humans, there is a sex difference in the nocturnal sensitivity of the pineal to light.

Keywords Circadian rhythm - light sensitivity - human melatonin - sex difference

Monteleone P, Martiadis V, Maj M

Year 2011

Authors Palmiero Monteleone, Vassilis Martiadis, Mario Maj

Report Name Circadian rhythms and treatment implications in depression

Publication Progress in Neuro-Psychopharmacology and Biological Psychiatry

Issue-page numbers Volume 35, Issue 7, 15 August 2011, Pages 1569-1574

URL http://www.sciencedirect.com/science/article/pii/S0278584610002940

Abstract In humans almost all physiological and behavioural functions occur on a rhythmic basis. Therefore the possibility that delays, advances or desynchronizations of circadian rhythms may play a role in the pathophysiology of psychiatric disorders is an interesting field of research. In particular mood disorders such as seasonal affective disorder and major depression have been linked to circadian rhythms alterations. Furthermore, the antidepressant efficacy of both pharmacological and non-pharmacological strategies affecting endogenous circadian rhythms, such as new antidepressant medications, light-therapy and sleep deprivation, is consistent with the idea that circadian alterations may represent a core component of depression, at least in a subgroup of depressed patients. This paper briefly describes the molecular and genetic mechanisms regulating the endogenous clock system, and reviews the literature supporting the relationships between depression, antidepressant treatments and changes in circadian rhythms.

Keywords Antidepressants; Circadian rhythms; Depression; Endogenous clock; Treatment

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Moore CB, Siopes TD

Year 2003

Authors Moore CB, Siopes TD

Report Name Melatonin enhances cellular and humoral immune responses in the Japanese quail (Coturnix coturnix japonica) via an opiatergic mechanism

Publication Gen Comp Endocrinol

Issue-page numbers 131:258–263 doi:10.1016/S0016-6480(03)00011-X. PMID:12714007

URL http://www.sciencedirect.com/science/article/pii/S001664800300011X

Abstract It is known that melatonin has important immunomodulatory properties in the Japanese quail. However, the mechanism of melatonin action on the immune system is not clearly understood in avian species. In mammals, the immunostimulatory properties of melatonin are mediated by the release of opioid peptides from activated T-lymphocytes. The present study was performed to determine if these same melatonin-induced opioids (MIO) are involved with the immunoenhancing effects of melatonin in quail. Three treatment groups were given melatonin (50 μg/ml) in the drinking water ad libitum along with naltrexone, a known opioid receptor-blocking agent. Melatonin was administered throughout the 3 week study and each bird received a daily intramuscular injection of naltrexone at a dose of 0.1, 1.0, or 10.0 mg/kg. In addition, three control groups were established that received only melatonin, naltrexone, or diluent. Evaluation of the cellular and humoral immune responses was initiated after 2 weeks of treatments. A cutaneous basophil hypersensitivity reaction to phytohemagglutinin (PHA-P) was measured to evaluate the cellular immune response. To evaluate the humoral immune response, primary antibody titers were determined 7 days post-intravenous injection with a Chukar red blood cell (CRBC) suspension. Both the cellular and humoral immune responses were significantly increased by 22 and 34%, respectively, upon melatonin exposure as compared to quail receiving diluent only. Concomitant administration of naltrexone and melatonin significantly reduced the immunoenhancing effect of melatonin across all naltrexone doses. We conclude that melatonin enhances a cellular and humoral immune response in Japanese quail via an opiatergic mechanism.

Keywords

Authors Moore CB, Siopes TD, Steele CT, Underwood H

Report Name Pineal melatonin secretion, but not ocular melatonin secretion, is sufficient to maintain normal immune responses in Japanese quail (Coturnix coturnix japonica)

Publication Gen Comp Endocrinol

Issue-page numbers 126:352–358 doi:10.1016/S0016-6480(02)00011-4. PMID:12093123

URL http://www.sciencedirect.com/science/article/pii/S0016648002000114

Abstract Reports that plasma melatonin is an important immune regulator in avian species have been rather sparse and contradictory. Also, the primary source of immune-modulating melatonin has yet to be determined in birds. In Japanese quail (Coturnix coturnix japonica), the pineal gland and eyes contribute roughly two thirds and one third of the melatonin found in the blood, respectively. Two experiments were conducted to evaluate melatonin as an immune modulator in Japanese quail and to determine the primary source of immune-modulating melatonin in this species. Experiment 1 was designed to evaluate the involvement of the pineal gland and the eyes in immunocompetence. Each of three groups of quail was assigned a surgical treatment and the cellular and humoral immune responses were determined 8 weeks following surgery. The surgical treatments were pinealectomy (Px), sham pinealectomy (SH-Px), and ocular enucleation (eye removal (Ex)). Experiment 2 utilized exogenous melatonin as a replacement to reconstitute immune responses in surgically immunocompromised birds. In this experiment, 50.0 μg/ml of melatonin, or diluent only, was provided to Px and SH-Px birds in the drinking water ad libitum. The cellular and humoral immune responses were determined after 8 weeks of melatonin treatment. In both experiments, a cutaneous basophil hypersensitivity reaction to phytohemagglutinin was measured to evaluate the cellular immune response. To evaluate the humoral immune response, primary antibody titers were determined 7 days postintravenous injection with a Chukar red blood cell suspension. Flow cytometric analysis of peripheral blood lymphocytes was performed to determine the relative percentage of CD4+ and CD8+ T- and B-lymphocytes in all treatments of Experiment 2. In Experiment 1, both the SH-Px and Ex surgical treatments produced similar cellular and humoral immune responses, and these responses were significantly greater than those in Px-treated birds. Pinealectomy significantly reduced the cellular and humoral immune responses from SH-Px by 25.8% and 41.3%, respectively. In Experiment 2, Px again resulted in depressed cellular and humoral immune responses. In addition, Px significantly reduced CD8+ T-lymphocyte numbers compared to SH-Px, while B-lymphocytes remained unchanged. Melatonin administration to Px birds increased the cellular (32.9%) and humoral (30.6%) immune responses to the level of control (SH-Px) birds, although this reconstitution was not due to increased CD8+ T- or B-lymphocytes. From these data, it was clear that removal of the pineal gland, but not the eyes, reduced cellular and humoral immune responses, which were reconstituted to normal levels by exogenous melatonin. These data suggest that immunodepression is only observed in birds with two thirds of the plasma melatonin removed by pinealectomy. Removal of one third of the plasma melatonin (by ocular enucleation) is not sufficient to reduce cellular and humoral responses in the Japanese quail.

Keywords Melatonin; Immune response; Japanese quail; Pineal; Eye

Moore DE

Year 2002

Authors Moore DE.

Report Name Drug-induced cutaneous photosensitivity: incidence, mechanism, prevention and management

Publication Drug Saf

Issue-page numbers 2002;25(5):345-72.

URL http://www.ncbi.nlm.nih.gov/pubmed/12020173

Abstract

The interaction of sunlight with drug medication leads to photosensitivity responses in susceptible patients, and has the potential to increase the incidence of skin cancer. Adverse photosensitivity responses to drugs occur predominantly as a phototoxic reaction which is more immediate than photoallergy, and can be reversed by withdrawal or substitution of the drug. The bias and inaccuracy of the reporting procedure for these adverse reactions is a consequence of the difficulty in distinguishing between sunburn and a mild drug photosensitivity reaction, together with the patient being able to control the incidence by taking protective action. The drug classes that currently are eliciting a high level of adverse photosensitivity are the diuretic, antibacterial and nonsteroidal anti-inflammatory drugs (NSAIDs). Photosensitising chemicals usually have a low molecular weight (200 to 500 Daltons) and are planar, tricyclic, or polycyclic configurations, often with heteroatoms in their structures enabling resonance stabilisation. All absorb ultraviolet (UV) and/or visible radiation, a characteristic that is essential for the chemical to be regarded as a photosensitiser. The photochemical and photobiological mechanisms underlying the adverse reactions caused by the more photoactive drugs are mainly free radical in nature, but reactive oxygen species are also involved. Drugs that contain chlorine substituents in their chemical structure, such as hydrochlorthiazide, furosemide and chlorpromazine, exhibit photochemical activity that is traced to the UV-induced dissociation of the chlorine substituent leading to free radical reactions with lipids, proteins and DNA. The photochemical mechanisms for the NSAIDs that contain the 2-aryl propionic acid group involve decarboxylation as the primary step, with subsequent free radical activity. In aerated systems, the reactive excited singlet form of oxygen is produced with high efficiency. This form of oxygen is highly reactive towards lipids and proteins. NSAIDs without the 2-arylpropionic acid group are also photoactive, but with differing mechanisms leading to a less severe biological outcome. In the antibacterial drug class, the tetracyclines, fluoroquinolones and sulfonamides are the most photoactive. Photocontact dermatitis due to topically applied agents interacting with sunlight has been reported for some sunscreen and cosmetic ingredients, as well as local anaesthetic and anti-acne agents. Prevention of photosensitivity involves adequate protection from the sun with clothing and sunscreens. In concert with the preponderance of free radical mechanisms involving the photosensitising drugs, some recent studies suggest that diet supplementation with antioxidants may be beneficial in increasing the minimum erythemal UV radiation dose.

Keywords

Authors Moreno CRC, Louzada FM, Teixeira LR et al.

Report Name Short sleep is associated with obesity among truck drivers

Publication Chronobiol Int

Issue-page numbers 23:1295–1303 doi:10.1080/07420520601089521. PMID:17190714

URL http://informahealthcare.com/doi/abs/10.1080/07420520601089521

Abstract Recent studies suggest that short-sleep duration is independently associated with obesity in the general population. The population of truck drivers is of particular interest, because they frequently work irregular shifts that in turn are associated with short-sleep duration. In addition, truck drivers have a high prevalence of sedentary habits, poor diet, and obesity. The present study aimed at verifying the association between sleep patterns and factors associated with obesity in this population. The study sample consisted in 4,878 truck drivers who participated in a campaign promoted by a highway company in the State of São Paulo, Brazil. This campaign offered highway truck drivers a medical and laboratorial evaluation. The truck drivers completed a questionnaire concerning demographic data, sleep duration, consumption of medications, and medical problems, such as diabetes, cardiopathy, and hypertension; as well as the Berlin questionnaire, which is able to discriminate low and high risk for obstructive sleep apnea. Blood samples were collected to measure glucose and cholesterol levels. Also, body weight and height were registered to calculate the body mass index (BMI). The mean age (+/-SD) of the truck drivers studied was 40+/-10 years. Out of the truck drivers analyzed, 28.3% (n = 1,379) had a BMI > or =30.0 Kg/m2 (obesity). Among the 4,878 drivers included in the study, 1,199 (24.6%) were on medications and 334 (6.8%) were diabetic. Drivers (26.9%) with the greater BMI had a short sleep length. The independent factors associated with obesity were sleep duration <8 h/day (OR = 1.24), age >40 years (OR = 1.20), glucose levels >200 (OR = 2.02), cholesterol levels >240 (OR = 1.57), snoring (OR = 1.74), and hypertension (OR = 2.14). Smoking was not associated with obesity (OR = 0.69), and diabetes was considered a control variable. In conclusion, this study supports the hypothesis that short sleep duration as well as age >40 years are independently associated with obesity. This particular combination (short-sleep duration and obesity) is independently associated with several healthcare problems, including high levels of cholesterol, glucose, snoring, and hypertension. However, due to the cross-sectional nature of this study, no cause-effect relationship can be drawn from these results.

Keywords

Morgan L, Hampton S, Gibbs M, Arendt J

Year 2003

Authors Linda Morgan, Shelagh Hampton, Michelle Gibbs and Josephine Arendt

Report Name Circadian Aspects of Postprandial Metabolism

Publication Chronobiology International

Issue-page numbers 20:5, 795-808

URL http://informahealthcare.com/doi/abs/10.1081/CBI-120024218

Abstract Time-dependent variations in the hormonal and metabolic responses to food are of importance to human health, as postprandial metabolic responses have been implicated as risk factors in a number of major diseases, including cardiovascular disease. Early work reported decreasing glucose tolerance in the evening and at night with evidence for insulin resistance at night. Subsequently an endogenous circadian component, assessed in constant routine (CR), as well as an influence of sleep time, was described for glucose and insulin. Plasma triacylglycerol (TAG), the major lipid component of dietary fat circulating after a meal, also appears to be influenced by both the circadian clock and sleep time with higher levels during biological night (defined as the time between the onset and offset of melatonin secretion) despite identical hourly nutrient intake. These time-dependent differences in postprandial responses have implications for shiftworkers. In the case of an unadapted night shift worker, meals during work time will be taken during biological night. In simulated night shift conditions the TAG response to a standard meal, preceded by either a low-fat or a high-fat premeal, was higher after a nighttime meal than during a daytime meal, and the day/night difference was larger in men than in women. In real night shift workers in Antarctica, insulin, glucose, and TAG all showed an increased response after a nighttime meal (second day of night shift) compared to a daytime meal. Night shift workers are reported to have an approximately 1.5 times higher incidence of heart disease risk and also demonstrate higher TAG levels compared with matched dayworkers. As both insulin resistance and elevated circulating TAG are independent risk factors for heart disease, it is possible that meals at night may contribute to this risk.

Keywords Circadian, Insulin, Glucose, Triacylglycerol (TAG), Heart disease

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Morgan PJ

Year 2000

Authors Morgan PJ

Report Name The pars tuberalis: the missing link in the photoperiodic regulation of prolactin secretion? [Review]

Publication J Neuroendocrinol

Issue-page numbers 12:287–295 doi:10.1046/j.1365-2826.2000.00459.x. PMID:10718925

URL The pars tuberalis: the missing link in the photoperiodic regulation of prolactin secretion? [Review]

Abstract The endocrine function of the pars tuberalis of the pituitary gland has been an enigma for many years. Recent work suggests that one of its primary functions in seasonal mammals is to mediate photoperiodically regulated changes in prolactin secretion via an unidentified factor called tuberalin.

Keywords

Authors Morgan PJ, Barrett P, Howell HE, Helliwell R

Report Name Melatonin receptors: localization, molecular pharmacology and physiological significance

Publication Neurochem Int

Issue-page numbers 24:101–146 doi:10.1016/0197-0186(94)90100-7. PMID:8161940

URL http://www.sciencedirect.com/science/article/pii/0197018694901007

Abstract

A pre-requisite to understanding the physiological mechanisms of action of melatonin is the identification of the target sites where the hormone acts. The radioligand 2-[125I]iodomelatonin has been used extensively to localize binding sites in both the brain and peripheral tissues. In general these binding sites have been found to be high affinity, with Kd in the low picomolar range, and selective for structural analogues of melatonin. Also the affinity of these sites can generally be modulated by guanine nucleotides, consistent with the notion that they are putative G-protein coupled receptors. However, only a few studies have demonstrated that these putative receptors mediate biochemical and cellular responses. In the pars tuberalis (PT) and pars distalis (PD) of the pituitary, the amphibian melanophore and vertebrate retina, evidence indicates that melatonin acts to inhibit intracellular cyclic AMP through a G-protein coupled mechanism, demonstrating that this is a common signal transduction pathway for many melatonin receptors. However in the pars distalis the inhibition of calcium influx and membrane potential are also important mediators of melatonin effects.

How many different forms or states of the melatonin receptor exist is unknown, but clearly the identification of the structure of the melatonin receptor(s) and its ability to interact with different G-proteins and signal transduction pathways are quintessential to our understanding of the physiological mechanisms of action of melatonin. In parallel the recent development of new melatonin analogues will greatly aid our understanding of the pharmacology of the melatonin receptor both in terms of the development of potent melatonin receptor antagonists and for the definition of receptor sub-types.

The wide species and phylogenic diversity of melatonin binding sites in the brain has probably generated more questions than answers. Nevertheless the localization of melatonin receptors to the suprachiasmatic nucleus of the hypothalamus is at least consistent with circadian effects within the foetus and the adult. In contrast the PT of the pituitary presents an enigma in relation to the seasonal effects of melatonin. A model of how melatonin might mediate the timing of the circannual events through the PT is proposed.

Keywords

Authors Morgan PJ, Williams LM

Report Name The pars tuberalis of the pituitary: a gateway for neuroendocrine output

Publication Rev Reprod

Issue-page numbers 1:153–161 doi:10.1530/ror.0.0010153. PMID:9414453

URL http://ror.reproduction-online.org/cgi/content/abstract/1/3/153

Abstract The pars tuberalis is a structurally distinct region of the adenohypophysis, the function of which has been unclear for decades. Recent studies, which demonstrate the localization of melatonin receptors on the pars tuberalis, suggest a photoperiodic function. The principal cell type of the pars tuberalis is morphologically distinct from others in the pituitary and is thought to secrete a specific product. In support of this, evidence is emerging that ovine pars tuberalis cells secrete a factor ('tuberalin') that exerts hormonal control over both gene expression and prolactin release from the pars distalis lactotrophs. These data in conjunction with physiological studies, which show that photoperiodically driven cycles in prolactin secretion can occur in the absence of an intact hypothalamic-pituitary axis, suggest that the function of the pars tuberalis is to act as an endocrine intermediate in the photoperiodic effects of melatonin on prolactin secretion. Studies of the cellular biochemistry of the ovine pars tuberalis suggest that the main function of melatonin is to prevent or terminate transcriptional and translational activation by an unidentified factor (Stim X). On the basis of these physiological and biochemical studies, a hypothetical model is proposed to account for the mechanism of photoperiodic regulation of prolactin secretion by melatonin.

Keywords

Morghen I, Turola MC, Forini E, et al. **Year** 2009

Authors Ilaria Morghen, Maria Cristina Turola, Elena Forini, Piero Di Pasquale, Paolo Zanatta, and Teresa Matarazzo

Report Name Ill-lighting syndrome: prevalence in shift-work personnel in the anaesthesiology and intensive care department of three Italian hospitals

Publication J Occup Med Toxicol.

Issue-page numbers 2009; 4: 6.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2666745/

Abstract

Background
Light is one of the most important factors in our interaction with the environment; it is indispensable to visual function and neuroendocrine regulation, and is essential to our emotional perception and evaluation of the environment. Previous studies have focussed on the effects of prolonged anomalous exposure to artificial light and, in the field of work-related illness. Studies have been carried out on shift-work personnel, who are obliged to experience alterations in the physiological alternation of day and night, with anomalous exposure to light stimuli in hours normally reserved for sleep. In order to identify any signs and symptoms of the so-called ill-lighting syndrome, we carried out a study on a sample of anaesthesiologists and nurses employed in the operating theatres and Intensive Care Departments of three Italian hospitals. We measured the subjective emotional discomfort (stress) experienced by these subjects, and its correlation with environmental discomfort factors, in particular the level of lighting, in their workplace.
Methods
We used a questionnaire developed by the Scandinavian teams who investigated Sick-Building Syndrome, that was self-administered on one day in the environments where the degree of illumination was measured according to UNIEN12464-1 regulations.
Results
Upon comparison of the types of exposure with the horizontal luminance values (lux) measured (< 700 lux, between 1000–1500 lux, > 1500 lux) and the degree of stress reported, (Intensive Care: mean stress = 55.8%, high stress = 34.6%; Operating Theatres: mean stress = 51.5%, high stress = 33.8%), it can be observed that the percentage of high stress was reduced as the exposure to luminance was increased, although this finding was not statistically significant.
Conclusion
We cannot share other authors' enthusiasm regarding the effects on workers well-being correlated to the use of fluorescent lighting. The stress level of our workers was found to be more heavily influenced by their familial and working conditions, irrespective of the ambient light stimulus.

Keywords

Morin D, Simon N, Deprés-Brummer P et al. **Year** 1997

Authors Morin D, Simon N, Deprés-Brummer P et al.

Report Name Melatonin high-affinity binding to alpha-1-acid glycoprotein in human serum

Publication Pharmacology

Issue-page numbers 54:271–275 doi:10.1159/000139495. PMID:9380773

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=139495

Abstract The binding of 3H-melatonin to human serum proteins was investigated by equilibrium dialysis at 37 °C and pH 7.4. The binding to serum was moderate (53%) for physiological melatonin concentrations below 1 nmol/l. α1-Acid glycoprotein and albumin bound melatonin with high 27 ± 3 and low 1.5 ± 0.1 (mmol/l)–1 affinity, respectively. Melatonin binding to other serum proteins, γ-globulins and lipoproteins was not significant. The serum binding was characterized by a saturable and a nonsaturable component. The saturable component resulted from the high-affinity binding to α1-acid glycoprotein and the nonsaturable component resulted from the low-affinity binding to albumin. The number of binding sites was 0.36/molecule of α1-acid glycoprotein, when either pure α1-acid glycoprotein or serum were studied, indicating that only a fraction of α1-acid glycoprotein bound melatonin. The observed binding parameters did not enable simulation of the observed serum binding, and melatonin binding to an α1-acid glycoprotein-albumin mixture was higher than that expected from the binding to each isolated protein. The high-affinity melatonin binding to αi-acid glycoprotein might result from a potentiation of the binding interaction by albumin and the amount of melatonin bound in plasma might vary according to the α1-acid glycoprotein concentration.

Keywords

Morin PJ **Year** 1999

Authors Morin PJ

Report Name beta-catenin signaling and cancer

Publication Bioessays

Issue-page numbers 21:1021–1030 doi:10.1002/(SICI)1521-1878(199912)22:1<1021::AID-BIES6>3.0.CO;2-P. PMID:10580987

URL http://www.ncbi.nlm.nih.gov/pubmed/10580987

Abstract Since its discovery as a protein associated with the cytoplasmic region of E-cadherin, beta-catenin has been shown to perform two apparently unrelated functions: it has a crucial role in cell-cell adhesion in addition to a signaling role as a component of the Wnt/wg pathway. Wnt/wg signaling results in beta-catenin accumulation and transcriptional activation of specific target genes during development. It is now apparent that deregulation of beta-catenin signaling is an important event in the genesis of a number of malignancies, such as colon cancer, melanoma, hepatocellular carcinoma, ovarian cancer, endometrial cancer, medulloblastoma pilomatricomas, and prostate cancer. beta-catenin mutations appear to be a crucial step in the progression of a subset of these cancers, suggesting an important role in the control of cellular proliferation or cell death. The APC/beta-catenin pathway is highly regulated and includes players such as GSK3-beta, CBP, Groucho, Axin, Conductin, and TCF. c-MYC and cyclin D1 were recently identified as a key transcriptional targets of this pathway and additional targets are likely to emerge.

Keywords

Moriwaki SI, Misawa J, Yoshinari Y, et al. **Year** 2001

Authors Moriwaki SI, Misawa J, Yoshinari Y, Yamada I, Takigawa M, Tokura Y.

Report Name Analysis of photosensitivity in Japanese cancer-bearing patients receiving photodynamic therapy with porfimer sodium (Photofrin)

Publication Photodermatol Photoimmunol Photomed

Issue-page numbers 2001 Oct;17(5):241-3.

URL http://www.ncbi.nlm.nih.gov/pubmed/11555335

Abstract A major disadvantage of a new cancer treatment, porfimer sodium (Photofrin)-mediated photodynamic therapy (PF-PDT), is photosensitivity for several weeks after cessation of the treatment. To characterize persistent sensitivity to visible light following PF-PDT, phototestings were performed in 59 Japanese cancer-bearing patients with a slide projector lamp 3 weeks or more after the treatment. The duration of photosensitivity was analyzed in relation to the patients' sex, skin phototype (SPT), site of tumor and liver function. There was no correlation of the photosensitivity persistency with the site of cancers and the function of liver. However, female subjects needed significantly longer recovery periods than male subjects from potential photosensitivity after PF-PDT. Patients with SPT2 were significantly more sensitive than patients with SPT3 and 4. These results suggest that the prolonged photosensitivity occurs after PF-PDT especially in female patients and in cases with a lighter SPT. Such patients should be carefully followed up for post-PDT photosensitivity.

Keywords

Mormont MC, Lévi F **Year** 1997

Authors Mormont MC, Lévi F

Report Name Circadian-system alterations during cancer processes: a review

Publication Int J Cancer

Issue-page numbers 70:241–247. PMID:9009166 doi:10.1002/(SICI)1097-0215(19970117)70:2<241::AIDIJC16> 3.0.CO;2-L

URL http://onlinelibrary.wiley.com/doi/10.1002/%28SICI%291097-0215%2819970117%2970:2%3C241::AID-IJC16%3E3.0.CO;2-L/abstract

Abstract Murine and human data have indicated that tumors and tumor-bearing hosts may exhibit nearly normal or markedly altered circadian rhythms. Amplitude damping, phase shifts, and/or period (τ) change, including appearance of ultradian rhythms (with $\tau < 20$ hr) usually become more prominent at late stages of cancer development. The extent of rhythm alterations also varies according to tumor type, growth rate and level of differentiation. While “group chronotherapy,” i.e., administration of the same chronomodulated schedule to cancer patients, has increased chemotherapy efficacy and/or tolerability, cancer patients' individual circadian rhythms now need to be explored on a large scale, in order to estimate the incidence of cancer-associated circadian-system alterations and to understand the underlying mechanisms. Correlations between such alterations and patient outcome must be established in order to specify the need for individualized chronomodulated delivery schedules and/or specific rhythm-oriented therapy, especially in patients with circadian-system disturbance.

Keywords

Mormont MC, Waterhouse J **Year** 2002

Authors Mormont MC, Waterhouse J

Report Name Contribution of the rest-activity circadian rhythm to quality of life in cancer patients

Publication Chronobiol Int

Issue-page numbers 19:313–323 doi:10.1081/CBI-120002606. PMID:11962684

URL http://informahealthcare.com/doi/abs/10.1081/CBI-120002606?journalCode=cbi

Abstract Quality of life (QoL) is estimated from patients scores to items related to everyday life, including rest and activity. The rest–activity rhythm reflects endogenous circadian clock function. The relation between the individual rhythm in activity and QoL was investigated in 200 patients with metastatic colorectal cancer. Patients wore a wrist actigraph (Ambulatory Monitoring Inc., New York, NY) for 3–5 d before chronotherapy, and completed a QoL questionnaire developed by the European Organization for Research and Treatment of Cancer (QLQ-C30) plus the Hospital Anxiety and Depression Scale. The rest–activity circadian rhythm was characterized by the mean activity level (m), autocorrelation coefficient at 24h (r24), and the dichotomy index (I<O), a ratio between the amount of activity while in and out of bed. The distribution of the rest–activity cycle parameters and that of QoL scores was independent of sex, age, primary tumor, number of metastatic sites, and prior treatment. Both the 24h rhythm indicators were positively correlated with global QoL score as well as physical, emotional, and social functioning. Negative correlations were found between m, r24, or I<O and fatigue, appetite loss, and nausea. The rest–activity circadian rhythm appeared to be an objective indicator of physical welfare and QoL. This analysis suggests that circadian function may be one of the biological determinants of QoL in cancer patients.

Keywords Circadian rest/activity rhythm, Fatigue, Metastatic colorectal cancer, Quality of life

Morrey KM, McLachlan JA, Serkin CD, Bakouche O **Year** 1994

Authors Morrey KM, McLachlan JA, Serkin CD, Bakouche O

Report Name Activation of human monocytes by the pineal hormone melatonin

Publication J Immunol

Issue-page numbers 153:2671–2680. PMID:8077674

URL http://www.jimmunol.org/content/153/6/2671.abstract

Abstract To determine the effects of the pineal hormone melatonin on human monocytes, human monocytes were activated by different concentrations of melatonin. Above the activation threshold of 5 x 10(-11) M, melatonin was able to induce the cytotoxicity of human monocytes, the secretion of IL-1, and the production of reactive oxygen intermediates. Melatonin and LPS seemed to have a synergistic effect on human monocyte activation. Indeed, below their respective monocyte activation threshold (5 x 10(-11) M and 0.625 ng/ml), melatonin (10(-12) M) in association with LPS (0.2 ng/ml) was able to induce cytotoxicity, IL-1 secretion, and reactive oxygen intermediates production. Melatonin alone at 10(-12) M or LPS alone at 0.2 ng/ml did not activate monocytes. Furthermore, melatonin was able to prime the monocytes for a subsequent activation by LPS. When monocytes were activated by LPS (0.25 ng/ml) at the time that they were plated and then activated by melatonin (10(-12) M) 8 h later, no IL-1 secretion and no cytotoxicity were detected. However, when the cells were first activated by melatonin (10(-12) M), and then 8 h later by LPS (0.25 ng/ml), IL-1 secretion and monocyte cytotoxicity were observed. Above its monocyte activation threshold, melatonin induces both cell-associated IL-1 alpha and IL-1 beta activities. Below this activation threshold, i.e., at 10(- 12) M, melatonin does not induce the cell-associated IL-1 alpha and IL- 1 beta activities, but does induce the mRNA for both IL-1 (alpha and beta). It seems that melatonin activates monocytes through protein kinase C. These data suggest that melatonin activates monocytes and induces their cytotoxic properties, along with the IL-1 secretion.

Keywords

Motohashi Y, Kawakami T, Miyazaki Y, et al. **Year** 1990

Authors Y Motohashi, T Kawakami, Y Miyazaki, T Takano, W Ekataksin

Report Name Circadian variations in trichloroethylene toxicity under a 12:12 hr light-dark cycle and their alterations under constant darkness in rats.

Publication Toxicology and Applied Pharmacology

Issue-page numbers Volume: 104, Issue: 1, Pages: 139-148 PubMed: 2360203

URL http://www.mendeley.com/research/circadian-variations-in-trichloroethylene-toxicity-under-a-1212-hr-lightdark-cycle-and-their-alterations-under-constant-darkness-in-rats/

Abstract In order to investigate the circadian variations in acute toxicity of trichloroethylene (TRI), TRI (1.2 g/kg weight) or saline was injected intraperitoneally in a total of 88 male Wistar rats at four circadian stages (03.00, 09.00, 15.00, and 21.00:hr.min) under two different lighting regimens of a 12:12 hr light-dark cycle (LD; light from 06.00 to 18.00) and of constant darkness (DD). Circadian variations in TRI toxicity were confirmed in both LD and DD. The toxicity of TRI evaluated by the increase in glutamic-pyruvate transaminase activity (GPT) was greatest when injected at 09.00 in LD while at 21.00 in DD. The increases in blood urea nitrogen, serum total cholesterol and triglyceride concentrations reached peaks when injected at 09.00 in LD and 03.00 in DD. The circadian variations in serum trichloroethanol concentration were very similar to those in GPT in both LD and DD, showing a significant correlation (p less than 0.05). The present study revealed that circadian variations in TRI toxicity existed in LD and that these variations persisted in a free-running condition. The peak phase of TRI toxicity was located in a trough phase (09.00) in LD and in a peak phase (21.00 or 03.00) in DD of temperature rhythm. Thus, the phase relationship changed in DD, showing a desynchronization between TRI toxicity rhythm and temperature rhythm, which is an unusual phenomenon. This means that an unexpected potentiation of TRI toxicity during active phase which is not a critical phase in a well-synchronized state could occur in a free-running condition.

Keywords

Motta M **Year** 2012

Authors Motta, M.

Report Name Adverse Health Effects of Nighttime Lighting

Publication The Journal of the American Association of Variable Star Observers

Issue-page numbers electronic edition, accepted for publication

URL http://adsabs.harvard.edu/abs/2012JAVSO.tmp..186M

Abstract The effects of poor lighting and glare on public safety are well-known, as are the harmful environmental effects on various species and the environment in general. What is less well-known is the potential harmful medical effects of excessive poor nighttime lighting. A significant body of research has been developed over the last few years regarding this problem. One of the most significant effects is the startling increased risk for breast cancer by excessive exposure to nighttime lighting. The mechanism is felt to be by disruption of the circadian rhythm and suppression of melatonin production from the pineal gland. Melatonin has an anticancer effect that is lost when its production is disrupted. I am in the process of developing a monograph that will summarize this important body of research, to be presented and endorsed by the American Medical Association, and its Council of Science and Public health. This paper is a brief overall summary of this little known potential harmful effect of poor and excessive nighttime lighting.

Keywords light pollution

Mottram V, Middleton B, Williams P, Arendt J **Year** 2011

Authors Mottram V, Middleton B, Williams P, Arendt J.

Report Name The impact of bright artificial white and 'blue-enriched' light on sleep and circadian phase during the polar winter

Publication Journal of Sleep Research

Issue-page numbers Volume 20, Issue 1pt2, pages 154–161, March 2011

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2869.2010.00875.x/abstract

Abstract Delayed sleep phase (and sometimes free-run) is common in the Antarctic winter (no natural sunlight) and optimizing the artificial light conditions is desirable. This project evaluated sleep when using 17 000 K blue-enriched lamps compared with standard white lamps (5000 K) for personal and communal illumination. Base personnel, 10 males, five females, 32.5 ± 8 years took part in the study. From 24 March to 21 September 2006 light exposure alternated between 4–5-week periods of standard white (5000 K) and blue-enriched lamps (17 000 K), with a 3-week control before and after extra light. Sleep and light exposure were assessed by actigraphy and sleep diaries. General health (RAND 36-item questionnaire) and circadian phase (urinary 6-sulphatoxymelatonin rhythm) were evaluated at the end of each light condition. Direct comparison (rmanova) of blue-enriched light with white light showed that sleep onset was earlier by 19 min ($P = 0.022$), and sleep latency tended to be shorter by 4 min ($P = 0.065$) with blue-enriched light. Analysing all light conditions, control, blue and white, again provided evidence for greater efficiency of blue-enriched light compared with white ($P < 0.05$), but with the best sleep timing, duration, efficiency and quality in control natural light conditions. Circadian phase was earlier on average in midwinter blue compared with midwinter white light by 45 min ($P < 0.05$). Light condition had no influence on general health. We conclude that the use of blue-enriched light had some beneficial effects, notably earlier sleep, compared with standard white light during the polar winter.

Keywords

Movshon JA, Lennie P **Year** 1979

Authors Movshon JA, Lennie P.

Report Name Pattern-selective adaptation in visual cortical neurones

Publication Nature

Issue-page numbers 278, 850 - 852 (26 April 1979); doi:10.1038/278850a0

URL http://www.nature.com/nature/journal/v278/n5707/abs/278850a0.html

Abstract PROLONGED viewing of a grating pattern produces striking ‘after-effects’, involving changes in the detectability, apparent size, orientation and contrast of subsequently viewed gratings1–3. Studies of perceptual after-effects have been used to infer properties of neurones in the human visual cortex2,4,5 similar to those pattern-selective neurones whose sensitivities have been directly measured in the visual cortex of cats and monkeys6,7. Such inferences are based on two assumptions: first, that perceptual changes result from changes in the distribution of activity within the responding population of neurones; second, that the effect of adaptation on each neurone of the population is to reduce its sensitivity uniformly to all stimuli. The experimental results reported here support the first but challenge the second assumption, as they show that after adaptation to a particular grating the sensitivity of a single neurone to that grating may be reduced more than its sensitivity to other gratings.

Keywords

Münch M, Bromundt V

Year 2012

Authors Mirjam Münch, Vivien Bromundt

Report Name Light and chronobiology: implications for health and disease

Publication Dialogues Clin Neurosci

Issue-page numbers 2012;14:448-453

URL http://www.dialogues-cns.com/wp-content/uploads/2013/01/DialoguesClinNeurosci-14-448.pdf

Abstract Environmental light synchronizes the primary mammalian biological clock in the suprachiasmatic nuclei, as
well as many peripheral clocks in tissues and cells, to the solar 24-hour day. Light is the strongest synchronizing agent (zeitgeber) for the circadian system, and therefore keeps most biological and psychological rhythms internally synchronized, which is important for optimum function. Circadian sleep-wake disruptions and chronic circadian misalignment, as often observed in psychiatric and neurodegenerative illness, can be treated with light therapy. The beneficial effect on circadian synchronization, sleep quality, mood, and cognitive performance depends on timing, intensity, and spectral composition of light exposure. Tailoring and optimizing indoor lighting conditions may be an approach to improve wellbeing, alertness, and cognitive performance and, in the long term, producing health benefits.

Keywords circadian rhythm; daylight; bright light; indoor lighting; zeitgeber; entrainment; intrinsically photosensitive retinal ganglion cell

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Münch M, Kobialka S, Steiner R, et al.

Year 0

Authors Münch M, Kobialka S, Steiner R, Oelhafen P, Wirz-Justice A, Cajochen C

Report Name Wavelength-dependent effects of evening light exposure on sleep architecture and sleep EEG power density in men.

Publication AJP - Regu Physiol

Issue-page numbers May 2006 vol. 290 no. 5 R1421-R1428

URL http://ajpregu.physiology.org/content/290/5/R1421.abstract

Abstract Light strongly influences the circadian timing system in humans via non-image-forming photoreceptors in the retinal ganglion cells. Their spectral sensitivity is highest in the short wavelength range of the visible light spectrum as demonstrated by melatonin suppression, circadian phase shifting, acute physiological responses, and subjective alertness. We tested the impact of short wavelength light (460 nm) on sleep EEG power spectra and sleep architecture. We hypothesized that its acute action on sleep is similar in magnitude to reported effects for polychromatic light at higher intensities and stronger than longer wavelength light (550 nm). The sleep EEGs of eight young men were analyzed after 2-h evening exposure to blue (460 nm) and green (550 nm) light of equal photon densities (2.8 x 1013 photons·cm–2·s–1) and to dark (0 lux) under constant posture conditions. The time course of EEG slow-wave activity (SWA; 0.75–4.5 Hz) across sleep cycles after blue light at 460 nm was changed such that SWA was slightly reduced in the first and significantly increased during the third sleep cycle in parietal and occipital brain regions. Moreover, blue light significantly shortened rapid eye movement (REM) sleep duration during these two sleep cycles. Thus the light effects on the dynamics of SWA and REM sleep durations were blue shifted relative to the three-cone visual photopic system probably mediated by the circadian, non-image-forming visual system. Our results can be interpreted in terms of an induction of a circadian phase delay and/or repercussions of a stronger alerting effect after blue light, persisting into the sleep episode.

Keywords monochromatic light; non-image-forming visual system; spectral analysis; sleep electroencephalogram

Munch M, Leon L, Crippa SV, Kawasaki A

Year 2012

Authors Mirjam Munch, Lorette Leon, Sylvain V. Crippa and Aki Kawasaki

Report Name Circadian and wake-dependent effects on the pupil light reflex in response to narrow-bandwidth light pulses

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers June 5, 2012 IOVS-12-9494

URL http://www.iovs.org/content/early/2012/06/04/iovs.12-9494.abstract

Abstract Purpose: Non-visual light-dependent functions in humans are mainly conveyed by intrinsically photosensitive retinal ganglion cells which express melanopsin as photopigment. We aimed to identify the effects of circadian phase and sleepiness across 24-h on various aspects of the pupil response tolight stimulation. Methods: Ten healthy adults were tested hourly in two 12-h sessions covering a 24-h period. Pupil responses to narrow bandwidth red (635±18nm) and blue (463±24nm) light (duration of 1s and 30s) at equal photon fluxes were recorded and correlated to salivary melatonin concentrations at the same circadian phases and to subjective sleepiness ratings. The magnitude of pupil constriction was determined from minimal pupil size. The post-stimulus pupil response was assessed from the pupil size at 6s following light offset, the area within the re-dilation curve, and the exponential rate of re-dilation. Results: Amongst the measured parameters, the pupil size 6s after light offset correlated with melatonin concentrations ($p<0.05$) and showed a significant modulation over 24h with maximal values after the nocturnal peak of melatonin secretion. In contrast, the post-stimulus pupil response following red light stimulation correlated with subjective sleepiness ($p<0.05$) without significant changes over 24h. Conclusion: The post-stimulus pupil response to blue light as a marker of intrinsic melanopsin activity demonstrated a circadian modulation. In contrast, the effect of sleepiness was more apparent in the cone contribution to the pupil response. Thus, pupillary responsiveness to light is under influence of both the endogenous circadian clock and subjective sleepiness.

Keywords

Murphy GM, Anderson KE

Year 0

Authors Murphy GM, Anderson KE

Report Name Cutaneous porphyrias

Publication In: Lim HW, Honigsmann H, Hawk JLM, editors. Photodermatology

Issue-page numbers New York: Informa; 2007. p.219-38.

URL N/A

Abstract book

Keywords

Nagano M, Adachi A, Nakahama K et al. **Year** 2003

Authors Nagano M, Adachi A, Nakahama K et al.

Report Name An abrupt shift in the day/night cycle causes desynchrony in the mammalian circadian center

Publication J Neurosci

Issue-page numbers 23:6141–6151. PMID:12853433

URL http://www.jneurosci.org/content/23/14/6141.abstract

Abstract The suprachiasmatic nucleus (SCN) is the neuroanatomical locus of the mammalian circadian pacemaker. Here we demonstrate that an abrupt shift in the light/dark (LD) cycle disrupts the synchronous oscillation of circadian components in the rat SCN. The phases of the RNA cycles of the period genes Per1 and Per2 and the cryptochrome gene Cry1 shifted rapidly in the ventrolateral, photoreceptive region of the SCN, but were relatively slow to shift in the dorsomedial region. During the period of desynchrony, the animals displayed increased nighttime rest, the timing of which was inversely correlated with the expression of Per1 mRNA in the dorsomedial SCN. Molecular resynchrony required ~6 d after a 10 hr delay and 9~13 d after a 6 hr advance of the LD cycle and was accompanied by the reemergence of normal rest–activity patterns. This dissociation and slow resynchronization of endogenous oscillators within the SCN after an LD cycle shift suggests a mechanism for the physiological symptoms that constitute jet lag.

Keywords

Nagashima K, Matsue K, Konishi M et al. **Year** 2005

Authors Nagashima K, Matsue K, Konishi M et al.

Report Name The involvement of Cry1 and Cry2 genes in the regulation of the circadian body temperature rhythm in mice

Publication Am J Physiol Regul Integr Comp Physiol

Issue-page numbers 288:R329–R335. PMID:15331384

URL http://ajpregu.physiology.org/content/288/1/R329.short

Abstract The criptochrome genes (Cry1 and Cry2) are involved in the molecular mechanism that controls the circadian clock, and mice lacking these genes (Cry1–/–/Cry2–/–) are behaviorally arrhythmic. It has been speculated that the circadian clock modulates the characteristics of thermoregulation, resulting in body temperature (Tb) rhythm. However, there is no direct evidence proving this speculation. We show here that Tb and heat production in Cry1–/–/Cry2–/– mice are arrhythmic under constant darkness. In contrast, both rhythms occur under a light-dark cycle and/or periodical food restriction linked with spontaneous activity and/or eating, although they are not robust as those in wild-type mice. The relationship between heat production and Tb in Cry1–/–/Cry2–/– mice is linear and identical under any conditions, indicating that their Tb rhythm is determined by heat production rhythm associated with activity and eating. However, Tb in wild-type mice is maintained at a relatively higher level in the active phase than the inactive phase regardless of the heat production level. These results indicate that the thermoregulatory responses are modulated according to the circadian phase, and the Cry genes are involved in this mechanism.

Keywords circadian clock; thermoregulation; metabolism

Nagata C, Nagao Y, Yamamoto S **Year** 0

Authors Chisato Nagata, Yasuko Nagao, Satoru Yamamoto, Chiken Shibuya, Yoshitomo Kashiki and Hiroyuki Shimizu

Report Name Light Exposure at Night, Urinary 6-Sulfatoxymelatonin, and Serum Estrogens and Androgens in Postmenopausal Japanese Women

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers June 2008 17; 1418

URL http://cebp.aacrjournals.org/content/17/6/1418.short

Abstract It has been hypothesized that exposure to light at night increases the risk of breast cancer by suppressing the normal nocturnal increase in melatonin production and release, thereby resulting in increased levels of circulating estrogen. We assessed associations among concentrations of serum estrogen and androgen and the principal metabolite of melatonin in urine, 6-sulfatoxymelatonin, and exposure to light at night based on information regarding the sleeping habits and history of graveyard-shift work of 206 postmenopausal Japanese women. Serum estradiol level was significantly higher in women who were not asleep at or after 1:00 a.m. (the approximate time of the melatonin peak) than those who were asleep after controlling for covariates. Significantly increased estrone levels were observed in women who had worked graveyard shift. Serum testosterone and DHEA sulfate were unrelated to sleeping habits and history of graveyard-shift work. Urinary 6-sulfatoxymelatonin was lower in women who were not asleep at or after 1:00 a.m. on weekends than those who were asleep at this time, but the difference was of borderline significance (P = 0.08). There was no significant association between urinary 6-sulfatoxymelatonin and any serum hormone levels. These data suggest that exposure to light at night has implications for the risk of breast cancer in postmenopausal women. However, the potential role of melatonin as an intervening factor between light exposure at night and the serum concentrations of estrogen was equivocal.

Keywords breast cancer, estrogen, light at night, melatonin

Nakamura W, Yamazaki S, Takasu NN et al. **Year** 2005

Authors Nakamura W, Yamazaki S, Takasu NN et al.

Report Name Differential response of Period 1 expression within the suprachiasmatic nucleus

Publication J Neurosci

Issue-page numbers 25:5481–5487 doi:10.1523/JNEUROSCI.0889-05.2005. PMID:15944376

URL http://www.jneurosci.org/content/25/23/5481.full.pdf+html

Abstract The suprachiasmatic nuclei (SCNs) of the hypothalamus contain a circadian clock that exerts profound control over rhythmic physiology and behavior. The clock consists of multiple autonomous cellular pacemakers distributed throughout the rat SCN. In response to a shift in the light schedule, the SCN rapidly changes phase to achieve the appropriate phase relationship with the shifted light schedule. Through use of a transgenic rat in which rhythmicity in transcription of the Period 1 gene was measured with a luciferase reporter (Per1-luc), we have been successful in tracking the time course of molecular rhythm phase readjustments in different regions of the SCN that occur in response to a shift in the light schedule. We find that different regions of the SCN phase adjust at different rates, leading to transient internal desynchrony in Per1-luc expression among SCN regions. This desynchrony among regions is most pronounced and prolonged when the light schedule is advanced compared with light schedule delays. A similar asymmetry in the speed of phase resetting is observed with locomotor behavior, suggesting that phase shifting kinetics within the SCN may underlay the differences observed in behavioral resetting to advances or delays in the light schedule.

Keywords

Nakano Y, Miura T, Hara I et al. ***Year*** 1982

Authors Nakano Y, Miura T, Hara I et al.

Report Name The effect of shift work on cellular immune function

Publication J Hum Ergol (Tokyo)

Issue-page numbers 11 Suppl;131–137. PMID:6985367

URL http://www.ncbi.nlm.nih.gov/pubmed/6985367

Abstract N/A

Keywords

Nakatani M, Ohara Y, Katagiri E et al. ***Year*** 1940

Authors Nakatani M, Ohara Y, Katagiri E et al.

Report Name Studies on pinealectomized white rat

Publication Nippon Byori Gakkai Kaishi

Issue-page numbers 30:232–236

URL N/A

Abstract N/A

Keywords

Nathan PJ, Burrows GD, Norman TR — ***Year*** 1999

Authors Pradeep J Nathan Ph.D, Graham D Burrows MD and Trevor R Norman

Report Name Melatonin Sensitivity to Dim White Light in Affective Disorders

Publication Neuropsychopharmacology

Issue-page numbers (1999) 21 408-413

URL http://www.nature.com/npp/journal/v21/n3/full/1395342a.html

Abstract Both dim and bright light has been shown to suppress the nocturnal secretion of the pineal hormone melatonin. Early reports suggests that an abnormal response to light occurs in patients with bipolar affective disorder, where as patients with major depressive disorder respond similarly to controls. It has been suggested that this abnormal sensitivity of the melatonin response to light could be a trait marker of bipolar affective disorder. However reports lack consistency. Hence, we investigated the melatonin suppression by dim light (200 lux) in patients with bipolar affective disorder, seasonal affective disorder and major depressive disorder. Results suggest that a supersensitive melatonin suppression to light in bipolar affective disorder ($p < .005$), and seasonal affective disorder ($p < .05$), whereas patients with major depressive disorder display similar suppression to controls. The supersensitivity may be a mechanism where by phase-delayed rhythms, are re-synchronised to a new circadian position. Conversely, an abnormality may exist in the pathway from the retina to the suprachiamatic nucleus.

Keywords Melatonin; Suppression; Dim-light; Affective disorders; Circadian rhythms; Biological marker; Light-sensitivity

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Nathan PJ, Wyndham EL, Burrows GD, Norman TR — ***Year*** 2000

Authors Nathan PJ, Wyndham EL, Burrows GD, Norman TR

Report Name The effect of gender on the melatonin suppression by light: a dose response relationship

Publication J Neural Transm

Issue-page numbers 107:271–279 doi:10.1007/s007020050022. PMID:10821436

URL http://www.ncbi.nlm.nih.gov/pubmed/10821436

Abstract It is well known that light is an inhibitor of pineal melatonin secretion in humans. However, the effect of gender on the melatonin suppression by dim and bright light is still controversial. The present study investigated the effect of gender on the suppression of melatonin at five light intensities (0, 200, 500, 1,000, 3,000 lux). Five healthy men and women attended five testing sessions separated by one week. At each session, subjects were exposed to light from midnight to 0100 hours in a sitting position. Blood samples where collected at regular intervals and plasma melatonin concentration was measured using a specific radioimmunoassay. No gender differences were found in melatonin suppression by light at any of the five light intensities ($p > 0.1$). Furthermore, the mean melatonin suppression by light in both males and females was dose dependent (17% [200 lux], 40% [500 lux], 56% [1,000 lux] and 74% [3,000 lux]). Our findings suggest that melatonin suppression by light in intensity dependent, with no gender differences in light sensitivity.

Keywords

Navara KJ, Nelson RJ — **Year** 2007

Authors Navara KJ, Nelson RJ

Report Name The dark side of light at night: physiological, epidemiological, and ecological consequences

Publication J Pineal Res

Issue-page numbers 43:215–24. doi: 10.1111/j.1600-079X.2007.00473.x.

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2007.00473.x/full

Abstract Abstract: Organisms must adapt to the temporal characteristics of their surroundings to successfully survive and reproduce. Variation in the daily light cycle, for example, acts through endocrine and neurobiological mechanisms to control several downstream physiological and behavioral processes. Interruptions in normal circadian light cycles and the resulting disruption of normal melatonin rhythms cause widespread disruptive effects involving multiple body systems, the results of which can have serious medical consequences for individuals, as well as large-scale ecological implications for populations. With the invention of electrical lights about a century ago, the temporal organization of the environment has been drastically altered for many species, including humans. In addition to the incidental exposure to light at night through light pollution, humans also engage in increasing amounts of shift-work, resulting in repeated and often long-term circadian disruption. The increasing prevalence of exposure to light at night has significant social, ecological, behavioral, and health consequences that are only now becoming apparent. This review addresses the complicated web of potential behavioral and physiological consequences resulting from exposure to light at night, as well as the large-scale medical and ecological implications that may result.

Keywords cancer, endocrine disruptor, immune, light pollution, melatonin

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Neale RE, Purdie JL, Hirst LW, Green AC — **Year** 2003

Authors Rachel E. Neale, Jennifer L. Purdie, Lawrence W. Hirst and Adèle C. Green

Report Name Sun exposure as a risk factor for nuclear cataract

Publication Epidemiology

Issue-page numbers Vol. 14, No. 6 (Nov., 2003), pp. 707-712

URL http://www.jstor.org/pss/3703431

Abstract Background: Cataracts are the leading cause of blindness and visual impairment throughout the world. An association of sun exposure with cortical cataract has been well established, but the association with nuclear cataract remains unclear. Methods: This case-control study was nested within the Nambour (Australia) Trial of Skin Cancer Prevention conducted between 1992 and 1996. We compared 195 cases who had a nuclear opacity of grade 2.0 or greater with 159 controls. Structured questionnaires were used to ascertain lifetime sun exposure history, eyeglasses and sunglasses use, and potentially confounding variables such as education and smoking. Results: There was a strong positive association of occupational sun exposure between the ages of 20 and 29 years with nuclear cataract (odds ratio = 5.9; 95% confidence interval = 2.1-17.1). Exposure later in life resulted in weaker associations. Wearing sunglasses, particularly during these early years, afforded some protective effect. Conclusions: This study provides new evidence to support a link between sun exposure and nuclear cataract. Risk was highest among those with high sun exposure at younger ages.

Keywords

Nelson RJ

Year 2004

Authors Nelson RJ

Report Name Seasonal immune function and sickness responses

Publication Trends Immunol

Issue-page numbers 25:187–192 doi:10.1016/j.it.2004.02.001. PMID:15039045

URL http://www.sciencedirect.com/science/article/pii/S1471490604000511

Abstract Winter is a particularly difficult time to breed and survive. Animals monitor day length (photoperiod) to engage seasonally appropriate adaptations in anticipation of harsh winter conditions. I propose that photoperiodic information, mediated by melatonin, might also influence immune responses. Individuals could improve survival if seasonally recurring stressors were anticipated and countered. Recent studies suggest that short day lengths reroute energy from reproduction and growth to bolster immune function during winter. Short days can either enhance or suppress components of immune function, as well as reduce fever and the expression of sickness behaviors. The net result of these photoperiod-mediated adjustments is enhanced immune function and increased survival. Melatonin appears to be part of an integrated system that coordinates reproductive, immunological and other processes to cope successfully with energetic stressors during winter and to balance trade-offs between reproductive success and survival.

Keywords

Nelson RJ, Drazen DL

Year 2000

Authors Nelson RJ, Drazen DL

Report Name Melatonin mediates seasonal changes in immune function

Publication Ann N Y Acad Sci

Issue-page numbers 917:404–415 doi:10.1111/j.1749-6632.2000.tb05405.x. PMID:11268368

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.2000.tb05405.x/full

Abstract Field studies indicate that immune function is compromised and the prevalence of many diseases are elevated during winter when energetic stressors are extensive. Presumably, individuals would enjoy a survival advantage if seasonally recurring stressors could be anticipated and countered by shunting energy reserves to bolster immune function. The primary environmental cue that permits physiological anticipation of season is daily photoperiod, a cue that is mediated by melatonin. However, other environmental factors, including low food availability and ambient temperatures, may interact with photoperiod to affect immune function and disease processes. This paper will review laboratory studies that consistently report enhanced immune function in short day lengths. Prolonged melatonin treatment mimics short days, and both in vitro and in vivo melatonin treatment enhances various aspects of immune function, especially cell-mediated immune function, in non-tropical rodents. Reproductive responsiveness to melatonin appears to affect immune function. In sum, melatonin may be part of an integrative system to coordinate reproductive, immunologic, and other physiological processes to cope successfully with energetic stressors during winter.

Keywords

Nelson W, Tong YL, Lee JK, Halberg F | ***Year*** 1979

Authors Nelson W, Tong YL, Lee JK, Halberg F

Report Name Methods for cosinor-rhythmometry

Publication Chronobiologia

Issue-page numbers 6:305–323. PMID:548245

URL http://www.ncbi.nlm.nih.gov/pubmed/548245

Abstract N/A

Keywords

Nguyen ATH, Campbell M, Kenna PF, Kiang A, et al. | ***Year*** 2012

Authors Anh T. H. Nguyen, Matthew Campbell, Paul F. Kenna, Anna-Sophia Kiang, Lawrence Tam, Marian M. Humphries and Peter Humphries

Report Name Calpain and Photoreceptor Apoptosis

Publication Retinal Degenerative Diseases

Issue-page numbers 2012, Volume 723, Part 8, 547-552, DOI: 10.1007/978-1-4614-0631-0_69

URL http://www.springerlink.com/content/j4412141355w273q/

Abstract Photoreceptor apoptosis is present in various retinopathies such as retinitis pigmentosa and glaucoma where caspases are generally considered to be the main executioners of apoptosis in various tissues. However, accumulating evidence suggests apoptosis could occur in a caspase-independent fashion. In this view, many studies have shown that calpain activation is associated with photoreceptor apoptosis in various animal and light-induced retinal degeneration models. Thus, calpain could be a potential target for treatment and may promote cell survival in cases where caspase inhibition has failed. Herein, we review current thinking on this topic and also present data showing protection of photoreceptors to apoptosis by systemic delivery of a calpain inhibitor in a light-induced model of retinal degeneration by modulation of the inner blood retina barrier (iBRB).

Keywords Calpain - Photoreceptor apoptosis - Light-induced retinal damage - Blood retina barrier - Barrier modulation - Claudin-5

Nicolau GY, Haus E | ***Year*** 1992

Authors Nicolau GY, Haus E

Report Name Chronobiology of the hypothalamic-pituitary-thyroid axis

Publication In: Touitou Y & Haus E, Eds. Biologic Rhythms in Clinical and Laboratory Medicine

Issue-page numbers 2nd Ed. New York: Springer-Verlag. pp. 330–347

URL N/A

Abstract N/A

Keywords

Nicoletti I, Gerli R, Orlandi S et al. | ***Year*** 1989

Authors Nicoletti I, Gerli R, Orlandi S et al.

Report Name Defective natural killer cell activity in puerperal hyperprolactinemia

Publication J Reprod Immunol

Issue-page numbers 15:113–121 doi:10.1016/0165-0378(89)90031-4. PMID:2788740

URL http://www.jrijournal.org/article/0165-0378%2889%2990031-4/abstract

Abstract

Prolactin (PRL) influences immune reactivity in animals and in humans and both T-cell abnormalities and reduced natural killer (NK) cell activity have been reported in women with pathological hyperprolactinemia. To investigate further the possible interactions between PRL and the immune system in humans, we analysed T-cell phenotypes and NK cell activity in 15 women with physiological hyperprolactinemia of the puerperium and in 45 age-matched healthy normal cycling women.

Puerperal women displayed a normal T-cell phenotype but a significant reduction in the number of Leu-7+ and Leu-11+ cells, associated with a decreased NK cell activity, as measured against K-562 target cells. There was a significant inverse correlation between the raised serum PRL levels and both the number of Leu-7+ cells and NK cell activity.

These data confirm an important immunoregulatory role for PRL in humans and suggest a direct inhibitory effect of the chronically raised PRL concentrations on the maturation of NK cells.

Keywords NK cell activity, hyperprolactinemia, puerperium

Niles LP, Wang J, Shen L et al. **Year** 1999

Authors Niles LP, Wang J, Shen L et al.

Report Name Melatonin receptor mRNA expression in human granulosa cells

Publication Mol Cell Endocrinol

Issue-page numbers 156:107–110 doi:10.1016/S0303-7207(99)00135-5. PMID:10612428

URL http://ukpmc.ac.uk/abstract/MED/10612428

Abstract We have shown that the melatonin receptor agonist, 2-[125I] iodomelatonin, binds to high-affinity guanine nucleotide-sensitive sites on human granulosa (HG) cell membranes. In order to confirm the presence of melatonin receptors in HG cells, we have now used a reverse transcriptase-polymerase chain reaction (RT-PCR) procedure to examine receptor subtype expression. RT-PCR studies revealed the presence of the mt1 (Mel1alpha) melatonin receptor subtype in ten single or pooled HG cell samples which were obtained from 14 patients. In contrast, expression of MT2 (Mel1b) mRNA was observed in only two of these HG samples. DNA sequencing of the mt1 PCR product confirmed its identity with the reported human mt1 melatonin receptor. The expression of mt1 and MT2 receptor mRNA in HG cells and the reported presence of melatonin in human follicular fluid indicate a potentially important role for this hormone in regulating human ovarian and reproductive function.

Keywords

Nissen C, Sander B, Lund-Andersen H **Year** 2012

Authors Nissen C, Sander B, Lund-Andersen H.

Report Name The effect of pupil size on stimulation of the melanopsin containing retinal ganglion cells, as evaluated by monochromatic pupillometry.

Publication Front Neurol

Issue-page numbers 2011;2:92. Epub 2012 Feb 2.

URL http://www.ncbi.nlm.nih.gov/pubmed/22319506

Abstract Purpose: To evaluate the influence of the size of the light exposed pupil in one eye on the pupillary light reflex of the other eye. Method: Using a monochromatic pupillometer, the left eye in each of 10 healthy subjects was exposed to 20 s of monochromatic light of luminance 300 cd/m(2), first red (660 nm) and in a following session, blue (470 nm) light. The consensual pupillary diameter in the right eye was continuously measured before, during, and after light exposure. Subsequently, Tropicamide 1% or Pilocarpine 2% was instilled into the left eye and when the pupil was either maximally dilated or contracted, the entire sequence of red and blue light exposure repeated. After at least 3 days, when the effect of the eye drop had subsided, the entire experiment was repeated, this time employing the other substance. Results: Prior dilatation of the left pupil augmented the post light contraction to blue ($p < 0.0001$), but not to red light. The contraction during light exposure did not change. Prior contraction of the left pupil decreased the post-stimulus contraction to blue light ($p < 0.04$). Conclusion: The size of the light exposed pupil influences the magnitude of the response to blue, but not to red light. Prior dilatation may therefore prove useful, when the response to blue light - as a marker of melanopsin containing retinal ganglion cell function - is of interest, especially when this response is weak.

Keywords

Noell WK

Year 0

Authors Noell WK.

Report Name Aspects of experimental and hereditary degeneration

Publication In: Raymore C, editor. Biochemistry of the Retina

Issue-page numbers London: Academic Press; 1965, p.51-72.

URL N/A

Abstract Book

Keywords

Noell WK, Walker VS, Kang BS, Berman S

Year 1966

Authors Noell WK, Walker VS, Kang BS, Berman S

Report Name Retinal damage by light in rats

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers October 1966 vol. 5 no. 5 450-473

URL http://www.iovs.org/content/5/5/450.abstract

Abstract The retina of laboratory rats is affected irreversibly by intense light applied for less than 1 hour or for up to 2 days depending upon experimental conditions. Exposure of unanesthetized and unrestrained animals was in chambers surrounded by a green filter and circular fluorescent lamps of a nominal brightness of 2,040 footlamberts. Eyes of anesthetized animals were exposed diffusely to either the light from a 100 w. zirconium arc passing through filters or monochromatic light of various wavelengths. Irreversible reduction in ERG amplitudes and degeneration of visual cells and pigment epithelium indicated the severity of the light damage. The effect was very dependent upon the body (eye) temperature during exposure. Hyperthermia greatly accelerated and intensified the damaging action of light and for this reason most experiments reported in this paper were performed at a high body temperature. At a body temperature around 104° F. severe damage was produced with exposures to 5 to 10 μw per square centimeter retina for 1 hour. The minimal damaging dose at a high temperature was estimated to be about 1 μw per square centimeter. The action spectrumof the damaging effect approximated that of visual excitation as measured by the ERG. Hooded (pigmented) animals were no more affected than albinos of different strains. Recovery in the dark from a just subliminally damaging dose of light at a high body temperature required about 24 hours and was preceded by a period of time during which the retina was "sensitized" to an additional dose. Duringjrrfollowing exposure to light at a high body temperature visual cell and pigiiient_epithelial_dmxage developed about simultaneously and was first indicated bu pyknosis and cell swelling followed rapidly by the dissolution of nuclei and cytoplasm. The crucial reaction in producing the damage is considered a "dark-reaction" initiated by light of an intensity which bleaches measurabLiirhodopsin. Hypotheses on the reaction sequence which leads to damage are briefly discussed.

Keywords

Nolan JM

Year 0

Authors J. M. Nolan

Report Name The Role of the Macular Carotenoids as a Blue Light Filter and an Antioxidant

Publication Studies on Retinal and Choroidal Disorders

Issue-page numbers Oxidative Stress in Applied Basic Research and Clinical Practice, 2012, 595-611, DOI: 10.1007/978-1-61779-606-7_30

URL http://www.springerlink.com/content/h115666x65705018/

Abstract It is now accepted that age-related macular degeneration (AMD) is the result of (photo)oxidative-induced retinal injury. However, the anatomic (central retinal), biochemical (antioxidant), and optical (short-wavelength-filtering) properties of the macular carotenoids suggest that these pigments may confer protection against AMD. Also, their optical (short-wavelength-filtering) properties suggest that they play a role in visual performance and experience.

Keywords

Norval M

Year 2006

Authors Norval M.

Report Name The mechanisms and consequences of ultraviolet-induced immunosuppression

Publication Prog Biophys Mol Biol

Issue-page numbers 2006 Sep;92(1):108-18. Epub 2006 Feb 28.

URL http://www.ncbi.nlm.nih.gov/pubmed/16564073

Abstract Exposure to ultraviolet radiation (UVR) can result in immune suppression to antigens encountered within a few days of the irradiation. The process leading to the down-regulation in immune responses is complex. It is initiated by several photoreceptors located in the skin surface, namely DNA, trans-urocanic acid and membrane components. The absorption of UVR by these chromophores then leads to the release of a wide range of mediators that can affect antigen presenting cells locally or systemically. The final steps include the generation of antigen-specific T cells capable of regulating immunity. The consequences of the UV-induced changes in the skin immune system for the control of skin cancers, infectious diseases including vaccination, and autoimmune diseases are considered. Finally, the effects of active vitamin D, synthesised in the epidermis following UVR, are discussed in the context of the skin immune response.

Keywords

Norval M

Year 2006

Authors Norval M.

Report Name The effect of ultraviolet radiation on human viral infections

Publication Photochemistry and Photobiology

Issue-page numbers 2(6):1495-1504. 2006 doi: 10.1562/2006-07-28-IR-987

URL http://www.bioone.org/doi/abs/10.1562/2006-07-28-IR-987?journalCode=phot

Abstract

Exposure to UV radiation is recognized to suppress cell-mediated immunity and therefore could adversely affect the course of a viral infection. Rodent models of viral infection confirm this possibility but the situation in human subjects is not so clear, apart from two exceptions. These are herpes simplex, in which sunlight exposure can cause reactivation, and certain papillomavirus types in which sunlight exposure can lead to the development of nonmelanoma skin cancer. In both cases, there are UV response elements in the viral genomes that alter the normal interactions between the viruses and the host following exposure, and UV-induced effects on the immune response occur in addition. These complex mechanisms are discussed, and the situation regarding UV radiation and viral exanthems plus other viruses, including the retroviruses, summarized. Finally viral vaccination is considered in the context of UV exposure and the importance of the host's genetic background emphasized. Further research is required to evaluate whether sunlight can significantly affect the resistance to common viral infections and vaccines.

Keywords

Norval M, Lucas RM, Cullen AP, et al. **Year** 2011

Authors Norval M, Lucas RM, Cullen AP, de Gruijl FR, Longstreth J, Takizawa Y, et al.

Report Name The human health effects of ozone depletion and interactions with climate change

Publication Photochem. Photobiol. Sci.

Issue-page numbers 10, 199-225

URL http://pubs.rsc.org/en/Content/ArticleLanding/2011/PP/c0pp90044c

Abstract

Depletion of the stratospheric ozone layer has led to increased solar UV-B radiation (280–315 nm) at the surface of the Earth. This change is likely to have had an impact on human exposure to UV-B radiation with consequential detrimental and beneficial effects on health, although behavioural changes in society over the past 60 years or so with regard to sun exposure are of considerable importance. The present report concentrates on information published since our previous report in 2007. The adverse effects of UV radiation are primarily on the eye and the skin. While solar UV radiation is a recognised risk factor for some types of cataract and for pterygium, the evidence is less strong, although increasing, for ocular melanoma, and is equivocal at present for age-related macular degeneration. For the skin, the most common harmful outcome is skin cancer, including melanoma and the non-melanoma skin cancers, basal cell carcinoma and squamous cell carcinoma. The incidence of all three of these tumours has risen significantly over the past five decades, particularly in people with fair skin, and is projected to continue to increase, thus posing a significant world-wide health burden. Overexposure to the sun is the major identified environmental risk factor in skin cancer, in association with various genetic risk factors and immune effects. Suppression of some aspects of immunity follows exposure to UV radiation and the consequences of this modulation for the immune control of infectious diseases, for vaccination and for tumours, are additional concerns In a common sun allergy (polymorphic light eruption), there is an imbalance in the immune response to UV radiation, resulting in a sun-evoked rash. The major health benefit of exposure to solar UV-B radiation is the production of vitamin D. Vitamin D plays a crucial role in bone metabolism and is also implicated in protection against a wide range of diseases. Although there is some evidence supporting protective effects for a range of internal cancers, this is not yet conclusive, but strongest for colorectal cancer, at present. A role for vitamin D in protection against several autoimmune diseases has been studied, with the most convincing results to date for multiple sclerosis. Vitamin D is starting to be assessed for its protective properties against several infectious and coronary diseases. Current methods for protecting the eye and the skin from the adverse effects of solar UV radiation are evaluated, including seeking shade, wearing protective clothing and sunglasses, and using sunscreens. Newer possibilities are considered such as creams that repair UV-induced DNA damage, and substances applied topically to the skin or eaten in the diet that protect against some of the detrimental effects of sun exposure. It is difficul to provide easily understandable public health messages regarding “safe” sun exposure, so that the positive effects of vitamin D production are balanced against the negative effects of excessive exposure. The international response to ozone depletion has included the development and deployment of replacement technologies and chemicals. To date, limited evidence suggests that substitutes for the ozone-depleting substances do not have significant effects on human health. In addition to stratospheric ozone depletion, climate change is predicted to affect human health, and potential interactions between these two parameters are considered. These include altering the risk of developing skin tumours, infectious diseases and various skin diseases, in addition to altering the efficiency by which pathogenic microorganisms are inactivated in the environment.

Keywords

Authors Nosjean O, Ferro M, Coge F et al.

Report Name Identification of the melatonin-binding site MT3 as the quinone reductase 2

Publication J Biol Chem

Issue-page numbers 275:31311–31317 doi:10.1074/jbc.M005141200. PMID:10913150

URL http://www.jbc.org/content/275/40/31311.full.pdf

Abstract

The regulation of the circadian rhythm is relayed from the central nervous system to the periphery by melatonin, a hormone synthesized at night in the pineal gland. Besides two melatonin G-coupled receptors, mt1 and MT2, the existence of a novel putative melatonin receptor, MT3, was hypothesized from the observation of a binding site in both central and peripheral hamster tissues with an original binding profile and a very rapid kinetics of ligand exchange compared with mt1 and MT2.

In this report, we present the purification of MT3 from Syrian hamster kidney and its identification as the hamster homologue of the human quinone reductase 2 (QR2, EC 1.6.99.2). Our purification strategy included the use of an affinity chromatography step which was crucial in purifying MT3 to homogeneity. The protein was sequenced by tandem mass spectrometry and shown to align with 95% identity with human QR2. After transfection of CHO-K1 cells with the human QR2 gene, not only did the QR2 enzymatic activity appear, but also the melatonin-binding sites with MT3 characteristics, both being below the limit of detection in the native cells. We further confronted inhibition data from MT3 binding and QR2 enzymatic activity obtained from samples of Syrian hamster kidney or QR2-overexpressing Chinese hamster ovary cells, and observed an overall good correlation of the data. In summary, our results provide the identification of the melatonin-binding site MT3 as the quinone reductase QR2 and open perspectives as to the function of this enzyme, known so far mainly for its detoxifying properties.

Keywords

Nováková M, Paclt I, Ptáček R, et al. **Year** 2011

Authors Marta Nováková, Ivo Paclt, Radek Ptáček, Hana Kuželová, Ivan Hájek and Alena Sumová

Report Name Salivary Melatonin Rhythm as a Marker of the Circadian System in Healthy Children and Those With Attention-Deficit/Hyperactivity Disorder

Publication Chronobiology International

Issue-page numbers 28:7, 630-637

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.596983

Abstract Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood. Problems with sleep structure, efficiency, and timing have been reported in some, but not all, studies on ADHD children. As the sleep-wake cycle belongs to circadian rhythms, the timekeeping circadian system might be involved in ADHD. To assess whether the circadian system of ADHD children differs from that of controls, the rhythm of the pineal hormone melatonin was used as a reliable marker of the system. Saliva from 34 ADHD and 43 control 6- to 12-yr-old children was sampled at 2-h intervals throughout the entire 24-h cycle, and the melatonin profiles of the ADHD and control children were compared. The nocturnal melatonin peaks of the ADHD and control group did not differ significantly. The high nocturnal interindividual variability of the peaks seen in adulthood was present already in the studied children. The 24-h melatonin profiles of all the ADHD subjects did not differ significantly from those of the control subjects. Categorization of subjects according to age, into groups of 6- to 7-yr-old (9 ADHD, 5 control), 8- to 9-yr-old (16 ADHD, 26 control), and 10- to 12-yr-old (9 ADHD, 12 control) children, revealed significant differences between the ADHD and control group in the melatonin rhythm waveform, but not in nocturnal melatonin peaks; the peaks were about the same in both groups and did not change significantly with increasing age. In the oldest, but not in the younger, children, the melatonin signal duration in the ADHD group was shorter than in the control group. The difference might be due to the fact that whereas in the control group both the evening melatonin onset and the morning offset phase delayed in the oldest children relative to those in the youngest children, in the ADHD group only the onset, but not the offset, phase delayed with increasing age. The data may indicate subtle differences between the circadian system of ADHD and control children during development.

Keywords Attention-deficit/hyperactivity disorder, Children, Melatonin

Novotny P, Plischke H, Schwarz MJ, Kohls N **Year** 2013

Authors Novotny, Philipp; Plischke, Herbert; Schwarz, Markus J.; Kohls, Niko

Report Name Impact of the solid angle of light sources upon the suppression of melatonin in adults – a feasibility study

Publication Conference: Lebensqualität im Wandel von Demografie und Technik

Issue-page numbers 6. Deutscher AAL-Kongress mit Ausstellung

URL http://www.vde-verlag.de/proceedings-en/453484062.html

Abstract In this feasibility study we intended to test the effect of exposure to different lighting scenarios upon the suppression of melatonin in adults in relationship to the solid angle in an experimental setting. High quality empirical and experimental deisgns are necessary in order to improve our knowledge about optimal lighting scenarios with regard to needs and demands of humans. Our experimental setup allowed us to investigate six participants under two different melatonin suppressing lighting conditions: a) a large solid angle, b) and a small solid angle (ie. how large the light source appears to the observer). Results suggest that a large solid angle could be more effective for suppressing melatonin in humans. Further elucidation of the mechanisms could be useful for developing and designing lighting scenarios for residential care homes or other specialized caretaking facilities. Particularly specialized nursing homes for individuals suffering from dementia could take advantage of with the optimal lighting scenarios, not only for the psychological and physical health of their residents in care but in order to support the care takers.

Keywords

Authors Nowak R, McMillen IC, Redman J, Short RV

Report Name The correlation between serum and salivary melatonin concentrations and urinary 6-hydroxymelatonin sulphate excretion rates: two noninvasive techniques for monitoring human

Publication Clin Endocrinol (Oxf)

Issue-page numbers 27:445–452 doi:10.1111/j.1365-2265.1987.tb01172.x. PMID:3436070

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1987.tb01172.x/abstract

Abstract Athough there is a circadian rhythm in blood melatonin concentrations in humans, the problems associated with frequent blood collection limit the use of this rhythm in the investigation of the circadian system and in the diagnosis and treatment of chronobiological disorders. Therefore, to establish a convenient, non-invasive technique for monitoring melatonin circadian rhythmicity, we compared the melatonin concentrations in blood samples collected from five subjects every 2-4 h over a 26 h period, with the melatonin concentrations in saliva samples and with the total amount of 6-hydroxymelatonin sulphate excreted in the urine during 2-h periods. There was significant correlation between serum and salivary melatonin concentrations (r= 0.81, P < 0.001), and between serum melatonin concentrations and 6-hydroxymelatonin sulphate excretion rates (r= 0-72, P<0001). The results demonstrate that both salivary melatonin concentrations and urinary 6-hydroxymelatonin sulphate excretion rates are reliable indices of serum melatonin concentrations. These measurements, in combination with frequent sample collection, provide two convenient, non-invasive techniques for monitoring melatonin circadian rhythmicity.

Keywords

NRPB **Year** 2002

Authors NRPB

Report Name Health Effects from Ultraviolet Radiation: Report of an Advisory Group on Non-Ionising Radiation

Publication Documents of the NRPB: Volume 13, No. 1

Issue-page numbers ISBN: 0-85951-475-7

URL http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1254510590307

Abstract

1. The National Radiological Protection Board has a statutory responsibility to provide advice and information on standards of protection for exposure to non-ionising radiation. This includes the health effects and hazards associated with exposure to ultraviolet radiation (UVR). UVR is radiation in the range of wavelengths 100-400 nm. It is divided by wavelength into UVA 315-400 nm, UVB 280-315 nm and UVC 100-280 nm. Blue light lies in the range of about 400-500 nm.

2. The Board's Advisory Group on Non-Ionising Radiation has a remit:

to review work on the biological effects of non-ionising radiation relevant to human health and to advise on research priorities

3. In this, its seventh report, the Advisory Group has updated its previous review of the health effects from UVR (NRPB, 1995). It has considered both natural and artificial sources of exposure, as well as experimental studies relevant to understanding the effects of UVR on cells and tissues. It has examined information on the clinical effects of UVR and the results of epidemiological studies with the aim of providing advice on the health effects of exposure. The Advisory Group has also made recommendations for further research aimed at improving the basis for assessing exposures to natural and artificial sources as well as furthering knowledge of the effects of UVR on health through experimental and epidemiological studies.

4. This summary reviews the main conclusions of the Advisory Group. At the specific request of the Board it also gives advice on the means of protection of human health. This applies both to members of the public and to those who are occupationally exposed and is intended to provide a practical basis for reducing UVR exposure and increasing awareness of its effects.

Keywords

O'Steen WK, Anderson KV, Shear CR **Year** 1974

Authors O'Steen WK, Anderson KV, Shear CR.

Report Name Photoreceptor degeneration in albino rats: dependency on age

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers May 1974 vol. 13 no. 5 334-339

URL http://www.iovs.org/content/13/5/334

Abstract Exposure of adult, albino rats to fluorescent and incandescent illuminance causes photoreceptor degeneration, which is followed by active phagocytosis of the fragmented cells. Male and female rats from 3 weeks of age to adulthood were exposed to a lighting schedule and an elevated environmental temperature known to induce receptor destruction in adult animals; control groups were exposed to cyclic lighting and room temperature. Retinas of 3- and 4-weekold experimental animals were apparently unaffected by light exposure. Outer and inner segments were fragmented and receptor nuclei were pyknotic in localized areas of the central retina of some 5- and most 6-week-old rats; areas of focal damage were more severe in 7-weekold rats. At 8 weeks of age, the reduction in average thickness of the outer nuclear layer (ONL) first became statistically significant. Thereafter, photoreceptor destruction and reduction in OLN thickness became progressively more severe as the rats aged. Reduction in the overall thickness of the retina as a result of light exposure was not as impressive as the effect on the ONL. Photoreceptor damage apparently was not influenced by the animal's gender.

Keywords retina, retinal damage, retinal degeneration, photoreceptor damage, rat retina, age dependency, photoperiod

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Obál F Jr, Payne L, Kacsoh B et al. **Year** 1994

Authors F. Obál Jr.a, b, L. Paynec, B. Kacsohd, M. Oppe, L. Kapásb, C.E. Grosvenorf, J.M. Krueger

Report Name Involvement of prolactin in the REM sleep-promoting activity of systemic vasoactive intestinal peptide (VIP)

Publication Brain Res

Issue-page numbers 143–149 doi:10.1016/0006-8993(94)91647-0. PMID:8062077

URL http://www.sciencedirect.com/science/article/pii/0006899394916470

Abstract The involvement of pituitary prolactin (PRL) in systemic vasoactive intestinal peptide (VIP)-induced sleep was studied. Male rats were implanted with electrodes for EEG-recording, with brain thermistors to record cortical temperature (Tcrt) and with chronic intracardial catheters to obtain blood samples and to deliver substances. One group of rats (n = 8) received normal rabbit serum (NS) + physiological saline (SAL) on the baseline day and was injected with NS + VIP on the experimental day. In the other group of rats (n = 6), the baseline day was followed by administration of PRL-antiserum (PRL-AS) + VIP on the experimental day. The sera and VIP or SAL were injected 30 min before and at light onset, respectively. Sleep-wake activity was then recorded for the next 12-h light period. Systemic VIP-stimulated PRL secretion as measured by RIA in serial samples obtained hour 1 postinjection. VIP also elicited selective increases in REM sleep (REMS) in the rats pretreated with NS. Tcrt was not affected by VIP. Administration of PRL-AS blocked the increase in circulating levels of free (non-IgG-bound) PRL and prevented VIP-enhanced REMS. Comparisons of the sleep effects of PRL-AS + VIP with the previously reported changes in sleep after PRL-AS alone indicate that PRL has a major role in the mediation of the REMS-promoting activity of systemic VIP. The results suggest that an increased release of endogenous pituitary PRL modulates REMS.

Keywords Prolactin; Sleep; VIP; REM

Obana A; Brinkmann R; Gohto Y; Nishimura K

Year 2011

Authors Obana, Akira ; Brinkmann, Ralf ; Gohto, Yuko; Nishimura, Kasumi

Report Name A Case of Retinal Injury By A Violet Light-Emitting Diode

Publication RETINAL Cases & Brief Reports:

Issue-page numbers Summer 2011 - Volume 5 - Issue 3 - pp 223-226

URL http://journals.lww.com/retinalcases/Abstract/2011/00530/A_Case_of_Retinal_Injury_By_A_Violet.11.aspx

Abstract

Purpose: To describe the first case of retinal injury by a misuse of a toy using light-emitting diode.

Methods: A 15-year-old male Japanese student received irradiation on his right eye by a 5 mW light-emitting diode of 410 nm wavelength for 20 seconds in 2 days. He noticed decreased vision and central scotoma approximately 2 weeks later from these events. The mechanism of injury was evaluated from the estimated irradiance on the retina by comparison with experimental threshold data published.

Results: Chorioretinal atrophy with visual loss and central scotoma has remained on the fovea. The patient received an estimated dose of 1.58 J/cm2 2 times, which was close tc the experimentally determined radiant exposure for photochemical injury of rat retina.

Conclusion: The violet light from light-emitting diodes is a potential hazard for the retina, and thus, direct viewing into the beam should be avoided. Children, especially, should not be allowed to play with such toys without being carefully instructed about their proper use and fully supervised.

Keywords

Authors Obayashi K, Saeki K, Iwamoto J, Okamoto N, Tomioka K, Nezu S, Ikada Y, Kurumatani N

Report Name Exposure to Light at Night, Nocturnal Urinary Melatonin Excretion, and Obesity/Dyslipidemia in the Elderly: A Cross-Sectional Analysis of the HEIJO-KYO Study.

Publication J Clin Endocrinol Metab

Issue-page numbers 2013 Jan;98(1):337-44. doi: 10.1210/jc.2012-2874. Epub 2012 Nov 1

URL http://www.ncbi.nlm.nih.gov/pubmed/23118419

Abstract Context: Obesity and exposure to light at night (LAN) have increased globally. Although LAN suppresses melatonin secretion and disturbs body mass regulation in experimental settings, its associations with melatonin secretion, obesity, and other metabolic consequences in uncontrolled home settings remain unclear. Objective: The aim of this study was to determine the association of exposure to LAN in an uncontrolled home setting with melatonin secretion, obesity, dyslipidemia, and diabetes. Design and Participants: A cross-sectional study was performed in 528 elderly individuals (mean age, 72.8 yr). Measures: The intensity of LAN in the bedroom was measured at 1-min intervals during two consecutive nights, along with overnight urinary melatonin excretion and metabolic parameters. Results: Compared with the Dim group (average <3 lux; n = 383), the LAN group (average ≥3 lux; n = 145) showed significantly higher body weight (adjusted mean, 58.8 vs. 56.6 kg; P = 0.01), body mass index (23.3 vs. 22.7 kg/m(2); P = 0.04), waist circumference (84.9 vs. 82.8 cm; P = 0.01), triglyceride levels (119.7 vs. 99.5 mg/dl; P < 0.01), and low-density lipoprotein cholesterol levels (128.6 vs. 122.2 mg/dl; P = 0.04), and showed significantly lower high-density lipoprotein cholesterol levels (57.4 vs. 61.3 mg/dl; P = 0.02). These associations were independent of numerous potential confounders, including urinary melatonin excretion. Furthermore, LAN exposure is associated with higher odds ratios (ORs) for obesity (body mass index: OR, 1.89; P = 0.02; abdominal: OR, 1.62; P = 0.04) and dyslipidemia (OR, 1.72; P = 0.02) independent of demographic and socioeconomic parameters. In contrast, urinary melatonin excretion and glucose parameters did not show significant differences between the two groups. Conclusions: Exposure to LAN in an uncontrolled home setting is associated with impaired obese and lipid parameters independent of nocturnal urinary melatonin excretion in elderly individuals. Moreover, LAN exposure is associated with higher ORs for obesity and dyslipidemia independent of demographic and socioeconomic parameters.

Keywords

Authors Ocampo-Lim B, Guo W, DeMott-Friberg R et al.

Report Name Nocturnal growth hormone (GH) secretion is eliminated by infusion of GH-releasing hormone antagonist

Publication J Clin Endocrinol Metab

Issue-page numbers 81:4396–4399 doi:10.1210/jc.81.12.4396. PMID:8954048

URL http://www.ncbi.nlm.nih.gov/pubmed/8954048

Abstract The neuroendocrine mechanisms underlying the generation of pulsatile GH secretion in humans are poorly understood. GH secretory pulses are likely to result from acute GHRH secretory episodes, acute decreases in hypothalamic somatostatin secretion, or a combination of these mechanisms. In earlier studies we demonstrated that a single i.v. bolus o a competitive GHRH antagonist [N-Ac-Tyr1,D-Arg2)GHRH-(1-29); GHRH-Ant] blocked 40% of the nocturnal GH release. Failure to more completely eliminate nocturnal GH secretion could be due to either incomplete antagonism of endogenous GHRH action by GHRH-Ant or a non-GHRH component of GH release. We subsequently investigated whether a continuous infusion of GHRH-Ant would more completely eliminate nocturnal GH secretion. Eight men were given a 400 micrograms/kg i.v. bolus of GHRH-Ant at 2300 h, followed by a 50 micrograms/kg.h i.v. infusion of GHRH-Ant between 2300-0700 h or a saline bolus followed by a saline infusion. An i.v. bolus of GHRH (1 microgram/kg) was given at 0500 h on both occasions. Blood was sampled every 10 min between 2300-0700 h. As measured by the area under the curve (AUC) from 2400-0500 h, GHRH-Ant suppressed GH secretion by an average of 89% (1795 +/- 412 vs. 164 +/- 46 micrograms/min.L; P = 0.004). The response to GHRH was suppressed by 79% (484 +/- 140 vs. 64 +/- 19 micrograms/min.L; P = 0.02). These data demonstrate that the previously observed nonsuppressible GH secretion was probably due to incomplete blockade of pituitary GHRH receptors and that all or nearly all of nocturnal GH pulsatility can be attributed to the effect of hypothalamic GHRH.

Keywords

OECD/IEA **Year** 2006

Authors Organization for Economic Co-operation and Development (OECD)/International Energy Agency (IEA)

Report Name Light's labour's lost - policies for energy-efficient lighting

Publication OECD/IEA

Issue-page numbers Paris, France, 2006

URL http://www.iea.org/work/2007/cfl/Waide.pdf

Abstract

When William Shakepeare wrote Love's Labour's Lost he would have used light from tallow candles at a cost (today) of £12,000 per million-lumen hours. The same amount of light from electric lamps now costs only £2! But today's low-cost illumination still has a dark side. Globally, lighting consumes more electricity than is produced by either hydro or nuclear power and results in CO2 emissions equivalent to two thirds of the world's cars.

A standard incandescent lamp may be much more efficient than a tallow candle, but it is far less efficient than a high-pressure sodium lamp. Were inefficient light sources to be replaced by the equivalent efficient ones, global lighting energy demand would be up to 40% less at a lower overall cost. Larger savings still could be realised through the intelligent use of controls, lighting levels and daylight.

But achieving efficient lighting is not just a question of technology; it requires policies to transform current practice. This book documents the broad range of policy measures to stimulate efficient lighting that have already been implemented around the world and suggests new ways these could be strengthened to prevent light's labour's from being lost.

Keywords

Ohlendorf R, Vidavski RR, Eldar A, et al. **Year** 2012

Authors Robert Ohlendorf, Roee R. Vidavski, Avigdor Eldar,

Report Name From Dusk till Dawn: One-Plasmid Systems for Light-Regulated Gene Expression

Publication Journal of Molecular Biology

Issue-page numbers Available online 8 January 2012

URL http://lehre.biologie.hu-berlin.de/biophyschem/papers/Ohlendorf_JMB2012.pdf

Abstract

Signaling photoreceptors mediate diverse organismal adaptations in response to light. As light-gated protein switches, signaling photoreceptors provide the basis for optogenetics, a term that refers to the control of organismal physiology and behavior by light. We establish as novel optogenetic tools the plasmids pDusk and pDawn, which employ bluelight photoreceptors to confer light-repressed or light-induced gene expression in Escherichia coli with up to 460-fold induction upon illumination. Key features of these systems are low background activity, high dynamic range, spatial control on the 20-μm scale, independence from exogenous factors, and ease of use. In optogenetic experiments, pDusk and pDawn can be used to specifically perturb individual nodes of signaling networks and interrogate their role. On the preparative scale, pDawn can induce by light the production of recombinant proteins and thus represents a cost-effective and readily automated alternative to conventional induction systems.

Keywords gene expression; light-oxygen-voltage; optogenetics; photoreceptor; protein engineering

Authors Okatani Y, Sagara Y

Report Name Amplification of nocturnal melatonin secretion in women with functional secondary amenorrhoea: relation to endogenous oestrogen concentration

Publication Clin Endocrinol (Oxf)

Issue-page numbers 41:763–770 doi:10.1111/j.1365-2265.1994.tb02791.x. PMID:7889612

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1994.tb02791.x/abstract

Abstract

BACKGROUND AND OBJECTIVE Although there is extensive evidence that melatonin inhibits gonadotrophin secretion in animals, there is a parity of data on the relation between melatonin and ovarian function in humans. The purpose of this study was to evaluate the relation between endogenous oestrogen concentrations and nocturnal melatonin secretion occurring in patients with secondary amenorrhoea (SA).

DESIGN AND PATIENTS Nocturnal serum melatonin concentrations were determined in 20 women with SA, 5 women with endometriosis showing normal menstrual cycles and 11 volunteers with normal menstrual cycles.

MEASUREMENT Serum melatonin concentrations were determined by high performance liquid chromatography with electrochemical detection. Differences in melatonin concentrations were examined by analysis of variance.

RESULTS Nocturnal melatonin concentrations in patients with SA were significantly higher than in normal women ($P < 0{\cdot}01$ vs women with normal menstrual cycles). There were significant negative correlations between cummulative melatonin levels (between 2000 and 0800 h) and serum 17β-oestradiol ($r = -0{\cdot}561$, $p < 0{\cdot}01$) and between peak serum melatonin values and the serum 17β-oestradiol ($r = -0{\cdot}608$, $P < 0{\cdot}01$) in SA. Intravenous administration of a conjugated oestrogen (Premarin 20 mg) significantly suppressed nocturnal melatonin secretion ($P < 0{\cdot}05$). A low oestrogen state, induced by long-term (3·5 months) GnRH agonist treatment (900 μg/day of buserelin acetate) of the women with endometriosis produced an increase in nocturnal melatonin secretion comparable to that found in SA women.

CONCLUSION Our findings suggest that elevated nocturnal melatonin secretion in women with secondary amenorrhoea may be related to their low oestrogen concentrations.

Keywords

Okuno T, Saito H, Ojima J

Year 2002

Authors Okuno T, Saito H, Ojima J.

Report Name Evaluation of blue-light hazards from various light sources

Publication Dev Ophthalmol

Issue-page numbers 2002;35:104-12.

URL http://www.ncbi.nlm.nih.gov/pubmed/12061267

Abstract Visible light of short wavelength (blue light) may cause a photochemical injury to the retina, called photoretinitis or blue-light hazard. In this study, various light sources were evaluated for blue-light hazard. These sources include the sun, the arc associated with arc welding and plasma cutting, molten steel, iron and glass, the interior of furnaces, the arc or envelope of discharge lamps, the filament or envelope of incandescent lamps, the envelope of fluorescent lamps and light-emitting diodes. The spectral radiance of each light source was measured, and blue-light effective radiance and the corresponding permissible exposure time per day were calculated in accordance with the ACGIH (American Conference of Governmental Industrial Hygienists) standard. The sun, arc welding, plasma cutting and the arc of discharge lamps were found to have extremely high effective radiances with corresponding permissible exposure times of only 0.6-40 s, suggesting that viewing these light sources is very hazardous to the retina. Other light sources were found to have low effective radiances under the study conditions and would pose no hazard, at least for short exposure times.

Keywords

O'Leary ES, Schoenfeld ER, Stevens RG, et al.

Year 2006

Authors Erin S. O'Leary, Elinor R. Schoenfeld, Richard G. Stevens, Geoffrey C. Kabat, Kevin Henderson, Roger Grimson, Marilie D. Gammon, M. Cristina Leske

Report Name Shift Work, Light at Night, and Breast Cancer on Long Island, New York

Publication American Journal of Epidemiology

Issue-page numbers Volume164, Issue4 Pp. 358-366

URL http://aje.oxfordjournals.org/content/164/4/358.full

Abstract The hypothesized association between breast cancer and circadian disruption was evaluated in the Electromagnetic Fields and Breast Cancer on Long Island Study. Participants included 576 women with breast cancer diagnosed from August 1996 to June 1997 and 585 population-based controls (87% and 83% participation rates, respectively) aged <75 years and living in the same Long Island, New York, home for ≥15 years. An in-person interview ascertained light-at-night exposure histories through shift work (previous 15 years) and at home (previous 5 years). Odds ratios and 95% confidence intervals were estimated by unconditional multivariate logistic regression. Breast cancer was not associated with overall shift work (odds ratio (OR) = 1.04, 95% confidence interval (CI): 0.79, 1.38) or evening shift work (OR = 1.08, 95% CI: 0.81, 1.44). However, overnight shift workers were at lower risk than women never working shifts (OR = 0.55, 95% CI: 0.32, 0.94). Women who frequently turned on lights at home during sleep hours (≥twice/week and ≥twice/night) had increased risks (OR = 1.65, 95% CI: 1.02, 2.69). The latter results suggest positive associations with residential light-at-night exposure, or they could reflect response biases. Furthermore, overall and evening shift work were not significant factors, and analyses of overnight shift workers yielded reduced risk estimates. The study thus provides mixed evidence for the light-at-night hypothesis.

Keywords breast neoplasms, case-control studies, circadian rhythm, electromagnetic fields, light, melatonin, occupation, women

Oliveira C, Ortega A, López-Olmeda JF, et al. **Year** 2007

Authors Catarina Oliveira, Aurelio Ortega, José Fernando López-Olmeda, Luisa María Vera and Dr. Francisco Javier Sánchez-Vázquez

Report Name Influence of Constant Light and Darkness, Light Intensity, and Light Spectrum on Plasma Melatonin Rhythms in Senegal Sole

Publication Chronobiology International

Issue-page numbers 24:4, 615-627

URL http://informahealthcare.com/doi/abs/10.1080/07420520701534657

Abstract Light is the most important synchronizer of melatonin rhythms in fish. This paper studies the influence of the characteristics of light on plasma melatonin rhythms in sole. The results revealed that under long-term exposure to constant light conditions (LL or DD), the total 24 h melatonin production was significantly higher than under LD, but LL and DD conditions influenced the rhythms differently. Under LL, melatonin remained at around 224 pg/ml throughout the 24 h, while under DD a significant elevation (363.6 pg/ml) was observed around the subjective evening. Exposure to 1 h light pulses at MD (mid-dark) inhibited melatonin production depending on light intensity (3.3, 5.3, 10.3, and 51.9 μW/cm2). The light threshold required to reduce nocturnal plasma melatonin to ML (mid-light) values was 5.3 μW/cm2. Melatonin inhibition by light also depended on the wavelength of the light pulses: while a deep red light (λ>600 nm) failed to reduce plasma melatonin significantly, far violet light (λmax=368 nm) decreased indoleamine's concentration to ML values. These results suggest that dim light at night (e.g., moonlight) may be perceived and hence affect melatonin rhythms, encouraging synchronization to the lunar cycle. On the other hand, deep red light does not seem to inhibit nocturnal melatonin production, and so it may be used safely during sampling at night.

Keywords Circadian rhythms, Melatonin, Senegal sole (Solea senegalensis), Photoperiod, Light pulses

Opländer C, Hidding S, Werners FB, et al. **Year** 2011

Authors Christian Opländer, Sarah Hidding, Frauke B. Werners, Matthias Born, Norbert Pallua, Christoph V. Suschek

Report Name Effects of blue light irradiation on human dermal fibroblasts

Publication Journal of Photochemistry and Photobiology B: Biology

Issue-page numbers Volume 103, Issue 2, 3 May 2011, Pages 118-125

URL http://www.sciencedirect.com/science/article/pii/S1011134411000698

Abstract Previous studies have reported that separately from UV-radiation also blue light influences cellular physiology in different cell types. However, little is known about the blue light action spectrum. The purpose of this study was to investigate effects of blue light at distinct wavelengths (410, 420, 453, 480 nm) emitted by well defined light-emitting-diodes on viability, proliferation and antioxidative capacity of human dermal fibroblasts. We found that irradiation with blue light (410, 420 nm) led to intracellular oxidative stress and toxic effects in a dose and wavelength dependent manner. No toxicity was observed using light at 453 nm and 480 nm. Furthermore, blue light (410, 420, 453 nm) at low doses reduced the antioxidative capacity of fibroblasts. At non-toxic doses, irradiations at 410, 420 and 453 nm reduced proliferation indicating a higher susceptibility of proliferating fibroblasts to blue light. Our results show that blue light at different wavelengths may induce varying degrees of intracellular oxidative stress with different physiological outcome, which could contribute to premature skin photoaging. On the other hand, the use of blue light due to its antiproliferative and toxic properties may represent a new approach in treatment and prevention of keloids, hypertrophic scars and fibrotic skin diseases.

Keywords Fibroblasts; Visible light; Blue light

Opp MR, Kapás L, Toth LA — *Year* 1992

Authors Opp MR, Kapás L, Toth LA

Report Name Cytokine involvement in the regulation of sleep

Publication Proc Soc Exp Biol Med

Issue-page numbers 201:16–27. PMID:1382300

URL http://www.ncbi.nlm.nih.gov/pubmed/1382300

Abstract N/A

Keywords

Organisciak D., Wong P, Rapp C, et al. — *Year* 2012

Authors Daniel Organisciak, Paul Wong, Christine Rapp, Ruth Darrow, Alison Ziesel, Rekha Rangarajan, John Lang

Report Name Light-Induced Retinal Degeneration Is Prevented by Zinc, a Component in the Age-related Eye Disease Study Formulation

Publication Photochemistry and Photobiology

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2012.01134.x/abstract

Abstract Mineral supplements are often included in multivitamin preparations because of their beneficial effects on metabolism. In this study, we used an animal model of light-induced retinal degeneration to test for photoreceptor cell protection by the essential trace element zinc. Rats were treated with various doses of zinc oxide and then exposed to intense visible light for as long as 8 h. Zinc treatment effectively prevented retinal light damage as determined by rhodopsin and retinal DNA recovery, histology and electrophoretic analysis of DNA damage and oxidized retinal proteins. Zinc oxide was particularly effective when given before light exposure and at doses two- to four-fold higher than recommended by the age-related eye disease study group. Treated rats exhibited higher serum and retinal pigment epithelial zinc levels and an altered retinal gene expression profile. Using an Ingenuity database, 512 genes with known functional annotations were found to be responsive to zinc supplementation, with 45% of these falling into a network related to cellular growth, proliferation, cell cycle and death. Although these data suggest an integrated and extensive regulatory response, zinc induced changes in gene expression also appear to enhance antioxidative capacity in retina and reduce oxidative damage arising from intense light exposure.

Keywords

Authors Organisciak DT, Jiang YL, Wang HM, Pickford M, Blanks JC.

Report Name Retinal light damage in rats exposed to intermittent light. Comparison with continuous light exposure

Publication Invest Ophthalmol Vis Sci

Issue-page numbers 1989 May;30(5):795-805.

URL http://www.iovs.org/content/30/5/795.full.pdf

Abstract Visible light-induced photoreceptor cell damage resulting from exposure to multiple intermittent light-dark periods was compared with damage resulting from continuous light in albino rats maintained in a weak cyclic-light environment or in darkness before light treatment. The time course of retinal damage was determined by correlative measurements of rhodopsin and visual cell DNA at various times after light exposure, and by histopathological evaluation. The effect of intense light exposures on rhodopsin regeneration and on the level of rod outer segment docosahexaenoic acid was also determined. For rats previously maintained in weak cyclic light, 50% visual cell loss was measured 2 weeks after 12 1 hr light/2 hr dark periods, or following 24 hr of continuous light. A comparable 50% loss of visual cells was found in dark-reared rats after only 5 hr of continuous illumination or 2-3 hr of intermittent light. As judged by histology, cyclic-light-reared rats incurred less retinal pigment epithelial cell damage than dark-reared animals. In both experimental rat models intermittent light exposure resulted in greater visual cell damage than continuous exposure. Visual cell damage from intermittent light was found to depend on the duration of light exposure and on the number of light doses administered. Measurements of rhodopsin and DNA 2 hr and 2 weeks after light exposure of up to 8 hr duration revealed that visual cell loss occurs largely during the 2 week dark period following light treatment. The loss of docosahexaenoic acid from rod outer segments was also greater in rats exposed to intermittent light than in animals treated with continuous light. It is concluded that intermittent light exposure exacerbates Type I light damage in rats (involving the retina and retinal pigment epithelium) and the schedule of intense light exposure is a determinant of visual cell death.

Keywords

Organisciak DT, Vaughan DK

Year 2010

Authors Daniel T. Organisciak and Dana K. Vaughan

Report Name Retinal light damage: mechanisms and protection

Publication Prog Retin Eye Res

Issue-page numbers 2010 March; 29(2): 113–134.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2831109/

Abstract By its action on rhodopsin, light triggers the well-known visual transduction cascade, but can also induce cell damage and death through phototoxic mechanisms -- a comprehensive understanding of which is still elusive despite more than 40 years of research. Herein, we integrate recent experimental findings to address several hypotheses of retinal light damage, premised in part on the close anatomical and metabolic relationships between the photoreceptors and the retinal pigment epithelium. We begin by reviewing the salient features of light damage, recently joined by evidence for retinal remodeling which has implications for the prognosis of recovery of function in retinal degenerations. We then consider select factors that influence the progression of the damage process and the extent of visual cell loss. Traditional, genetically-modified, and emerging animal models are discussed, with particular emphasis on cone visual cells. Exogenous and endogenous retinal protective factors are explored, with implications for light damage mechanisms and some suggested avenues for future research. Synergies are known to exist between our long term light environment and photoreceptor cell death in retinal disease. Understanding the molecular mechanisms of light damage in a variety of animal models can provide valuable insights into the effects of light in clinical disorders and may form the basis of future therapies to prevent or delay visual cell loss.

Keywords

Ortiz-Tudela E, Bonmatí-Carrión MD, De la Fuente M, Mendiola P

Year 2011

Authors Ortiz-Tudela E, Bonmatí-Carrión MD, De la Fuente M, Mendiola P

Report Name [Chronodisruption and ageing.]

Publication Rev Esp Geriatr Gerontol

Issue-page numbers 2011 Dec 15. [Epub ahead of print]

URL http://www.ncbi.nlm.nih.gov/pubmed/22177973

Abstract Modern life leads to a more active nocturnal lifestyle, reduced sleep hours and sometimes abrupt shifts across time zones (such as jet lag and shift work) that generate chronodisruption (CD) which can result in premature ageing. CD is defined as a significant disturbance of the internal temporal order of biochemical, physiological and behavioural circadian rhythms. Epidemiological studies show that CD induced by shift work, chronic jet lag, social jet lag and excessive exposure of bright light at night is associated with an increased incidence of metabolic syndrome, cardiovascular disease, cognitive and affective impairment, sleep disorders, some cancers and premature ageing. CD may be the result of disturbances in different components of the circadian system (central pacemaker and peripheral oscillators, inputs to central clock, mainly due to visual deficiencies, and output signals from the pacemaker and oscillators). Exposure to different synchronizers (light, meal times, physical and social activities) with a regular pattern results in a chronoenhacement that can prevent age-related CD.

Keywords

Osborne NN

Year 2010

Authors Neville N Osborne

Report Name Mitochondria: Their role in ganglion cell death and survival in primary open angle glaucoma

Publication Experimental Eye Research

Issue-page numbers Volume: 90, Issue: 6, Publisher: Elsevier Ltd, Pages: 750-757

URL http://www.mendeley.com/research/mitochondria-their-role-in-ganglion-cell-death-and-survival-in-primary-open-angle-glaucoma/

Abstract Retinal ganglion cell axons within the globe are functionally specialised being richly provided with many mitochondria. Mitochondria produce the high energy that is required for nerve conduction in the unmylenated part of the ganglion cell axons and for the maintenance of optimum neuronal function. We proposed that in the initiation of glaucoma (POAG) an alteration in the quality of blood flow dynamics in the optic nerve head results in sustained or intermittent ischemia of a defined nature. This results in normal mitochondrial function being negatively affected and as a consequence retinal ganglion cell function is compromised. Ganglion cells in this state are now susceptible to secondary insults which they would normally tolerate. One secondary insult to ganglion cell mitochondria in such a state might be light entering the eye. Other insults to the ganglion cells might come from substances such as glutamate, prostaglandins and nitric oxide released from astrocytes and microglia in the optic nerve head region. Such cascades of events initiated by ischemia to the optic nerve head region ultimately cause ganglion cells to die at different rates.

Keywords

Osborne NN, Lascaratos G, Bron AJ, et al.

Year 2006

Authors N N Osborne, G Lascaratos, A J Bron, G Chidlow, J P M Wood

Report Name A hypothesis to suggest that light is a risk factor in glaucoma and the mitochondrial optic neuropathies.

Publication Br J Ophthalmol

Issue-page numbers 2006;90:237-241 doi:10.1136/bjo.2005.082230

URL http://bjo.bmj.com/content/90/2/237.abstract

Abstract The authors propose that light entering the eye interacts with retinal ganglion cell (RGC) axon mitochondria to generate reactive oxygen intermediates (ROI) and that when these neurons are in an energetically low state, their capacity to remove these damaging molecules is exceeded and their survival is compromised. They suggest that in the initial stages of glaucoma, RGCs exist at a low energy level because of a reduced blood flow at the optic nerve head and that in the mitochondrial optic neuropathies (MONs), this results from a primary, genetic defect in aerobic metabolism. In these states RGCs function at a reduced energy level and incident light on the retina becomes a risk factor. Preliminary laboratory studies support this proposition. Firstly, the authors have shown that light is detrimental to isolated mitochondria in an intensity dependent manner. Secondly, light triggers apoptosis of cultured, transformed RGCs and this effect is exacerbated when the cells are nutritionally deprived. Detailed studies are under way to strengthen the proposed theory. On the basis of this proposal, the authors suggest that patients with optic neuropathies such as glaucoma or at risk of developing a MON may benefit from the use of spectral filters and reducing the intensity of light entering the eye.

Keywords

Osborne NN, Li GY, Ji D, et al. ***Year*** 2008

Authors Osborne NN, Li GY, Ji D, Mortiboys HJ, Jackson S.

Report Name Light affects mitochondria to cause apoptosis to cultured cells: possible relevance to ganglion cell death in certain optic neuropathies

Publication Journal of Neurochemistry

Issue-page numbers Volume 105, Issue 5, pages 2013–2028, June 2008

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1471-4159.2008.05320.x/abstract

Abstract Retinal ganglion cell axons within the globe are laden with mitochondria that are unprotected from light (400–760 nm) impinging onto the retina. Light can be absorbed by mitochondrial enzymes such as cytochrome and flavin oxidases causing the generation of reactive oxygen species, and we have suggested this may pose a risk to ganglion cell survival if their energy state is compromised, as may be so in glaucoma or in Leber's Hereditary Optic Neuropathy. Here, we demonstrate that light (400–760 nm) provokes apoptosis in cultured retinal ganglion-5 cells, and that this effect is enhanced in low serum, and attenuated by various antioxidants. Apoptosis is shown to be caspase independent, involving reactive oxygen species generation and the activation of poly(ADP-ribose) polymerase-1 and apoptosis-inducing factor. We further show that light-induced apoptosis requires the participation of the mitochondrial respiratory chain. This was demonstrated by culturing fibroblasts (BJhTERT cells) in ethidium bromide for 40 days to deplete their mitochondrial DNA and perturb their mitochondrial respiratory chain function (BJhTERT rh0 cells). Only BJhTERT cells, with intact mitochondrial respiratory chain function were affected by light insult. Finally, we show that exposure of anaesthetized pigmented rat eye to white, but not red light, causes changes in the expression of certain retinal mRNAs (neurofilament light, Thy-1 and melanopsin) and optic nerve proteins (neurofilament light and tubulin), suggesting that ganglion cell survival is affected. Our findings support the proposal that the interaction of light, particularly the blue component, with intra-axonal ganglion cell mitochondria may be deleterious under certain circumstances, and suggest that reducing the light energy impinging upon the retina might benefit patients with certain optic neuropathies.

Keywords apoptosis; ganglion cells; glaucoma; light; mitochondria; retina

Owen J, Arendt J ***Year*** 1992

Authors Owen J, Arendt J

Report Name Melatonin suppression in human subjects by bright and dim light in Antarctica: time and season-dependent effects

Publication Neurosci Lett

Issue-page numbers 137:181–184 doi:10.1016/0304-3940(92)90399-R. PMID:1584458

URL http://www.mendeley.com/research/melatonin-suppression-human-subjects-bright-dim-light-antartica-time-seasondependent-effects/

Abstract Full-spectrum light, of sufficiently high intensity, will suppress the secretion of melatonin at night in humans. Individual sensitivity to such suppression is variable, and the factors determining such sensitivity are largely unknown.

Keywords light, light health, melatonin, season

Ozturk L, Pelin Z, Karadeniz D et al. **Year** 1999

Authors Oztürk L, Pelin Z, Karadeniz D, Kaynak H, Cakar L, Gözükirmizi E.

Report Name Effects of 48 hours sleep deprivation on human immune profile

Publication Sleep Res

Issue-page numbers 2:107–111. PMID: 11382891

URL http://www.ncbi.nlm.nih.gov/pubmed/11382891

Abstract It is a common belief that sleep deprivation increases the susceptibility to diseases. In order to evaluate the effects of sleep deprivation on immune profile in humans, peripheral venous blood was obtained from sixteen healthy young male volunteers. Ten of the volunteers underwent 48 hours of sleep deprivation and the other six maintained their regular sleep schedule and acted as controls. The first blood samples were taken at the end of the first polysomnographic recording at 8:00 a.m. After this sampling, ten subjects were sleep deprived for 48 hours in sedentary conditions. The second and third blood samples were taken at the 24th and 48th hours. The subjects were recorded again to verify rebound effects of sleep deprivation after the third blood sampling. In this second polysomnographic recording, all sleep-deprived subjects showed slow wave and REM sleep rebound. The last blood samples were taken at the 72nd hour of study at 8:00 a.m. CD4, CD8, CD5, CD16, CD19 surface antigen positive lymphocyte subsets, serum IgG, IgM, and cortisol levels were assessed in all samples. Our results showed that the proportion of NK cells were decreased during sleep deprivation and returned to normal values after recovery sleep. In the control group, we did not observe any changes in the same direction as the sleep-deprived group.

Keywords

Pääkkönen T, Mäkinen TM, Leppäluoto J et al. **Year** 2006

Authors Pääkkönen T, Mäkinen TM, Leppäluoto J et al.

Report Name Urinary melatonin: a noninvasive method to follow human pineal function as studied in three experimental conditions

Publication J Pineal Res

Issue-page numbers 40:110–115 doi:10.1111/j.1600-079X.2005.00300.x. PMID:16441547

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2005.00300.x/full

Abstract The aim of this study was to examine whether urinary melatonin, rather than urinary 6-sulfatoxymelatonin (aMT6s), can be used as an indicator of diurnally and seasonally changing melatonin secretion. The subjects (n = 15) spent three separate 24-hr periods in a climatic chamber during winter (n = 7) and summer (n = 8). Blood and urine samples were obtained during each period at 2- to 5-hr intervals. Serum melatonin and urinary melatonin and aMT6s were assayed by radioimmunoassay. The serum melatonin levels increased nearly 10-fold from low daytime to high nocturnal values. The mean nocturnal increase of urinary melatonin was 1.7-fold and that of urinary aMT6s was 4.6-fold. Both urinary melatonin and aMT6s correlated significantly with area under the curve melatonin in serum during the night, during the day and throughout the entire 24-hr observation period in all cases. The ratio between urinary melatonin and aMT6s excretion showed significant diurnal variation, being ninefold higher at 16:00 hr than at 07:00 or at 09:00 hr. The ninefold decrease in the urinary melatonin/aMT6s excretion ratio between the evening and the morning may reflect increased liver metabolism of melatonin during the night. Both urinary melatonin and aMT6s are good indicators of melatonin secretion, but the variation is significantly smaller for the former molecule.

Keywords diurnal rhythm; radioimmuno assay; serum melatonin; urinary 6-sulfatoxymelatonin; urinary melatonin

Palmblad J, Cantell K, Strander H et al. ***Year*** 1976

Authors Jan Palmblad∗, ‡, Kari Cantell§, Hans Strander†, Jan Fröberg‡, Claes-Göran Karlsson‡, Lennart Levi‡, Marta Granström‖, Peter Unger

Report Name Stressor exposure and immunological response in man: interferon-producing capacity and phagocytosis

Publication J Psychosom Res

Issue-page numbers 20:193–199 doi:10.1016/0022-3999(76)90020-9. PMID:972359

URL http://www.sciencedirect.com/science/article/pii/0022399976900209

Abstract Exposure of 8 healthy human females to a moderately stressful 77-hr vigil under strictly controlled conditions was accompanied by changes in adrenal cortical and medullary hormones compatible with a stress reaction. The ability of the lymphocytes to procedure interferon in response to the addition of Sendai virus to blood samples rose during the stressor exposure and was highest after this. Phagocytosis by peripheral blood phagocytes showed a decrease during the vigil and was followed in post-exposure samples by a rise to levels above pre-exposure values.

Keywords

Palmblad J, Petrini B, Wasserman J, Akerstedt T ***Year*** 1979

Authors Palmblad J, Petrini B, Wasserman J, Akerstedt T

Report Name Lymphocyte and granulocyte reactions during sleep deprivation

Publication Psychosom Med

Issue-page numbers 41:273–278. PMID:482523

URL http://www.psychosomaticmedicine.org/content/41/4/273.full.pdf

Abstract The possible influence of 48 hr of sleep deprivation on in vitro DNA synthesis of blood lymphocytes and on the adhesiveness and intracellular, stainable activity of alkaline phosphatase in blood granulocytes was studied in twelve young male volunteers. Following the sleep deprivation, all 12 subjects showed marked reductions of DNA synthesis after stimulation with phytohemagglutinin. Pre-exposure levels were regained 5 days after terminating the vigil. No changes were noted in granulocyte adherence or alkaline phosphatase activity. The results suggest that sleep deprivation may decrease cell-mediated immune reactions and thereby impair some aspects of host defense.

Keywords

Pan A, Schernhammer ES, Sun Q, Hu FB **Year** 2011

Authors An Pan, Eva S. Schernhammer, Qi Sun, and Frank B. Hu

Report Name Rotating Night Shift Work and Risk of Type 2 Diabetes: Two Prospective Cohort Studies in Women

Publication PLoS Med

Issue-page numbers 2011 December; 8(12): e1001141.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3232220/

Abstract

ackground
Rotating night shift work disrupts circadian rhythms and has been associated with obesity, metabolic syndrome, and glucose dysregulation. However, its association with type 2 diabetes remains unclear. Therefore, we aimed to evaluate this association in two cohorts of US women.
Methods and Findings
We followed 69,269 women aged 42–67 in Nurses' Health Study I (NHS I, 1988–2008), and 107,915 women aged 25–42 in NHS II (1989–2007) without diabetes, cardiovascular disease, and cancer at baseline. Participants were asked how long they had worked rotating night shifts (defined as at least three nights/month in addition to days and evenings in that month) at baseline. This information was updated every 2–4 years in NHS II. Self-reported type 2 diabetes was confirmed by a validated supplementary questionnaire. We documented 6,165 (NHS I) and 3,961 (NHS II) incident type 2 diabetes cases during the 18–20 years of follow-up. In the Cox proportional models adjusted for diabetes risk factors, duration of shift work was monotonically associated with an increased risk of type 2 diabetes in both cohorts. Compared with women who reported no shift work, the pooled hazard ratios (95% confidence intervals) for participants with 1–2, 3–9, 10–19, and ≥20 years of shift work were 1.05 (1.00–1.11), 1.20 (1.14–1.26), 1.40 (1.30–1.51), and 1.58 (1.43–1.74, p-value for trend <0.001), respectively. Further adjustment for updated body mass index attenuated the association, and the pooled hazard ratios were 1.03 (0.98–1.08), 1.06 (1.01–1.11), 1.10 (1.02–1.18), and 1.24 (1.13–1.37, p-value for trend <0.001).
Conclusions
Our results suggest that an extended period of rotating night shift work is associated with a modestly increased risk of type 2 diabetes in women, which appears to be partly mediated through body weight. Proper screening and intervention strategies in rotating night shift workers are needed for prevention of diabetes.

Keywords

Panda S, Antoch MP, Miller BH et al. **Year** 2002

Authors Panda S, Antoch MP, Miller BH et al.

Report Name Coordinated transcription of key pathways in the mouse by the circadian clock

Publication Cell

Issue-page numbers 109:307–320 doi:10.1016/S0092-8674(02)00722-5. PMID:12015981

URL http://www.cell.com/abstract/S0092-8674%2802%2900722-5

Abstract In mammals, circadian control of physiology and behavior is driven by a master pacemaker located in the suprachiasmatic nuclei (SCN) of the hypothalamus. We have used gene expression profiling to identify cycling transcripts in the SCN and in the liver. Our analysis revealed ~650 cycling transcripts and showed that the majority of these were specific to either the SCN or the liver. Genetic and genomic analysis suggests that a relatively small number of output genes are directly regulated by core oscillator components. Major processes regulated by the SCN and liver were found to be under circadian regulation. Importantly, rate-limiting steps in these various pathways were key sites of circadian control, highlighting the fundamental role that circadian clocks play in cellular and organismal physiology.

Keywords

Panda S, Hogenesch JB, Kay SA **Year** 0

Authors Panda S, Hogenesch JB, Kay SA.

Report Name Circadian rhythms from flies to human

Publication Nature

Issue-page numbers 417, 329-335 (16 May 2002) | doi:10.1038/417329a

URL http://www.nature.com/nature/journal/v417/n6886/full/417329a.html

Abstract In this era of jet travel, our body 'remembers' the previous time zone, such that when we travel, our sleep–wake pattern, mental alertness, eating habits and many other physiological processes temporarily suffer the consequences of time displacement until we adjust to the new time zone. Although the existence of a circadian clock in humans had been postulated for decades, an understanding of the molecular mechanisms has required the full complement of research tools. To gain the initial insights into circadian mechanisms, researchers turned to genetically tractable model organisms such as Drosophila.

Keywords

Authors Rohit Kumar Pandey and Sanjay Kumar Bhardwaj

Report Name Circadian and Seasonal Responses in Indian Weaver Bird: Subjective Interpretation of Day and Night Depends Upon Both Light Intensity and Contrast Between Illuminations

Publication Chronobiology International

Issue-page numbers Posted online on August 30, 2011. (doi:10.3109/07420528.2011.603873)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.603873

Abstract This study investigated whether changes in illumination modify perception of day and night conditions in a diurnal species, the Indian weaver bird. Birds were initially subjected to a 12-h light:12-h dark regime (12L:12D; L = 20 lux, D = 0.5 lux). After every 2 wks, the combinations of light illumination in L and D phases were changed as follows: 20:2 lux, 20:5 lux, 20:10 lux, 20:20 lux, 20:100 lux, and 20:200 lux. Finally, birds were released into dim constant light (0.5 lux) for 2 wks to determine the phase and period of the circadian activity rhythm. They were also laparotomized at periodic intervals to examine the effects of the light regimes on the seasonal testicular cycle. All individuals showed a consistently similar response. As evident by the activity pattern under these light regimes, both in total activity during contrasting light phases and during the 2 h in the beginning and end of first light phase, birds interpreted the period of higher light intensity as day, and the period of lower intensity as the night. During the period of similar light intensity, i.e., under LL, birds free-ran with a circadian period (24 h). In bright LL (20 lux), the activity rhythm was less distinct, but periodogram analysis revealed the circadian period for the group as 24.46 ± 0.41 h (mean ± SE). However, in dim LL at the end of the experiment, all birds exhibited a circadian pattern with average period of 25.52 ± 0.70 h. All birds also showed testicular growth and regression during the 16-wks study. It is suggested that weaver birds interpret day and night subjectively based on both the light intensity and contrast between illuminations during two phases over the 24 h.

Keywords Circadian rhythm, Indian weaver bird, Light intensity, Locomotor activity, Zeitgeber time

Authors Seithikurippu R. Pandi-Perumal, Ahmed S. BaHammam, Gregory M. Brown, D. Warren Spence, Vijay K. Bharti, Charanjit Kaur, Rüdiger Hardeland and Daniel P. Cardinali

Report Name Melatonin Antioxidative Defense: Therapeutical Implications for Aging and Neurodegenerative Processes

Publication Neurotoxicity Research

Issue-page numbers 2012, DOI: 10.1007/s12640-012-9337-4

URL http://www.springerlink.com/content/162166j698r01607/

Abstract The pineal product melatonin has remarkable antioxidant properties. It is secreted during darkness and plays a key role in various physiological responses including regulation of circadian rhythms, sleep homeostasis, retinal neuromodulation, and vasomotor responses. It scavenges hydroxyl, carbonate, and various organic radicals as well as a number of reactive nitrogen species. Melatonin also enhances the antioxidant potential of the cell by stimulating the synthesis of antioxidant enzymes including superoxide dismutase, glutathione peroxidase, and glutathione reductase, and by augmenting glutathione levels. Melatonin preserves mitochondrial homeostasis, reduces free radical generation and protects mitochondrial ATP synthesis by stimulating Complexes I and IV activities. The decline in melatonin production in aged individuals has been suggested as one of the primary contributing factors for the development of age-associated neurodegenerative diseases. The efficacy of melatonin in preventing oxidative damage in either cultured neuronal cells or in the brains of animals treated with various neurotoxic agents, suggests that melatonin has a potential therapeutic value as a neuroprotective drug in treatment of Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), Huntington's disease (HD), stroke, and brain trauma. Therapeutic trials with melatonin indicate that it has a potential therapeutic value as a neuroprotective drug in treatment of AD, ALS, and HD. In the case of other neurological conditions, like PD, the evidence is less compelling. Melatonin's efficacy in combating free radical damage in the brain suggests that it can be a valuable therapeutic agent in the treatment of cerebral edema following traumatic brain injury or stroke. Clinical trials employing melatonin doses in the range of 50–100 mg/day are warranted before its relative merits as a neuroprotective agent is definitively established.

Keywords Melatonin, Mitochondria, Free radicals, Oxidative stress, Aging, Parkinson's disease, Alzheimer's disease, Huntington's disease

Pandi-Perumal SR, Smits M, Spence W et al. *Year* 2007

Authors Pandi-Perumal SR, Smits M, Spence W et al.

Report Name Dim light melatonin onset (DLMO): a tool for the analysis of circadian phase in human sleep and chronobiological disorders

Publication Prog Neuropsychopharmacol Biol Psychiatry

Issue-page numbers 31:1–11 doi:10.1016/j.pnpbp.2006.06.020. PMID:16884842

URL http://www.sciencedirect.com/science/article/pii/S0278584606002831

Abstract The circadian rhythm of melatonin in saliva or plasma, or of the melatonin metabolite 6-sulphatoxymelatonin (aMT6S) in urine, is a defining feature of suprachiasmatic nucleus (SCN) function, the endogenous oscillatory pacemaker. A substantial number of studies have shown that, within this rhythmic profile, the onset of melatonin secretion under dim light conditions (the dim light melatonin onset or DLMO) is the single most accurate marker for assessing the circadian pacemaker. Additionally, melatonin onset has been used clinically to evaluate problems related to the onset or offset of sleep. DLMO is useful for determining whether an individual is entrained (synchronized) to a 24-h light/dark (LD) cycle or is in a free-running state. DLMO is also useful for assessing phase delays or advances of rhythms in entrained individuals. Additionally, it has become an important tool for psychiatric diagnosis, its use being recommended for phase typing in patients suffering from sleep and mood disorders. More recently, DLMO has also been used to assess the chronobiological features of seasonal affective disorder (SAD). DLMO marker is also useful for identifying optimal application times for therapies such as bright light or exogenous melatonin treatment.

Keywords Circadian rhythms; Delayed sleep phase syndrome; Dim light melatonin onset; Light/dark cycle; Melatonin; Mood disorders; Seasonal affective disorder

Panzer A, Lottering ML, Bianchi P et al. *Year* 1998

Authors Panzer A, Lottering ML, Bianchi P et al.

Report Name Melatonin has no effect on the growth, morphology or cell cycle of human breast cancer (MCF-7), cervical cancer (HeLa), osteosarcoma (MG-63) or lymphoblastoid (TK6) cells

Publication Cancer Lett

Issue-page numbers 122:17–23 doi:10.1016/S0304-3835(97)00360-1. PMID:9464486

URL http://www.cancerletters.info/article/S0304-3835%2897%2900360-1/abstract

Abstract Melatonin was previously shown to inhibit proliferation of MCF-7 human breast cancer cells. In this study the effect of melatonin on MCF-7 cells was further examined, while human cervical carcinoma (HeLa), osteosarcoma (MG-63) and lymphoblastoid (TK6) cells were tested for the first time. Haemocytometer counts, DNA content, flow cytometry and indirect immunofluorescence for nucleolar proteins, actin and β-tubulin showed no differences in the growth, cell cycle or morphology between melatonin-exposed and control cells. The direct antiproliferative effect of melatonin thus seems to be confined to a melatonin-responsive subclone of MCF-7 cells and not applicable to the majority of cancer cells.

Keywords Melatonin, Cancer, Cell culture

Pao C, Norris PG, Corbett M, Hawk JL

Year 1994

Authors Pao C, Norris PG, Corbett M, Hawk JL.

Report Name Polymorphic light eruption: prevalence in Australia and England

Publication British Journal of Dermatology

Issue-page numbers Volume 130, Issue 1, pages 62–64, January 1994

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.1994.tb06884.x/abstract

Abstract Summary The prevalence and clinical characteristics of polymorphic light eruption were assessed by a questionnaire survey of 172, 196 and 182 subjects in Perth, Ballarat and London, respectively. The prevalence was 5·2% in Perth (latitude 32°), 3·6% in Ballarat (37·5°) and 14·8% in London (51·5°). The age distribution (mostly first three decades) and male: female ratio (1:3) was similar for affected individuals in all three areas. Development of tolerance during the summer was more common in Perth (66·7%) and Ballarat (71·4%) than in London (40·7%).

Keywords

Papamichael C, Skene DJ, Revell VL

Year 2012

Authors Christiana Papamichael, Debra J. Skene, Victoria L. Revell

Report Name Human Nonvisual Responses to Simultaneous Presentation of Blue and Red Monochromatic Light

Publication J Biol Rhythms

Issue-page numbers February 2012 vol. 27 no. 1 70-78

URL http://jbr.sagepub.com/content/27/1/70.abstract

Abstract Blue light sensitivity of melatonin suppression and subjective mood and alertness responses in humans is recognized as being melanopsin based. Observations that long-wavelength (red) light can potentiate responses to subsequent short-wavelength (blue) light have been attributed to the bistable nature of melanopsin whereby it forms stable associations with both 11-cis and all-trans isoforms of retinaldehyde and uses light to transition between these states. The current study examined the effect of concurrent administration of blue and red monochromatic light, as would occur in real-world white light, on acute melatonin suppression and subjective mood and alertness responses in humans. Young healthy men (18-35 years; n = 21) were studied in highly controlled laboratory sessions that included an individually timed 30-min light stimulus of blue (λmax 479 nm) or red (λmax 627 nm) monochromatic light at varying intensities (1013-1014 photons/cm2/sec) presented, either alone or in combination, in a within-subject randomized design. Plasma melatonin levels and subjective mood and alertness were assessed at regular intervals relative to the light stimulus. Subjective alertness levels were elevated after light onset irrespective of light wavelength or irradiance. For melatonin suppression, a significant irradiance response was observed with blue light. Co-administration of red light, at any of the irradiances tested, did not significantly alter the response to blue light alone. Under the current experimental conditions, the primary determinant of the melatonin suppression response was the irradiance of blue 479 nm light, and this was unaffected by simultaneous red light administration.

Keywords light, monochromatic, humans, melanopsin, bistability, melatonin suppression

Parent M, El-Zein M, Rousseau M, et al. **Year** 2012

Authors Marie-Élise Parent, Mariam El-Zein, Marie-Claude Rousseau, Javier Pintos and Jack Siemiatycki

Report Name Night Work and the Risk of Cancer Among Men

Publication Am. J. Epidemiol.

Issue-page numbers doi: 10.1093/aje/kws318 First published online: October 3, 2012

URL http://aje.oxfordjournals.org/content/early/2012/10/02/aje.kws318.abstract

Abstract Night work might influence cancer risk, possibly via suppression of melatonin release. In a population-based case-control study conducted in Montreal, Quebec, Canada, between 1979 and 1985, job histories, including work hours, were elicited from 3,137 males with incident cancer at one of 11 anatomic sites and from 512 controls. Compared with men who never worked at night, the adjusted odds ratios among men who ever worked at night were 1.76 (95% confidence interval (CI): 1.25, 2.47) for lung cancer, 2.03 (95% CI: 1.43, 2.89) for colon cancer, 1.74 (95% CI: 1.22, 2.49) for bladder cancer, 2.77 (95% CI: 1.96, 3.92) for prostate cancer, 2.09 (95% CI: 1.40, 3.14) for rectal cancer, 2.27 (95% CI: 1.24, 4.15) for pancreatic cancer, and 2.31 (95% CI: 1.48, 3.61) for non-Hodgkin's lymphoma. Equivocal evidence or no evidence was observed for cancers of the stomach (odds ratio (OR) = 1.34, 95% CI: 0.85, 2.10), kidney (OR = 1.42, 95% CI: 0.86, 2.35), and esophagus (OR = 1.51, 95% CI: 0.80, 2.84) and for melanoma (OR = 1.04, 95% CI: 0.49, 2.22). There was no evidence of increasing risk with increasing duration of night work, with risks generally being increased across all duration categories. Results suggest that night work may increase cancer risk at several sites among men.

Keywords case-control studies, circadian rhythm, men, neoplasms, night work, occupations, shift work

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Parish CA, Hashimoto M, Nakanishi K, et al. **Year** 1998

Authors Parish CA, Hashimoto M, Nakanishi K, Dillon J, Sparrow J.

Report Name Isolation and one-step preparation of A2E and iso-A2E, fluorophores from human retinal pigment epithelium

Publication PNAS

Issue-page numbers December 8, 1998 vol. 95 no. 25 14609-14613

URL http://www.pnas.org/content/95/25/14609.abstract

Abstract Age-related macular degeneration, a major cause of blindness for which no satisfactory treatments exist, leads to a gradual decrease in central high acuity vision. The accumulation of fluorescent materials, called lipofuscin, in retinal pigment epithelial cells of the aging retina is most pronounced in the macula. One of the fluorophores of retinal pigment epithelial lipofuscin has been characterized as A2E, a pyridinium bis-retinoid, which is derived from two molecules of vitamin A aldehyde and one molecule of ethanolamine. An investigation aimed at optimizing the in vitro synthesis of A2E has resulted in the one-step biomimetic preparation of this pigment in 49% yield, readily producing more than 50 mg in one step. These results have allowed for the optimization of HPLC conditions so that nanogram quantities of A2E can be detected from extracts of tissue samples. By using 5% of the extract from individual aged human eyes, this protocol has led to the quantification of A2E and the characterization of iso-A2E, a new A2E double bond isomer; all-trans-retinol and 13-cis-retinol also have been identified in these HPLC chromatograms. Exposure of either A2E or iso-A2E to light gives rise to 4:1 A2E:iso-A2E equilibrium mixtures, similar to the composition of these two pigments in eye extracts. A2E and iso-A2E may exhibit surfactant properties arising from their unique wedge-shaped structures.

Keywords

Year 2001

Authors Parisi A, Green A, Kimlin M.

Report Name Diffuse solar UV radiation and implications for preventing human eye damage

Publication Photochemistry and Photobiology

Issue-page numbers Volume 73, Issue 2, pages 135–139, February 2001

URL http://onlinelibrary.wiley.com/doi/10.1562/0031-8655(2001)0730135DSURAI2.0.CO2/abstract?

Abstract

Ocular UV exposure is a function of both the direct and diffuse components of solar radiation. Broadband global and diffuse UV measurements were made in the morning, noon and afternoon. Thirty sets of measurements were made in summer and 50 in each of the other seasons at each of the periods in full sun. Corresponding sets were made in the shade of Australian evergreen trees: 42 trees in summer and 50 in each of the other seasons. The percentage diffuse UV was higher for the shorter 320–400 nm range (UVB) than for 280–320 nm (UVA). The percentage diffuse UVB ranged from 23 to 59%, whereas the percentage diffuse UVA ranged from 17 to 31%. The percentage diffuse UV was lower at noon than in the morning and afternoon with the difference more pronounced for the UVB. The average percentage diffuse UVB over all the measurements in the tree shade for the morning, noon and afternoon was 62, 58 and 71%, respectively, and the average percentage diffuse UVA was 52, 51 and 59%, respectively.

Keywords

Authors Parkes KR

Report Name Shift work and age as interactive predictors of body mass index among offshore workers

Publication Scand J Work Environ Health

Issue-page numbers 28:64–71

URL http://www.ncbi.nlm.nih.gov/pubmed/11871855

Abstract

OBJECTIVES:
This study investigated shift pattern (day shifts versus day-night rotation) and its interactions with age, and with years of shiftwork exposure, as predictors of body mass index (BMI).
METHODS:

Survey data were collected from offshore personnel working day shifts (N=787) or day-night shifts (N=787); information was obtained about shift pattern and years of shiftwork exposure, height, weight, demographic factors, and smoking habits. Hierarchical multiple regression was used to test a model in which BMI was predicted by additive and interactive effects of shift pattern, age, and exposure years with control for confounding variables.
RESULTS:

In a multivariate analysis (controlling for job type, education and smoking), BMI was predicted by the main effects of age and years of shiftwork exposure. Shift pattern was not significant as a main effect, but it interacted significantly with the curvilinear age term and with the linear and curvilinear components of shiftwork exposure. In the day shift group, age but not exposure predicted BMI; the opposite was true of the day-night shift group. The increase in BMI with an increase in age and exposure years was steeper for the day-night shift group than for the day shift group.
CONCLUSIONS:

The significant interaction effects found in this study were consistent with the view that continued exposure to day-night shift work gives rise to increases in BMI, over and above the normative effects of ageing on BMI shown by day-shift workers.

Keywords

Paskowitz DM, LaVail MM, Duncan JL

Year 2006

Authors Paskowitz DM, LaVail MM, Duncan JL.

Report Name Light and inherited retinal degeneration

Publication Br J Ophthalmol

Issue-page numbers 2006 August; 90(8): 1060–1066.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1857196/

Abstract Light deprivation has long been considered a potential treatment for patients with inherited retinal degenerative diseases, but no therapeutic benefit has been demonstrated to date. In the few clinical studies that have addressed this issue, the underlying mutations were unknown. Our rapidly expanding knowledge of the genes and mechanisms involved in retinal degeneration have made it possible to reconsider the potential value of light restriction in specific genetic contexts. This review summarises the clinical evidence for a modifying role of light exposure in retinal degeneration and experimental evidence from animal models, focusing on retinitis pigmentosa with regional degeneration, Oguchi disease, and Stargardt macular dystrophy. These cases illustrate distinct pathophysiological roles for light, and suggest that light restriction may benefit carefully defined subsets of patients.

Keywords light, retinal degeneration, retinitis pigmentosa, Stargardt disease, Oguchi disease

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Patel JB, Mehta J, Belosay A, et al.

Year 2007

Authors Patel JB, Mehta J, Belosay A, Sabnis G, Khandelwal A, Brodie AM, Soprano DR, Njar VC.

Report Name Novel retinoic acid metabolism blocking agents have potent inhibitory activities on human breast cancer cells and tumour growth

Publication Br J Cancer

Issue-page numbers Apr 23;96(8):1204-15. Epub 2007 Mar 27.

URL http://www.ncbi.nlm.nih.gov/pubmed/17387344

Abstract Antitumour effects of retinoids are attributed to their influence on cell proliferation, differentiation, apoptosis and angiogenesis. In our effort to develop useful agents for breast cancer therapy, we evaluated the effects of four representative retinoic acid metabolism blocking agents (RAMBAs, VN/14-1, VN/50-1, VN/66-1 and VN/69-1) on growth inhibition of oestrogen receptor positive (ER +ve, MCF-7 and T-47D) and oestrogen receptor negative (ER -ve, MDA-MB-231) human breast cancer cells. Additionally, we investigated the biological effects/molecular mechanism(s) underlying their growth inhibitory properties as well as their antitumour efficacies against MCF-7 and MCF-7Ca tumour xenografts in nude mice. We also assessed the effect of combining VN/14-1 and all-trans-retinoic acid (ATRA) on MCF-7 tumour xenografts. The ER +ve cell lines were more sensitive (IC(50) values between 3.0 and 609 nM) to the RAMBAs than the ER -ve MDA-MB-231 cell line (IC(50)=5.6-24.0 microM). Retinoic acid metabolism blocking agents induced cell differentiation as determined by increased expression of cytokeratin 8/18 and oestrogen receptor-alpha (ER-alpha). Similar to ATRA, they also induced apoptosis via activation of caspase 9. Cell cycle analysis indicated that RAMBAs arrested cells in the G1 and G2/M phases and caused significant downregulation (>80%) of cyclin D1 protein. In vivo, the growth of MCF-7 mammary tumours was dose-dependently and significantly inhibited (92.6%, P<0.0005) by VN/14-1. The combination of VN/14-1 and ATRA also inhibited MCF-7 breast tumour growth in vivo (up to 120%) as compared with single agents (P<0.025). VN/14-1 was also very effective in preventing the formation of MCF-7Ca tumours and it significantly inhibited the growth of established MCF-7Ca tumours, being as effective as the clinically used aromatase inhibitors, anastrozole and letrozole. Decrease in cyclin D1 and upregulation of cytokeratins, Bad and Bax with VN/14-1 may be responsible for the efficacy of this compound in inhibiting breast cancer cell growth in vitro and in vivo. Our results suggest that our RAMBAs, especially VN/14-1 may be useful novel therapy for breast cancer.

Keywords

Authors Patel SR, Ayas NT, Malhotra MR et al.

Report Name A prospective study of sleep duration and mortality risk in women

Publication Sleep

Issue-page numbers 27:440–444. PMID:15164896

URL http://www.journalsleep.org/Articles/270310.pdf

Abstract

Study Objectives: It is commonly believed that 8 hours of sleep per night is optimal for good health. However, recent studies suggest the risk of death is lower in those sleeping 7 hours. We prospectively examined the association between sleep duration and mortality in women to better understand the effect of sleep duration on health.
Design: Prospective observational study.
Setting: Community-based.
Participants: Women in the Nurses Health Study who answered a mailed questionnaire asking about sleep duration in 1986.
Interventions: None.
Measurements and Results: Vital status was ascertained through questionnaires, contact with next of kin, and the National Death Index. During the 14 years of this study (1986-2000), 5409 deaths occurred in the 82,969 women who responded to the initial questionnaire. Mortality risk was lowest among nurses reporting 7 hours of sleep per night. After adjusting for age, smoking, alcohol, exercise, depression, snoring, obesity, and history of cancer and cardiovascular disease, sleeping less than 6 hours or more than 7 hours remained associated with an increased risk of death. The relative mortality risk for sleeping 5 hours or less was 1.15 (95% confidence interval [CI], 1.02-1.29) for 6 hours, 1.01 (95% CI, 0.94-1.08), for 7 hours, 1.00 (reference group), for 8 hours, 1.12 (95% CI, 1.05-1.20), and for 9 or more hours 1.42 (95% CI, 1.27-1.58).
Conclusions: These results confirm previous findings that mortality risk in women is lowest among those sleeping 6 to 7 hours. Further research is needed to understand the mechanisms by which short and long sleep times can affect health.

Keywords Sleep, sleep deprivation, proportional hazards models, women, survival rate

Pauers MJ, Kuchenbecker JA, Neitz M, Neitz J

Year 2012

Authors Michael J. Pauers, James A. Kuchenbecker, Maureen Neitz, Jay Neitz

Report Name Changes in the colour of light cue circadian activity

Publication Animal Behaviour

Issue-page numbers Available online 18 February 2012

URL http://www.sciencedirect.com/science/article/pii/S0003347212000553

Abstract

The discovery of melanopsin, the nonvisual opsin present in intrinsically photosensitive retinal ganglion cells (ipRGCs), has created great excitement in the field of circadian biology. Now, researchers have emphasized melanopsin as the main photopigment governing circadian activity in vertebrates. Circadian biologists have tested this idea under standard 12:12 h light:dark cycles in the laboratory that lack the dramatic daily colour changes of natural skylight. Here we used a stimulus paradigm in which the colour of the illumination changed throughout the day, thus mimicking natural skylight, but luminance, sensed intrinsically by melanopsin containing ganglion cells, was kept constant. We show in two species of cichlid, Aequidens pulcher and Labeotropheus fuelleborni, that changes in light colour, not intensity, are the primary determinants of natural circadian activity. Moreover, opponent-cone photoreceptor inputs to ipRGCs mediate the sensation of wavelength change, and not the intrinsic photopigment, melanopsin. These results have implications for understanding the evolutionary biology of nonvisual photosensory pathways and answer long-standing questions about the nature and distribution of photopigments in organisms, including providing a solution to the mystery of why nocturnal animals routinely have mutations that interrupt the function of their short-wavelength-sensitive photopigment gene.

Keywords

Pauley SM

Year 2004

Authors Stephen M. Pauley

Report Name Lighting for the human circadian clock: recent research indicates that lighting has become a public health issue

Publication J Medical Hypotheses

Issue-page numbers 63, 588-596

URL http://www.skykeepers.org/handouts/pauleylhh.pdf

Abstract

Summary The hypothesis that the suppression of melatonin (MLT) by exposure to light at night (LAN) may be one reason for the higher rates of breast and colorectal cancers in the developed world deserves more attention. The literature supports raising this subject for awareness as a growing public health issue. Evidence now exists that indirectly links exposures to LAN to human breast and colorectal cancers in shift workers. The hypothesis begs an even larger question: has medical science overlooked the suppression of MLT by LAN as a contributor to the overall incidence of cancer?
The indirect linkage of breast cancer to LAN is further supported by laboratory rat experiments by David E. Blask and colleagues. Experiments involved the implanting of human MCF-7 breast cancer cell xenografts into the groins of rats and measurements were made of cancer cell growth rates, the uptake of linoleic acid (LA), and MLT levels. One group of implanted rats were placed in light–dark (12L:12D) and a second group in light–light (12L:12L) environments. Constant light suppressed MLT, increased cancer cell growth rates, and increased LA uptake into cancer cells. The opposite was seen in the light–dark group. The proposed mechanism is the suppression of nocturnal MLT by exposure to LAN and subsequent lack of protection by MLT on cancer cell receptor sites which allows the uptake of LA which in turn enhances the growth of cancer cells.
MLT is a protective, oncostatic hormone and strong antioxidant having evolved in all plants and animals over the millennia. In vertebrates, MLT is normally produced by the pineal gland during the early morning hours of darkness, even in nocturnal animals, and is suppressed by exposure to LAN.
Daily entrainment of the human circadian clock is important for good human health. These studies suggest that the proper use and color of indoor and outdoor lighting is important to the health of both humans and ecosystems. Lighting fixtures should be designed to minimize interference with normal circadian rhythms in plants and animals. New discoveries on blue-light-sensitive retinal ganglion cell light receptors that control the circadian clock and how those receptors relate to today's modern high intensity discharge (HID) lamps are discussed. There is a brief discussion of circadian rhythms and light pollution. With the precautionary principle in mind, practical suggestions are offered for better indoor and outdoor lighting practices designed to safeguard human health.

Keywords light at night, LAN, cancer, dark

Pavel S

Year 2006

Authors Pavel S.

Report Name Light therapy (with UVA-1) for SLE patients: is it a good or bad idea?

Publication Rheumatology

Issue-page numbers (June 2006) 45 (6): 653-655. doi: 10.1093/rheumatology/kel063

URL http://rheumatology.oxfordjournals.org/content/45/6/653.full

Abstract The development of skin rash—an unusual reaction to sunlight—is one of the criteria used in the diagnosis of systemic lupus erythematosus (SLE). In addition, exposure to sunlight is a risk factor for the induction or exacerbation of the disease. Patients with SLE who regularly protect themselves against sunlight appear to have significantly less renal involvement, thrombocytopenia, hospitalization and requirement for cyclophosphamide treatment [1]. All these facts support the importance of photoprotection in patients with SLE and suggest that light therapy in SLE patients may be more detrimental than beneficial.

Keywords

Pavlova M, Sheikh LS

Year 2011

Authors Milena Pavlova, Lubna S. Sheikh

Report Name Sleep in Women

Publication Semin Neurol

Issue-page numbers 31(4): 397-403 DOI: 10.1055/s-0031-1293539

URL https://www.thieme-connect.com/ejournals/abstract/sin/doi/10.1055/s-0031-1293539

Abstract The timing and continuity of sleep in healthy individuals is regulated by the synchronous function of the sleep homeostasis and the endogenous circadian rhythms. Multiple factors affect these two processes and the way they interact. Sleep disorders may manifest differently in men and women and these differences are particularly notable during pregnancy, lactation, and menopause. Insomnia may occur relatively commonly during pregnancy and in the postpartum, and may be the result of either a primary sleep disorder, such as obstructive sleep apnea (OSA), movement disorders such as restless legs syndrome (RLS), or sometimes depression, especially in the postpartum period. Obstructive sleep apnea may contribute to a higher risk of hypertension during pregnancy and doubles the risk for preeclampsia and preterm birth. Snoring, a frequent symptom of OSA, increases in frequency during pregnancy. Restless legs syndrome is more common in pregnant women, is more frequent in the third trimester of pregnancy, and tends to improve dramatically after delivery. Factors associated with increased RLS in pregnancy may be related to iron and folate metabolism. Risk for OSA increases after menopause and presentation with insomnia can delay the diagnosis of OSA. Various treatment options for sleep disorders in women are discussed.

Keywords Sleep - pregnant - women - biologic rhythms

Peng M, Tsai C, Chien C, et al. **Year** 2012

Authors Mei-Ling Peng, Cheng-Yu Tsai, Chung-Liang Chien, John Ching-Jen Hsiao, Shuan-Yu Huang, Ching-Ju Lee, Hsiang-Yin Lin, Yang-Cheng Wen, Kuang-Wen Tseng

Report Name http://www.lifesciencesite.com/lsj/life0901/072_8366life0901_477_482.pdf

Publication Life Science Journal

Issue-page numbers 2012;9(1)

URL http://www.lifesciencesite.com/lsj/life0901/072_8366life0901_477_482.pdf

Abstract Ocular tissue damage because of exposure to visible light has been demonstrated by the results of human and animal studies. The short-wavelength visible light between 430 nm to 500 nm (blue light) is especially associated with retina damage. Recently, new powerful sources and relatively inexpensive blue energy of LED (light emitting diodes) family lamps in home illumination are available. The aim of this study is to investigate the effects of illumination source from the low-powered and the conscious spectrum source of LED family lamps on retina tissues. The illumination source of LED family lamps was analyzed from 300 nm to 800 nm using an UV-visible spectrophotometer. In animal experiments, young adult mice were assigned to expose to family LED light for 2h every day ranging 2 to 4 weeks or light environment using LED family lamps for 39 weeks. After LED light treatment, sections of eyes were stained with hematoxylin and examined using histopathology. The data clearly demonstrated irradiation of the white LED is above 400 nm and is not within the ultraviolet light region. However, the analysis of spectrum distribution demonstrated that the family LED lighting exhibited power-peak at 450 nm is within the blue light region. Histological results showed that the photoreceptor layer is significantly reduced in thickness after 4 weeks of LED exposure 2h every day or LED illuminated environment. This study provides important data regarding the efficacy and safety of LED light in family illumination. It is impossible to consider these degenerative changes are related unavoidably part of their mechanism of action or an avoidable toxic effect.

Keywords Light emitting diodes, Photoreceptor, Blue light

Pepe IM **Year** 1999

Authors Pepe IM.

Report Name Rhodopsin and phototransduction

Publication J Photochem Photobiol B

Issue-page numbers 1999 Jan;48(1):1-10.

URL http://www.ncbi.nlm.nih.gov/pubmed/10205874

Abstract Recent studies on rhodopsin structure and function are reviewed and the properties of vertebrate as well as invertebrate rhodopsin described. Open issues such as the 'red shift' of the absorbance spectra are emphasized in the light of the present model of the retinal-binding pocket. The processes that restore the rhodopsin content in photoreceptors are also presented with a comparison between vertebrate and invertebrate visual systems. The central role of rhodopsin in the phototransduction cascade becomes evident by examining the main reports on light-activated conformational changes of rhodopsin and its interaction with transducin. Shut-off mechanisms are considered by reporting the studies on the sites of rhodopsin phosphorylation and arrestin binding. Furthermore, recent findings on the energetics of phototransduction point out that the ATP needed for photoreception in vertebrates is synthesized in the outer segments where phototransduction events take place.

Keywords

Authors Beata Peplonska, Agnieszka Bukowska, Jolanta Gromadzinska, Wojciech Sobala, Edyta Reszka, Jenny-Anne Lie, Helge Kjuus, Wojciech Wasowicz

Report Name Night shift work characteristics and 6-sulfatoxymelatonin (MT6s) in rotating night shift nurses and midwives

Publication Occup Environ Med

Issue-page numbers doi:10.1136/oemed-2011-100273

URL http://oem.bmj.com/content/early/2012/02/24/oemed-2011-100273.abstract

Abstract

Objectives Synthesis of melatonin follows a circadian cycle, with high melatonin levels during the night and low levels during the day. Light exposure at night has been hypothesised as one of potential mechanisms of breast carcinogenesis in the night shift workers through inhibition of melatonin synthesis. The aim of the study was to examine a number of determinants for night shift work in relation to 6-sulfatoxymelatonin (MT6s), primary melatonin metabolite.

Methods The cross-sectional study included 354 nurses and midwives (aged 40–60 years) currently working on rotating night shifts and 370 working days only. Data from questionnaires and 1-week diaries were used to characterise current job and total occupational history. Associations between rotating night shift work characteristics and MT6s (creatinine adjusted) in spot morning urine were tested in multiple linear regression models.

Results No significant differences were found for MT6s concentrations between women currently working on rotating night shifts and those working only day shifts (means 47.2 vs 45.7 ng/mg Cr, respectively). The adjusted means among rotating night shift nurses and midwives varied depending on the department of employment, from 35.1 ng/mg Cr in neonatology to 68.2 ng/mg Cr in the orthopaedics department. Women working eight or more night shifts per month had significantly lower MT6s levels than those having fewer night shifts per month (37.9 vs 47.4 ng/mg Cr, respectively). Total night shift work history was not associated with MT6s.

Conclusions The results of this study indicate that working eight or more night shifts per month may disrupt the synthesis of melatonin.

Keywords

Peplonska B, Bukowska A, Sobala W, et al. **Year** 0

Authors Beata Peplonska, Agnieszka Bukowska, Wojciech Sobala, Edyta Reszka, Jolanta Gromadzińska, Wojciech Wasowicz, Jenny Anne Lie, Helge Kjuus, and Giske Ursin

Report Name Rotating night shift work and mammographic density.

Publication Cancer Epidemiology, Biomarkers & Prevention

Issue-page numbers April 26, 2012; doi: 10.1158/1055-9965.EPI-12-0005

URL http://cebp.aacrjournals.org/content/early/2012/04/24/1055-9965.EPI-12-0005.abstract

Abstract

Background: An increased risk of breast cancer has been observed in night shift workers. Exposure to artificial light at night, disruption of the endogenous circadian rhythm with suppression of the melatonin synthesis have been suggested mechanisms. We investigated the hypothesis that rotating night shift work is associated with mammographic density. Methods:We conducted a cross-sectional study on the association between rotating night shift work characteristics, 6-sulfatoxymelatonin(6MTs) creatinine adjusted in a spot morning urine sample and a computer-assisted measure of mammographic density in 640 nurses and midwives aged 40-60. The associations were evaluated using regression models adjusted for age, BMI, menopausal status, age at menopause, age at menarche, smoking, and the calendar season of the year when mammography was performed. Results:The adjusted means of percent mammographic density and absolute density were slightly higher among women working rotating night shifts, but not statistically significant (percent mammographic density=23.6%, 95%CI: 21.9-25.4% vs. 22.5%, 95%CI: 20.8-24.3%; absolute density=23.9 cm2, 95%CI: 21.4-26.4 cm2, vs. 21.8 cm2, 95%CI: 19.4-24.3 cm2 in rotating night shift and day shift nurses, respectively). There were no significant associations between the current or cumulative rotating night shift work exposure metrics and mammographic density. No association was observed between morning MT6s and mammographic density. Conclusions:The hypothesis on the link between rotating night shift work, melatonin synthesis disruption and mammographic density is not supported by the results of the present study. Impact:It is unlikely that the development of breast cancer in nurses working rotating night shifts is mediated by an increase in mammographic density.

Keywords

Pereira MA, Barnes LH, Rassman VL et al. **Year** 1994

Authors Michael A. Pereira, Leta H. Barnes, Vicki L. Rassman, Gary V. Kelloff and Vernon E. Steele

Report Name Use of azoxymethane-induced foci of aberrant crypts in rat colon to identify potential cancer chemopreventive agents

Publication Carcinogenesis

Issue-page numbers 15:1049–1054 doi:10.1093/carcin/15.5.1049. PMID:8200067

URL http://carcin.oxfordjournals.org/content/15/5/1049.short

Abstract Foci of aberrant and/or hexosaminidase-negative crypts in rat colon are putative precancerous lesions that have been proposed as biomarkers for Short-term bioassays for chemical carcinogens and chemopreventive agents. The ability of a substance to reduce the yield of azoxymethane (AOM)- induced foci in the colon of male Fischer 344 rats, was evaluated as a screening assay for chemopreventive agents. Twenty-eight test agents were administered continuously in the diet from the start of the experiments until the animals were killed 35 days later. AOM was s.c. administered either as 15 mg/kg body wt on days 7 and 14 or as 30 mg/kg body wt on day 7 of the experiment. Foci of aberrant crypts were evaluated in whole mounts of methylene blue-stained colons. AOM induced twice as many foci when administered between 8.40 and 11.00 a.m. than between 2.45 and 5.55 p.m. Calcium salts of carbonate, chloride and glucarate decreased the yield of AOM-induced foci while the acidic salts of lactate and phosphate did not inhibit the formation of foci. Dimethyl fumarate, fumaric acid, genistein, piroxicam, simethicone, sodium suramin and sulindac reduced the yield of AOM induced foci of aberrant crypts with genistein being the most potent. Only piroxicam of this group has previously been shown to inhibit colon cancer, while the rest have yet to be evaluated. Ibuprofen did not inhibit the formation of foci, although it has been reported to inhibit AOM-induced colon cancer in rats. Piroxicam and sulindac appeared to reduce preferentially hexosaminidase-negative foci of aberrant crypts, compared with those of apparently normal morphology. The AOM-induced foci of aberrant crypts assay appears suitable for screening chemicals for chemopreventive action.

Keywords

Persengiev SP **Year** 1992

Authors Persengiev SP

Report Name 2-(125I) iodomelatonin binding sites in rat adrenals: pharmacological characteristics and subcellular distribution

Publication Life Sci

Issue-page numbers 51:647–651 doi:10.1016/0024-3205(92)90237-J. PMID:1323736

URL http://www.sciencedirect.com/science/article/pii/002432059290237J

Abstract Specific binding sites for 2-[125I] iodomelatonin, a selective radiolabeled melatonin receptor ligand, were detected and characterized in rat adrenal membranes. Saturation studies demonstrated that 2-[125I] iodomelatonin binds to a single class of sites with an affinity constant (Kd) of 541 pM and a total binding capacity (Bmax) of 3.23 fmol/mg protein. Competition experiments revealed that the relative order of potency of compounds tested was as follows: 6-chloromelatonin > 2-iodomelatonin > melatonin > 5-methoxytryptamine > 5-methoxytryptophol. The highest density of binding sites was found in membranes from nuclear (0.76 fmol/mg protein) and mitochondrial (1.82 fmol/mg protein) subcellular fractions.

Keywords

Persengiev SP, Kanchev LN **Year** 1991

Authors Persengiev SP, Kanchev LN

Report Name Melatonin and adrenal cortex steroid production: in vivo and in vitro studies

Publication Folia Histochem Cytobiol

Issue-page numbers 29:15–18. PMID:1783093

URL http://www.mendeley.com/research/melatonin-adrenal-cortex-steroid-production-vivo-vitro-studies/

Abstract The present study was designed to clarify the interaction between the pineal melatonin and adrenal cortex steroid production. Experiments with male rats under chronic stress conditions (sleep deprivation) revealed that melatonin circadian pattern was fully destroyed and daytime plasma concentration were significantly elevated. Constant illumination (2500 lux) during the nighttime was not able to suppress melatonin production in the stressed animals. Plasma concentration of corticosterone were increased in the stressed rats as well. The modulatory effect of melatonin on corticosterone and progesterone production by rat adrenals was studied in a superfusion system. During melatonin challenge progesterone secretion was two-three fold elevated with no effect on corticosterone content in the plasma samples. Pineal cytoplasmic glucocorticoid and progesterone receptors were investigated as well. A specific binding was not observed in that case. Presented data support the existence of direct communication between the pineal and adrenal glands.

Keywords

Pesch B, Harth V, Rabstein S, et al. **Year** 2010

Authors Beate Pesch, Volker Harth, Sylvia Rabstein, Christian Baisch, Markus Schiffermann, Dirk Pallapies, Nadine Bonberg, Evelyn Heinze, Anne Spickenheuer, Christina Justenhoven

Report Name Night work and breast cancer - results from the German GENICA study.

Publication Scandinavian journal of work environment health

Issue-page numbers Volume: 36, Issue: 2, Pages: 134-141

URL http://www.mendeley.com/research/night-work-and-breast-cancer-results-from-the-german-genica-study/

Abstract OBJECTIVES: Some epidemiological and animal data indicate that night work might increase the risk for breast cancer. We have investigated the risk in a German population-based case-control study known as GENICA (gene environment interaction and breast cancer). METHODS: The GENICA study involved interviews to assess shift work information in 857 breast cancer cases and 892 controls. We estimated risks of employment status and night shift characteristics using conditional logistic regression models, adjusting for potential confounders. Resampling and bootstrapping were applied to adjust the risk estimates for a potential selection bias. RESULTS: Among 1749 women, 56 cases and 57 controls worked in night shifts for > or =1 year, usually in the healthcare sector (63.0% of controls). Female night workers were more frequently nulliparous and low-educated than day workers (28.6% versus 17.8% and 12.3% versus 9.2%, respectively). Fewer women in night work had ever used post-menopausal hormone therapy (35.7% versus 51.9%). An elevated breast cancer risk was not associated with having ever done shift or night work when compared to women employed in day work only odds ratio (OR) 0.96, 95% confidence interval (95% CI) 0.67-1.38 and OR 0.91, 95% CI 0.55-1.49, respectively). Women who reported >807 night shifts, the third quartile of the distribution among controls, experienced a breast cancer risk of 1.73 (95% CI 0.71-4.22). Night work for > or =20 years was associated with an OR of 2.48 (95% CI 0.62-9.99) based on 12 cases and 5 controls. CONCLUSIONS: Long-term night work was associated with a modestly, but not significantly, increased breast cancer risk, while having ever done night work was not. The precision of the results was limited by a low prevalence of night work in this study population.inci

Keywords

Petrovsky N

Year 2001

Authors Petrovsky N

Report Name Towards a unified model of neuroendocrine-immune interaction

Publication Immunol Cell Biol

Issue-page numbers 79:350–357 doi:10.1046/j.1440-1711.2001.01029.x. PMID:11488982

URL http://www.nature.com/icb/journal/v79/n4/full/icb200152a.html

Abstract Although the neuroendocrine system has immunomodulating potential, studies examining the relationship between stress, immunity and infection have, until recently, largely been the preserve of behavioural psychologists. Over the last decade, however, immunologists have begun to increasingly appreciate that neuroendocrine–immune interactions hold the key to understanding the complex behaviour of the immune system in vivo. The nervous, endocrine and immune systems communicate bidirectionally via shared messenger molecules variously called neurotransmitters, cytokines or hormones. Their classification as neurotransmitters, cytokines or hormones is more serendipity than a true reflection of their sphere of influence. Rather than these systems being discrete entities we would propose that they constitute, in reality, a single higher-order entity. This paper reviews current knowledge of neuroendocrine–immune interaction and uses the example of T-cell subset differentiation to show the previously under-appreciated importance of neuroendocrine influences in the regulation of immune function and, in particular, Th1/Th2 balance and diurnal variation there of.

Keywords cytokine, immune, neuroendocrine, regulation, T-cell subsets

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Petrovsky N, Harrison LC

Year 1998

Authors Petrovsky N, Harrison LC

Report Name The chronobiology of human cytokine production

Publication Int Rev Immunol

Issue-page numbers 16:635–649 doi:10.3109/08830189809043012. PMID:9646180

URL http://www.ncbi.nlm.nih.gov/pubmed/9646180

Abstract Cytokine production in human whole blood exhibits diurnal rhythmicity. Peak production of the pro-inflammatory cytokines IFN-gamma, TNF-alpha, IL-1 and IL-12 occurs during the night and early morning at a time when plasma cortisol is lowest. The existence of a causal relationship between plasma cortisol and production is suggested by the finding that elevation of plasma cortisol within the physiological range by the administration of cortisone acetate results in a corresponding fall in pro-inflammatory cytokine production. Cortisol may not be the only neuroendocrine hormone that entrains cytokine rhythms; other candidates include 17-hydroxy progesterone, melatonin and dihydroepiandrostene dione (DHEAS). The finding of diurnal cytokine rhythms may be relevant to understanding why immuno-inflammatory disorders such as rheumatoid arthritis or asthma exhibit night-time or early morning exacerbations and to the optimisation of treatment for these disorders. Diurnal rhythmicity of cytokine production also has implications for the timing o blood samples drawn for diagnostic T-cell assays. Finally, diurnal rhythmicity of immune function suggests that the nature of an immune response, for example in response to vaccination, may be modified by the time of day of antigen administration and raises the possibility that immune responses could be therapeutically manipulated by co-administration of immuno-regulatory hormones such as glucocorticoids.

Keywords

Pévet P, Agez L, Bothorel B et al. **Year** 2006

Authors Pévet P, Agez L, Bothorel B et al.

Report Name Melatonin in the multi-oscillatory mammalian circadian world

Publication Chronobiol Int

Issue-page numbers 23:39–51 doi:10.1080/07420520500482074. PMID:16687278

URL http://www.mendeley.com/research/melatonin-multioscillatory-mammalian-circadian-world-1/

Abstract In mammals, the complex interaction of neural, hormonal, and behavioral outputs from the suprachiasmatic nucleus (SCN) drives circadian expression of events, either directly or through coordination of the timing of peripheral oscillators. Melatonin, one of the endocrine output signals of the clock, provides the organism with circadian information and can be considered as an endogenous synchronizer, able to stabilize and reinforce circadian rhythms and to maintain their mutual phase-relationship at the different levels of the circadian network. Moreover, exogenous melatonin, through an action on the circadian clock, affects all levels of the circadian network. The molecular mechanisms underlying this chronobiotic effect have also been investigated in rats. REV-ERB alpha seems to be the initial molecular target.

Keywords

Pevet P, Challet E **Year** 2011

Authors Pevet P, Challet E

Report Name Melatonin: Both master clock output and internal time-giver in the circadian clocks network

Publication J Physiol Paris

Issue-page numbers 2011 Jul 19

URL http://www.ncbi.nlm.nih.gov/pubmed/21914478

Abstract Daily rhythms in physiological and behavioral processes are controlled by a network of circadian clocks, reset by inputs and delivering circadian signals to the brain and peripheral organs. In mammals, at the top of the network is a master clock located in the suprachiasmatic nuclei (SCN) of the hypothalamus, mainly reset by ambient light. The nocturnal synthesis and release of melatonin by the pineal gland are tightly controlled by the SCN clock and inhibited by light exposure. Several roles of melatonin in the circadian system have been identified. As a major hormonal output, melatonin distributes temporal cues generated by the SCN to the multitude of tissue targets expressing melatonin receptors. In some target structures, like the Pars tuberalis of the adenohypophysis, these melatonin signals can drive daily rhythmicity that would otherwise be lacking. In other target structures, melatonin signals are used for the synchronization (i.e., adjustment of the timing of existing oscillations) of peripheral oscillators, such as the fetal adrenal gland. Due to the expression of melatonin receptors in the SCN, endogenous melatonin is also able to feedback onto the master clock, although its physiological significance needs further characterization. Of note, pharmacological treatment with exogenous melatonin can synchronize the SCN clock. From a clinical point of view, provided that the subject is not exposed to light at night, the daily profile of circulating melatonin provides a reliable estimate of the timing of the human SCN. During the past decade, a number of melatonin agonists have been developed for treating circadian, psychiatric and sleep disorders. These drugs may target the SCN for improving circadian timing or act indirectly at some downstream level of the circadian network to restore proper internal synchronization.

Keywords

Authors Pham TQ, Wang JJ, Rochtchina E, Mitchell P.

Report Name Pterygium/pinguecula and the five-year incidence of age-related maculopathy

Publication American Journal of Ophthalmology

Issue-page numbers Volume 139, Issue 3, March 2005, Pages 536-537

URL http://www.sciencedirect.com/science/article/pii/S0002939404010839

Abstract

Purpose

To assess the relationship between baseline pterygium and pinguecula and the five-year incidence of age-related maculopathy (ARM).
Design

Population-based longitudinal study.
Methods

The Blue Mountains Eye Study examined 3654 residents aged 49+ years during 1992 to 1994 and then re-examined 2335 (75.1% of survivors) after five years. Retinal photographs were graded using the Wisconsin Age-Related Maculopathy Grading System. Slit-lamp examination recorded pterygium and pinguecula. Eye-specific data were analyzed using generalized estimating equation models.
Results

After adjusting for age, gender, and smoking, eyes with pterygium or previous pterygium surgery had a higher risk of incident late ARM, odds ratio (OR) 3.3, 95% confidence interval (CI) 1.1 to 10.3, early ARM (OR 1.8, CI 1.1 to 2.9) and soft drusen (OR 2.0, CI 1.9 to 3.4), than eyes without pterygium. We found no association between pinguecula and incident ARM.
Conclusions

This study found that pterygium was associated with a two- to threefold increased risk of incident late and early ARM.

Keywords

Phillips MJ, Wilson DW, Simpson HW et al. **Year** 1981

Authors M. J. Phillips, D. W. Wilson, H. W. Simpson, D. R. Fahmy, G. V. Groom, M. E. A. Phillips, C. G. Pierrepoint, R. W. Blamey, F. Halberg and K. Griffiths

Report Name Characterisation of breast skin temperature rhythms of women in relation to menstrual status

Publication Acta Endocrinol (Copenh)

Issue-page numbers 96:350–360. PMID:7211096

URL http://www.eje-online.org/content/96/3/350.abstract

Abstract

Circadian breast skin temperature rhythms were characterised throughout the menstrual cycle, for various locations on the left breast of ambulatory women. All subjects exhibited highly significant circadian rhythms ($P < 0.001$). Changes in rhythm parameters, such as the mesor, amplitude and acrophase, were observed during the menstrual cycle. No consistent trend in these rhythm parameters was observed between subjects in relation to menstrual cycle stage. Experimental and statistical techniques used to characterise circadian rhythms in pre-menopausal women were applied to a post-menopausal woman with primary breast cancer. Comparison of rhythm parameters associated with the tumour area and corresponding site on the contralateral breast showed abnormal thermal characteristics such as elevated mesor values, decreased amplitude as well as changes in the timing of the acrophase. These properties may be exploited for the early detection of breast cancer. The project also involved the design and testing of an ambulatory device, known as the 'chronobra', for the measurement of breast skin temperature. The performance of the chronobra was in close agreement with reliable, conventional equipment. The chronobra now allows studies of breast skin temperature rhythms associated with breast disease to be extended.

Keywords

Pietroiusti A, Neri A, Somma G, et al. **Year** 2010

Authors A Pietroiusti, A Neri, G Somma, L Coppeta, I Iavicoli, A Bergamaschi, A Magrini

Report Name Incidence of metabolic syndrome among night-shift healthcare workers

Publication Occup Environ Med

Issue-page numbers 2010;67:54-57

URL http://oem.bmj.com/content/67/1/54.abstract

Abstract

Objective: Night-shift work is associated with ischaemic cardiovascular disorders. It is not currently known whether it may be causally linked to metabolic syndrome (MS), a risk condition for ischaemic cardiovascular disorders. The syndrome presents with visceral obesity associated with mild alterations in glucidic and lipidic homeostasis, and in blood pressure. The aim of this study was to assess whether a causal relationship exists between night-shift work and the development of MS.

Methods: Male and female nurses performing night shifts, free from any component of MS at baseline, were evaluated annually for the development of the disorder during a 4-year follow-up. Male and female nurses performing daytime work only, visited during the same time period, represented the control group.

Results: The cumulative incidence of MS was 9.0% (36/402) among night-shift workers, and 1.8% (6/336) among daytime workers (relative risk (RR) 5.0, 95% CI − 2.1 to 14.6). The annual rate of incidence of MS was 2.9% in night-shift workers and 0.5% in daytime workers. Kaplan–Meier survival curves of the two groups were significantly different (log-rank test; p<0.001). Multiple Cox regression analysis (forward selection method based on likelihood ratio) showed that among selected variables (age, gender, smoking, alcohol intake, familiar history, physical activity, and work schedule) the only predictors of occurrence of MS were sedentariness (hazard ratio (HR) 2.92; 95% CI 1.64 to 5.18; p=0.017), and night-shift work (HR 5.10; 95% CI 2.15 to 12.11; p<0.001).

Conclusions: The risk of developing MS is strongly associated with night-shift work in nurses. Medical counselling should be promptly instituted in night-shift workers with the syndrome, and in case of persistence or progression, a change in work schedule should be considered.

Keywords

Pioli C, Caroleo MC, Nistico G, Doria G **Year** 1993

Authors Pioli C, Caroleo MC, Nistico G, Doria G

Report Name Melatonin increases antigen presentation and amplifies specific and non specific signals for T-cell proliferation

Publication Int J Immunopharmacol

Issue-page numbers 15:463–468 doi:10.1016/0192-0561(93)90060-C. PMID:8365822

URL http://www.sciencedirect.com/science/article/pii/019205619390060C

Abstract Our preceding results have shown that melatonin administration to normal and immunodepressed mice increases significantly the antibody response. We also found that melatonin is able to restore the impaired T-helper cell activity in immunodepressed mice. The present study shows that melatonin enhances antigen presentation by splenic macrophages to T-cells. This effect is concomitant with an increase in the expression of MHC class II molecules and production of IL-1 and TNF-α. Considering the role of antigen presentation and cytokine production in the initiation of the immune response, the present findings provide evidence for relevant mechanisms that may account for the regulatory role of the pineal gland in immunoregulation.

Keywords

Pittendrigh CS **Year** 1967

Authors Pittendrigh CS

Report Name Circadian systems. I. The driving oscillation and its assay in Drosophila pseudoobscura

Publication Proc Natl Acad Sci USA

Issue-page numbers 58:1762–1767 doi:10.1073/pnas.58.4.1762. PMID:5237901

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC223992/

Abstract N/A

Keywords

Authors Plat L, Leproult R, L'Hermite-Baleriaux M et al.

Report Name Metabolic effects of short-term elevations of plasma cortisol are more pronounced in the evening than in the morning

Publication J Clin Endocrinol Metab

Issue-page numbers 84:3082–3092 doi:10.1210/jc.84.9.3082. PMID:10487669

URL http://jcem.endojournals.org/content/84/9/3082.full

Abstract

To determine whether elevations of cortisol levels have more pronounced effects on glucose levels and insulin secretion in the evening (at the trough of the daily rhythm) or in the morning (at the peak of the rhythm), nine normal men each participated in four studies performed in random order. In all studies, endogenous cortisol levels were suppressed by metyrapone administration, and caloric intake was exclusively under the form of a constant glucose infusion. The daily cortisol elevation was restored by administration of hydrocortisone (or placebo) either at 0500 h or at 1700 h. In each study, plasma levels of glucose, insulin, C-peptide, and cortisol were measured at 20-min intervals for 32 h.

The initial effect of the hydrocortisone-induced cortisol pulse was a short-term inhibition of insulin secretion without concomitant glucose changes and was similar in the evening and in the morning. At both times of day, starting 4–6 h after hydrocortisone ingestion, glucose levels increased and remained higher than under placebo for at least 12 h. This delayed hyperglycemic effect was minimal in the morning but much more pronounced in the evening, when it was associated with robust increases in serum insulin and insulin secretion and with a 30% decrease in insulin clearance.

Thus, elevations of evening cortisol levels could contribute to alterations in glucose tolerance, insulin sensitivity, and insulin secretion.

Keywords

Authors Poole EM, Schernhammer ES, Tworoger SS

Report Name Rotating night shift work and risk of ovarian cancer

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers May;20(5):934-8. Epub 2011 Apr 5.

URL http://www.ncbi.nlm.nih.gov/pubmed/21467237

Abstract

BACKGROUND:

Night shift work has been associated with higher risks of breast and endometrial cancer, but few studies have evaluated associations with other reproductive cancers.
METHODS:

We examined the association between rotating night shift work and risk of ovarian cancer during 20 years of follow-up in 181,548 women participating in two large cohort studies, the Nurses' Health Study (NHS) and NHSII. Number of years of rotating night shift work was queried in 1988 for NHS and in 1989, 1991, 1993, 2001, and 2005 for NHSII. We used Cox proportional hazards regression to model HRs and 95% CIs of ovarian cancer for each shift work category (1-2, 3-5, 6-9, 10-14, 15-19, and 20+ years).
RESULTS:

We confirmed 718 incident cases of ovarian cancer over 2,974,672 person-years of follow-up. Rotating shift work was not associated with ovarian cancer risk in either cohort individually. Combining both cohorts, compared with women without any night work, the HR for 15 to 19 years of rotating night shift work was 1.28 (95% CI: 0.84-1.94) and for 20+ years 0.80 (95% CI: 0.51-1.23).
CONCLUSIONS:

In this large prospective study, there was no association between duration of rotating night shift work and risk of ovarian cancer.
IMPACT:

Although associated with other cancers, night shift work does not appear to be associated with increased risk of ovarian cancer. However, further exploration of the association between melatonin and risk of ovarian cancer is warranted.

Keywords

Popovich I, Zabezhinski M, Panchenko A, et al. **Year** 2013

Authors Irina G. Popovich, Mark A. Zabezhinski, Andrei V. Panchenko, Tatiana S. Piskunova, Anna V. Semenchenko, Maragriata L. Tyndyk, Maria N. Yurova, Vladimir N. Anisimov

Report Name Exposure to light at night accelerates aging and spontaneous uterine carcinogenesis in female 129/Sv mice

Publication Cell Cycle

Issue-page numbers 12:1785 - 1790; PMID: 23656779; http://dx.doi.org/10.4161/cc.24879

URL http://www.landesbioscience.com/journals/cc/article/24879/

Abstract The effect of the constant illumination on the development of spontaneous tumors in female 129/Sv mice was investigated. Forty-six female 129/Sv mice starting from the age of 2 mo were kept under standard light/dark regimen [12 h light (70 lx):12hr dark; LD, control group], and 46 of 129/Sv mice were kept under constant illumination (24 h a day, 2,500 lx, LL) from the age of 5 mo until to natural death. The exposure to the LL regimen significantly accelerated body weight gain, increased body temperature as well as acceleration of age-related disturbances in estrous function, followed by significant acceleration of the development of the spontaneous uterine tumors in female 129/Sv mice. Total tumor incidence as well as a total number of total or malignant tumors was similar in LL and LD group ($p > 0.05$). The mice from the LL groups survived less than those from the LD group ($\chi 2 = 8.5$; $p = 0.00351$, log-rank test). According to the estimated parameters of the Cox's regression model, constant light regimen increased the relative risk of death in female mice compared with the control (LD) group ($p = 0.0041$). The data demonstrate in the first time that the exposure to constant illumination was followed by the acceleration of aging and spontaneous uterine tumorigenesis in female 129/Sv mice.

Keywords 129/Sv mice, lifespan, light at night, tumorigenesis

Portaluppi F, Cortelli P, Avoni P et al. **Year** 1994

Authors F Portaluppi, P Cortelli, P Avoni, L Vergnani, M Contin, P Maltoni, A Pavani, E Sforza, EC degli Uberti and P Gambetti

Report Name Diurnal blood pressure variation and hormonal correlates in fatal familial insomnia

Publication Hypertension

Issue-page numbers 23:569–576. PMID:8175163

URL http://hyper.ahajournals.org/content/23/5/569.short

Abstract Fatal familial insomnia is a prion disease in which a selective thalamic degeneration leads to total sleep deprivation, hypertension, dysautonomia, adrenal overactivity, and impaired motor functions. With patients under continuous recumbency and polysomnographic control, we assessed the changes in the 24-hour patterns of blood pressure, heart rate, plasma catecholamines, corticotropin, and serum cortisol in three patients at different stages of the disease. Six healthy volunteers were used as control subjects. A dominant 24-hour component was detected at rhythm analysis of all variables, both in patients and control subjects. In the patients, the amplitudes gradually decreased as the disease progressed, leading to the obliteration of any significant dirunal variation only in the preterminal stage. A shift in phase corresponded to the loss of the nocturnal fall in blood pressure in an early stage of the disease, when nocturnal bradycardia was still preserved. Plasma cortisol was high and became increasingly elevated, whereas corticotropin remained within normal levels; abnormal nocturnal peaks appeared in their circadian patterns. The disrupted patterns of cortisol and blood pressure preceded the development of hypertension and severe dysautonomia, which in turn were paralleled by increasing catecholamine and heart rate levels. Our data demonstrate that in patients with fatal familial insomnia the changes detectable in the rhythmic component of diurnal blood pressure variability result in a pattern of secondary hypertension. Disturbances in thalamic, pituitary- adrenal, and autonomic functions seem to be involved in mediating these changes.

Keywords

Pozo D, García-Mauriño S, Guerrero JM, Calvo JR *Year* 2004

Authors Pozo D, García-Mauriño S, Guerrero JM, Calvo JR

Report Name mRNA expression of nuclear receptor RZR/RORalpha, melatonin membrane receptor MT, and hydroxindole-O-methyltransferase in different populations of human immune cells

Publication J Pineal Res

Issue-page numbers 37:48–54 doi:10.1111/j.1600-079X.2004.00135.x. PMID:15230868

URL http://www.mendeley.com/research/mrna-expression-nuclear-receptor-rzrroralpha-melatonin-membrane-receptor-mt-hydroxindoleomethyltransferase-different-populations-humar

Abstract We characterized the expression levels of the retinoid Z receptor alpha (RZR alpha), RORalpha mRNA isoforms (RORalpha1, RORalpha2, and RORalpha3), and both melatonin receptor MT1 and hydroxindole-O-methyltransferase (HIOMT) genes. For this purpose, the following human peripheral blood mononuclear cells populations were isolated: monocytes (CD14+ cells), B lymphocytes (CD19+ cells), T helper lymphocytes (CD14(-) CD4+), cytotoxic T lymphocytes (CD56(-) CD8+ cells), and natural killer (NK) lymphocytes (CD56+ cells). PBMCs subsets were obtained by Dynabeads M-450 (Dynal) isolation procedure. We observed a strong gene expression signal for RZRalpha in all subpopulations studied, whereas both RORalpha1 and RORalpha2 transcripts were amplified only in CD8+ cells. Specific signal for RORalpha2 was obtained in all subpopulations studied, but we were not able to detect the RORalpha3 mRNA transcript in human immune cells studied. A weaker signal (especially in CD19+ cells) was also detected in all subsets of cells for the MT1 gene. With regard to HIOMT, a strong signal was achieved among all but one subpopulation of cells; the only exception was CD14+ cells. Thus, in addition to its classical function in the nervous and endocrine system, melatonin could act directly as a paracrine and/or autocrine agent in the human immune system.

Keywords

Preitner N, Damiola F, Lopez-Molina L et al. *Year* 2002

Authors Preitner N, Damiola F, Lopez-Molina L et al.

Report Name The orphan nuclear receptor REV-ERBalpha controls circadian transcription within the positive limb of the mammalian circadian oscillator

Publication Cell

Issue-page numbers 110:251–260 doi:10.1016/S0092-8674(02)00825-5. PMID:12150932

URL http://www.mendeley.com/research/the-orphan-nuclear-receptor-reverb-controls-circadian-transcription-within-the-positive-limb-of-the-mammalian-circadian-oscillator/

Abstract Mammalian circadian rhythms are generated by a feedback loop in which BMAL1 and CLOCK, players of the positive limb, activate transcription of the cryptochrome and period genes, components of the negative limb. Bmal1 and Per transcription cycles display nearly opposite phases and are thus governed by different mechanisms. Here, we identify the orphan nuclear receptor REV-ERBalpha as the major regulator of cyclic Bmal1 transcription. Circadian Rev-erbalpha expression is controlled by components of the general feedback loop. Thus, REV-ERBalpha constitutes a molecular link through which components of the negative limb drive antiphasic expression of components of the positive limb. While REV-ERBalpha influences the period length and affects the phase-shifting properties of the clock, it is not required for circadian rhythm generation.

Keywords

Prendergast BJ, Hotchkiss AK, Nelson RJ **Year** 2003

Authors Prendergast BJ, Hotchkiss AK, Nelson RJ

Report Name Photoperiodic regulation of circulating leukocytes in juvenile Siberian hamsters: mediation by melatonin and testosterone

Publication J Biol Rhythms

Issue-page numbers 18:473–480 doi:10.1177/0748730403258486. PMID:14667148

URL http://jbr.sagepub.com/content/18/6/473

Abstract The reproductive system of Siberian hamsters (Phodopus sungorus) undergoes rapid phenotypic responses to changes in day length that occur around the time of weaning. The present experiments tested whether the immune system of Siberian hamsters is similarly photoperiodicearly in life and whether photoperiodic changes in melatonin or gonadal hormone secretions mediate any such responses to day length. Circulating blood leukocyte concentrations (WBC) were measured in juvenile male Siberian hamsters that were gestated in long-days (LD), transferred to short-days (SD) on the day of birth, and subsequently either remained in SD or were transferred fromSD toLDat 18 days of age (day 18). WBC values were comparable between LD and SD hamsters on day 18. Between day 18 and day 32, SD hamsters exhibited a 3-fold increase in WBC, whereas LD hamsters failed to undergo a significant increase inWBCduring this interval. WBC of LD hamsters was significantly lower than that of SD hamsters on day 25 and on day 32. In LD housed males, peripheral injections of melatonin delivered so as to extend the nocturnal duration of elevated endogenous melatonin secretion (i.e., provided in late afternoon) on days 18-31 increasedWBCas measured on day 32. Peripubertal (day 17) gonadectomy abolished the immunosuppressive effect of LD exposure on WBC, and treatment with silasticimplants containing testosterone suppressed WBC independent of photoperiod treatment. These data indicate that juvenile Siberian hamsters are immunologically responsive to photoperiod and that the leukocyte responses to day length are the result of melatonin-mediated effects of photoperiod on testicular hormone secretion.

Keywords immune function, photoperiodism, puberty, seasonal rhythms, Phodopus sungorus

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Price LL, Khazova M, O'Hagan JB **Year** 2012

Authors L. L. Price, M. Khazova, J. B. O'Hagan

Report Name Performance assessment of commercial circadian personal exposure devices

Publication Lighting Research and Technology

Issue-page numbers January 11, 2012, doi: 10.1177/1477153511433171

URL http://lrt.sagepub.com/content/early/2012/01/06/1477153511433171.abstract

Abstract Through the influence on circadian rhythms, natural and artificial lighting, as well as lifestyle and architecture, affect health and performance. Epidemiological and interventional studies of light-initiated circadian biological outcomes require robust 24-hour data on personal light exposures, including blue light weighted irradiance data. The performance of the detection systems used is a key factor. We assessed the performance of 16 Actiwatch Spectrum™ devices for spectral response, directional response and dynamic range and propose techniques for calibration, deployment and data analysis for use of the watches in circadian studies. The results are presented, followed by a discussion of applicability focussing on spectral response for circadian studies

Keywords

Priebe LA, Cain CP, Welch AJ

Year 1975

Authors Priebe LA, Cain CP, Welch AJ.

Report Name Temperature rise required for production of minimal lesions in the Macaca mulatta retina

Publication Am J Ophthalmol

Issue-page numbers 1975 Mar;79(3):405-13.

URL http://www.ncbi.nlm.nih.gov/pubmed/804816

Abstract Fundus temperatures of the rhesus monkey were measured with argon laser (488 nm) irradiations that produced minimal, ophthalmoscopically visible lesions five minutes after exposure. Measurements were made with 10- to 20-mu tip diameter, copper-nickel thermocouples. Preliminary data included measurements at eight paramacular sites and seven macular sites. The threshold temperature rise was 17 to 26 degrees C for a ten-second exposure at these sites. Decreasing the exposure duration to 20 msec increased the threshold temperature rise range to the interval between 30 and 40 degrees C. The temperature measurements in the eye were compared to a computer solution of the heat conduction equation.

Keywords

Pronk A, Ji B, Shu X, et al.

Year 2010

Authors Anjoeka Pronk, Bu-Tian Ji, Xiao-Ou Shu, Shouzheng Xue, Gong Yang, Hong-Lan Li, Nathaniel Rothman, Yu-Tang Gao, Wei Zheng and Wong-Ho Chow

Report Name Night-Shift Work and Breast Cancer Risk in a Cohort of Chinese Women

Publication American Journal of Epidemiology

Issue-page numbers Volume171, Issue9 Pp. 953-959

URL http://aje.oxfordjournals.org/content/171/9/953.full

Abstract Shift work involving disruption of circadian rhythms has been classified as a probable cause of human cancer by the International Agency for Research on Cancer, based on limited epidemiologic evidence and abundant experimental evidence. The authors investigated this association in a population-based prospective cohort study of Chinese women. At baseline (1996–2000), information on lifetime occupational history was obtained from 73,049 women. Lifetime night-shift exposure indices were created using a job exposure matrix. During 2002–2004, self-reported data on frequency and duration of night-shift work were collected. Hazard ratios and 95% confidence intervals, adjusted for major breast cancer risk factors, were calculated. During follow-up through 2007, 717 incident cases of breast cancer were diagnosed. Breast cancer risk was not associated with ever working the night shift on the basis of the job exposure matrix (adjusted hazard ratio = 1.0, 95% confidence interval: 0.9, 1.2) or self-reported history of night-shift work (adjusted hazard ratio = 0.9, 95% confidence interval: 0.7, 1.1). Risk was also not associated with frequency, duration, or cumulative amount of night-shift work. There were no indications of effect modification. The lack of an association between night-shift work and breast cancer adds to the inconsistent epidemiologic evidence. It may be premature to consider shift work a cause of cancer.

Keywords breast neoplasms, China, prospective studies, work schedule tolerance

Authors Ignacio Provencio, Ignacio R. Rodriguez, Guisen Jiang, William Pa¨r Hayes, Ernesto F. Moreira, and

Report Name A Novel Human Opsin in the Inner Retina

Publication The Journal of Neuroscience

Issue-page numbers January 15, 2000, 20(2):600-605

URL http://www.jneurosci.org/content/20/2/600.full.pdf

Abstract

Here we report the identification of a novel human opsin, melanopsin, that is expressed in cells of the mammalian inner retina. The human melanopsin gene consists of 10 exons and is mapped to chromosome 10q22. This chromosomal localization and gene structure differs significantly from that of other human opsins that typically have four to seven exons. A survey of 26 anatomical sites indicates that, in humans, melanopsin is expressed only in the eye. In situ hybridization histochemistry shows that melanopsin expression is restricted to cells within the ganglion and amacrine cell layers of the primate and murine retinas. Notably, expression is not observed in retinal photoreceptor cells, the opsin-containing cells of the outer retina that initiate vision. The unique inner retinal localization of melanopsin suggests that it is not involved in image formation but rather may mediate nonvisual photoreceptive tasks, such as the regulation of circadian rhythms and the acute suppression of pineal melatonin. The anatomical distribution of melanopsinpositive retinal cells is similar to the pattern of cells known to project from the retina to the suprachiasmatic nuclei of the hypothalamus, a primary circadian pacemaker.

Keywords circadian; melanopsin; opsin; photoreceptor; retina;

Provencio I, Warthen DM

Year 2012

Authors Ignacio Provencio, Daniel M. Warthen

Report Name Melanopsin, the photopigment of intrinsically photosensitive retinal ganglion cells

Publication Wiley Interdisciplinary Reviews: Membrane Transport and Signaling

Issue-page numbers Article first published online: 11 JAN 2012

URL http://onlinelibrary.wiley.com/doi/10.1002/wmts.29/full

Abstract Melanopsin (gene symbol: Opn4) is the G protein-coupled photopigment that confers photosensitivity upon intrinsically photosensitive retinal ganglion cells (ipRGCs). ipRGCs are the third class of retinal photoreceptor in mammals, complementing the two previously identified classes, the rods and cones. This novel class, however, differs from rods and cones in many significant ways. First, ipRGCs are more similar morphologically to other retinal ganglion cell classes than to other retinal photoreceptors, i.e., rods and cones. Instead of having photopigment concentrated in a specialized light-absorbing cellular domain such as the outer segment, ipRGCs have photopigment distributed throughout the plasma membrane of the cell. Second, the phototransduction cascade of ipRGCs more closely resembles that of the rhabdomeric photoreceptors that are typically found in the invertebrates rather than that of ciliary photoreceptors typical of vertebrate visual systems. Accordingly, like the rhabdomeric photoreceptors of invertebrates, ipRGCs depolarize in response to illumination while rods and cones hyperpolarize. Third, in addition to their inherent light sensitivity, ipRGCs also function as a conduit for information that originates in the rods and cones and is conveyed to the brain for the purposes of generating non-visual light responses. WIREs Membr Transp Signal 2012 doi: 10.1002/wmts.29

Keywords

Pruessner JC, Wolf OT, Hellhammer DH et al.

Year 1997

Authors Pruessner JC, Wolf OT, Hellhammer DH et al.

Report Name Free cortisol levels after awakening: a reliable biological marker for the assessment of adrenocortical activity

Publication Life Sci

Issue-page numbers 61:2539–2549 doi:10.1016/S0024-3205(97)01008-4. PMID:9416776

URL http://www.sciencedirect.com/science/article/pii/S0024320597010084

Abstract In three independent studies, free cortisol levels after morning awakening were repeatedly measured in children, adults and elderly subjects (total n= 152). Cortisol was assessed by sampling saliva at 10 or 15 minute intervals for 30–60 minutes, beginning at the time of awakening for two days (Study 1 and 2) or one (Study 3) day, respectively. In all three studies, free cortisol levels increased by 50–75% within the first 30 minutes after awakening in both sexes on all days. Premenopausal women consistently showed a stronger increase with a delayed peak after awakening compared to men on all days. In Study 2, there was a tendency for lower early morning free cortisol levels for women taking oral contraceptives (p=.10). Stability of the area under the curve (AUC) of the early morning free cortisol levels over the three (Study 1 and 2) or two (Study 3) days ranged between r=.39 and r=.67 (p<.001). Neither age, weight, nor smoking showed an effect on baseline or peak cortisol levels. Sleep duration, time of awakening and alcohol consumption also appeared to be unrelated to early morning free cortisol levels. From these data we conclude that in contrast to single assessments at fixed times, early morning cortisol levels can be a reliable biological marker for the individual's adrenocortical activity when measured repeatedly with strict reference to the time of awakening.

Keywords

Pudroma X, Juzeniene A, Ma L, et al. **Year** 2011

Authors Xiao Pudroma, Asta Juzeniene, Li-Wei Ma, Vladimir Iani, Johan Moan

Report Name Fluorescence Photobleaching of ALA and ALA-Heptyl Ester Induced Protoporphyrin IX During Photodynamic Therapy of Normal Hairless Mouse Skin: A Comparison of Two Ligh

Publication Journal of Environmental Pathology, Toxicology and Oncology

Issue-page numbers Issue 3, pages 235-240

URL http://www.dl.begellhouse.com/journals/0ff459a57a4c08d0,28d5b25a1eb31fda,2790dc6d5a3921d4.html

Abstract This study investigated photobleaching of protoporphyrin IX (PpIX) induced by 5-aminolevulinic acid (ALA) and ALA-heptyl ester during superficial photodynamic therapy (PDT) in normal skin of the female BALB/c-nu/nu athymic mouse. We examined the effects of two light sources (laser and broadband lamp) and two different illumination schemes (fractionated light and continuous irradiation) on the kinetics of photobleaching. Our results show that light exposure (0−30 minutes, 10 mW/cm2) of wavelengths of approximately 420 nm (blue light) and 635 nm (red light) induced time-dependent PpIX photobleaching for mouse skin of 2% ALA and ALA-heptyl ester. Blue light (10 mW/cm2) caused more rapid PpIX photobleaching than did red light (100 mW/cm2), which is attributed to stronger absorption at 407 nm than at 632 nm for PpIX. In the case of light fractionation, fractionated light induced faster photobleaching compared with continuous light exposure after topical application of 2% ALA and ALA-heptyl ester in vivo. These have been suggested to allow reoxygenation of the irradiated tissue, with a consequent enhancement of singlet oxygen production in the second and subsequent fractions.

Keywords photobleaching, photodynamic therapy, red light, blue light, fractionation

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Puig-Domingo M, Webb SM, Serrano J et al. **Year** 1992

Authors Puig-Domingo M, Webb SM, Serrano J et al.

Report Name Brief report: melatonin-related hypogonadotropic hypogonadism

Publication N Engl J Med

Issue-page numbers 1356–1359 doi:10.1056/NEJM199211053271905. PMID:1406837

URL http://www.nejm.org/doi/full/10.1056/NEJM199211053271905

Abstract THE secretion of melatonin from the pineal gland is linked to the light–dark cycle, being greater at night in all species, including humans, and it is pulsatile.1 In humans the peak nocturnal plasma melatonin concentration declines progressively with age, being highest in infants and prepubertal children and lowest in elderly people. Melatonin profoundly influences reproductive function in seasonally breeding mammals. One such species is the Syrian hamster, in which pinealectomy leads to sustained reproductive activity and in which appropriately timed injections of melatonin inhibit reproductive function.2 It is less clear whether melatonin has regulatory actions on the reproductive system in species that breed nonseasonally, such as humans. Some patients with hypothalamic hypogonadism have unusually high plasma melatonin concentrations,3 4 5 6 suggesting that increased pineal activity may be involved in the pathogenesis of this condition. Some boys with delayed puberty have elevated daytime plasma melatonin concentrations,7 and more than half of children with precocious sexual development have plasma melatonin concentrations lower than those of age-matched normal children.8 These data suggest that melatonin is important in pathologic conditions of the human reproductive system.

We describe a young man who had high plasma melatonin concentrations, delayed puberty, and hypogonadotropic hypogonadism, whose clinical abnormalities reversed spontaneously when the secretion of melatonin decreased.

Keywords

Authors Pukkala E, Aspholm R, Auvinen A et al.

Report Name Incidence of cancer among Nordic airline pilots over five decades: occupational cohort study

Publication BMJ

Issue-page numbers 325:567.doi:10.1136/bmj.325.7364.567 PMID:12228131

URL http://www.bmj.com/content/325/7364/567.full

Abstract

Objective: To assess the incidence of cancer among male airline pilots in the Nordic countries, with special reference to risk related to cosmic radiation.

Design: Retrospective cohort study, with follow up of cancer incidence through the national cancer registries.

Setting: Denmark, Finland, Iceland, Norway, and Sweden.

Participants: 10 032 male airline pilots, with an average follow up of 17 years.

Main outcome measures: Standardised incidence ratios, with expected numbers based on national cancer incidence rates; dose-response analysis using Poisson regression.

Results: 466 cases of cancer were diagnosed compared with 456 expected. The only significantly increased standardised incidence ratios were for skin cancer: melanoma 2.3 (95% confidence interval 1.7 to 3.0), non-melanoma 2.1 (1.7 to 2.8), basal cell carcinoma 2.5 (1.9 to 3.2). The relative risk of skin cancers increased with the estimated radiation dose. The relative risk of prostate cancer increased with increasing number of flight hours in long distance aircraft.

Conclusions: This study does not indicate a marked increase in cancer risk attributable to cosmic radiation, although some influence of cosmic radiation on skin cancer cannot be entirely excluded. The suggestion of an association between number of long distance flights (possibly related to circadian hormonal disturbances) and prostate cancer needs to be confirmed.

Keywords

Authors Pukkala E, Auvinen A, Wahlberg G

Report Name Incidence of cancer among Finnish airline cabin attendants, 1967–92

Publication BMJ

Issue-page numbers 311:649–652 http://www.bmj.com/cgi/content/full/311/7006/649. PMID:7549630

URL http://www.bmj.com/content/311/7006/649.abstract

Abstract

Objective: To assess whether occupational exposure among commercial airline cabin attendants are associated with risk of cancer.

Design: Record linkage study.

Setting: Finland.

Subjects: 1577 female and 187 male cabin attendants who had worked for the Finnish airline companies.

Main outcome measure: Standardised incidence ratio; expected number of cases based on national cancer incidences.

Results: A significant excess of breast cancer (standardised incidence ratio 1.87 (95% confidence interval 1.15 to 2.23)) and bone cancer (15.10 (1.82 to 54.40)) was found among female workers. The risk of breast cancer was most prominent 15 years after recruitment. Risks of leukaemia (3.57 (0.43 to 12.9)) and skin melanoma (2.11 (0.43 to 6.15 were not significantly raised. Among men, one lymphoma and one Kaposi's sarcoma were found (expected number of cases 1.6).

Conclusions: Although the lifestyle of cabin attendants is different from that of the reference population—for example, in terms of social status and parity—concentration of the excess risks to primary sites sensitive to radiation suggests that ionising radiation during flights may add to the cancer risk of all flight personnel. Otherwise the lifestyle of cabin attendants did not seem to affect their risks of cancer. Estimates of the effect of reproductive risk factors only partly explained the

Keywords

Authors Eero Pukkala, Matti Ojamo, Sirkka-Liisa Rudanko, Richard G. Stevens and Pia K. Verkasalo

Report Name Does Incidence of Breast Cancer and Prostate Cancer Decrease with Increasing Degree of Visual Impairment

Publication Cancer Causes and Control

Issue-page numbers Volume 17, Number 4, 573-576, DOI: 10.1007/s10552-005-9005-6

URL http://www.springerlink.com/content/m658956088146627/

Abstract

Objective
The issue of light at night and cancer continuously attracts discussion. The major hypotheses are that melatonin may decrease risk of hormone-related cancers, particularly breast cancer, or even act as a potent antioxidant and thus have a protective effect against cancer development in general.
Methods
We tested the hypothesis that blind persons are at lower risk of cancer in a follow-up study linking a cohort of 17,557 persons with visual impairment identified from the Finnish Register of Visual Impairment with cancer incidence data of the Finnish Cancer Registry for years 1983–2003.
Results
Breast cancer risk in females decreased by degree of visual impairment, and a similar but less consistent trend was observed for prostate cancer in males. The incidence for the remaining cancers among nearly to totally blind persons was significantly higher than in average Finnish population.
Conclusions
Our findings add to the suggestive epidemiological evidence for a decreased risk of hormone-related cancers in people with visual impairment and, consequently, a relationship between visible light at night and breast cancer risk. The result is strongly against the hypothesis of a systemic protective effect related lack of visible light.

Keywords Blindness - Neoplasms - Epidemiology - medical record linkage - Melatonin - Vision disorders

Authors Putilov AA, Danilenko KV, Protopopova AY, Kripke DF

Report Name Menstrual phase response to nocturnal light

Publication Biol Rhythm Res

Issue-page numbers 33:23–38 doi:10.1076/brhm.33.1.23.1324

URL http://www.lighttherapy.com.au/pdf_documents/PutilovMenstrualProof.pdf

Abstract

The aims of the study were to test whether nocturnal white light can normalize menstrual cycles in oligomenorrheic women, and whether the phase of the menstrual cycle in which light is given is important for the shortening effect. Twenty-five women with long menstrual cycles (35.9–53.4 days on average) were treated for 1–3 cycles, each of which was preceded and followed by at least two untreated cycles. Treatments were 100 watt bedside lights administered for 5 consecutive nights. They centered at three different phases of the menstrual cycle: 6–7th, 14–17th or 23–25th days of the treated cycle (early, middle or late treatment, respectively). On average, the treatment cycle lengths were modestly, but significantly reduced compared to the duration of baseline cycles (more than 11%). The difference in the effects of the early, middle and late treatment was not significant. However, if middle or late treatments were administered in the latter half of the interval between the menstrual cycle onset and probable time of ovulation, reductions of the treated cycle length were substantial (more than 20%, resulting in cycles less than 33 days on average; $p < 0.001$). Other treatments produced only weak (up to 7%), if any, cycle reductions. Moreover, we found a strong correlation ($p < 0.001$) between the duration of baseline cycle and differential effect of middle treatment (compared to early or late treatment). Middle treatments reduced treated cycle duration to the normal range in the subjects with shorter mean baseline cycles (<42 days), while in the subjects with longer duration of baseline cycle the shortening effect was produced by late treatments ($p = 0.005$ and $p = 0.001$, respectively). The results support the suggestion that a bedside lamp used on nights prior to ovulation can cause reduction of long menstrual cycles.

Keywords

Qian J, Block GD, Colwell CS, Matveyenko AV **Year** 2013

Authors Jingyi Qian, Gene D. Block, Christopher S. Colwell and Aleksey V. Matveyenko

Report Name Consequences of exposure to light at night on the pancreatic islet circadian clock and function in rats

Publication Diabetes

Issue-page numbers Published online before print June 17, 2013, doi: 10.2337/db12-1543

URL http://diabetes.diabetesjournals.org/content/early/2013/06/12/db12-1543.short

Abstract There is a correlation between circadian disruption, Type 2 Diabetes (T2DM) and islet failure. However the mechanisms underlying this association are largely unknown. Pancreatic islets express self-sustained circadian clocks essential for proper beta-cell function and survival. We hypothesized that exposure to enviromental conditions associated with disruption of circadian rhythms and susceptibility to T2DM in humans disrupts islet clock and beta-cell function. To address this hypothesis, we validated the use of Per-1:LUC transgenic rats for continuous longitudinal assessment of islet circadian clock function ex-vivo. Using this methodology we subsequently examined effects of the continuous exposure to light at night (LL) on islet circadian clock and insulin secretion in-vitro in rat islets. Our data show that changes in the light dark cycle (LD) cycles in-vivo entrain the phase of islet clock transcriptional oscillations, whereas prolonged exposure (10 weeks) to LL disrupts islet circadian clock function through impairment in the amplitude, phase and inter-islet synchrony of clock transcriptional oscillations. We also report that exposure to LL leads to diminished glucose-stimulated insulin secretion due to decrease in insulin secretory pulse mass. Our studies identify potential mechanisms by which disturbances in circadian rhythms common to modern life can predispose to islet failure in T2DM.

Keywords

Quera-Salva MA, Defrance R, Claustrat B et al. **Year** 1996

Authors Quera-Salva MA, Defrance R, Claustrat B et al.

Report Name Rapid shift in sleep time and acrophase of melatonin secretion in short shift work schedule

Publication Sleep

Issue-page numbers 19:539–543. PMID:8899932

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24408

Abstract Tolerance to shift work and adaptability to shifting schedules is an issue of growing importance in industrialized society. We studied 40 registered nurses, 20 on fixed day-shifts and 20 on fixed night-shifts, to assess whether workers with rapidly shifting schedules were able to adapt their melatonin secretion and sleep-wake cycles. The day-shift worked 5 days with 2 days off and the night-shift worked 3 nights with 2 off. All night-shift personnel acknowledged shifting back to daytime schedules on their days off. Sleep-wake was determined by sleep logs and actigraphy. To measure 6-sulfatoxymelatonin levels, urine was collected at 2-hour intervals on the last work day and on the last day off. Night-shift workers slept significantly more on days off. Napping on the job occurred in 9/20 night-shift workers (mean 114 minutes) between 3 and 6 a.m. The acrophase of 6-sulfatoxymelatonin in day-shift nurses occurred at similar times on workdays and off days. In night- shift nurses, the acrophase was about 7 a.m. on days off, but had a random distribution on workdays. Further analysis revealed two subgroups of night-shift nurses: six subjects (group A).demonstrated a rapid shift in melatonin secretion (acrophase at near 12 noon on work days and at near 7 a.m. on days off) while 14 nurses (group B) did not shift. Group A nurses slept more in the daytime on work days and their total sleep time was the same as day-shift nurses. Group A was slightly younger and was composed solely of women (there were nine women and five men in group B). Age may be a factor in the ability to adapt to rapidly shifting schedules.

Keywords

Quera-Salva MA, Guilleminault C, Claustrat B et al. **Year** 1997

Authors Maria Antonia Quera-Salva, †Christian Guilleminault, ‡Bruno Claustrat, §Remy Defrance; *Philippe Gajdos, *Catherine Crowe McCann and *Jacques De Lattre

Report Name Rapid shift in peak melatonin secretion associated with improved performance in short shift work schedule

Publication Sleep

Issue-page numbers 20:1145–1150. PMID:9493924

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24004

Abstract We studied the performance and adaptability of 40 nurses (median age 35 years), 20 on permanent day shift and 20 on permanent night shift with fast rotation of work and days off, matched for age, gender, and socio- familial responsibilities. For 15 days prior to the study, subjects maintained sleep logs and trained for performance tests. Questionnaires were administered to evaluate adaptability to shift work. During the experimental phase, sleep/wake patterns were monitored using sleep logs and activity/inactivity with wrist actigraphy. Performance levels were measured with the four choice reaction time and memory test for seven letters, eight times/day during the wake period, days on and off. On the last day of work and first day off, 6-sulfatoxy-melatonin levels were assayed from urine samples collected every 2 hours. Estimated total sleep time during the 15-day experimental period was not significantly different in the dayshift and nightshift nurses. Night nurses shifted regularly to daytime activities on days off and, as a group, were significantly sleep deprived on work days with napping on the job in 9 of the 20 night shift nurses (mean of 114 ± 45 minutes per shift) and a significant performance decrement during the work period. Further analysis revealed two subgroups of night nurses: The majority (14 nurses) had a mean peak of 6-sulfatoxy-melatonin at 0718 hours on days off and no peak during night work while the other 6 night shift nurses presented a fast melatonin shift with two clear peaks on both work and days off. Comparison of performance scores revealed that all nurses performed similarly on days off. Daytime nurses and fast- shifting night nurses had similar scores on work days, while nonshifting night nurses had significantly lower scores at work. Despite similar gender, age, social conditions, and light exposure levels, a minority of the nurses studied possessed the physiological ability to adapt to a fast-shifting sleep-wake schedule of more than 8 hours and were able to perform appropriately in both conditions. This shift was associated with a change in the acrophase of 6-sulfatoxy- melatonin.

Keywords

Quinn GE, Shin CH, Maguire MG, Stone RA **Year** 0

Authors Graham E. Quinn, Chai H. Shin, Maureen G. Maguire & Richard A. Stone

Report Name Myopia and ambient lighting at night

Publication Nature

Issue-page numbers 399, 113-114 (13 May 1999) | doi:10.1038/20094

URL http://www.nature.com/nature/journal/v399/n6732/abs/399113a0.html

Abstract Myopia, or short-sightedness, occurs when the image of distant objects, focused by the cornea and lens, falls in front of the retina. It commonly arises from excessive postnatal eye growth, particularly in the vitreous cavity. Its prevalence is increasing and now reaches 70-90% in some Asian populations1,2. As well as requiring optical correction, myopia is a leading risk factor for acquired blindness in adults because it predisposes individuals to retinal detachment, retinal degeneration and glaucoma. It typically develops in the early school years but can manifest into early adulthood2. Its aetiology is poorly understood but may involve genetic and environmental factors1,2, such as viewing close objects, although how this stimulates eye growth is not known3. We have looked at the effects of light exposure on vision, and find a strong association between myopia and night-time ambient light exposure during sleep in children before they reach two years of age.

Keywords

Authors Rabstein S, Harth V, Pesch B, Pallapies D, Lotz A, Justenhoven C, Baisch C, Schiffermann M, Haas S, Fischer H-P, Heinze E, Pierl C, Brauch H, Hamann U, Ko Y, Brüning T

Report Name Night work and breast cancer estrogen receptor status – results from the German GENICA study

Publication Scand J Work Environ Health

Issue-page numbers Online-first -article doi:10.5271/sjweh.3360

URL http://www.sjweh.fi/show_abstract.php?abstract_id=3360

Abstract

Objectives The potential mechanisms that link night-shift work with breast cancer have been extensively discussed. Exposure to light at night (LAN) depletes melatonin that has oncostatic and anti-estrogenic properties and may lead to a modified expression of estrogen receptor (ER) α. Here, we explored the association between shift work and breast cancer in subgroups of patients with ER-positive and -negative tumors.

Methods GENICA (Gene–Environment Interaction and breast Cancer) is a population-based case–control study on breast cancer with detailed information on shift work from 857 breast cancer cases and 892 controls. ER status was assessed by immunohistochemical staining. Associations between night-shift work and ER-positive and -negative breast cancer were analyzed with conditional logistic regression models, adjusted for potential confounders.

Results ER status was assessed for 827 cases and was positive in 653 and negative in 174 breast tumors. Overall, 49 cases and 54 controls were “ever employed” in shift work including night shifts for ≥1 year. In total, “ever shift work” and “ever night work” were not associated with an elevated risk of ER-positive or -negative breast tumors. Night work for ≥20 years was associated with a significantly elevated risk of ER-negative breast cancer [odds ratio (OR) 4.73, 95% confidence interval (95% CI) 1.22–18.36].

Conclusions Our case–control study suggests that long-term night-shift work is associated with an increased risk of ER-negative breast cancers. Further studies on histological subtypes and the analysis of other potentially relevant factors are crucial for discovering putative mechanisms

Keywords breast cancer; case–control study; circadian disruption; estrogen receptor; estrogen receptor status; GENICA

Authors Radespiel-Tröger M, Meyer M, Pfahlberg A, Lausen B, Uter W, Gefeller O.

Report Name Outdoor work and skin cancer incidence: a registry-based study in Bavaria

Publication International Archives of Occupational and Environmental Health

Issue-page numbers Volume 82, Number 3, 357-363, DOI: 10.1007/s00420-008-0342-0

URL http://www.springerlink.com/content/5v6467443034x773/

Abstract

Objective
To analyse the association between occupational ultraviolet (UV) light exposure and skin cancer (basal cell carcinoma, BCC; squamous cell carcinoma, SCC; cutaneous malignant melanoma, CMM) based on data from the Bavarian population-based cancer registry.
Methods
The population-based cancer registry of Bavaria (Germany) provided data on incident cases of BCC, SCC, and CMM, respectively, during the period 2001 until 2005. Eleven Bavarian districts with complete skin cancer registration were included in this analysis based on 2,156,336 person years. Cases were assigned to “indoor”, “mixed indoor/outdoor”, and “outdoor” exposure categories according to their job title. We computed age-specific and age-adjusted incidence rates of BCC (n = 1,641), SCC (n = 499), and CMM (n = 454) by work type, and the relative risk (RR) of skin cancer occurrence for “outdoor” and “mixed indoor/outdoor” workers, respectively, compared to “indoor” workers.
Results
The risk of BCC was substantially elevated in male (RR, 2.9; 95% CI, 2.2–3.9) and female (RR, 2.7; 95% CI, 1.8–4.1) outdoor workers compared to male and female indoor workers, respectively. We also found an elevated risk of similar magnitude for SCC in male (RR, 2.5; 95% CI, 1.4–4.7) and female (RR, 3.6; 95% CI, 1.6–8.1) outdoor workers compared to male and female indoor workers, respectively. CMM risk was not significantly associated with outdoor work.
Conclusion
Our study confirms previous reports on the increased risk of BCC and SCC in outdoor workers compared to indoor workers.

Keywords

Authors Rafnsson V, Hrafnkelsson J, Tulinius H

Report Name Incidence of cancer among commercial airline pilots

Publication Occup Environ Med

Issue-page numbers 57:175–179.doi:10.1136/oem.57.3.175 PMID:10810099

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1739925/

Abstract

OBJECTIVES—To describe the cancer pattern in a cohort of commercial pilots by follow up through the Icelandic Cancer Registry.
METHODS—This is a retrospective cohort study of 458 pilots with emphasis on subcohort working for an airline operating on international routes. A computerised file of the cohort was record linked to the Cancer Registry by making use of personal identification numbers. Expected numbers of cancer cases were calculated on the basis of number of person-years and incidences of cancer at specific sites for men provided by the Cancer Registry. Numbers of separate analyses were made according to different exposure variables.
RESULTS—The standardised incidence ratio (SIR) for all cancers was 0.97 (95% confidence interval (95% CI) 0.62 to 1.46) in the total cohort and 1.16 (95% CI 0.70 to 1.81) among those operating on international routes. The SIR for malignant melanoma of the skin was 10.20, 95% CI 3.29 to 23.81 in the total cohort and 15.63, 95% CI 5.04 to 36.46 in the restricted cohort. Analyses according to number of block-hours and radiation dose showed that malignant melanomas were found in the subgroups with highest exposure estimates, the SIRs were 13.04 and 28.57 respectively. The SIR was 25.00 for malignant melanoma among those who had been flying over five time zones.
CONCLUSIONS—The study shows a high occurrence of malignant melanoma among pilots. It is open to discussion what role exposure of cosmic radiation, numbers of block-hours flown, or lifestyle factors—such as possible excessive sunbathing—play in the aetiology of cancer among pilots. This calls for further and more powerful studies. The excess of malignant melanoma among those flying over five time zones suggests that the importance of disturbance of the circadian rhythm should be taken into consideration in future studies.

Keywords cancer registry; malignant melanoma of the skin; cosmic radiation; block-hours; time zones

Authors Rafnsson V, Sulem P, Tulinius H, Hrafnkelsson J

Report Name Breast cancer risk in airline cabin attendants: a nested case-control study in Iceland

Publication Occup Environ Med

Issue-page numbers 60:807–809.doi:10.1136/oem.60.11.807 PMID:14573709

URL http://oem.bmj.com/content/60/11/807.abstract

Abstract

Aims: To investigate whether length of employment as a cabin attendant was related to breast cancer risk, when adjusted for reproductive factors.

Methods: Age matched case-control study nested in a cohort of cabin attendants. The cases were found from a nationwide cancer registry (followed up to end of year 2000) and the reproductive factors (age at first childbirth and number of children) from a registry of childbirth, in both instances by record linkage with the cabin attendants' identification numbers. The employment time of the cabin attendants at the airline companies and the reproductive factors had been systematically recorded prior to the diagnosis of breast cancer in the cohort. A total of 35 breast cancer cases and 140 age matched controls selected from a cohort of 1532 female cabin attendants were included in the study.

Results: The matched odds ratio from conditional logistic regression of breast cancer risk among cases and controls of cabin attendants was 5.24 (95% CI 1.58 to 17.38) for those who had five or more years of employment before 1971 compared with those with less than five years of employment before 1971, adjusted for age at first childbirth and length of employment from 1971 or later.

Conclusions: The association between length of employment and risk of breast cancer, adjusted for reproductive factors, indicates that occupational factors may be an important cause of breast cancer among cabin attendants; the association is compatible with a long induction period.

Keywords

Authors Rafnsson V, Tulinius H, Jónasson JG, Hrafnkelsson J

Report Name Risk of breast cancer in female flight attendants: a population-based study (Iceland)

Publication Cancer Causes Control

Issue-page numbers 12:95–101.doi:10.1023/A:1008983416836 PMID:11246849

URL http://www.jstor.org/pss/3554148

Abstract

OBJECTIVES:

To study whether increased cancer risk, particularly of cancer types previously related to radiation, was found among cabin attendants, using employment time as a surrogate of exposure to cosmic radiation.
METHODS:

A cohort of 1690 cabin attendants, 158 men and 1532 women from the Icelandic Cabin Crew Association and two airline companies in Iceland, was established. Cancer sites were ascertained between 1955 and 1997 by follow-up in a cancer registry. The personal identification number of each subject was used in record linkage to population-based registers containing vital and emigration status, reproductive factors and histologically verified cancer diagnosis. Standardized incidence rates (SIR) of different cancer sites in relation to employment time and year of hiring were calculated, as well as predictive values of breast cancer risk for evaluating possible confounding due to reproductive factors.
RESULTS:

The total number of person-years was 27,148. Among the women, 64 cancers were observed whereas 51.63 were expected (SIR 1.2, 95% CI 1.0-1.6), and significantly increased risk for malignant melanoma (SIR 3.0, 95% CI 1.2-6.2) was found. Significantly increased risks of overall cancers (SIR 1.3, 95% CI 1.0-1.8) and breast cancer (SIR 1.6, 95% CI 1.0-2.4) were observed among the female cabin attendants when 15 years lag time was applied. Those hired in 1971 or later had the heaviest exposure to cosmic radiation at a young age and had significantly increased risk of overall cancer (SIR 2.8, 95% CI 1.4-4.9) and breast cancer (SIR 4.1, 95% CI 1.7-8.5). Predictive values calculated on the basis of reproductive factors among the cabin attendants and the population, and risk of breast cancer were 1.0 for parous vs. nulliparous, 1.0 for number of children, and 1.1 for age at birth of first child.
CONCLUSION:

The increased risk of breast cancer and malignant melanoma among cabin attendants seems to be occupationally related. The part played by occupational exposures, i.e. cosmic radiation, disturbance of the circadian rhythm, and electromagnetic fields or combination of these factors in the etiology of breast cancer among the cabin crew, is still a puzzle as confounding due to parity appears to be ruled out. The relationship between the sunbathing habits of the cabin crew and the increased risk of malignant melanoma needs to be clarified. There is also an urgent need to elucidate the importance of these findings for today's aviation.

Keywords

Raghavendra V, Singh V, Kulkarni SK, Agrewala JN **Year** 2001

Authors Raghavendra V, Singh V, Kulkarni SK, Agrewala JN

Report Name Melatonin enhances Th2 cell mediated immune responses: lack of sensitivity to reversal by naltrexone or benzodiazepine receptor antagonists

Publication Mol Cell Biochem

Issue-page numbers 221:57–62 doi:10.1023/A:1010968611716. PMID:11506187

URL http://www.springerlink.com/content/k272048720323787/

Abstract Chronic administration of melatonin for 5 days to antigen-primed mice increased the production of pro-inflammatory cytokine ILdash10 but decreased the secretion of antidashinflammatory cytokine TNF-agr. These results further confirm that melatonin activates Th2dashlike immune response. Whether melatonindashmediated Th2 response is dependent on opioid or central and peripheral benzodiazepine receptors was also examined. Hence, melatonin was administered to antigen-sensitised mice with either naltrexone (a mgr opioid receptor antagonist) or flumazenil (a central benzodiazepine receptor antagonist) or PK11195 (a peripheral benzoidiazepine receptor antagonist). No significant difference in melatonin-induced Th2 cell response was observed by naltrexone, flumazenil or PK11195 treatment. These findings suggest that the Th2 cell response induced by melatonin in antigen sensitised mice neither dependent on endogenous opioid system nor is modulated through the central or peripheral benzodiazepine receptors.

Keywords

Raghavendra V, Singh V, Shaji AV et al. **Year** 2001

Authors Raghavendra V, Singh V, Shaji AV et al.

Report Name Melatonin provides signal 3 to unprimed CD4(+) T cells but failed to stimulate LPS primed B cells

Publication Clin Exp Immunol

Issue-page numbers 124:414–422 doi:10.1046/j.1365-2249.2001.01519.x. PMID:11472402

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2249.2001.01519.x/abstract

Abstract Growing evidence has supported the conclusion that melatonin, a pineal hormone, modulates the immune function. In our previous study, we evaluated in vivo the potential role of melatonin in the regulation of the antigen specific T and B cells. In the present study, we observe that melatonin down-regulated the expression of the co-stimulatory molecule B7-1 but not B7-2 on macrophages. Further, melatonin encouraged the proliferation of anti-CD3 antibody activated CD4+ T cells only in the presence of antigen-presenting cells and promoted the production of Th2-like cytokines. Furthermore, it failed to influence the activity of B cells in a T-independent manner. Melatonin suppressed the release of TNF-α by LPS or IFN-γ activated macrophages but failed to inhibit nitric oxide (NO) release. Thus the study shows that melatonin can engineer the growth of unprimed CD4+ T cells if both the signals are provided by antigen-presenting cells. However, it could not regulate the function of B cells.

Keywords B cells and macrophages; CD4+ T cells; melatonin; unprimed Th1 and Th2 cells

Rahman SA, Marcu S, Shapiro CM, et al. **Year** 2011

Authors Shadab A. Rahman, Shai Marcu, Colin M. Shapiro, Theodore J. Brown, Robert F. Casper

Report Name Spectral modulation attenuates molecular, endocrine and neurobehavioral disruption induced by nocturnal light exposure

Publication AJP - Endo

Issue-page numbers March 2011 vol. 300 no. 3 E518-E527

URL http://ajpendo.physiology.org/content/300/3/E518?cited-by=yes&legid=ajpendo;300/3/E518

Abstract

The human eye serves distinctly dual roles in image forming (IF) and non-image-forming (NIF) responses when exposed to light. Whereas IF responses mediate vision, the NIF responses affect various molecular, neuroendocrine, and neurobehavioral variables. NIF responses can have acute and circadian phase-shifting effects on physiological variables. Both the acute and phase-shifting effects induced by photic stimuli demonstrate short-wavelength sensitivity peaking ≈450–480 nm. In the current study, we examined the molecular, neuroendocrine, and neurobehavioral effects of completely filtering (0% transmission) all short wavelengths <480 nm and all short wavelengths <460 nm or partially filtering (~30% transmission) <480 nm from polychromatic white light exposure between 2000 and 0800 in healthy individuals. Filtering short wavelengths <480 nm prevented nocturnal light-induced suppression of melatonin secretion, increased cortisol secretion, and disrupted peripheral clock gene expression. Furthermore, subjective alertness, mood, and errors on an objective vigilance task were significantly less impaired at 0800 by filtering wavelengths <480 nm compared with unfiltered nocturnal light exposure. These changes were not associated with significantly increased sleepiness or fatigue compared with unfiltered light exposure. The changes in molecular, endocrine, and neurobehavioral processes were not significantly improved by completely filtering <460 nm or partially filtering <480 nm compared with unfiltered nocturnal light exposure. Repeated light-dark cycle alterations as in rotating nightshifts can disrupt circadian rhythms and induce health disorders. The current data suggest that spectral modulation may provide an effective method of regulating the effects of light on physiological processes.

Keywords circadian rhythms, short-wavelength light, melatonin, cortisol, alertness, mood, sleepiness

Rai S, Haldar C **Year** 2003

Authors Rai S, Haldar C

Report Name Pineal control of immune status and hematological changes in blood and bone marrow of male squirrels (Funambulus pennanti) during their reproductively active phase

Publication Comp Biochem Physiol C Toxicol Pharmacol

Issue-page numbers 136:319–328 doi:10.1016/j.cca.2003.10.008. PMID:15012903

URL http://www.ncbi.nlm.nih.gov/pubmed/15012903

Abstract In addition to pineal control of reproduction in seasonal breeders, melatonin is also known to influence various immune parameters. In the present experiment, we assessed the effect of exogenous melatonin treatment on different hematological parameters of peripheral blood and bone marrow cells, together with histological observations of spleen and thymus blastogenic response and stimulation ratio, and hormonal assays (melatonin and testosterone) of Indian palm squirrel (Funambulus pennanti) during their reproductively active phase when endogenous melatonin levels are low. Daily subcutaneous injection of melatonin (25 microg/100 g body mass.) at 17.30-18.00 h to adult male squirrels for 60 consecutive days during May-June significantly increased the lymphocyte count of blood and bone marrow and the blastogenic response/percent stimulation ratio of spleen and thymus. Histological observation showed densely packed thymocytes and splenocytes. During this period, peripheral testosterone level was high and melatonin was low establishing an inverse relationship as noted earlier for this squirrel. In pinealectomized squirrels, decreased total leukocyte count and percent lymphocyte count in peripheral blood and bone marrow, along with a decreased cell density in spleen and thymus was observed histologically. Further, melatonin treatment of pinealectomized squirrels resulted in restoration of the immune parameters in line with a normal control level. We suggest that during the reproductively active period of male Indian palm squirrels the lymphoid organs were sensitive to melatonin; hence, the exogenous melatonin treatment had an immuno-enhancing effect.

Keywords

Raloff J **Year** 1998

Authors Raloff, J.

Report Name Does light have a dark side? Nighttime illumination might elevate cancer risk

Publication Science News Online

Issue-page numbers Week of Oct. 17, 1998; Vol. 154, No. 16

URL http://www.sciencenews.org/sn_arc98/10_17_98/19981017fob.asp

Abstract Since life began, one pattern has dominated Earth&#65533;s natural environment—a daily rhythm of intense sunlight alternating with nights of near-total darkness. As a source of heat and energy, sunlight powers a majority of the planet&#65533;s biological activities. When that light disappears, much of the world rests.

Keywords

Ralph MR, Foster RG, Davis FC, Menaker M

Year 1990

Authors Ralph MR, Foster RG, Davis FC, Menaker M

Report Name Transplanted suprachiasmatic nucleus determines circadian period

Publication Science

Issue-page numbers 247:975–978 doi:10.1126/science.2305266. PMID:2305266

URL http://www.sciencemag.org/content/247/4945/975.short

Abstract The pacemaker role of the suprachiasmatic nucleus in a mammalian circadian system was tested by neural transplantation by using a mutant strain of hamster that shows a short circadian period. Small neural grafts from the suprachiasmatic region restored circadian rhythms to arrhythmic animals whose own nucleus had been ablated. The restored rhythms always exhibited the period of the donor genotype regardless of the direction of the transplant or genotype of the host. The basic period of the overt circadian rhythm therefore is determined by cells of the suprachiasmatic region.

Keywords

Ram PT, Dai J, Yuan L et al.

Year 2002

Authors Ram PT, Dai J, Yuan L et al.

Report Name Involvement of the mt1 melatonin receptor in human breast cancer

Publication Cancer Lett

Issue-page numbers 179:141–150 doi:10.1016/S0304-3835(01)00873-4. PMID:11888668

URL http://www.sciencedirect.com/science/article/pii/S0304383501008734

Abstract Two putative melatonin receptors have been described including the cell surface G-protein-linked receptors, mt1 and MT2, and the nuclear retinoic orphan receptor alpha (RORα). The mt1 receptor, but not the MT2 receptor, is expressed in human breast tumor cell lines, and melatonin-induced growth suppression can be mimicked by the mt1 and MT2 agonist, AMMTC, and blocked by the antagonist, CBPT. RORα receptors are also expressed in MCF-7 breast cancer cells and the putative RORα agonist CPG-52608 inhibits MCF-7 cell growth but with a very different dose-response than melatonin. Finally, melatonin and AMMTC, but not CPG-52608, can repress RORα transcriptional activity in MCF-7 cells.

Keywords Melatonin; Breast cancer; mt1 receptors; Retinoic orphan receptor alpha

Ramírez F, Fowell DJ, Puklavec M et al. | ***Year*** 1996

Authors F Ramirez, DJ Fowell, M Puklavec, S Simmonds and D Mason

Report Name Glucocorticoids promote a TH2 cytokine response by CD4+ T cells in vitro

Publication J Immunol

Issue-page numbers 156:2406–2412. PMID:8786298

URL http://www.jimmunol.org/content/156/7/2406.abstract

Abstract Purified rat CD4+ T cells were activated in vitro in the presence or absence of the glucocorticoid dexamethasone. They were then expanded in IL-2 and subsequently restimulated, this time in the absence of the hormone. The results indicate that the exposure of the cells to dexamethasone in the primary stimulation changed the cytokine synthesis induced by the secondary stimulation. The mRNA levels for IL-4, IL-10, and IL-13 were all increased by the pretreatment, whereas synthesis of IFN-gamma and TNF-alpha was diminished. Further studies in which IL-4 was used together with dexamethasone showed that the cytokine potentiated the effect of the hormone. These data suggest that the neuroendocrine system can influence the cytokine response to pathogens and autoantigens in a way that favors Th2-type reactions. There are similar implications for therapy with glucocorticoids, and these drugs may be expected to have long term immunologic effects as well as short- lived immunosuppressive ones. The production of a mouse mAb, MRC-OX81, against rat IL-4 is also described.

Keywords

Rana S, Mahmood S | ***Year*** 2010

Authors Rana S, Mahmood S.

Report Name Circadian rhythm and its role in malignancy

Publication Journal of Circadian Rhythms

Issue-page numbers 2010, 8:3 doi:10.1186/1740-3391-8-3

URL http://www.jcircadianrhythms.com/content/8/1/3

Abstract Circadian rhythms are daily oscillations of multiple biological processes directed by endogenous clocks. The circadian timing system comprises peripheral oscillators located in most tissues of the body and a central pacemaker located in the suprachiasmatic nucleus (SCN) of the hypothalamus. Circadian genes and the proteins produced by these genes constitute the molecular components of the circadian oscillator which form positive/negative feedback loops and generate circadian rhythms. The circadian regulation extends beyond clock genes to involve various clock-controlled genes (CCGs) including various cell cycle genes. Aberrant expression of circadian clock genes could have important consequences on the transactivation of downstream targets that control the cell cycle and on the ability of cells to undergo apoptosis. This may lead to genomic instability and accelerated cellular proliferation potentially promoting carcinogenesis. Different lines of evidence in mice and humans suggest that cancer may be a circadian-related disorder. The genetic or functional disruption of the molecular circadian clock has been found in various cancers including breast, ovarian, endometrial, prostate and hematological cancers. The acquisition of current data in circadian clock mechanism may help chronotherapy, which takes into consideration the biological time to improve treatments by devising new therapeutic approaches for treating circadian-related disorders, especially cancer.

Keywords

Rato AG, Pedrero JG, Martinez MA et al. **Year** 1999

Authors AVELINA GARCÍA RATO*1, JUANA GARCÍA PEDRERO*, M. ARÁNTZAZU MARTÍNEZ†, BEATRIZ DEL RIO, PEDRO S. LAZO* and SOFÍA RAMOS*

Report Name Melatonin blocks the activation of estrogen receptor for DNA binding

Publication FASEB J

Issue-page numbers 13:857–868. PMID:10224229

URL http://www.fasebj.org/content/13/8/857

Abstract The present study shows that melatonin prevents, within the first cell cycle, the estradiol-induced growth of synchronized MCF7 breast cancer cells. By using nuclear extracts of these cells, we first examined the binding of estradiol–estrogen receptor complexes to estrogen-responsive elements and found that the addition of estradiol to whole cells activates the binding of the estrogen receptor to DNA whereas melatonin blocks this interaction. By contrast, melatonin neither affects the binding of estradiol to its receptor nor the receptor nuclear localization. Moreover, we also show that addition of estradiol to nuclear extracts stimulates the binding of estrogen receptor to DNA, but this activation is also prevented by melatonin. The inhibitory effect caused by melatonin is saturable at nanomolar concentrations and does not appear to be mediated by RZR nuclear receptors. The effect is also specific, since indol derivatives do not cause significant inhibition. Furthermore, we provide evidence that melatonin does not interact with the estrogen receptor in the absence of estradiol. Together, these results demonstrate that melatonin interferes with the activation of estrogen receptor by estradiol. The effect of melatonin suggests the presence of a receptor that, upon melatonin addition, destabilizes the binding of the estradiol–estrogen receptor complex to the estrogen responsive element.—Rato, A. G., Pedrero, J. G., Martínez, M. A., del Rio, B., Lazo, P. S., Ramos, S. Melatonin blocks the activation of estrogen receptor for DNA binding.

Keywords

Rea MS, Brons JA, Figueiro MG — ***Year*** 2011

Authors Mark S. Rea, Jennifer A. Brons and Mariana G. Figueiro

Report Name Measurements of Light at Night (LAN) for a Sample of Female School Teachers

Publication Chronobiology International

Issue-page numbers 28:8, 673-680

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.602198

Abstract Epidemiological studies have shown an association between rotating shiftwork and breast cancer (BC) risk. Recently, light at night (LAN) measured by satellite photometry and by self-reports of bedroom brightness has been shown to be associated with BC risk, irrespective of shiftwork history. Importance has been placed on these associations because retinal light exposures at night can suppress the hormone melatonin and/or disrupt circadian entrainment to the local 24-h light-dark cycle. The present study examined whether it was valid to use satellite photometry and self-reports of brightness to characterize light, as it might stimulate the circadian system and thereby affect BC incidence. Calibrated photometric measurements were made at the bedroom windows and in the bedrooms of a sample of female school teachers, who worked regular dayshifts and lived in a variety of satellite-measured sky brightness categories. The light levels at both locations were usually very low and were independent of the amount of satellite-measured light. Calibrated photometric measurements were also obtained at the corneas of these female school teachers together with calibrated accelerometer measurements for seven consecutive days and evenings. Based upon these personal light exposure and activity measurements, the female teachers who participated in this study did not have disrupted light-dark cycles like those associated with rotating shiftworkers who do exhibit a higher risk for BC. Rather, this sample of female school teachers had 24-h light-dark and activity rest patterns very much like those experienced by dayshift nurses examined in an earlier study who are not at an elevated risk of BC. No relationship was found between the amount of satellite-measured light levels and the 24-h light-dark patterns these women experienced. It was concluded from the present study that satellite photometry is unrelated to personal light exposures as they might affect melatonin suppression and/or circadian disruption. More generally, photometric devices calibrated in terms of the operational characteristics of the human circadian system must be used to meaningfully link LAN and BC incidence.

Keywords Breast cancer, Circadian light, Circadian light levels, Light pollution, Melatonin

Rea MS, Figueiro MG, Bierman A, Hamner R — ***Year*** 2011

Authors M. S. Rea, M. G. Figueiro, A. Bierman, R. Hamner

Report Name Modeling the spectral sensitivity of the human circadian system

Publication Lighting Research and Technology

Issue-page numbers December 14, 2011, doi: 10.1177/1477153511430474

URL http://lrt.sagepub.com/content/early/2011/12/14/1477153511430474.abstract

Abstract It is now well established that the spectral, spatial, temporal and absolute sensitivities of the human circadian system are very different from those of the human visual system. Although qualitative comparisons between the human circadian and visual systems can be made, there still remains some uncertainty in quantitatively predicting exactly how the circadian system will respond to different light exposures reaching the retina. This paper discusses attempts to model the spectral sensitivity of the circadian system. Each of the models discussed here varies in terms of its complexity and its consideration of retinal neuroanatomy and neurophysiology. Future testing to validate or improve any of these computational models will require a targeted hypothesis, as well as a suitably high level of experimental control before one model can be rejected in favour of another. Until specific hypotheses are formulated and tested, it would be premature to recommend international acceptance of any model or system of circadian photometry.

Keywords

Reaven GM, Lithell H, Landsberg L | *Year* 1996

Authors Reaven GM, Lithell H, Landsberg L

Report Name Hypertension and associated metabolic abnormalities– the role of insulin resistance and the sympathoadrenal system

Publication N Engl J Med

Issue-page numbers 334:374–381 doi:10.1056/NEJM199602083340607. PMID:8538710

URL Hypertension and associated metabolic abnormalities– the role of insulin resistance and the sympathoadrenal system

Abstract N/A

Keywords

Rechtschaffen A, Bergmann BM | *Year* 1995

Authors Rechtschaffen A, Bergmann BM

Report Name Sleep deprivation in the rat by the disk-over-water method

Publication Behav Brain Res

Issue-page numbers 69:55–63 doi:10.1016/0166-4328(95)00020-T. PMID:7546318

URL http://www.mendeley.com/research/sleep-deprivation-in-the-rat-by-the-diskoverwater-method/

Abstract Chronic sleep deprivation may be required to reveal the most serious physiological consequences of sleep loss, but it usually requires strong stimulation which can obscure the interpretation of effects. The disk-over-water method permits chronic sleep deprivation of rats with gentle physical stimulation that can be equally applied to yoked control rats. A series of studies with this method has revealed little or no pathology in the control rats. The deprived rats show a reliable syndrome that includes temperature changes (which vary with the sleep stages that are lost); heat seeking behavior; increased food intake; weight loss; increased metabolic rate; increased plasma norepinephrine; decreased plasma thyroxine; an increased triiodothyronine-thyroxine ratio; and an increase of an enzyme which mediates thermogenesis by brown adipose tissue. The temperature changes are attributable to excessive heat loss and an elevated thermoregulatory setpoint, both of which increase thermoregulatory load, and the other changes are interpretable as responses to this increased load. This pattern indicates that sleep serves a thermoregulatory function in the rat. The sleep deprived rats also show stereotypic ulcerative and hyperkeratotic lesions localized to the tail and plantar surfaces of the paws, and they die within a matter of weeks; the mediation of these changes is unresolved.

Keywords

Reddy AB, Field MD, Maywood ES, Hastings MH **Year** 2002

Authors Reddy AB, Field MD, Maywood ES, Hastings MH

Report Name Differential resynchronisation of circadian clock gene expression within the suprachiasmatic nuclei of mice subjected to experimental jet lag

Publication J Neurosci

Issue-page numbers 22:7326–7330. PMID:12196553

URL http://www.jneurosci.org/content/22/17/7326.short

Abstract Disruption of the circadian timing system arising from travel between time zones ("jet lag") and rotational shift work impairs mental and physical performance and severely compromises long-term health. Circadian disruption is more severe during adaptation to advances in local time, because the circadian clock takes much longer to phase advance than delay. The recent identification of mammalian circadian clock genes now makes it possible to examine time zone adjustments from the perspective of molecular events within the suprachiasmatic nucleus (SCN), the principal circadian oscillator. Current models of the clockwork posit interlocked transcriptional/post-translational feedback loops based on the light-sensitive Period (Per) genes and the Cryptochrome (Cry) genes, which are indirectly regulated by light. We show that circadian cycles ofmPer expression in the mouse SCN react rapidly to an advance in the lighting schedule, whereas rhythmic mCry1expression advances more slowly, in parallel to the gradual resetting of the activity–rest cycle. In contrast, during a delay in local time the mPer and mCry cycles react rapidly, completing the 6 hr shift together by the second cycle, in parallel with the activity–rest cycle. These results reveal the potential for dissociation of mPer and mCry expression within the central oscillator during circadian resetting and a differential molecular response of the clock during advance and delay resetting. They highlight the indirect photic regulation ofmCry1 as a potentially rate-limiting factor in behavioral adjustment to time zone transitions.

Keywords entrainment, period, cryptochrome, circadian, suprachiasmatic nuclei, jet lag

Reddy AB, O'Neill JS **Year** 2010

Authors Reddy AB, O'Neill JS.

Report Name Healthy clocks, healthy body, healthy mind

Publication Trends Cell Biol

Issue-page numbers 2010 Jan;20(1):36-44. Epub 2009 Nov 16.

URL http://www.ncbi.nlm.nih.gov/pubmed/19926479

Abstract Circadian rhythms permeate mammalian biology. They are manifested in the temporal organisation of behavioural, physiological, cellular and neuronal processes. Whereas it has been shown recently that these approximately 24-hour cycles are intrinsic to the cell and persist in vitro, internal synchrony in mammals is largely governed by the hypothalamic suprachiasmatic nuclei that facilitate anticipation of, and adaptation to, the solar cycle. Our timekeeping mechanism is deeply embedded in cell function and is modelled as a network of transcriptional and/or post-translational feedback loops. Concurrent with this, we are beginning to understand how this ancient timekeeper interacts with myriad cell systems, including signal transduction cascades and the cell cycle, and thus impacts on disease. An exemplary area where this knowledge is rapidly expanding and contributing to novel therapies is cancer, where the Period genes have been identified as tumour suppressors. In more complex disorders, where aetiology remains controversial, interactions with the clockwork are only now starting to be appreciated

Keywords

Reddy AB, Wong GKY, O'Neill J et al. **Year** 2005

Authors Reddy AB, Wong GKY, O'Neill J et al.

Report Name Circadian clocks: neural and peripheral pacemakers that impact upon the cell division cycle

Publication Mutat Res

Issue-page numbers 574:76–91. PMID:15914209

URL http://www.sciencedirect.com/science/article/pii/S0027510705000916

Abstract Circadian clocks are pervasive entities that allow organisms to maintain rhythms of approximately 24 h, independently of external cues, thereby adapting them to the solar cycle. Recent studies have shown that molecular circadian clocks are important for the proper orchestration of the cell division cycle. For the first time, this provides a framework to understand the interactions between these two evolutionarily linked timers. Here we review the current model of the circadian clock and the molecular methods that can be used to investigate its function. We then map out links to the cell cycle at the cellular level. Furthermore, we review recent progress that has linked dysfunction of the clockwork with the pathogenesis of cancer. Disruption of circadian timing (as occurs in jet-lag, shift work and dementia) thus has far reaching consequences for normal regulation of cell division. The implications of this for the health of a "24-h society" are apparent.

Keywords Cell cycle; Cell division; Circadian; Clock; Cryptochrome; Cyclin D1; E-box; Luciferase; Per2; Period; Suprachiasmatic; Wee1

Reddy P, Zehring WA, Wheeler DA et al. **Year** 1984

Authors Pranhitha Reddy*, William A. Zehring†, David A. Wheeler†, Vincent Pirrotta‡, Christopher Hadfield‡, Jeffrey C. Hall† and Michael Rosbash

Report Name Molecular analysis of the period locus in Drosophila melanogaster and identification of a transcript involved in biological rhythms

Publication Cell

Issue-page numbers 38:701–710 doi:10.1016/0092-8674(84)90265-4. PMID:6435882

URL http://www.cell.com/abstract/0092-8674%2884%2990265-4

Abstract We have isolated and analyzed DNA sequences encompassing the period (per) locus of Drosophila melanogaster. The location of this clock gene was delimited by the molecular mapping of chromosome aberrations at or very near the per locus. At least five RNAs are transcribed from this region. One of these transcripts, a 0.9 kb species, is strongly implicated in per's control of biological rhythms. Two independently isolated arrhythmic mutations at the per locus dramatically reduce the level of this transcript. Furthermore, the level of the 0.9 kb transcript is strongly modulated during a light/dark cycle. We discuss evidence, from previously reported genetic and phenotypic analysis of per's function, suggesting that this region may be complex and that several gene products from the per region, including this 0.9 kb transcript, may be involved in the different aspects of normal rhythmicity influenced by this clock gene.

Keywords

Redlin U

Year 2001

Authors Uwe Redlin

Report Name NEURAL BASIS AND BIOLOGICAL FUNCTION OF MASKING BY LIGHT IN MAMMALS: SUPPRESSION OF MELATONIN AND LOCOMOTOR ACTIVITY

Publication Chronobiology International

Issue-page numbers Vol. 18, No. 5 , Pages 737-758

URL http://informahealthcare.com/doi/abs/10.1081/CBI-100107511

Abstract Light influences mammalian circadian rhythms in two different ways: (1) It entrains endogenous oscillators (clocks), which regulate physiology and behavior; and (2) it affects directly and often immediately physiology and behavior (these effects are also referred to as masking). Masking effects of light on pineal melatonin, locomotor activity, and the sleep-wake cycle in mammals and man are reviewed. They seem to represent a universal response in this group. The review reveals that the mechanism of photic inhibition of melatonin is fairly well understood, whereas only little is known about the influence of light on other circadian rhythm outputs, such as locomotor activity.

Keywords Diurnal, Irradiance detection, Light, Locomotor activity, Masking, Melatonin, Nocturnal, Photoreception

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Reed VA

Year 2011

Authors Virginia A. Reed

Report Name Shift Work, Light at Night, and the Risk of Breast Cancer: A Guide to Administrative Action for Health Care Institutions

Publication AAOHN Journal

Issue-page numbers January 2011 - Volume 59 · Issue 1: 37-45 DOI: 10.3928/08910162-20101216-01

URL http://www.slackjournals.com/article.aspx?rid=78886

Abstract Studies of the effect of shift work have identified several negative health outcomes, most notably breast cancer. Disruption of circadian rhythm by exposure to light at night has been identified as the mechanism likely responsible for this outcome. This article recommends that health care institutions work with occupational health nurses to develop and implement hazard communication and policies concerning shift work, exposure to light at night, and increased risk for negative health outcomes, particularly breast cancer.

Keywords

Year 1968

Authors Regan D.

Report Name A high frequency mechanism which underlies visual evoked potentials

Publication Electroencephalography and Clinical Neurophysiology

Issue-page numbers Volume 25, Issue 3, September 1968, Pages 231-237

URL http://www.sciencedirect.com/science/article/pii/0013469468900205

Abstract

Dynamic steady-state scalp potentials were evoked in man by sinusoidally modulated light. An averaging computer was used to obtain average response waves; the amplitude and phase of individual harmonic components of the waves were measured with a cross-correlator.

Evidence was found for a high frequency system which could be distinguished from a lower frequency system. The peak amplitude of the high frequency responses occurred at around 45–55 c/sec, and their apparent latency was about 77 msec (61 msec after correction for phase shifts). The lower frequency responses had an apparent latency of about 120 msec (about 100 msec after correction for phase shifts) and could occur simultaneously with high frequency responses.

The amplitude of the high frequency responses was less dependent on stimulus intensity than that of the lower frequency responses, but was more dependent on field size.

Evidence was found that the generators of the two types of response had different spatial distributions or orientations in the brain.

The high frequency responses were generally in accord with Spekreijse's theoretical short latency system.

The amplitude of the high frequency evoked responses increased as stimulus frequency was increased near and beyond the point of fusion of perceived flicker; some possible implications of this are discussed.

Keywords

Reick M, Garcia JA, Dudley C, McKnight SL — *Year* 2001

Authors Reick M, Garcia JA, Dudley C, McKnight SL

Report Name NPAS2: an analog of clock operative in the mammalian forebrain

Publication Science

Issue-page numbers 293:506–509 doi:10.1126/science.1060699. PMID:11441147

URL http://www.sciencemag.org/content/293/5529/506.abstract

Abstract Neuronal PAS domain protein 2 (NPAS2) is a transcription factor expressed primarily in the mammalian forebrain. NPAS2 is highly related in primary amino acid sequence to Clock, a transcription factor expressed in the suprachiasmatic nucleus that heterodimerizes with BMAL1 and regulates circadian rhythm. To investigate the biological role of NPAS2, we prepared a neuroblastoma cell line capable of conditional induction of the NPAS2:BMAL1 heterodimer and identified putative target genes by representational difference analysis, DNA microarrays, and Northern blotting. Coinduction of NPAS2 and BMAL1 activated transcription of the endogenous Per1,Per2, and Cry1 genes, which encode negatively activating components of the circadian regulatory apparatus, and repressed transcription of the endogenous BMAL1 gene. Analysis of the frontal cortex of wild-type mice kept in a 24-hour light-dark cycle revealed that Per1, Per2, andCry1 mRNA levels were elevated during darkness and reduced during light, whereas BMAL1 mRNA displayed the opposite pattern. In situ hybridization assays of mice kept in constant darkness revealed that Per2 mRNA abundance did not oscillate as a function of the circadian cycle in NPAS2-deficient mice. Thus, NPAS2 likely functions as part of a molecular clock operative in the mammalian forebrain.

Keywords

Reilly JJ, Armstrong J, Dorosty AR et al — *Year* 2005

Authors Reilly JJ, Armstrong J, Dorosty AR et al

Report Name Avon Longitudinal Study of Parents and Children Study Team (2005). Early life risk factors for obesity in childhood: cohort study

Publication BMJ

Issue-page numbers 330:1357–1364 doi:10.1136/bmj.38470.670903.E0. PMID:15908441

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC558282/

Abstract Objective To identify risk factors in early life (up to 3 years of age) for obesity in children in the United Kingdom.
Design Prospective cohort study.
Setting Avon longitudinal study of parents and children, United Kingdom.
Participants 8234 children in cohort aged 7 years and a subsample of 909 children (children in focus) with data on additional early growth related risk factors for obesity.
Main outcome measures Obesity at age 7 years, defined as a body mass index 3 95th centile relative to reference data for the UK population in 1990.
Results Eight of 25 putative risk factors were associated with a risk of obesity in the final models: parental obesity (both parents: adjusted odds ratio, 10.44, 95% confidence interval 5.11 to 21.32), very early (by 43 months) body mass index or adiposity rebound (15.00, 5.32 to 42.30), more than eight hours spent watching television per week at age 3 years (1.55, 1.13 to 2.12), catch-up growth (2.60, 1.09 to 6.16), standard deviation score for weight at age 8 months (3.13, 1.43 to 6.85) and 18 months (2.65, 1.25 to 5.59); weight gain in first year (1.06, 1.02 to 1.10 per 100 g increase); birth weight, per 100 g (1.05, 1.03 to 1.07); and short (< 10.5 hours) sleep duration at age 3 years (1.45, 1.10 to 1.89).
Conclusion Eight factors in early life are associated with an increased risk of obesity in childhood.

Keywords

Reinberg A, Migraine C, Apfelbaum M et al. **Year** 1979

Authors Reinberg A, Migraine C, Apfelbaum M et al.

Report Name Circadian and ultradian rhythms in the feeding behaviour and nutrient intakes of oil refinery operators with shift-work every 3--4 days

Publication Diabete Metab

Issue-page numbers 5:33–41. PMID:446831

URL http://www.ncbi.nlm.nih.gov/pubmed/446831

Abstract Seven healthy adult men, five shift-workers and two non-shift-workers (from 21 to 36 years; mean = 26.4) volunteered to record what and when they ate, both at work and at home, every day, during eight consecutive weeks (Oct. - Dec. 1974). 1) All the subjects maintained the timing of main-meal (lunch and supper) during all shifts. 2) The major intake of protein and lipid was concentrated on the two main meals during all shifts. 3) Only the pattern of carbohydrate intake was modified by the shift-work: e.g. night-shift is associated with nibbling behaviour. 4) However, shift-work and in particular the occurence of nibbling behaviour did not result in change either in the mean 24 h caloric intake, or in the percentage of protein calories. 5) The comparison between the constancy of the timing of major meals and the shift of the timing of circadian rhythm acrophases of the 5 shift-workers leads to conclude that meal timing had a poor synchronizing effect, if any.

Keywords

Reitav J **Year** 2012

Authors Jaan Reitav

Report Name Managing Sleep Problems Among Cardiac Patients

Publication Behavioral Science

Issue-page numbers 2012, Part 2, 281-317, DOI: 10.1007/978-1-4419-5650-7_13

URL http://www.springerlink.com/content/w3672837gwh24266/

Abstract Sleep problems are common among cardiac patients, and treating them is important to both risk reduction and quality of life. This chapter will review the evidence supporting this statement and educate the cardiac frontline health-care provider (physician, psychologist, nurse) about how to manage these problems.

Keywords

Reiter RJ

Year 2001

Authors Russel J. Reiter

Report Name Reactive oxygen species, DNA damage and carcinogenesis

Publication In: Bartsch C, Bartsch H, Blask DE, et al., Eds. Pineal Gland and Cancer

Issue-page numbers Neuroimmunoendocrine Mechanisms in Malignancy. Heidelberg: Springer. pp. 442–455

URL N/A

Abstract N/A

Keywords

Reiter RJ

Year 1991

Authors Russel J. Reiter

Report Name Pineal melatonin: cell biology of its synthesis and of its physiological interactions

Publication Endocr Rev

Issue-page numbers 12:151–180 doi:10.1210/edrv-12-2-151. PMID:1649044

URL http://edrv.endojournals.org/content/12/2/151.abstract

Abstract

I. Introduction UNTIL 35 yr ago, most scientists did not take research on the pineal gland seriously. The decade beginning in 1956, however, provided several discoveries that laid the foundation for what has become a very active area of investigation. These important early observations included the findings that, 1), the physiological activity of the pineal is influenced by the photoperiodic environment (1–5); 2), the gland contains a substance, N-acetyl-5-methoxytryptamine or melatonin, which has obvious endocrine capabilities (6, 7); 3), the function of the reproductive system in photoperiodically dependent rodents is inextricably linked to the physiology of the pineal gland (5, 8, 9); 4), the sympathetic innervation to the pineal is required for the gland to maintain its biosynthetic and endocrine activities (10, 11); and 5), the pineal gland can be rapidly removed from rodents with minimal damage to adjacent neural structures using a specially designed trephine (12).

Since the mid 1960s, research on the pineal gland has increased exponentially, and its association with a wide variety of physiological systems has been documented (13–18). Proof that melatonin is the hormone of pineal origin that accounts for many of the endocrine manifestations of the gland, however, came somewhat later. Thus, whereas some early studies certainly suggested that melatonin had modulatory effects on the neuroendocrine- reproductive axis (19, 20), these actions were questioned when it was observed that in hamsters bearing sc placed melatonin pellets, which release the indole continuously, the ability of short day exposure and the pineal to suppress reproductive physiology was unexpectedly negated (21–23). These observations were, however, followed closely by studies showing that melatonin, administered as a single daily injection at a precise time with regard to the light-dark cycle, induced quiescence of the neuroendocrine-reproductive axis just as did short day exposure (24, 25).

Keywords

Reiter RJ

Year 1972

Authors Russel J. Reiter

Report Name Evidence for refractoriness of the pituitary-gonadal axis to the pineal gland in golden hamsters and its possible implications in annual reproductive rhythms

Publication Anat Rec

Issue-page numbers 173:365–371 doi:10.1002/ar.1091730311. PMID:5039088

URL http://onlinelibrary.wiley.com/doi/10.1002/ar.1091730311/abstract?

Abstract The testes of adult hamsters maintained in short daily photo-periods (light:dark “LD” cycles of 1:23, in hours) undergo regression within ten weeks and spontaneous regeneration within about 30 weeks. Thereafter (at least up to 80 weeks), as long as these animals are kept in short photoperiods the gonads do not experience a second atrophic response. After the 30 week period of dark exposure, if the hamsters are moved into a long photoperiodic environment (LD 14:10) for either one or ten weeks and are then returned to short photoperiods, the gonads do not involute a second time. However, if the duration of exposure to LD 14:10 is increased to 22 weeks, the return to LD 1:23 causes the gonads to degenerate. The regressive responses of the testes never occur in hamsters that have been pinealectomized indicating that the observed changes are mediated by this gland. The inability of darkness and, thus the pineal gland, to induce a second gonadal involution unless the hamsters are maintained in LD cycles of 14:10 for 22 weeks (after a 30 week period of dark exposure) may be explicable in terms of (1), a transient refractoriness of the brain to the pineal antigonadotropic principle or (2), the temporary failure of the pineal to be activated by short daily photoperiods.

Keywords

Reiter RJ

Year 1980

Authors Russel J. Reiter

Report Name The pineal and its hormones in the control of reproduction in mammals

Publication Endocr Rev

Issue-page numbers 1:109–131 doi:10.1210/edrv-1-2-109. PMID:6263600

URL http://edrv.endojournals.org/content/1/2/109.abstract

Abstract ONLY A LITTLE over a decade ago, any discussion of the function of the pineal gland included qualifying adjectives such as alleged, supposed, and putative. In the same vein, since it connoted a hormonal function, rather than referring to the pineal as a gland, the phrase pineal organ was usually employed to describe this portion of the epithalamus. However, this is no longer the case, at least in mammals. By the usual criteria in endocrinology, the pineal now fulfills all the qualifications of an organ of internal secretion.

Several major discoveries revolutionized ideas concerning the function of the pineal gland. Certainly, as noted frequently in other reviews, the isolation and identification of N-acetyl-5-methoxytryptamine (melatonin), a pineal hormone, from bovine pineal tissue by Lerner et al. (1, 2) provided a strong impetus for subsequent investigations on this sometimes exasperating organ. At least as important as this discovery, however, were the observations that light and darkness govern both the biosynthetic activity (3, 4) and endocrine capability (5, 6) of the gland. These findings provided the scientific community with a heretofore unknown handle that could be used to exploit and elucidate the functions of the pineal. Indeed, it is my conviction that the one major factor that stymied pineal research until the mid-1960s was the lack of the basic knowledge that the endocrine output of the pineal gland is determined by the photoperiod to which the experimental subjects, be they animals or man, are exposed.

Keywords

Reiter RJ

Year 1993

Authors R.J. Reiter

Report Name Electromagnetic fields and melatonin production

Publication Biomedicine & Pharmacotherapy

Issue-page numbers Volume 47, Issue 10, 1993, Pages 439-444

URL http://www.sciencedirect.com/science/article/pii/075333229390340Q

Abstract The pineal gland, which in humans is located near the anatomical center of the brain, is normally responsive to visible electromagnetic fields (ie light) since the eyes are functionally connected to the pineal gland by a series of neurons. Normally, the pineal gland produces low amounts of melatonin during the day and high amounts at night; this rhythm is reflected in the blood melatonin concentrations which are higher at night than during the day. In both man and lower mammals, their exposure to light at night is followed by a drop in pineal melatonin production and blood melatonin levels. Likewise, exposure of non-human mammals to sinusoidal electric and/or magnetic fields as well as pulsed static magnetic fields often reduces pineal melatonin production. Melatonin has many functions in the organism and any perturbation (not only electromagnetic fields) which causes levels of melatonin to be lower than normal may have significant physiological consequences. Melatonin, because it is a potent antioxidant, may provide significant protection against cancer initiation as well as promotion. However, it is premature to conclude that the alleged increased cancer risk reported in individuals living in higher than normal electromagnetic environments relate to reduced melatonin levels caused by such field exposures.

Keywords electromagnetic fields; melatonin

Reiter RJ, Acuña-Castroviejo D, Tan DX, Burkhardt S

Year 2001

Authors Reiter RJ, Acuña-Castroviejo D, Tan DX, Burkhardt S

Report Name Free radical-mediated molecular damage. Mechanisms for the protective actions of melatonin in the central nervous system

Publication Ann N Y Acad Sci

Issue-page numbers 939:200–215 doi:10.1111/j.1749-6632.2001.tb03627.x. PMID:11462772

URL http://www.mendeley.com/research/free-radicalmediated-molecular-damage-mechanisms-protective-actions-melatonin-central-nervous-system-1/

Abstract This review briefly summarizes the multiple actions by which melatonin reduces the damaging effects of free radicals and reactive oxygen and nitrogen species. It is well documented that melatonin protects macromolecules from oxidative damage in all subcellular compartments. This is consistent with the protection by melatonin of lipids and proteins, as well as both nuclear and mitochondrial DNA. Melatonin achieves this widespread protection by means of its ubiquitous actions as a direct free radical scavenger and an indirect antioxidant. Thus, melatonin directly scavenges a variety of free radicals and reactive species including the hydroxyl radical, hydrogen peroxide, singlet oxygen, nitric oxide, peroxynitrite anion, and peroxynitrous acid. Furthermore, melatonin stimulates a number of antioxidative enzymes including superoxide dismutase, glutathione peroxidase, glutathione reductase, and catalase. Additionally, melatonin experimentally enhances intracellular glutathione (another important antioxidant) levels by stimulating the rate-limiting enzyme in its synthesis, gamma-glutamylcysteine synthase. Melatonin also inhibits the proxidative enzymes nitric oxide synthase and lipoxygenase. Finally, there is evidence that melatonin stabilizes cellular membranes, thereby probably helping them resist oxidative damage. Most recently, melatonin has been shown to increase the efficiency of the electron transport chain and, as a consequence, to reduce election leakage and the generation of free radicals. These multiple actions make melatonin a potentially useful agent in the treatment of neurological disorders that have oxidative damage as part of their etiological basis.

Keywords

Reiter RJ, King TS, Richardson BA, Hurlbut EC

Year 1982

Authors R. J. Reiter, T. S. King, B. A. Richardson and E. C. Hurlbut

Report Name Studies on pineal melatonin levels in a diurnal species, the Eastern chipmunk (Tamias striatus): Effects of light at night, propranolol administration or superior cervical ganglionec

Publication Journal of Neural Transmission

Issue-page numbers Volume 54, Numbers 3-4, 275-284, DOI: 10.1007/BF01254936

URL http://www.springerlink.com/content/784041977x300602/

Abstract Five experiments were carried out on the control of melatonin levels in the pineal gland of a diurnal species, the Eastern chipmunk (Tamias striatus). We confirmed that the exposure of chipmunks to fluorescent white light of 3,981–4,304 lux during the normal dark period does not prevent the rise in pineal melatonin levels normally associated with darkness. Also, the administration of propranolol (20mg/kg) at 8 p.m. did not block the rise in pineal melatonin in animals exposed to either dark or light at night. Similarly, if chipmunks received propranolol 4 hours into the dark phase, pineal melatonin levels were not depressed 2 hours later. When animals were superior cervical ganglionectomized, however, the pineal content of melatonin remained low regardless of whether the animals were exposed to darkness or light at night. The exposure of chipmunks acutely to light at midnight (4 hours after darkness onset) had only a slight depressive effect on pineal melatonin 30 min later; by comparison, when chipmunks were acutely exposed to light at 3 a.m. (7 hours after darkness onset) daytime pineal melatonin levels were reached within 15 min after light onset. These findings in a diurnal species, the Eastern chipmunk, differ markedly when compared to previously reported observations on nocturnal laboratory rodents.

Keywords Pineal gland - melatonin - Eastern chipmunk - propranolol - superior cervical ganglionectomy - beta-adrenergic receptors

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Reiter RJ, Korkmaz A, Ma S, et al.

Year 2011

Authors Russel J. Reiter, Ahmet Korkmaz, Shuran Ma, Sergio Rosales-Corral, Dun-Xian Tan

Report Name Melatonin protection from chronic, low-level ionizing radiation

Publication Mutation Research/Reviews in Mutation Research

Issue-page numbers In Press, Uncorrected Proof - Note to users doi:10.1016/j.mrrev.2011.12.002

URL http://www.sciencedirect.com/science/article/pii/S1383574211001001

Abstract In the current survey, we summarize the published literature which supports the use of melatonin, an endogenously produced molecule, as a protective agent against chronic, low-level ionizing radiation. Under in vitro conditions, melatonin uniformly was found to protect cellular DNA and plasmid super coiled DNA from ionizing radiation damage due to Cs137 or X-radiation exposure. Likewise, in an in vivo/in vitro study in which humans were given melatonin orally and then their blood lymphocytes were collected and exposed to Cs137 ionizing radiation, nuclear DNA from the cells of those individuals who consumed melatonin (and had elevated blood levels) was less damaged than that from control individuals. In in vivo studies as well, melatonin given to animals prevented DNA and lipid damage (including limiting membrane rigidity) and reduced the percentage of animals that died when they had been exposed to Cs137 or Co60 radiation. Melatonin's ability to protect macromolecules from the damage inflicted by ionizing radiation likely stems from its high efficacy as a direct free radical scavenger and possibly also due to its ability to stimulate antioxidative enzymes. Melatonin is readily absorbed when taken orally or via any other route. Melatonin's ease of self administration and its virtual absence of toxicity or side effects, even when consumed over very long periods of time, are essential when large populations are exposed to lingering radioactive contamination such as occurs as a result of an inadvertent nuclear accident, an intentional nuclear explosion or the detonation of a radiological dispersion device, i.e., a “dirty” bomb.

Keywords

Reiter RJ, Liu X, Manchester LC, et al. **Year** 2013

Authors Russel J. Reiter, Xiaoyan Liu, Lucien C. Manchester, Sergio A. Rosales-Corral, Dun-Xian Tan, Juan Antonio Madrid Pérez

Report Name Processes Underlying Chronodisruption and Their Proposed Association with Illness

Publication Chronobiology and Obesity

Issue-page numbers 2013, pp 55-73

URL http://link.springer.com/chapter/10.1007%2F978-1-4614-5082-5_4?LI=true

Abstract Regularly alternating periods of light and darkness, such as normally occur with the rising and the setting of the sun, are essential for the maintenance of undisturbed circadian rhythms in all organisms including humans. The light–dark environment, as detected by specialized photoreceptors in the retinas, impacts the endogenous circadian clock in the anterior hypothalamus, the suprachiasmatic nuclei. These nuclei, via both neural and humoral signals, communicate with cells throughout the organism to establish regular circadian rhythms. The introduction of artificial sources of light roughly 150 years ago has significantly undermined the naturally occurring light–dark environment and, likewise, has disturbed circadian rhythms since light is now available at unusual times, i.e., at night. Light at night is known to cause circadian disruption and melatonin suppression. Of many potentially pathophysiological consequences of these artificial light-mediated changes, female breast cancer has become of major interest. Additionally, however, there is currently data suggesting that not only breast cancer, but cancer in general, cardiovascular diseases, insomnia, metabolic syndrome, and affective and cognitive disorders may be aggravated by the increased exposure to light at night, which is inevitable in well-developed societies that have undergone extensive electrification.

Keywords

Reiter RJ, Richardon BA **Year** 1992

Authors Russel J. Reiter and Bruce A. Richardson

Report Name Some Perturbations That Disturb the Circadian Melatonin Rhythm

Publication Chronobiology International

Issue-page numbers 9:4, 314-321

URL http://informahealthcare.com/doi/abs/10.3109/07420529209064541

Abstract The circadian melatonin rhythm is highly reproducible and generally not easily altered. The few perturbations that are capable of significantly changing either the amplitude or the pattern of the 24-h melatonin rhythm are summarized herein. Aging alters cyclic melatonin production by decreasing the amplitude of the nocturnal melatonin peak in all species in which it has been studied. The best known acute suppressor of nocturnal melatonin is light exposure. The brightness of light required to acutely depress pineal melatonin production is species dependent; of the visible wavelengths, those in the blue range (500-520 nm) seem most effective in suppressing melatonin production. Nonvisible, nonionizing radiation in the extremely low frequency range (e.g., 60 Hz) seems also capable of altering pineal melatonin synthesis. Hormones have relatively little influence on the circadian production of melatonin, although either adrenalectomy or hypo-physectomy does attenuate the amplitude of the melatonin cycle. Exercise at the time of high melatonin production rapidly depresses pineal concentrations of the indole without influencing its synthesis; the mechanism of this suppression remains unknown.

Keywords Melatonin, Circadian rhythm

Reiter RJ, Rosales-Corral S, Coto-Montes A, et al. **Year** 2011

Authors Reiter RJ, Rosales-Corral S, Coto-Montes A, Boga JA, Tan DX, Davis JM, Konturek PC, Konturek SJ, Brzozowski T.

Report Name The photoperiod, circadian regulation and chronodisruption: the requisite interplay between the suprachiasmatic nuclei and the pineal and gut melatonin

Publication J Physiol Pharmacol

Issue-page numbers Jun;62(3):269-74.

URL http://www.ncbi.nlm.nih.gov/pubmed/21893686

Abstract The current scientific literature is replete with investigations providing information on the molecular mechanisms governing the regulation of circadian rhythms by neurons in the suprachiasmatic nucleus (SCN), the master circadian generator. Virtually every function in an organism changes in a highly regular manner during every 24-hour period. These rhythms are believed to be a consequence of the SCN, via neural and humoral means, regulating the intrinsic clocks that perhaps all cells in organisms possess. These rhythms optimize the functions of cells and thereby prevent or lower the incidence of pathologies. Since these cyclic events are essential for improved cellular physiology, it is imperative that the SCN provide the peripheral cellular oscillators with the appropriate time cues. Inasmuch as the 24-hour light:dark cycle is a primary input to the central circadian clock, it is obvious that disturbances in the photoperiodic environment, e.g., light exposure at night, would cause disruption in the function of the SCN which would then pass this inappropriate information to cells in the periphery. One circadian rhythm that transfers time of day information to the organism is the melatonin cycle which is always at low levels in the blood during the day and at high levels during darkness. With light exposure at night the amount of melatonin produced is compromised and this important rhythm is disturbed. Another important source of melatonin is the gastrointestinal tract (GIT) that also influences the circulating melatonin is the generation of this hormone by the entero-endocrine (EE) cells in the gut following ingestion of tryptophan-containing meal. The consequences of the altered melatonin cycle with the chronodisruption as well as the alterations of GIT melatonin that have been linked to a variety of pathologies, including those of the gastrointestinal tract.

Keywords

Reiter RJ, Steinlechner S, Richardson BA, King TS **Year** 1983

Authors Russel J. Reiter, Stephan Steinlechner, Bruce A. Richardson, Thomas S. King

Report Name Differential response of pineal melatonin levels to light at night in laboratory-raised and wild-captured 13-lined ground squirrels (Spermophilus Tridecemlineatus)

Publication Life Sciences

Issue-page numbers Volume 32, Issue 23, 6 June 1983, Pages 2625-2629

URL http://www.sciencedirect.com/science/article/pii/0024320583903533

Abstract Pineal melatonin levels were compared in laboratory-raised or wild-captured 13-lined ground squirrels (Spermophilus tridecemlineatus) that were either exposed to 10 h of darkness at night or to light which had an irradiance of 400 μW/cm2. In laboratory-born squirrels the period of darkness was associated with a gradual rise in pineal melatonin levels with peak values being reached at 0200 h, 6 h after darkness onset. Thereafter, melatonin levels decreased and were back to low daytime levels by 0800 h, 2 h after light onset. The exposure of laboratory-raised animals to an irradiance of 400 μW/cm2 during the night totally prevented the nocturnal rise in pineal melatonin levels in these animals. In wild-captured ground squirrels the period of darkness at night was associated with a rapid rise in pineal melatonin such that by 2200 h, 2 h after lights out, peak melatonin values were already attained; additionally, melatonin levels remained high throughout the period of darkness but returned to daytime values by 0800 h. Exposure of wild-captured squirrels to a light irradiance of 400 μW/cm2 during the normal dark period was completely incapable of suppressing pineal melatonin levels. The difference in the sensitivity of the pineal gland of laboratory-raised and wild-captured ground squirrels may relate to their previous lighting history.

Keywords

Reiter RJ, Tan D, Fuentes-Broto L

Year 2010

Authors Russel J. Reiter, Dun-Xian Tan, Lorena Fuentes-Broto

Report Name Chapter 8 - Melatonin: A Multitasking Molecule

Publication Progress in Brain Research

Issue-page numbers Volume 181, 2010, Pages 127-151

URL http://www.sciencedirect.com/science/article/pii/S0079612308810084

Abstract Melatonin (N-acetyl-5-methoxytryptamine) has revealed itself as an ubiquitously distributed and functionally diverse molecule. The mechanisms that control its synthesis within the pineal gland have been well characterized and the retinal and biological clock processes that modulate the circadian production of melatonin in the pineal gland are rapidly being unravelled. A feature that characterizes melatonin is the variety of mechanisms it employs to modulate the physiology and molecular biology of cells. While many of these actions are mediated by well-characterized, G-protein coupled melatonin receptors in cellular membranes, other actions of the indole seem to involve its interaction with orphan nuclear receptors and with molecules, for example calmodulin, in the cytosol. Additionally, by virtue of its ability to detoxify free radicals and related oxygen derivatives, melatonin influences the molecular physiology of cells via receptor-independent means. These uncommonly complex processes often make it difficult to determine specifically how melatonin functions to exert its obvious actions. What is apparent, however, is that the actions of melatonin contribute to improved cellular and organismal physiology. In view of this and its virtual absence of toxicity, melatonin may well find applications in both human and veterinary medicine.

Keywords melatonin; melatonin receptors; seasonal reproduction; circadian rhythms; sleep; cancer; free radicals; antioxidant

Reiter RJ, Tan DX

Year 2008

Authors R.J. Reiter, D.-X. Tan

Report Name Pineal Gland and Melatonin

Publication Encyclopedia of Neuroscience

Issue-page numbers Pages 713-717

URL http://www.sciencedirect.com/science/article/pii/B9780080450469011931

Abstract This article succinctly summarizes what is known about the pineal gland and its secretory product melatonin. The pineal gland, a small dorsal outgrowth of the brain stem, is an end organ of the visual system; its function is determined by light and darkness as perceived by the retinas. The neural connections between the eyes and the pineal gland involve the peripheral sympathetic nervous system and an important synaptic relay in the suprachiasmatic nuclei, the biological clock. During darkness at night, the pineal gland, in response to norepinephrine released onto pineal cells by postganglionic sympathetic nerve fibers, produces melatonin and discharges it into the blood; as a consequence, blood levels of melatonin are elevated at night. The 24 h cycle of blood melatonin functions in the regulation of circadian rhythms and in promoting nighttime sleep. In addition, melatonin inhibits growth of some tumors, has modulatory effects on the immune system, and functions as a direct free-radical scavenger and as an indirect antioxidant. Some o melatonin's actions are mediated via specific receptors while others are receptor independent.

Keywords Free-radical scavenger; Immune physiology; Seasonal reproduction; Sleep; Suprachiasmatic nuclei; Sympathetic nervous system; Tumor inhibition

Reiter RJ, Tan DX, Erren TC, et al. **Year** 2009

Authors Reiter RJ, Tan DX, Erren TC, Fuentes-Broto L, Paredes SD

Report Name Light-mediated perturbations of circadian timing and cancer risk: a mechanistic analysis

Publication Integr Cancer Ther

Issue-page numbers 2009 Dec;8(4):354-60.

URL http://www.ncbi.nlm.nih.gov/pubmed/20042411

Abstract In industrialized countries, certain types of cancer, most notably, breast and prostate, are more frequent than in poorly developed nations. This high cancer frequency is not explained by any of the conventional causes. Within the past decade, numerous reports have appeared that link light at night with an elevated cancer risk. The three major consequences of light at night are sleep deprivation, chronodisruption, and melatonin suppression. Each of these individually or in combination may contribute to the reported rise in certain types of cancer. In this article, the potential mechanisms underlying the basis of the elevated cancer risk are briefly discussed. Finally, if cancer is a consequence of excessive nighttime light, it is likely that other diseases/conditions may also be exaggerated by the widespread use of light after darkness onset.

Keywords

Reiter RJ, Tan DX, Fuentes-Broto L **Year** 2010

Authors Reiter RJ, Tan DX, Fuentes-Broto L.

Report Name Melatonin: a multitasking molecule

Publication Progress in Brain Research

Issue-page numbers Volume 181, 2010, Pages 127-151

URL http://www.sciencedirect.com/science/article/pii/S0079612308810084

Abstract Melatonin (N-acetyl-5-methoxytryptamine) has revealed itself as an ubiquitously distributed and functionally diverse molecule. The mechanisms that control its synthesis within the pineal gland have been well characterized and the retinal and biological clock processes that modulate the circadian production of melatonin in the pineal gland are rapidly being unravelled. A feature that characterizes melatonin is the variety of mechanisms it employs to modulate the physiology and molecular biology of cells. While many of these actions are mediated by well-characterized, G-protein coupled melatonin receptors in cellular membranes, other actions of the indole seem to involve its interaction with orphan nuclear receptors and with molecules, for example calmodulin, in the cytosol. Additionally, by virtue of its ability to detoxify free radicals and related oxygen derivatives, melatonin influences the molecular physiology of cells via receptor-independent means. These uncommonly complex processes often make it difficult to determine specifically how melatonin functions to exert its obvious actions. What is apparent, however, is that the actions of melatonin contribute to improved cellular and organismal physiology. In view of this and its virtual absence of toxicity, melatonin may well find applications in both human and veterinary medicine.

Keywords

Authors Reiter RJ, Tan DX, Korkmaz A, Erren TC, Piekarski C, Tamura H, Manchester LC

Report Name Light at night, chronodisruption, melatonin suppression, and cancer risk: a review

Publication Crit Rev Oncog

Issue-page numbers Dec;13(4):303-28.

URL http://www.ncbi.nlm.nih.gov/pubmed/18540832/

Abstract Light exposure during the night is becoming progressively more common throughout the world, particularly in areas where electricity is commonly used. Also, the availability of artificial light has allowed humans to work or recreate throughout the 24-hour day. Based on photographs taken of the Earth from outer space, it is also apparent that true darkness is disappearing. For years it was assumed that polluting the daily dark period with light was inconsequential in terms of animal/human physiology. That assumption, however, has proven incorrect. Light at night has two major physiological actions, i.e., it disrupts circadian rhythms and suppresses the production of melatonin by the pineal gland. Moreover, both these changes are light intensity and wavelength dependent. Both human epidemiological and experimental studies on animals have documented that a potential negative consequence of chronodisruption and nocturnal melatonin inhibition is cancer initiation and growth. In epidemiological studies, the frequency of each of the following cancers has been reportedly increased in individuals who routinely work at night or whose circadian rhythms are disrupted for other reasons (e.g., due to jet lag): breast, prostate, endometrial, and colorectal. Likewise, in experimental animals, cancer growth is exaggerated when the animals are repeatedly phase advanced (as occurs during easterly flights) or exposed to light at night. A variety of mechanisms have been examined to explain how the suppression of melatonin exaggerates cancer risk. Mechanistically, how chronodisruption (without a consideration of melatonin suppression) would enhance cancer frequency is less clear. In addition to cancer, there may be other diseases that result from the chronic suppression of melatonin by light at night.

Keywords

Reiter RJ, Tan DX, Korkmaz A, Ma S. ***Year*** 2011

Authors Reiter RJ, Tan DX, Korkmaz A, Ma S.

Report Name Obesity and metabolic syndrome: Association with chronodisruption, sleep deprivation, and melatonin suppression

Publication Ann Med

Issue-page numbers 2011 Jun 13.

URL http://informahealthcare.com/doi/abs/10.3109/07853890.2011.586365

Abstract Abstract Obesity has become an epidemic in industrialized and developing countries. In 30 years, unless serious changes are made, a majority of adults and many children will be classified as overweight or obese. Whereas fatness alone endangers physiological performance of even simple tasks, the associated co-morbidity of obesity including metabolic syndrome in all its manifestations is a far more critical problem. If the current trend continues as predicted, health care systems may be incapable of handling the myriad of obesity-related diseases. The financial costs, including those due to medical procedures, absenteeism from work, and reduced economic productivity, will jeopardize the financial well-being of industries. The current review summarizes the potential contributions of three processes that may be contributing to humans becoming progressively more overweight: circadian or chronodisruption, sleep deficiency, and melatonin suppression. Based on the information provided in this survey, life-style factors (independent of the availability of abundant calorie-rich foods) may aggravate weight gain. Both epidemiological and experimental data support associations between disrupted physiological rhythms, a reduction in adequate sleep, and light-at-night-induced suppression of an essential endogenously produced molecule, melatonin. The implication is that if these problems were corrected with life-style changes, body-weight could possibly be more easily controlled.

Keywords Brown adipose tissue, circadian rhythms, light:dark cycle, melatonin, metabolic syndrome, obesity, sleep

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Reiter RJ, Tan DX, Sanchez-Barcelo E. et al. ***Year*** 2011

Authors Russel J. Reiter, Dun Xian Tan, Emilio Sanchez-Barcelo, Maria D. Mediavilla, Eloisa Gitto, Ahmet Korkmaz

Report Name Circadian mechanisms in the regulation of melatonin synthesis: disruption with light at night and the pathophysiological consequences

Publication J Exp Integr Med

Issue-page numbers 1(1): 13-22

URL http://www.scopemed.org/?mno=2587

Abstract In the past two decades, the results of a number of epidemiological studies have uncovered an association between excessive light exposure at night and the prevalence of cancer. Whereas the evidence supporting this link is strongest between nighttime light and female breast and male prostate cancer, the frequency of other tumor types may also be elevated. Individuals who have the highest reported increase in cancer are chronic night shift workers and flight attendants who routinely fly across numerous time zones. There are at least two obvious physiological consequences of nighttime light exposure, i.e., a reduction in circulating melatonin levels and disruption of the circadian system (chronodisruption). Both these perturbations in experimental animals aggravate tumor growth. Melatonin has a long investigative history in terms of its ability to stymie the growth of many tumor types. Likewise, in the last decade chronodisruption has been unequivocally linked to a variety of abnormal metabolic conditions including excessive tumor growth This brief review summarizes the processes by which light after darkness onset impedes melatonin production and disturbs circadian rhythms. The survey also reviews the evidence associating the ostensible danger of excessive nighttime light pollution to cancer risk. If an elevated tumor frequency is definitively proven to be a consequence of light at night and/or chronodisruption, it seems likely that cancer will not be the exclusive pathophysiological change associated with the rampant light pollution characteristic of modern societies.

Keywords Biological clock; Cancer, Circadian rhythm; Light pollution; Melatonin

Reppert SM, Godson C, Mahle CD et al. **Year** 1995

Authors S M Reppert, C Godson, C D Mahle, D R Weaver, S A Slaugenhaupt, and J F Gusella

Report Name Molecular characterization of a second melatonin receptor expressed in human retina and brain: the Mel1b melatonin receptor

Publication Proc Natl Acad Sci USA

Issue-page numbers 92:8734–8738 doi:10.1073/pnas.92.19.8734. PMID:7568007

URL http://www.pnas.org/content/92/19/8734

Abstract A G protein-coupled receptor for the pineal hormone melatonin was recently cloned from mammals and designated the Mel1a melatonin receptor. We now report the cloning of a second G protein-coupled melatonin receptor from humans and designate it the Mel1b melatonin receptor. The Mel1b receptor cDNA encodes a protein of 362 amino acids that is 60% identical at the amino acid level to the human Mel1a receptor. Transient expression of the Mel1b receptor in COS-1 cells results in high-affinity 2-[125I]iodomelatonin binding (Kd = 160 +/- 30 pM). In addition, the rank order of inhibition of specific 2-[125I]iodomelatonin binding by eight ligands is similar to that exhibited by the Mel1a melatonin receptor. Functional studies of NIH 3T3 cells stably expressing the Mel1b melatonin receptor indicate that it is coupled to inhibition of adenylyl cyclase. Comparative reverse transcription PCR shows that the Mel1b melatonin receptor is expressed in retina and, to a lesser extent, brain. PCR analysis of human-rodent somatic cell hybrids maps the Mel1b receptor gene (MTNR1B) to human chromosome 11q21-22. The Mel1b melatonin receptor may mediate the reported actions of melatonin in retina and participate in some of the neurobiological effects of melatonin in mammals.

Keywords

Reppert SM, Weaver DR **Year** 2001

Authors Reppert SM, Weaver DR

Report Name Molecular analysis of mammalian circadian rhythms

Publication Annu Rev Physiol

Issue-page numbers 63:647–676 doi:10.1146/annurev.physiol.63.1.647. PMID:11181971

URL http://www.ncbi.nlm.nih.gov/pubmed/11181971

Abstract In mammals, a master circadian "clock" resides in the suprachiasmatic nuclei (SCN) of the anterior hypothalamus. The SCN clock is composed of multiple, single-cell circadian oscillators, which, when synchronized, generate coordinated circadian outputs that regulate overt rhythms. Eight clock genes have been cloned that are involved in interacting transcriptional-/translational-feedback loops that compose the molecular clockwork. The daily light-dark cycle ultimately impinges on the control of two clock genes that reset the core clock mechanism in the SCN. Clock-controlled genes are also generated by the central clock mechanism, but their protein products transduce downstream effects. Peripheral oscillators are controlled by the SCN and provide local control of overt rhythm expression. Greater understanding of the cellular and molecular mechanisms of the SCN clockwork provides opportunities for pharmacological manipulation of circadian timing.

Keywords

Reppert SM, Weaver DR

Year 2002

Authors Reppert SM, Weaver DR

Report Name Coordination of circadian timing in mammals

Publication Nature

Issue-page numbers 418:935–941 doi:10.1038/nature00965. PMID:12198538

URL http://www.mendeley.com/research/coordination-of-circadian-timing-in-mammals-1/

Abstract Time in the biological sense is measured by cycles that range from milliseconds to years. Circadian rhythms, which measure time on a scale of 24 h, are generated by one of the most ubiquitous and well-studied timing systems. At the core of this timing mechanism is an intricate molecular mechanism that ticks away in many different tissues throughout the body. However, these independent rhythms are tamed by a master clock in the brain, which coordinates tissue-specific rhythms according to light input it receives from the outside world.

Keywords

Reppert SM, Weaver DR, Ebisawa T

Year 1994

Authors Reppert SM, Weaver DR, Ebisawa T

Report Name Cloning and characterization of a mammalian melatonin receptor that mediates reproductive and circadian responses

Publication Neuron

Issue-page numbers 13:1177–1185 doi:10.1016/0896-6273(94)90055-8. PMID:7946354

URL http://www.cell.com/neuron/abstract/0896-6273%2894%2990055-8

Abstract The pineal hormone melatonin regulates seasonal reproductive function and modulates circadian rhythms in mammals. We now report the cloning and characterization of a high affinity receptor for melatonin from the sheep and human. The receptor cDNAs encode proteins that are members of a newly discovered group within the G protein-coupled receptor family. Expression of the sheep and human receptors in COS-7 cells results in high affinity 2-[125I]iodomelatonin binding and pharmacological characteristics similar to endogenous high affinity receptors. Functional studies of NIH 3T3 cells stably expressing the sheep receptor show that the mammalian melatonin receptor is coupled to inhibition of adenylyl cyclase through a pertussis toxin-sensitive mechanism. In situ hybridization studies of melatonin receptor mRNA in several mammals reveal hybridization signals in the hypophyseal pars tuberalis and hypothalamic suprachiasmatic nucleus. The cloned high affinity receptor likely mediates the reproductive and circadian actions of melatonin in mammals.

Keywords

Authors Reszka E, Peplonska B, Weiczorek E, Sobala W, Bukowska A, Gromadzinska J, Lie J-A, Kjuus H, Wasowicz W

Report Name Rotating night shift work and polymorphism of genes important for the regulation of circadian rhythm

Publication Scand J Work Environ Health

Issue-page numbers Online-first -article

URL http://scholar.google.com/scholar_url?hl=en&q=http://www.sjweh.fi/download.php%3Fabstract_id%3D3299%26file_nro%3D1&sa=X&scisig=AAGBfm3xuv0_ftkyyQIIAW_Hoegxo

Abstract

Objective People living in industrialized societies have developed specific working schedules during the day and at night, including permanent night shifts and rotating night shifts. The aim of this study was to examine the association between circadian polymorphisms and rotating night shift work.
Methods This cross-sectional study comprised 709 nurses and midwives (348 current rotating and 361 current day workers). Genetic polymorphism of selected clock genes BMAL1 (rs2279287), CLOCK (rs1801260), PER1 (rs2735611), PER2 (rs2304672), PER3 (rs10462020), CRY1 (rs8192440), CRY2 (rs10838527, rs10838527) was determined using real-time polymerase chain reaction (PCR) assays.
Results There were no differences in BMAL1, CLOCK, CRY2, PER1, PER2, and PER3 genotypes among nurses and midwives working rotating night and day shifts. The frequency of women with rare CRY1 TT genotype was higher in the group of rotating night shift than day workers (17.0% versus 13.9%, P=0.06). Moreover, CRY1 TT genotype was associated with the total rotating shift-work duration, compared to women rarely working night shifts.
Conclusions These results suggest that CRY1 (rs8192440) polymorphism may influence the adaptation to the rotating night shift work among nurses and midwives.

Keywords cancer; chronotype; night work; nurse; rotating shift; shift worker; sleep

Reszka E, Peplonska B, Wieczorek E, et al. **Year** 2012

Authors Edyta Reszka, Beata Peplonska, Edyta Wieczorek, Wojciech Sobala, Agnieszka Bukowska, Jolanta Gromadzinska, Jenny-Anne Lie, Helge Kjuus, Wojciech Wasowicz

Report Name Circadian gene expression in peripheral blood leukocytes of rotating night shift nurses

Publication Scand J Work Environ Health

Issue-page numbers online first. doi:10.5271/sjweh.3303

URL http://scholar.google.com/scholar_url?hl=en&q=http://www.sjweh.fi/download.php%3Fabstract_id%3D3303%26file_nro%3D1&sa=X&scisig=AAGBfm2ZAb3rKkpPUxVCNKRY3N

Abstract

Objective It has been hypothesized that the underlying mechanism of elevated breast cancer risk among longterm, night-working women involves circadian genes expression alteration caused by exposure to light at night and/or irregular work hours. The aim of the present study was to determine the effect of rotating night shift work on expression of selected core circadian genes.
Methods The cross-sectional study was conducted on 184 matched nurses and midwives, who currently work either day or rotating night shifts, to determine the effect of irregular work at night on circadian gene expression in peripheral blood leukocytes. Transcript levels of BMAL1, CLOCK, CRY1, CRY2, PER1, PER2, and PER3 were determined by means of quantitative real-time polymerase chain reaction (PCR).
Results After adjusting for hour of blood collection, there were no statistically significant changes of investigated circadian genes among nurses and midwives currently working rotating night shifts compared to nurses working day shifts. The highest expression of PER1 messanger ribonucleic acid (mRNA) was observed for women currently working shifts who had worked >15 years in rotating night shift work. PER1 gene expression was associated with the lifetime duration of rotating night shift work among women currently working night shifts (P=0.04). PER1 and PER3 transcript levels in blood leukocytes were significantly down-regulated in the later versus early hours of the morning between 06.00–10.00 hours (β-coefficient -0.226, P=0.001 and β-coefficient -0.181, P<0.0001, respectively).
Conclusions These results suggest that current rotating night shift work does not affect circadian gene expression in human circulating leukocytes. In analysis of the peripheral clock in human studies, the hour of blood collection should be precisely specified.

Keywords cancer; chronotype; night work; nurse; shift work; shift worker; sleep.

Reszka K, Eldred G, Wang RH, et al. **Year** 1995

Authors Reszka K, Eldred G, Wang RH, Chignell C, Dillon J.

Report Name The photochemistry of human retinal lipofuscin as studied by EPR

Publication Photochemistry and Photobiology

Issue-page numbers Volume: 62, Issue: 6, Pages: 1005-1008

URL http://www.mendeley.com/research/the-photochemistry-of-human-retinal-lipofuscin-as-studied-by-epr/

Abstract Fluorescent material generated in the human retina accumulates within lipofuscin (HLF) granules of the retinal pigment epithelium (RPE) during aging. We have been investigating the possible light-induced contribution of these fluorophores to various diseases including age-related macular degeneration. Our studies have shown that some of the fluorescent components of HLF are products of the reaction of retinaldehyde with ethanolamine and that synthetic mixtures of this reaction can serve as a useful model for photophysical studies. Previous research by us has demonstrated that irradiation of either natural or synthetic lipofuscin resulted in the formation of a triplet state and possibly a free radical. Here EPR studies were performed to verify the formation of that radical. The UV irradiation of either synthetic or natural human retinal lipofuscin extracts in oxygen-free methanol led to the formation of a 5,5-dimethylpyrroline-N-oxide (DMPO) spin-trapped carbon-centered radical resulting from either hydrogen atom or electron abstraction from solvent molecules. In the presence of oxygen superoxide was formed, which was observed as a DMPO adduct. It is concluded that certain components of the chloroform-soluble fluorophores of human RPE lipofuscin granules and the fluorescent reaction products of retinaldehyde and ethanolamine are photophysically similar but not the same. Electron or hydrogen abstraction from a substrate by these fluorophores in vivo and the resulting radical products may contribute to the age-related decline of RPE function and blue light damage in the retina.

Keywords

Revell VL, Arendt J, Fogg LF, Skene DJ **Year** 2006

Authors Victoria L. Revell, Josephine Arendt, Louis F. Fogg, Debra J. Skene

Report Name Alerting effects of light are sensitive to very short wavelengths

Publication Neuroscience Letters

Issue-page numbers Volume 399, Issues 1-2, 15 May 2006, Pages 96-100

URL http://www.sciencedirect.com/science/article/pii/S0304394006000668

Abstract In humans a range of non-image-forming (NIF) light responses (melatonin suppression, phase shifting and alertness) are short wavelength sensitive (440–480 nm). The aim of the current study was to assess the acute effect of three different short wavelength light pulses (420, 440 and 470 nm) and 600 nm light on subjective alertness. Healthy male subjects (n = 12, aged 27 ± 4 years, mean ± S.D.) were studied in 39, 4-day laboratory study sessions. The subjects were maintained in dim light (<8 lx) and on day 3 they were exposed to a single 4-h light pulse (07:15–11:15 h). Four monochromatic wavelengths were administered at two photon densities: 420 and 440 nm at 2.3 × 1013 photons/cm2/s and 440, 470 and 600 nm at 6.2 × 1013 photons/cm2/s. Subjective mood and alertness were assessed at 30 min intervals during the light exposure, using four 9-point VAS scales. Mixed model regression analysis was used to compare alertness and mood ratings during the 470 nm light to those recorded with the other four light conditions. There was a significant effect of duration of light exposure ($p < 0.001$) on alertness but no significant effect of subject. Compared to 470 nm light, alertness levels were significantly higher in 420 nm light and significantly lower in the 600 nm light ($p < 0.05$). These data (420 nm > 470 nm > 600 nm) suggest that subjective alertness may be maximally sensitive to very short wavelength light.

Keywords Human; Alertness; Light; Spectral sensitivity; Short wavelength light

Revell VL, Arendt J, Terman M, Skene DJ

Year 2005

Authors Revell VL, Arendt J, Terman M, and Skene DJ

Report Name Short-Wavelength Sensitivity of the Human Circadian System to Phase-Advancing Light

Publication J Biol Rhythms

Issue-page numbers June 2005 vol. 20 no. 3 270-272

URL http://jbr.sagepub.com/content/20/3/270.extract

Abstract Letter

Keywords

Revell VL, Eastman CI

Year 2005

Authors Revell VL, Eastman CI

Report Name How to trick mother nature into letting you fly around or stay up all night

Publication J Biol Rhythms

Issue-page numbers 20:353–365 doi:10.1177/0748730405277233. PMID:16077154

URL http://jbr.sagepub.com/content/20/4/353.short

Abstract Night shift work and rapid transmeridian travel result in a misalignment between circadian rhythms and the new times for sleep, wake, and work, which has health and safety implications for both the individual involved and the general public. Entrainment to the new sleep/wake schedule requires circadian rhythms to be phase-shifted, but this is often slow or impeded. The authors show superimposed light and melatonin PRCs to explain how to appropriately time these zeitgebers to promote circadian adaptation. They review studies in which bright light and melatonin were administered to try to counteract jet lag or to produce circadian adaptation to night work. They demonstrate how jet lag could be prevented entirely if rhythms are shifted before the flight using their preflight plan and discuss the combination of interventions that they now recommend for night shift workers.

Keywords

Authors Revell VL, Skene DJ.

Report Name Light-induced melatonin suppression in humans with polychromatic and monochromatic light

Publication Chronobiology International

Issue-page numbers 2007, Vol. 24, No. 6 , Pages 1125-1137 (doi:10.1080/07420520701800652)

URL http://informahealthcare.com/doi/abs/10.1080/07420520701800652?journalCode=cbi

Abstract The relative contribution of rods, cones, and melanopsin to non-image-forming (NIF) responses under light conditions differing in irradiance, duration, and spectral composition remains to be determined in humans. NIF responses to a polychromatic light source may be very different to that predicted from the published human action spectra data, which have utilized narrow band monochromatic light and demonstrated short wavelength sensitivity. To test the hypothesis that only melanopsin is driving NIF responses in humans, monochromatic blue light (λmax 479 nm) was matched with polychromatic white light for total melanopsin-stimulating photons at three light intensities. The ability of these light conditions to suppress nocturnal melatonin production was assessed. A within-subject crossover design was used to investigate the suppressive effect of nocturnal light on melatonin production in a group of diurnally active young male subjects aged 18–35 yrs (24.9±3.8 yrs; mean±SD; n=11). A 30 min light pulse, individually timed to occur on the rising phase of the melatonin rhythm, was administered between 23:30 and 01:30 h. Regularly timed blood samples were taken for measurement of plasma melatonin. Repeated measures two-way ANOVA, with irradiance and light condition as factors, was used for statistical analysis (n=9 analyzed). There was a significant effect of both light intensity ($p<0.001$) and light condition ($p<0.01$). Polychromatic light was more effective at suppressing nocturnal melatonin than monochromatic blue light matched for melanopsin stimulation, implying that the melatonin suppression response is not solely driven by melanopsin. The findings suggest a stimulatory effect of the additional wavelengths of light present in the polychromatic light, which could be mediated via the stimulation of cone photopigments and/or melanopsin regeneration. The results of this study may be relevant to designing the spectral composition of polychromatic lights for use in the home and workplace, as well as in the treatment of circadian rhythm disorders.

Keywords Melatonin suppression, Light, Melanopsin, Human

Authors Reynolds P, Cone J, Layefsky M et al.

Report Name Cancer incidence in California flight attendants (United States)

Publication Cancer Causes Control

Issue-page numbers 13:317–324.doi:10.1023/A:1015284014563 PMID:12074501

URL http://www.jstor.org/pss/3553848

Abstract

OBJECTIVE:

To examine unusual exposure opportunities to flight crews from chemicals, cosmic radiation, and electric and magnetic fields.
METHODS:

This project evaluated the incidence of cancers of the breast and other sites among Association of Flight Attendants (AFA) members residing in California. AFA membership files were matched to California's statewide cancer registry to identify a total of 129 newly diagnosed invasive cancers among AFA members with California residential histories between 1988 and 1995.
RESULTS:

Compared to the general population, female breast cancer incidence was over 30% higher than expected, and malignant melanoma incidence was roughly twice that expected. Both of these are cancers that are associated with higher socioeconomic status and have been suggestively associated with various sources of radiation.
CONCLUSIONS:

Consistent with the results from Nordic studies of cabin crews and a recent meta-analysis of prior studies, these data suggest that follow-up investigations should focus on the potential relative contribution of workplace exposures and lifestyle characteristics to the higher rates of disease for these two cancers.

Keywords

Rhodes LE, Bock M, Janssens AS, et al. **Year** 2010

Authors Rhodes LE, Bock M, Janssens AS, Ling TC, Anastasopoulou L, Antoniou C, et al.

Report Name Polymorphic light eruption occurs in 18% of Europeans and does not show higher prevalence with increasing latitude: Multicenter survey of 6,895 individuals residing from the Me

Publication Journal of Investigative Dermatology

Issue-page numbers (2010) 130, 626–628; doi:10.1038/jid.2009.250

URL http://www.nature.com/jid/journal/v130/n2/full/jid2009250a.html

Abstract TO THE EDITOR Polymorphic light eruption (PLE) is acknowledged to be the most common idiopathic photodermatosis, but epidemiological data are sparse. From surveys in 550 people in Perth and Ballarat (Australia) and London (UK), PLE prevalence was estimated at 5.2, 3.6, and 14.8%, respectively (Pao et al., 1994), whereas a postal questionnaire of 397 Swedish subjects showed symptoms of PLE in 21% (Ros and Wennersten, 1986), and from 271 Boston (USA) residents the prevalence of PLE was estimated at 11% (Morison and Stern, 1982). These investigations led to the assumption that PLE prevalence is lower in countries nearer the equator, whereas latitudes with higher seasonal UV radiation modulation may predispose to the condition. However, reliable data concerning this hypothesis are lacking. In our large-scale cross-sectional study, we assessed PLE prevalence in the adult population of six European countries located from the Mediterranean to Scandinavia.

Keywords

Rhodes LE, Webb AR, Fraser HI, et al. **Year** 2010

Authors Rhodes LE, Webb AR, Fraser HI, Kift R, Durkin MT, Allan D, et al.

Report Name Recommended summer sunlight exposure levels can produce sufficient (> or =20 ng ml(-1)) but not the proposed optimal (> or =32 ng ml(-1)) 25(OH)D levels at UK latitudes

Publication Journal of Investigative Dermatology

Issue-page numbers (2010) 130, 1411–1418; doi:10.1038/jid.2009.417

URL http://www.nature.com/jid/journal/v130/n5/abs/jid2009417a.html

Abstract Recommendations on limitation of summer sunlight exposure to prevent skin cancer may conflict with requirements to protect bone health through adequate vitamin D levels, the principal source being UVB in summer sunlight. We determined whether sufficient (greater than or equal to20 ng ml−1) and proposed optimal (greater than or equal to32 ng ml−1) 25(OH)D levels are attained by following UK guidance advising casual short exposures to UVB in summer sunlight, and performed the study under known conditions to enhance the specificity of future recommendations. During wintertime, when ambient UVB is negligible, 120 white Caucasians, aged 20–60 years, from Greater Manchester, UK (53.5°N) received a simulated summer's sunlight exposures, specifically 1.3 standard erythemal dose, three times weekly for 6 weeks, while wearing T-shirt and shorts. The baseline winter data predict that 5% (confidence interval (CI): 2.7–8.6) of Greater Manchester white Caucasians have deficient (<5 ng ml−1) 25(OH)D, 62.5% (CI: 55.2–69.4) have insufficient, and only 2.9% (CI: 1.4–5.6) have proposed optimal levels. After the simulated summer exposures, 90 (CI: 84.9–93.7) and 26.2% (CI: 20.1–33.2) reached 20 and 32 ng ml−1 25(OH)D, respectively. Assuming midday UVB levels, sufficient but suboptimal vitamin D status is attained after a summer's short (13 minutes) sunlight exposures to 35% skin surface area; these findings will assist future public health guidance on vitamin D acquisition.

Keywords

Authors Ribak J, Ashkenazi IE, Klepfish A et al.

Report Name Diurnal rhythmicity and Air Force flight accidents due to pilot error

Publication Aviat Space Environ Med

Issue-page numbers 54:1096–1099. PMID:6686440

URL http://www.ncbi.nlm.nih.gov/pubmed/6686440

Abstract In order to evaluate the possible role of an endogenous rhythmic factor in Air Force flight accidents a retrospective study was carried out. The study included all Air Force (aircraft) flying accidents which have been attributed to pilot's error and which occurred, in peace time missions, over a period of 12 years (1968-1980). The frequency of hourly accidents was computed separately, for each year, for each month, for each day of the week, and for each calendar day. Identical computations were carried out for the frequency of hourly flights. When the hourly ratios of these two parameters were computed, by dividing the value of one parameter to the other at each hour, a rhythmic (rather than constant) diurnal pattern was obtained. The pattern was defined as the "Hourly Accident Coefficient (HAC)". The HAC values ranged from 1.58 to 0.68 (pooled data for all surveyed aircrafts) and from 4.12 to 0.74 (data for fighter planes). The pattern, which exhibited a diurnal rhythm, was independent of the frequency of flights and appeared to be related to the sleep-wake cycle of the pilots, especially to the time of waking from the night sleep. The results are used as a directive for a progressive study aimed at evaluating the practical implications of the presented observations.

Keywords

Authors Christophe Ribelayga and Stuart C. Mangel

Report Name Identification of a Circadian Clock-Controlled Neural Pathway in the Rabbit Retina

Publication PLoS One

Issue-page numbers 2010; 5(6): e11020.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2883549/

Abstract

Background
Although the circadian clock in the mammalian retina regulates many physiological processes in the retina, it is not known whether and how the clock controls the neuronal pathways involved in visual processing.
Methodology/Principal Findings
By recording the light responses of rabbit axonless (A-type) horizontal cells under dark-adapted conditions in both the day and night, we found that rod input to these cells was substantially increased at night under control conditions and following selective blockade of dopamine D2, but not D1, receptors during the day, so that the horizontal cells responded to very dim light at night but not in the day. Using neurobiotin tracer labeling, we also found that the extent of tracer coupling between rabbit rods and cones was more extensive during the night, compared to the day, and more extensive in the day following D2 receptor blockade. Because A-type horizontal cells make synaptic contact exclusively with cones, these observations indicate that the circadian clock in the mammalian retina substantially increases rod input to A-type horizontal cells at night by enhancing rod-cone coupling. Moreover, the clock-induced increase in D2 receptor activation during the day decreases rod-cone coupling so that rod input to A-type horizontal cells is minimal.
Conclusions/Significance
Considered together, these results identify the rod-cone gap junction as a key site in mammals through which the retinal clock, using dopamine activation of D2 receptors, controls signal flow in the day and night from rods into the cone system.

Keywords

Richard D, Huang Q, Timofeeva E **Year** 2000

Authors Richard D, Huang Q, Timofeeva E

Report Name The corticotropin-releasing hormone system in the regulation of energy balance in obesity

Publication Int J Obes Relat Metab Disord

Issue-page numbers 24 Suppl 2;S36–S39. PMID:10997606

URL http://www.ncbi.nlm.nih.gov/pubmed/10997606

Abstract The view that energy balance is regulated has gained acceptance in recent years. An important role in this regulation is played by brain circuitries involved in the control of energy intake (food intake) and energy expenditure (thermogenesis) that are capable of integrating peripheral signals, produced by perturbations of adipose tissue mass, into messages to effectors of food intake and energy expenditure, so as to prevent substantial variations in the level of energy reserves. More than one neurosystem has been reported to genuinely participate in the regulation of energy balance. Among them is the corticotropin-releasing hormone (CRH) system. This system, with its numerous clusters of brain neurons, its closely related peptide urocortin, its two receptor types and its binding protein, all generally widely distributed throughout the brain, forms a network of neuronal pathways capable of interacting with the circuitries controlling food intake and energy expenditure. In addition, CRH and urocortin's anorectic and thermogenic actions appear to be coordinated to optimize energy losses. Finally, the CRH system seems to demonstrate a certain degree of plasticity in obesity and in response to food deprivation that is consistent with its action on food intake and thermogenesis. The observations have been made that food deprivation and obesity can blunt the expression of the CRH type 2alpha receptor in the ventromedial hypothalamic nucleus and can induce the expression of the CRH-binding protein (a CRH-inactivating protein) in brain areas involved in the anorectic and thermogenic actions of CRH.

Keywords

Richter K, Niklewski G **Year** 2012

Authors Kneginja Richter, Guenter Niklewski

Report Name Health Promotion and Prevention in Companies – Economic Aspects and Prevention Strategies for Shift Work Sleep Disorders

Publication Advances in Predictive, Preventive and Personalised Medicine

Issue-page numbers Volume 1, 2012, pp 423-467

URL http://link.springer.com/chapter/10.1007%2F978-94-007-4602-2_23?LI=true

Abstract The proper functioning of the human body is regulated by the rhythmical change of the rest and activity cycle called sleep-wake activity. Suprachiasmatic nucleus (SCN) is responsible for the central generation of the biorhythm/circadian rhythm while the peripheral “Zeitgeber” as light, social contacts and time of meal modulate the rhythmical activity of the body. The circadian rhythm in the SCN is generated by a gene expression cycle in individual SCN neurons.

Shift worker suffer from the disruption of the sleep-wake and 24-h rhythm and lack of melatonin which could be the trigger factor for development of sleep disorders and breast cancer in female shift worker.

The growing amount of data which indicate the high risk of sleep disorders and many other health related problems should empower the implementation of prevention strategies against sleep disorders caused by the disruption of the sleep-wake activity implementing regularly education courses for prevention of sleep disorders in the companies.

Keywords

Riegel KW

Year 1973

Authors Riegel KW.

Report Name Light Pollution: Outdoor lighting is a growing threat to astronomy.

Publication Science

Issue-page numbers 1973 Mar 30;179(4080):1285-91

URL http://www.sciencemag.org/content/179/4080/1285.short

Abstract There have been major qualitative and quantitative changes in outdoor lighting technology in the last decade. The level of skylight caused by outdoor lighting systems is growing at a very high rate, about 20 percent per year nationwide. In addition, the spectral distribution of man-made light pollution may change in the next decade from one containing a few mercury lines to one containing dozens of lines and a significantly increased continuum level. Light pollution is presently damaging to some astronomical programs, and it is likely to become a major factor limiting progress in the next decade. Suitable sites in the United States for new dark sky observing facilities are very difficult to find. Some of the increase in outdoor illumination is due to the character of national growth and development. Some is due to promotional campaigns, in which questionable arguments involving public safety are presented. There are protective measures which might be adopted by the government; these would significantly aid observational astronomy, without compromising the legitimate outdoor lighting needs of society. Observatories should establish programs to routinely monitor sky brightness as a function of position, wavelength, and time. The astronomical community should establish a mechanism by which such programs can be supported and coordinated.

Keywords astronomy, light at night, growth

Rihner M, McGrath H Jr

Year 1992

Authors Rihner M, McGrath H Jr.

Report Name Fluorescent light photosensitivity in patients with systemic lupus erythematosus

Publication Arthritis & Rheumatism

Issue-page numbers Volume 35, Issue 8, pages 949–952, August 1992

URL http://onlinelibrary.wiley.com/doi/10.1002/art.1780350816/abstract?

Abstract Objective. To determine the prevalence of fluorescent light toxicity in patients with systemic lupus erythematosus (SLE).

Methods. SLE patients were polled about their symptomatic responses to sunlight and cool white fluorescent light. Photometry was used to determine the levels of ultraviolet (UV) emissions from fluorescent lamps.

Results. Thirteen of 30 photosensitive SLE patients described increases in disease activity following exposure to unshielded fluorescent lamps. Photometry indicated that these lamps emit substantial levels of UV-B (280–320 nm) radiation, which is toxic to patients with SLE. Standard acrylic diffusers absorbed this radiation, and their use was associatec with almost no patient-reported problems.

Conclusion. Fluorescent lamps, emitting UV-B radiation, induce disease activity in photosensitive SLE patients. Standard acrylic diffusers absorb UV-B radiation and appear to be protective against induction of disease activity with the use of fluorescent lamps.

Keywords

Year 2000

Authors Rimmer DW, Boivin DB, Shanahan TL, Kronauer RE, Duffy JF, Czeisler CA.

Report Name Dynamic resetting of the human circadian pacemaker by intermittent bright light

Publication Am J Physiol Regul Integr Comp Physiol

Issue-page numbers 279:R1574-R1579, 2000.

URL http://ajpregu.physiology.org/content/279/5/R1574.full.pdf

Abstract In humans, experimental studies of circadian resetting typically have been limited to lengthy episodes of exposure to continuous bright light. To evaluate the time course of the human endogenous circadian pacemaker's resetting response to brief episodes of intermittent bright light, we studied 16 subjects assigned to one of two intermittent lighting conditions in which the subjects were presented with intermittent episodes of bright-light exposure at 25- or 90-min intervals. The effective duration of bright-light exposure was 31% or 63% compared with a continuous 5-h bright-light stimulus. Exposure to intermittent bright light elicited almost as great a resetting response compared with 5 h of continuous bright light. We conclude that exposure to intermittent bright light produces robust phase shifts of the endogenous circadian pacemaker. Furthermore, these results demonstrate that humans, like other species, exhibit an enhanced sensitivity to the initial minutes of bright-light exposure.

Keywords circadian rhythms; core body temperature; phototherapy

Year 2004

Authors Rivers JK.

Report Name Is there more than one road to melanoma?

Publication The Lancet

Issue-page numbers Volume 363, Issue 9410, Pages 728 - 730, 28 February 2004

URL http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2804%2915649-3/fulltext

Abstract CONTEXT: Sunlight is the main environmental cause of most cutaneous melanomas. Exposure to intense bursts of ultraviolet radiation, especially in childhood, starts the transformation of benign melanocytes into a malignant phenotype. Paradoxically, outdoor workers have a decreased risk of melanoma compared with indoor workers, suggesting that chronic sunlight exposure can have a protective effect. Further, some melanomas form on sun-exposed regions; others do not. Although some melanomas arise from pre-existing melanocytic naevi (moles), many arise de novo. These observations suggest that melanoma arises from multiple pathways, with initiating and promoting factors differing for each. STARTING POINT: Janet Maldonado and colleagues recently studied the distribution of BRAF gene mutations in 115 patients with invasive primary melanomas (J Natl Cancer Inst 2003; 95: 1878-80). These researchers found that BRAF mutations were statistically significantly more common in melanomas occurring on intermittently sun-exposed skin than elsewhere. By contrast, BRAF mutations in melanomas on chronically sun-damaged skin were rare. These findings strongly suggest that distinct genetic pathways lead to melanoma. WHERE NEXT? The study of gene-environment interactions is clearly the next arena for epidemiological research into melanoma. The recent identification of polymorphisms in the melanocortin-1 receptor could open up an avenue of investigation into a molecular distinction between those individuals whose melanomas arise on chronic sun-exposed skin from those in whom tumours will develop on sun-protected skin or from melanocytic naevi. If a dual pathway for melanoma is supported by other investigations, public-health messages can be tailored to the population at risk.

Keywords

Authors Rivest RW, Schulz P, Lustenberger S, Sizonenko PC

Report Name Differences between circadian and ultradian organization of cortisol and melatonin rhythms during activity and rest

Publication J Clin Endocrinol Metab

Issue-page numbers 68:721–729 doi:10.1210/jcem-68-4-721. PMID:2921307

URL http://www.ncbi.nlm.nih.gov/pubmed/2921307

Abstract

We compared the cortisol and melatonin circadian and ultradian rhythms in normal men using two approaches: 1) the men were exposed successively to two conditions, one normal and a second chosen to alter differently each of the hormones, i.e. complete bedrest for 34 h (supine, fasting, and under dim light), and 2) analyses of the rhythms using a combination of curve smoothing for the description of the 24-h rhythm, and peak detection and spectral analysis for the measurement of periodic phenomena. Blood was sampled every 30 min from 0700-0700 h. A diurnal rhythm was detected for both hormones, with different underlying frequencies. Plasma cortisol had an ultradian rhythm of 8 h. From 0000-0800 h (night) and 0830-1600 h (early day), the pulsatile activity and baseline values of cortisol were high, while from 1630-2400 h (late day), these variables were low. During complete bedrest, pulsatile activity and baseline values were even higher during the night period, and the nocturnal peak of cortisol, usually present between 0300-1000 h, was split in two, with an early peak at 0000-0400 h. There were two specific events during the day associated with synchronous, high amplitude pulses: awakening and eating at noon. No such pulses occurred at suppertime or when the men fasted. Melatonin secretion was organized around a 5.5-h period. In the rest condition, plasma melatonin values were higher during the night. The 24-h rhythms of cortisol and melatonin were temporally related. Plasma melatonin began to rise when plasma cortisol was at its lowest, it peaked when cortisol began to rise, and it began to decrease when cortisol reached its peak, with a 5-h phase delay between plasma cortisol and melatonin rise at night. In summary, melatonin and cortisol rhythms have different ultradian frequencies, suggesting an intrinsic difference in the mechanisms controlling their secretion. In addition, their responses to restricted physical activity in an environment with dim light were completely different; for plasma melatonin, the change was primarily quantitative, with an increase in total production especially at night, while for plasma cortisol, there was more of a qualitative change, with different patterns of pulsatile activity and possible splitting of the nocturnal peak. The differences in the ultradian organization of these two hormones imply that the correlation between their peaks must depend on a third factor, which is likely to be the 24-h organization of the day.

Keywords

Rivier C

Year 1993

Authors Rivier C

Report Name Neuroendocrine effects of cytokines in the rat

Publication Rev Neurosci

Issue-page numbers 4:223–237. PMID:9155864

URL http://www.ncbi.nlm.nih.gov/pubmed/9155864

Abstract The necessity ot maintain and/or restore homeostasis is an essential feature of mammals. This requires complex interactions between body cells, such as those from the immune and neuroendocrine systems, and in particular implies that the occurrence of immune activation be conveyed to the brain. It is now widely recognized that following infection, injury or inflammation, some immune cells (particularly macrophages) produce polypeptides called cytokines, interleukins or lymphokines /48/. These proteins provide the basis for intercellular communication between leukocytes (hence the name "interleukins") and mediate the immunoinflammatory responses (in particular T and B lymphocyte proliferation) /4,177/. In addition, interleukins (IL) can enter the general circulation and reach cells of the neuroendocrine axes, a phenomenon which represents one arm of the bidirectional communication links between the immune and the endocrine systems /25/. The early events which take place after presentation of an antigen (the so-called "acute-phase response" /89/) include metabolic and endocrine changes, such as changes in the circulating levels of insulin, TSH, GH, LH and ACTH, as well as adrenal and gonadal steroids /7,14/. This article reviews our present state of knowledge with regard to the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-gonadal (HPG) axes of the rodent in response to interleukins.

Keywords

Roach GD, Burgess H, Lamond N et al.

Year 2001

Authors Roach GD, Burgess H, Lamond N et al.

Report Name A week of simulated night work delays salivary melatonin onset

Publication J Hum Ergol (Tokyo)

Issue-page numbers 30:255–260. PMID:14564892

URL http://www.icts.uiowa.edu/Loki/publications/browsePublication.jsp?id=14564892

Abstract n most studies, the magnitude and rate of adaptation to various night work schedules is assessed using core body temperature as the marker of circadian phase. The aim of the current study was to assess adaptation to a simulated night work schedule using salivary dim light melatonin onset (DLMO) as an alternative circadian phase marker. It was hypothesised that the night work schedule would result in a phase delay, manifest in relatively later DLMO, but that this delay would be somewhat inhibited by exposure to natural light. Participants worked seven consecutive simulated 8-hour night shifts (23:00-07:00 h). By night 7, there was a mean cumulative phase delay of 5.5 hours, equivalent to an average delay of 0.8 hours per day. This indicates that partial circadian adaptation occurred in response to the simulated night work schedule. The radioimmunoassay used in the current study provides a sensitive assessment of melatonin concentration in saliva that can be used to determine DLMO, and thus provides an alternative phase marker to core body temperature, at least in laboratory studies.

Keywords

Roach GD, Lamond N, Dorrian J et al. **Year** 2005

Authors Roach GD, Lamond N, Dorrian J et al.

Report Name Changes in the concentration of urinary 6-sulphatoxymelatonin during a week of simulated night work

Publication Ind Health,

Issue-page numbers 43:193–196 doi:10.2486/indhealth.43.193. PMID:15732322

URL http://www.mendeley.com/research/changes-concentration-urinary-6sulphatoxymelatonin-during-week-simulated-night-work/

Abstract The aim of the study was to examine the adaptation of participants to a common night work schedule using urinary 6-sulphatoxymelatonin (aMT6s) concentration as the circadian phase marker. Fifteen adults (7 male, 8 female, age = 21.9 yr) spent nine consecutive nights in the laboratory, including: (i) adaptation sleep, (ii) baseline sleep, and (iii) seven simulated night shifts (23:00-07:00 h) followed by daytime sleep. During the baseline and daytime sleeps, participants collected urine samples which were subsequently assayed for aMT6s. The concentration of aMT6s in urine for the first three day sleeps was significantly lower than for the baseline sleep, but there was no difference in aMT6s concentrations between any of the last three day sleeps and the baseline sleep. The data indicate that people may adapt to a pattern of work that includes seven consecutive night shifts if they adhere to a fixed sleep schedule, if their exposure to morning sunlight is minimised, and if they are provided with an ideal sleep environment.

Keywords

Robbins JH, Kraemer KH, Lutzner MA, et al. **Year** 1974

Authors Robbins JH, Kraemer KH, Lutzner MA, Festoff BW, Coon HG.

Report Name Xeroderma pigmentosum: An inherited disease with sun sensitivity, multiple cutaneous neoplasms and abnormal DNA repair

Publication Ann Intern Med

Issue-page numbers 1974 Feb;80(2):221-48.

URL http://www.ncbi.nlm.nih.gov/pubmed/4811796

Abstract N/A

Keywords

Authors Robilliard DL, Archer SN, Arendt J et al.

Report Name The 3111 Clock gene polymorphism is not associated with sleep and circadian rhythmicity in phenotypically characterized human subjects

Publication J Sleep Res

Issue-page numbers 11:305–312 doi:10.1046/j.1365-2869.2002.00320.x. PMID:12464098

URL http://www.sciencesleep.org/ziliao/The%203111%20Clock%20gene%20polymorphism%20is%20not%20associated%20with%20sleep%20and%20circadian%20rhythmicity%20ir

Abstract Mutations in clock genes are associated with abnormal circadian parameters, including sleep. An association has been reported previously between a polymorphism (3111C), situated in the 3¢-untranslated region (3¢-UTR) of the circadian gene Clock and evening preference. In the present study, this polymorphism was assessed in: (1) 105 control subjects with defined diurnal preference, (2) 26 blind subjects with free-running circadian rhythms and characterized with regard to circadian period (s) and (3) 16 delayed sleep phase syndrome patients. The control group was chosen from a larger population (n ¼ 484) by Horne-O¨ stberg questionnaire analysis, from which three subgroups were selected (evening, intermediate and morning preference). Data from sleep diaries completed by 90% of these subjects showed a strong correlation between preferred and estimated timings of sleep and wake. The mean timings of activities for the evening group were at least 2 h later than the morning group. Genetic analysis showed that, in contrast with the previously published finding, there was no association between 3111C and eveningness. Neither was there an association between 3111C and s, nor a significant difference in 3111C frequency between the normal and delayed sleep phase syndrome groups. To assess the effect of this polymorphism on messenger RNA (mRNA) translatability, luciferase reporter gene constructs containing the two Clock polymorphic variants in their 3¢-UTR were transfected into COS-1 cells and luciferase activity measured. No significant difference was observed between the two variants. These results do not support Clock 3111C as a marker for diurnal preference, s, or delayed sleep phase syndrome in humans.

Keywords 3¢-untranslated region, circadian rhythm sleep disorder, messenger RNA,

Robinson JE, Kaynard AH, Karsch FJ **Year** 1986

Authors Robinson JE, Kaynard AH, Karsch FJ

Report Name Does melatonin alter pituitary responsiveness to gonadotropin-releasing hormone in the ewe?

Publication Neuroendocrinology

Issue-page numbers 43:635–640 doi:10.1159/000124593. PMID:3531906

URL http://www.ncbi.nlm.nih.gov/pubmed/3531906

Abstract The diurnal secretion of melatonin from the pineal gland transduces information about day length to the reproductive axis of many seasonal breeders including the ewe. In the sheep the target for melatonin is thought to be neural, such that the hormone acts through the GnRH pulse generator to produce seasonal alterations in the frequency of pulsatile LH secretion. These effects on the pulse generation mechanism take approximately 50 days to become evident. It is possible that melatonin also exerts direct effects at the level of the pituitary gland to alter responsiveness to GnRH. Such effects have been noted in other species. The site of action of melatonin to regulate pulsatile LH secretion was assessed in the ewe by determining whether the animal's endogenous melatonin acutely modifies pituitary responsiveness to sustained pulsatile administration of GnRH. Using an animal model in which endogenous GnRH was blocked, pituitary responsiveness to hourly pulses of exogenous GnRH was assessed under conditions of both high (dark period) and low (light period) melatonin. No evidence for acute effects of melatonin on pituitary response to GnRH was found. In another experiment, the amplitude and frequency of endogenously generated LH pulses in ovariectomized ewes was found not to change during the 24-hour light/dark cycle. These data lead to the conclusion that melatonin does not act at the pituitary gland to produce acute effects on LH secretion. Rather, our findings are consistent with the hypothesis that the action of melatonin, in this short-day breeder is long term, and is directed towards the neural elements of the hypothalamic pulse-generating mechanism.

Keywords

Rodin AE **Year** 1963

Authors Rodin AE

Report Name The Growth and spread of walker 256 carcinoma in pinealectomized rats

Publication Cancer Res

Issue-page numbers 23:1545–1548. PMID:14072694

URL http://cancerres.aacrjournals.org/content/23/9_Part_1/1545

Abstract Walker 256 carcinoma was injected into the thighs of control, sham-pinealectomized, and pinealectomized Sprague-Dawley rats weighing between 40 and 50 grams. The pinealectomized group had statistically significant shorter survival times, larger tumor diameters, and more extensive metastases than the control and sham-pinealectomized groups. Pineal cells of rats that had died of tumor had more vesicular nuclei, prominent nucleoli, and more abundant cytomplasm than tumor-free animals. These results are considered to be indicative of a relationship between the pineal gland and the growth and spread of Walker 256 carcinoma in the Sprague-Dawley rat.

Keywords

Roehlecke C, Schumann U, Ader M, et al. **Year** 2011

Authors Roehlecke C, Schumann U, Ader M, Knels L, Funk RH.

Report Name Influence of blue light on photoreceptors in a live retinal explant system

Publication Molecular Vision

Issue-page numbers 2011; 17:876-884

URL http://www.molvis.org/molvis/v17/a98/

Abstract

Purpose: The present study was performed to investigate the early effects of blue light irradiation of photoreceptors in retinal explant cultures.

Methods: Murine retinal explant cultures were irradiated with visible blue light (405 nm) with an output power of 1 mW/cm2. Dihydroethidium was used to determine the production of reactive oxygen species. Morphological alterations of photoreceptor outer segments were determined by live imaging microscopy with mitochondrial dye JC-1. Transmission and scanning electron microscopy were used for ultrastructural evaluations. Cell death in the retina was assessed by the terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate (dUTP) nick end labeling (TUNEL) assay method.

Results: Live retinal explants displayed an increase in reactive oxygen species production, as revealed by fluorescent dihydroethidium products in photoreceptor cells after 30 min of blue light exposure. After 3 h of exposure, blue light caused disorganization of the normally neatly stacked outer segments of living photoreceptors. Ultrastructural analysis revealed breaks in the cell membrane surrounding the outer segments, especially in the middle section. The outer segments appeared tortuous, and the lamellar structures had been disrupted. TUNEL-staining revealed that long-term blue light exposure induced photoreceptor cell death.

Conclusions: In vitro blue light irradiation of retinal explants is a suitable model system for investigating early ultrastructural changes, as well as damage that leads to cell death in photoreceptor cells.

Keywords

Roenneberg T, Foster RG **Year** 1977

Authors Till Roenneberg, Russell G. Foster

Report Name Twilight times: light and the circadian system

Publication Photochemistry and Photobiology

Issue-page numbers Volume 66, Issue 5, pages 549–561, November 1997

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.1997.tb03188.x/abstract

Abstract N/A

Keywords

Roh S, Weiter JJ

Year 1994

Authors Roh S, Weiter JJ.

Report Name Light damage to the eye

Publication J Fla Med Assoc

Issue-page numbers 1994 Apr;81(4):248-51.

URL http://www.ncbi.nlm.nih.gov/pubmed/8046363

Abstract The effects of light on the eye are being increasingly recognized. In addition to visible radiation, we are constantly exposed to infrared and ultraviolet radiation throughout life. Acute light damage such as sunburn of eyelids, photokeratitis and solar retinopathy are well recognized and fairly obvious. The effects of chronic light exposure have been more controversial. Recent epidemiologic studies are showing an association between long-term sunlight exposure and ocular diseases such as cataracts, age-related macular degeneration, pterygium and climatic droplet keratopathy. Furthermore, the role of photosensitizers contributing to light-induced ocular damage needs to be kept in mind. The ocular hazard from photosensitizing drugs and sunlight in general is greatest in aphakic eyes that have lost their natural ultraviolet filter (the ocular lens) and in young children, whose own lenses readily transmit ultraviolet light. At present, there is enough evidence to assume that chronic sunlight exposure contributes to ocular disease and to institute preventive measures.

Keywords

Roky R, Obál F Jr, Valatx JL et al.

Year 1995

Authors Roky R, Obál F Jr, Valatx JL et al.

Report Name Prolactin and rapid eye movement sleep regulation

Publication Sleep

Issue-page numbers 18:536–542. PMID:8552923

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24536

Abstract During the past few years data have accumulated suggesting the involvement of prolactin (PRL) in rapid eye movement sleep (REMS) regulation. Pituitary PRL secretion seems to be, at least in part, sleep-dependent. PRL is also found in the central nervous system. PRL- containing neurons in the hypothalamus project to various structures in the brain. Systemic injection of PRL promotes REMS in rats, cats and rabbits. Intracerebroventricular injection of PRL enhances REMS in rats. Stimulation of endogenous PRL secretion by vasoactive intestinal peptide (VIP) also promotes REMS. Immunoneutralization of blood-borne PRL slightly reduces REMS. Various observations (hypoprolactinemic and hyperprolactinemic rats) indicate that PRL may act on REMS via modulating the diurnal rhythms of REMS. It is likely that hypothalamic PRL is more important for sleep regulation than circulating PRL. Hypothalamic PRL is likely involved in the mediation of the REMS- promoting activity of VIP. We conclude that PRL has a role in REMS regulation.

Keywords

Romagnani S **Year** 1996

Authors Romagnani S

Report Name Development of Th 1- or Th 2-dominated immune responses: what about the polarizing signals?

Publication Int J Clin Lab Res

Issue-page numbers 26:83–98 doi:10.1007/BF02592350. PMID:8856361

URL http://www.mendeley.com/research/development-th-1-th-2dominated-immune-responses-about-polarizing-signals/

Abstract Type 1 helper T cells and type 2 helper T cells represent two extremely polarized forms of the effector specific immune response, based on a distinctive profile of cytokine production. Type 1- and type 2 helper T cell-dominated immune responses play a different role in both protection and immunopathology. The differentiation of effector phenotypes depends on a complex matrix of interconnecting factors resulting from the evolutionary interplay between vertebrates and microorganisms. These include the physical form of the antigen, as well as the density and affinity of the peptide ligand, the cytokines produced by "natural" immunity cells at the time of antigen presentation, costimulatory signals provided by antigen-presenting cells, and hormones released into the microenvironment. The elucidation of genetic and environmental factors that regulate type 1 or type 2 helper T cell development in response to different antigenic stimulation is the basis for new immunotherapeutic strategies in allergic and autoimmune disorders, as well as for the improvement of vaccines.

Keywords

Romeo S, Viaggi C, Di Camillo D, et al. **Year** 2013

Authors Stefania Romeo, Cristina Viaggi, Daniela Di Camillo, Allison W. Willis, Luca Lozzi, Cristina Rocchi, Marta Capannolo, Gabriella Aloisi, et al.

Report Name Bright light exposure reduces TH-positive dopamine neurons: implications of light pollution in Parkinson's disease epidemiology

Publication Sci Rep.

Issue-page numbers 2013; 3: 1395.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3589725/

Abstract This study explores the effect of continuous exposure to bright light on neuromelanin formation and dopamine neuron survival in the substantia nigra. Twenty-one days after birth, Sprague–Dawley albino rats were divided into groups and raised under different conditions of light exposure. At the end of the irradiation period, rats were sacrificed and assayed for neuromelanin formation and number of tyrosine hydroxylase (TH)-positive neurons in the substantia nigra. The rats exposed to bright light for 20 days or 90 days showed a relatively greater number of neuromelanin-positive neurons. Surprisingly, TH-positive neurons decreased progressively in the substantia nigra reaching a significant 29% reduction after 90 days of continuous bright light exposure. This decrease was paralleled by a diminution of dopamine and its metabolite in the striatum. Remarkably, in preliminary analysis that accounted for population density, the age and race adjusted Parkinson's disease prevalence significantly correlated with average satellite-observed sky light pollution.

Keywords

Romon M, Beuscart R, Frimat P et al. **Year** 1986

Authors Romon M, Beuscart R, Frimat P et al.

Report Name [Caloric intake and weight gain according to the shift schedule of shift workers]

Publication Rev Epidemiol Sante Publique

Issue-page numbers 34:324–331. PMID:3823526

URL http://www.ncbi.nlm.nih.gov/pubmed/3823526

Abstract Survey involved 84 workers matched for age, socio-occupational and families status and divided into 3 groups : A : 27 shift workers on 3 days rotating shift, B : 47 shift workers on 5 days rotating shift, C : 20 days workers. Each subject was submitted to dietary survey by means of 24 hours recall, realised 3 times for shift workers and once for control. Al workers were interviewed about caloric intake of the preceding day off caloric intake. Annual weight gain was studied through the use of occupational health service records. There was no significant difference between the 3 groups for working day caloric intake. Day-off intake was lower (p less than 0.05) in group A (day-off any day of the week). Annual weight gain was not different between the 3 groups. Shift workers with faster weight gain had a higher caloric intake on day-off and after evening meal.

Keywords

Ronkainen H, Pakarinen A, Kirkinen P, Kauppila A **Year** 1985

Authors Ronkainen H, Pakarinen A, Kirkinen P, Kauppila A

Report Name Physical exercise-induced changes and season-associated differences in the pituitary-ovarian function of runners and joggers

Publication J Clin Endocrinol Metab

Issue-page numbers 60:416–422 doi:10.1210/jcem-60-3-416. PMID:3919040

URL http://www.hopkinsguides.com/hopkins/ub/citation/3919040/Physical_exercise_induced_changes_and_season_associated_differences_in_the_pituitary_ovarian_function_of_run

Abstract The hormonal responses to energetic chronic exercise and to seasonal shift from autumn to spring were evaluated by measuring concentrations of serum FSH, LH, PRL, estradiol (E2), progesterone (P), testosterone (T), and sex hormone-binding globuline (SHBG) during 1 menstrual cycle in the autumn (light training season) and 1 in the spring (hard training season) in 18 endurance runners and 12 age-matched nonrunning women, and in 13 joggers and 11 age-matched nonjogging women. The appearance, growth, and maximal size of the ovarian follicles were monitored by ultrasonography. The high intensity training of the runners was associated with decreased concentrations of FSH on cycle days 7-8 in the autumn, E2 on cycle days 12-13 in the spring and days 22-23 in both seasons, P on cycle days 20-21 in both seasons and days 22-23 in the autumn, and T on cycle days 12-13, 14-15, and 22-23 in the spring. Jogging, however, did not alter the concentrations of these hormones. Using as criteria the presence of 2 or 3 abnormal values of the 3 indicators used for evaluation of folliculogenesis (midfollicular E2 lower than 0.09 nmol/liter, luteal phase P lower than 7 nmol/liter, and peak diameter of the largest ovarian follicle less than 15 mm), seriously disturbed folliculogenesis was found in 50% of the 32 study cycles of the runners and 9% of the 23 cycles of their controls (P less than 0.01). In all four study groups, there was a significant seasonal difference in the concentrations of ovarian hormones, with lowered E2, P, and T levels in the autumn. There were no differences in the serum concentrations of SHBG between the study groups or between the autumn and the spring. High training activity and a dark photoperiod appeared to independently suppress ovarian activity and were not associated with chronic changes in anterior pituitary hormone or SHBG concentrations.

Keywords

Rönnberg L, Kauppila A, Leppaluoto J et al. **Year** 1990

Authors Rönnberg L, Kauppila A, Leppaluoto J et al.

Report Name Circadian and seasonal variation in human preovulatory follicular fluid melatonin concentration

Publication J Clin Endocrinol Metab

Issue-page numbers 71:492–496 doi:10.1210/jcem-71-2-493. PMID: 2380343

URL http://jcem.endojournals.org/content/71/2/493.abstract

Abstract The concentrations of melatonin in 112 preovulatory follicular fluid (FF) samples obtained from 60 women undergoing in vitro fertilization and 27 patients at laparotomy during a spontaneous cycle were measured by RIA and compared with those in peripheral serum. The circadian and seasonal variations in FF melatonin were also analyzed.

The FF melatonin concentrations in stimulated (mean ± sem, 61.9 ± 6.4 pmol/L) and spontaneous cycles (98.1 ± 8.9 pmol/L) were significantly higher ($P < 0.005$) than those in peripheral serum (25.4 ± 1.2 and 38.6 ± 1.8 pmol/L, respectively), and in the stimulated cycles there was a positive correlation between them. The FF melatonin concentration in the morning (58.9 ± 3.8 pmol/L) was significantly higher ($P < 0.005$) than that in the daytime (23.2 ± 0.8 pmol/L), but the morning concentrations did not differ between the light and the dark seasons of the year, whereas the daytime values were higher ($P < 0.005$) during the dark season (27.1 ± 2.1 pmol/L) than during the light season (21.1 ± 2.1 pmol/L). The FF melatonin concentration did not correlate with follicular volume, and FF and serum melatonin concentrations showed no significant correlation with the serum concentrations of estradiol, progesterone, testosterone, or PRL. There were also no differences between FF melatonin concentrations in aspirates with or without an ovum.

In summary, significant circadian and circannual variations in high FF melatonin concentrations were found, which sugges that melatonin could potentially interfere with the regulation of reproduction in humans at the follicular level.

Keywords

Rosenthal N **Year** 1995

Authors N Rosenthal

Report Name Light and biological rhythms in psychiatry

Publication Harvard Mental Health Letter (1995)

Issue-page numbers Volume: 11, Issue: 9, Pages: 5

URL http://www.mendeley.com/research/light-and-biological-rhythms-in-psychiatry-1/

Abstract About twenty years ago, researchers began to suggest that disturbances in biological rhythms might be a cause of human psychiatric disorders, especially those of mood. Since that time, understanding of the subject has advanced greatly, especially with the discovery of seasonal affective disorder (SAD), a type of depression that occurs in winter and responds to trratment with bright light.

Keywords

Rosołowska-Huszcz D, Thaela MJ, Jagura M et al. **Year** 1991

Authors Rosołowska-Huszcz D, Thaela MJ, Jagura M et al.

Report Name Pineal influence on the diurnal rhythm of nonspecific immunity indices in chickens

Publication J Pineal Res

Issue-page numbers 10:190–195 doi:10.1111/j.1600-079X.1991.tb00815.x. PMID:1920042

URL http://www.ncbi.nlm.nih.gov/pubmed/1920042

Abstract The effect of pinealectomy and melatonin injections on the diurnal rhythms of serum lysozyme and blood granulocytes was examined in White Leghorn cockerels kept from time of hatching for 5 weeks in L:D 12:12 conditions and immunized twice with sheep red blood cells (SRBC). Pinealectomy or sham-operation was made during first week of life. Pinealectomized chickens were injected daily with a melatonin dosage increased over 4 consecutive weeks (the dosage was 10, 13, 16, and 20 ng per bird daily during the 4 weeks, respectively; MEL I) at the beginning of darkness. The same treatment was performed on chickens with an intact pineal gland using additional melatonin doses increased 10 times (MEL II) and 500 times (MEL III). Intact chickens were also injected with MEL II and MEL III 4 hr before the end of light. Control birds received equivalent injections of vehicle. Five-week-old chickens were sacrificed during a 24-hr period every 4 hr. The existence of diurnal rhythm was evaluated by cosinor analysis. Pinealectomy shifted the acrophase of the diurnal rhythm of granulocytes and abolished that of serum lysozyme. Both rhythms were restored in pinealectomized chickens by MEL I but not by vehicle injections. The same melatonin dose was unable to change the granulocyte rhythm but delayed the acrophase of that of serum lysozyme in chickens with an intact pineal gland. Two higher melatonin doses influenced the diurnal rhythm of granulocytes as a function of dose and time of administration. The rhythm of serum lysozyme was dependent only on the time of injection. The pineal gland seems to control, via its hormone melatonin, the diurnal rhythm of nonspecific immunity in chickens.

Keywords

Ross G, Foley P, Baker C **Year** 2008

Authors Ross G, Foley P, Baker C.

Report Name Actinic prurigo

Publication Photodermatology, Photoimmunology & Photomedicine

Issue-page numbers Volume 24, Issue 5, pages 272–275, October 2008

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0781.2008.00375.x/full

Abstract Actinic Prurigo (AP), an uncommon idiopathic photodermatosis, presents a distinct clinical picture and can be severely debilitating. The clinical features, investigation and treatment of AP are reviewed. We report the experience of an Australian photobiology unit with this condition.

Keywords HLA DRB1*0407; HLA typing; photodermatosis; photosensitivity; thalidomide

Authors Ross JK, Arendt J, Horne J, Haston W

Report Name Night-shift work in Antarctica: sleep characteristics and bright light treatment

Publication Physiol Behav

Issue-page numbers 57:1169–1174 doi:10.1016/0031-9384(95)00018-E. PMID:7652039

URL http://www.sciencedirect.com/science/article/pii/003193849500018E

Abstract Changes in sleep parameters during and after night-shift and the effects of bright white (2500–3000 1x) and dim red (>500 1x) light treatment on re adaptation after night-shift during winter were studied in 14 men on the British Antarctic Survey Base of Halley (75° south). Subjects kept daily sleep diaries and mood ratings from one week before to three weeks after night-shift and received either full-spectrum white or dim red light treatment from 1100 to 1300 h daily during the first week after night-shift. Plasma melatonin (for 24 h at the end of weeks 1, 2 and 4), and urinary 6-sulfatoxymelatonin (aMT6s, for 48 h weekly) were measured. A significant (MANOVA; $p < 0.05$) improvement in sleep was seen during night shift (latency and duration) and with bright light treatment (latency). Melatonin and aMT6s rhythms delayed by 7–8 h during night-shift. The white light group readapted slowly, apparently by phase delay, as assessed by aMT6s measurement. The red light group readapted slightly, but significantly (ANOVA, $p < 0.01$) faster than the white light group.

Keywords Melatonin; Circadian rhythm; Shift work; Light treatment

Roth T

Year 2012

Authors Thomas Roth

Report Name Appropriate therapeutic selection for patients with shift work disorder

Publication Sleep Medicine

Issue-page numbers Available online 20 February 2012

URL http://www.sciencedirect.com/science/article/pii/S1389945712000044

Abstract

Background

Shift work disorder (SWD) is characterized by symptoms of excessive sleepiness during work hours or insomnia during allotted daytime sleep hours, as well as by a disruption of the circadian rhythm. Many shift workers with SWD experience significant social, behavioral, and health problems as a result of this disorder. SWD is associated with a higher risk of occupational and motor vehicle accidents, and thus poses a public health risk.

Methods

Currently there are both pharmacologic and non-pharmacologic treatments for this disorder that can be used to normalize the disruption of the circadian cycle or alleviate the symptoms of excessive sleepiness or insomnia. The American Academy of Sleep Medicine and the British Society of Psychopharmacology have developed guidelines for the diagnosis and treatment of patients with SWD.

Results

Recommended therapies for altering the circadian cycle include chronobiotics such as melatonin or melatonin agonists and non-pharmacologic interventions such as timed light exposure. Other therapies, such as sedative hypnotics, target daytime insomnia, while pharmacologic agents such as modafinil, armodafinil, and caffeine and non-pharmacologic approaches such as napping promote nighttime alertness.

Conclusions

While no therapies (pharmacological or nonpharmacological) can restore altered circadian cycles to baseline levels, proper identification and management of SWD will likely reduce its co-morbidities and improve the quality of life for individuals with this disorder.

Keywords Shift work disorder; Circadian rhythm; Excessive sleepiness; Insomnia; Wakefulness

Roybal K, Theobold D, Graham A, et al. **Year** 2007

Authors Kole Roybal, David Theobold, Ami Graham, Jennifer A. DiNieri, Scott J. Russo, Vaishnav Krishnan, Sumana Chakravarty, Joseph Peevey, Nathan Oehrlein, Shari Birnbaum, Ma

Report Name Mania-like behavior induced by disruption of CLOCK

Publication Proc Natl Acad Sci USA

Issue-page numbers April 10; 104(15): 6406–6411.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1851061/

Abstract Circadian rhythms and the genes that make up the molecular clock have long been implicated in bipolar disorder. Genetic evidence in bipolar patients suggests that the central transcriptional activator of molecular rhythms, CLOCK, may be particularly important. However, the exact role of this gene in the development of this disorder remains unclear. Here we show that mice carrying a mutation in the Clock gene display an overall behavioral profile that is strikingly similar to human mania, including hyperactivity, decreased sleep, lowered depression-like behavior, lower anxiety, and an increase in the reward value for cocaine, sucrose, and medial forebrain bundle stimulation. Chronic administration of the mood stabilizer lithium returns many of these behavioral responses to wild-type levels. In addition, the Clock mutant mice have an increase in dopaminergic activity in the ventral tegmental area, and their behavioral abnormalities are rescued by expressing a functional CLOCK protein via viral-mediated gene transfer specifically in the ventral tegmental area. These findings establish the Clock mutant mice as a previously unrecognized model of human mania and reveal an important role for CLOCK in the dopaminergic system in regulating behavior and mood.

Keywords bipolar disorder, circadian rhythms, dopamine

Różanowski B, Cuenco J, Davies S, et al. **Year** 2008

Authors Bartosz Różanowski, Joyceline Cuenco, Sallyanne Davies, Farukh A. Shamsi, Andrzej Żądło, Pierrette Dayhaw-Barker, Małgorzata Róz˙anowska, Tadeusz Sarna, Michael E. Bo

Report Name The Phototoxicity of Aged Human Retinal Melanosomes

Publication Photochemistry and Photobiology

Issue-page numbers Volume 84, Issue 3, pages 650–657, May/June 2008

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2007.00259.x/full

Abstract The purpose of this study was to determine whether an age-related increase in photoreactivity of human retinal melanosomes (MS) can cause phototoxicity to retinal pigment epithelium (RPE) cells. MS were isolated post mortem from young (20–30 years, young human melanosomes [YHMs]) and old (60–90 years, old human melanosomes [OHMs]) human eyes and from young bovine eyes (bovine melanosomes [BMs]). Confluent cultured ARPE-19 cells were fed equivalent numbers of OHMs or BMs and accumulated similar amounts of melanin as determined by electron paramagnetic resonance assay. Cells with and without MS were either maintained in the dark or exposed to blue light for up to 96 h and assessed for alterations in cell morphology, cell viability and lysosomal integrity. Incubation of cells in dark in the presence of internalized MS or irradiation of cells with blue light in the absence or presence of BMs did not significantly affect cell viability. However, exposures to blue light in the presence of OHMs resulted in abnormal cell morphology, up to ~75% decrease in mitochondrial activity, loss of lysosomal pH and cell death. OHMs contained significantly less melanin than YHMs, supporting the hypothesis that melanin undergoes degradation during RPE aging. Our results demonstrate that aged MS can be phototoxic to human RPE cells and support a contributing role of MS in RPE aging and in the pathogenesis of age-related macular degeneration.

Keywords

Ruan G-X, Gamble KL, Risner ML, et al. **Year** 2012

Authors Guo-Xiang Ruan, Karen L. Gamble, Michael L. Risner, Laurel A. Young, Douglas G. McMahon

Report Name Divergent Roles of Clock Genes in Retinal and Suprachiasmatic Nucleus Circadian Oscillators

Publication PLoS ONE

Issue-page numbers 7(6): e38985. doi:10.1371/journal.pone.0038985

URL http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0038985

Abstract The retina is both a sensory organ and a self-sustained circadian clock. Gene targeting studies have revealed that mammalian circadian clocks generate molecular circadian rhythms through coupled transcription/translation feedback loops which involve 6 core clock genes, namely Period (Per) 1 and 2, Cryptochrome (Cry) 1 and 2, Clock, and Bmal1 and that the roles of individual clock genes in rhythms generation are tissue-specific. However, the mechanisms of molecular circadian rhythms in the mammalian retina are incompletely understood and the extent to which retinal neural clocks share mechanisms with the suprachiasmatic nucleus (SCN), the central neural clock, is unclear. In the present study, we examined the rhythmic amplitude and period of real-time bioluminescence rhythms in explants of retina from Per1-, Per2-, Per3-, Cry1-, Cry2-, and Clock-deficient mice that carried transgenic PERIOD2::LUCIFERASE (PER2::LUC) or Period1::luciferase (Per1::luc) circadian reporters. Per1-, Cry1- and Clock-deficient retinal and SCN explants showed weakened or disrupted rhythms, with stronger effects in retina compared to SCN. Per2, Per3, and Cry2 were individually dispensable for sustained rhythms in both tissues. Retinal and SCN explants from double knockouts of Cry1 and Cry2 were arrhythmic. Gene effects on period were divergent with reduction in the number of Per1 alleles shortening circadian period in retina, but lengthening it in SCN, and knockout of Per3 substantially shortening retinal clock period, but leaving SCN unaffected. Thus, the retinal neural clock has a unique pattern of clock gene dependence at the tissue level that it is similar in pattern, but more severe in degree, than the SCN neural clock, with divergent clock gene regulation of rhythmic period.

Keywords

Ruby NF, Brennan TJ, Xie X et al. **Year** 2002

Authors Ruby NF, Brennan TJ, Xie X et al.

Report Name Role of melanopsin in circadian responses to light

Publication Science

Issue-page numbers 298:2211–2213 doi:10.1126/science.1076701. PMID:12481140

URL http://www.sciencemag.org/content/298/5601/2211.abstract

Abstract Melanopsin has been proposed as an important photoreceptive molecule for the mammalian circadian system. Its importance in this role was tested in melanopsin knockout mice. These mice entrained to a light/dark cycle, phase-shifted after a light pulse, and increased circadian period when light intensity increased. Induction of the immediate-early gene c-fos was observed after a nighttime light pulse in both wild-type and knockout mice. However, the magnitude of these behavioral responses in knockout mice was 40% lower than in wild-type mice. Although melanopsin is not essential for the circadian clock to receive photic input, it contributes significantly to the magnitude of photic responses.

Keywords

Rüger M, Gordijn MCM, Beersma DGM

Year 2006

Authors Melanie Rüger, Marijke C. M. Gordijn, Domien G. M. Beersma, Bonnie de Vries, and Serge Daan

Report Name Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure

Publication AJP - Regu Physiol

Issue-page numbers May 2006 vol. 290 no. 5 R1413-R1420

URL http://ajpregu.physiology.org/content/290/5/R1413.short

Abstract Bright light can influence human psychophysiology instantaneously by inducing endocrine (suppression of melatonin, increasing cortisol levels), other physiological changes (enhancement of core body temperature), and psychological changes (reduction of sleepiness, increase of alertness). Its broad range of action is reflected in the wide field of applications, ranging from optimizing a work environment to treating depressed patients. For optimally applying bright light and understanding its mechanism, it is crucial to know whether its effects depend on the time of day. In this paper, we report the effects of bright light given at two different times of day on psychological and physiological parameters. Twenty-four subjects participated in two experiments (n = 12 each). All subjects were nonsmoking, healthy young males (18–30 yr). In both experiments, subjects were exposed to either bright light (5,000 lux) or dim light <10 lux (control condition) either between 12:00 P.M. and 4:00 P.M. (experiment A) or between midnight and 4:00 A.M. (experiment B). Hourly measurements included salivary cortisol concentrations, electrocardiogram, sleepiness (Karolinska Sleepiness Scale), fatigue, and energy ratings (Visual Analog Scale). Core body temperature was measured continuously throughout the experiments. Bright light had a time-dependent effect on heart rate and core body temperature; i.e., bright light exposure at night, but not in daytime, increased heart rate and enhanced core body temperature. It had no significant effect at all on cortisol. The effect of bright light on the psychological variables was time independent, since nighttime and daytime bright light reduced sleepiness and fatigue significantly and similarly.

Keywords sleepiness; core body temperature; cortisol; heart rate

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Rüger M, St. Hilaire MA, Brainard G, et al.

Year 2012

Authors Melanie Rüger, Melissa A St. Hilaire, George Brainard, Sat Bir S Khalsa, Richard E Kronauer, Charles A Czeisler and Steven W Lockley

Report Name Human phase response curve to a single 6.5-h pulse of short-wavelength light

Publication The Journal of Physiology,

Issue-page numbers Published online before print October 22, 2012, doi: 10.1113/jphysiol.2012.239046

URL http://jp.physoc.org/content/early/2012/10/17/jphysiol.2012.239046.abstract

Abstract The photic resetting response of the human circadian pacemaker depends on the timing of exposure, and the direction and magnitude of the resulting shift is described by a Phase Response Curve (PRC). Previous PRCs in humans have utilized high intensity polychromatic white light. Given that the circadian photoreception system is maximally sensitive to short-wavelength visible light, the aim of the current study was to construct a PRC to blue (480 nm) light and compare it to a 10,000 lux white light PRC constructed previously using a similar protocol. Eighteen young healthy participants (18-30 years) were studied for 9-10 days in a time-free environment. The protocol included 3 baseline days followed by a constant routine (CR) to assess initial circadian phase. Following CR1 participants were exposed to a 6.5-h 480 nm light exposure (11.8 μW/cm2, 11.2 lux) following mydriasis via a modified Ganzfeld dome. A second CR was conducted following the light exposure to re-assess circadian phase. Phase shifts were calculated from the difference in Dim Light Melatonin Onset (DLMO) between CRs. Exposure to 6.5 hours of 480 nm light reset the circadian pacemaker according to a conventional Type 1 PRC with fitted maximum delays and advances of -2.55 h and 1.29 h, respectively. The 480 nm PRC induced ~75% of the response of the 10,000 lux white light PRC.. These results may contribute to a re-evaluation of dosing guidelines for clinical light therapy and the use of light as a fatigue countermeasure.

Keywords Melatonin, Blue light, Phase Response Curve

Russell SC, Dawe RS, Collins P, et al. **Year** 1998

Authors Russell SC, Dawe RS, Collins P, Man I, Ferguson J.

Report Name The photosensitivity dermatitis and actinic reticuloid syndrome (chronic actinic dermatitis) occurring in seven young atopic dermatitis patients

Publication British Journal of Dermatology

Issue-page numbers Volume 138, Issue 3, pages 496–501, March 1998

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2133.1998.02132.x/abstract?

Abstract Seven young patients with atopic dermatitis (AD) who presented with a marked photoexposed site dermatitis have been investigated in detail. The results of phototesting, patch testing and other investigations were compatible with the diagnosis of photosensitivity dermatitis/actinic reticuloid syndrome (PD/AR) (chronic actinic dermatitis). It is known that AD patients may have photoaggravation of their dermatitis or exacerbation secondary to a photodermatosis, such as polymorphic light eruption, actinic prurigo or drug-induced phototoxicity. The patients we describe, however, appear to be an uncommon AD subgroup affected by PD/AR. We recommend that all AD patients who have a history of sunlight-induced exacerbation or marked intolerance of PUVA or ultraviolet B phototherapy should have phototesting and patch testing conducted.

Keywords

Saari JC, Bredberg DL, Noy N **Year** 1994

Authors Saari JC, Bredberg DL, Noy N.

Report Name Control of substrate flow at a branch in the visual cycle

Publication Biochemistry

Issue-page numbers 1994, 33 (10), pp 3106–3112 DOI: 10.1021/bi00176a045

URL http://pubs.acs.org/doi/abs/10.1021/bi00176a045

Abstract Photoisomerization of rhodopsin's chromophore, 11-cis-retinaldehyde, and subsequent regeneration of the 11-cis configuration are accomplished in vertebrates by a series of reactions known as the visual cycle. At one point in the cycle, 11-cis-retinol can either be enzymatically oxidized to 11-cis-retinaldehyde and exported for visual pigment regeneration or be enzymatically esterified and stored. Partition of substrate at this branch was examined in this study and found to be influenced by cellular retinaldehyde-binding protein (CRALBP), a retinoid-binding protein found in retina. Esterification was reduced to about 10% and oxidation stimulated 2-3-fold in the presence of this protein. Other experiments confirmed that "free" 11-cis-retinol was esterified more rapidly than 11-cis-retinol complexed with CRALBP and that CRALBP.11-cis-retinol was not an inhibitor of the esterification. Following oxidation of CRALBP.11-cis-retinol, the reaction product, 11-cis-retinaldehyde, was found associated with the binding protein. 11-cis-Retinaldehyde is not available for reaction with carbonyl reagents when the retinoid is bound to CRALBP. However, enzymatic oxidation of CRALBP.11-cis-retinol in the presence of O-ethylhydroxylamine produced ca. 30% retinaldehyde O-ethyloxime and 70% free 11-cis-retinaldehyde, suggesting that about one-third of the retinol oxidized had dissociated from the binding protein. Neither oxidation nor esterification of CRALBP.11-cis-retinol was inhibited by including CRALBP.11-cis-retinaldehyde in the reaction mixture.(ABSTRACT TRUNCATED AT 250 WORDS)

Keywords

Sack RL, Blood ML, Lewy AJ

Year 1992

Authors Sack RL, Blood ML, Lewy AJ

Report Name Melatonin rhythms in night shift workers

Publication Sleep

Issue-page numbers 15:434–441.PMID:1455127

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24833

Abstract

For some time, it has remained uncertain whether the circadian rhythms of permanent night shift workers are adapted to their night-active schedule. Previous studies of this question have often been limited by "masking" (evoked) effects of sleep and activity on body temperature and cortisol, used as marker rhythms. In this study, the problem of masking was minimized by measuring the timing of melatonin production under dim light conditions. Nine permanent night shift workers were admitted to the Clinical Research Center (CRC) directly from their last work shift of the week and remained in dim light while blood samples were obtained hourly for 24 hours. Melatonin concentrations were measured in these samples using a gas-chromatographic mass- spectrometric method. Sleep diaries were completed for two weeks prior to the admission to the CRC. Overall, the onset of the melatonin rhythm was about 7.2 hours earlier (or 16.8 hours later) in the night workers compared to day-active controls. It was not possible to know whether the phase of the melatonin rhythm was the result of advances or delays. In night shift workers, sleep was initiated (on average) about three hours prior to the onset of melatonin production. In contrast, day- active subjects initiated sleep (on average) about three hours after their melatonin onset. Thus, the sleep times selected by night shift workers may not be well-synchronized to their melatonin rhythm, assumed to mark the phase of their underlying circadian pacemaker.

Keywords

Authors Sack RL, Brandes RW, Kendall AR, Lewy AJ

Report Name Entrainment of free-running circadian rhythms by melatonin in blind people

Publication N Engl J Med

Issue-page numbers 343:1070–1077 doi:10.1056/NEJM200010123431503. PMID:11027741

URL http://www.nejm.org/doi/full/10.1056/NEJM200010123431503

Abstract

Background

Most totally blind people have circadian rhythms that are “free-running” (i.e., that are not synchronized to environmental time cues and that oscillate on a cycle slightly longer than 24 hours). This condition causes recurrent insomnia and daytime sleepiness when the rhythms drift out of phase with the normal 24-hour cycle. We investigated whether a daily dose of melatonin could entrain their circadian rhythms to a normal 24-hour cycle.

Full Text of Background...
Methods

We performed a crossover study involving seven totally blind subjects who had free-running circadian rhythms. The subjects were given 10 mg of melatonin or placebo daily, one hour before their preferred bedtime, for three to nine weeks. They were then given the other treatment. The timing of the production of endogenous melatonin was measured as a marker of the circadian time (phase), and sleep was monitored by polysomnography.

Full Text of Methods...
Results

At base line, the subjects had free-running circadian rhythms with distinct and predictable cycles averaging 24.5 hours (range, 24.2 to 24.9). These rhythms were unaffected by the administration of placebo. In six of the seven subjects the rhythm was entrained to a 24.0-hour cycle during melatonin treatment ($P<0.001$). After entrainment, the subjects spent less time awake after the initial onset of sleep ($P=0.05$) and the efficiency of sleep was higher ($P=0.06$). Three subjects subsequently participated in a trial in which a 10-mg dose of melatonin was given daily until entrainment was achieved. The dose was then reduced to 0.5 mg per day over a period of three months; the entrainment persisted, even at the lowest dose.

Full Text of Results...
Conclusions

Administration of melatonin can entrain circadian rhythms in most blind people who have free-running rhythms.

Keywords

Sack RL, Hughes RJ, Edgar DM, Lewy AJ **Year** 1997

Authors Sack RL, Hughes RJ, Edgar DM, Lewy AJ

Report Name Sleep-promoting effects of melatonin: at what dose, in whom, under what conditions, and by what mechanisms?

Publication Sleep

Issue-page numbers 20:908–915. PMID:9415954

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24166

Abstract Differing conclusions regarding the sleep-promoting effects of melatonin may be the result of the broad range of doses employed (0.1- 2000 mg), the differing categories of subjects tested (normal subjects, insomniac patients, elderly, etc.), and the varying times of administration (for daytime vs. nighttime sleep). We conclude that melatonin may benefit sleep by correcting circadian phase abnormalities and/or by a modest direct soporific effect that is most evident following daytime administration to younger subjects. We speculate that these effects are mediated by interactions with specific receptors concentrated in the suprachiasmatic nucleus (SCN) that result in resetting of the circadian pacemaker and/or attenuation of an SCN- dependent circadian alerting process.

Keywords

Sahar S, Sassone-Corsi P **Year** 2007

Authors Sahar S, Sassone-Corsi P

Report Name Circadian clock and breast cancer: a molecular link

Publication Cell Cycle

Issue-page numbers 6:1329–1331. PMID:17534151

URL https://www.landesbioscience.com/journals/cc/article/4295/

Abstract The circadian clock controls a large array of behavioral and physiological systems of fundamental importance to most organisms. Consequently, abnormal functioning of the clock results in severe dysfunctions and pathologies. Although epidemiological studies show a clear correlation between disruption of circadian rhythms and incidence of breast cancer, a molecular interpretation of how clock-related mechanisms may link to tumor development remains elusive. Here we speculate on the molecular pathways that may couple the circadian machinery to breast cancer.

Keywords

Sahar S, Sassone-Corsi P

Year 2011

Authors Saurabh Sahar, Paolo Sassone-Corsi

Report Name Regulation of metabolism: the circadian clock dictates the time

Publication Trends in Endocrinology & Metabolism

Issue-page numbers In Press, Corrected Proof - Note to users doi:10.1016/j.tem.2011.10.005

URL http://www.sciencedirect.com/science/article/pii/S1043276011001767

Abstract Circadian rhythms occur with a periodicity of approximately 24 h and regulate a wide array of metabolic and physiologic functions. Accumulating epidemiological and genetic evidence indicates that disruption of circadian rhythms can be directly linked to many pathological conditions, including sleep disorders, depression, metabolic syndrome and cancer. Intriguingly, several molecular gears constituting the clock machinery have been found to establish functional interplays with regulators of cellular metabolism. Although the circadian clock regulates multiple metabolic pathways, metabolite availability and feeding behavior can in turn regulate the circadian clock. An in-depth understanding of this reciprocal regulation of circadian rhythms and cellular metabolism may provide insights into the development of therapeutic intervention against specific metabolic disorders.

Keywords

Sakai N, Decatur J, Nakanishi K, Eldred GE

Year 1996

Authors Sakai N, Decatur J, Nakanishi K, Eldred GE.

Report Name Ocular age pigment A2-E: An unprecedented pyridinium bisretinoid

Publication J. Am. Chem. Soc.

Issue-page numbers 1996, 118, 1559-1560

URL http://www.columbia.edu/cu/chemistry/groups/nakanishi/publication/618-Ocular%20Age%20Pigment%20_A2-E_%20An%20Unprecedented%20Pyridinium%20Bisretinoid.pdf

Abstract With age, fluorescent granules called lipofuscin or age pigments accumulate in the retinal pigment epithelium (RPE).1 These granules are believed to lead to cellular aging processes and related diseases, notably age-related macular degeneration (AMD),2 the leading cause of blindness in elderly people for which no remedy exists. It is generally accepted that the pigments are formed as a consequence of accumulation of debris resulting from incomplete digestion of phagocytosed outer segment disks in lysosomes. Among the compounds that accumulate in lipofuscin, the orange fluorophores have attracted wide interest since they are considered to be the possible cause of age-related decline of cell functions. In this communication we report the structure of the major fluorophore.

Keywords

Sakami S, Ishikawa T, Kawakami N et al. **Year** 2003

Authors Sakami S, Ishikawa T, Kawakami N et al.

Report Name Coemergence of insomnia and a shift in the Th1/Th2 balance toward Th2 dominance.

Publication Neuroimmunomodulation

Issue-page numbers 10:337–343 doi:10.1159/000071474. PMID:12907840

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=71474

Abstract Objectives: Insomnia is associated with physical and mental disorders. We examined the effect of insomnia on immune functions, focusing on the T helper 1 (Th1)/ T helper 2 (Th2) balance, by a cross-sectional design. Methods: We provided a self-administered questionnaire to evaluate sleep habits, smoking and medical disorders to 578 men without any toxic exposure (20–64 years old), and measured natural killer (NK) cell activity in 324 men and production of interferon-gamma (IFN-=γ) and interleukin-4 (IL-4) after stimulation with phytohemagglutinin in 254 men. According to the criteria of DSM-IV, in which insomnia is classified into primary and secondary insomnia, we assessed the effect of insomnia on immune functions, controlling for age and smoking in groups with and without medical disorders. Results: The prevalence of insomnia in the present study was 9.2%. In the absence of medical disorders, insomniac men had a significantly lower IFN-=γ and ratio of IFN-=γ to IL-4 than noninsomniac men. Men with insufficient sleep or difficulty initiating sleep (DIS) had a significantly lower IFN-=γ to IL-4 ratio than those not suffering from insufficient sleep or DIS. In the presence of medical disorders, insomniac men had significantly higher IL-4 than noninsomniac men. Men with difficulty maintaining sleep (DMS) had a significantly lower IFN-=γ to IL-4 ratio than men without DMS. NK cell activity was independent of insomnia. Conclusions: The present results showed a link between insomnia unrelated to medical disorders and a shift in the Th1/Th2 balance toward Th2 dominance, indicating that the relationship between sleep quality and the etiology of immune-related diseases should be reconsidered.

Keywords

Sakamoto K, Ishida N **Year** 2000

Authors Sakamoto K, Ishida N

Report Name Light-induced phase-shifts in the circadian expression rhythm of mammalian period genes in the mouse heart

Publication Eur J Neurosci

Issue-page numbers 12:4003–4006 doi:10.1046/j.1460-9568.2000.00302.x. PMID:11069596

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1460-9568.2000.00302.x/abstract?

Abstract To investigate the molecular mechanism that regulates circadian rhythms in mammalian peripheral tissues, we examined the phase shifts evoked by light exposure in the circadian mRNA expression rhythms of mammalian Period genes (mPer1, mPer2 and mPer3) and a clock-controlled gene Dbp, in the mouse heart, by Northern blot analysis. The light pulse did not induce any acute mRNA expression of mPer in the heart, but the pulse gave rise to phase shifts in the circadian mRNA rhythms. On the first day after the exposure, only mPer1 mRNA showed a phase shift, whereas obvious phase shifts were not observed in the rhythms of mPer2, mPer3 and Dbp mRNAs. On the second day, phase shifts occurred to a similar extent in the mRNA rhythms of all four genes examined. The rhythm of mPer1 mRNA shifted fastest among those of the three mPers. Therefore mPer1 seems to play an important role in phase resetting of mammalian peripheral oscillators. Immediate responses to light pulses in mRNA expression of mPers may not be required for phase shifting of peripheral circadian oscillators. Our findings suggest that mammals require more than one day to have peripheral oscillators entrained to a new daily schedule.

Keywords circadian rhythms; mammals; Period; phase shift

Authors Sakamoto K, Nagase T, Fukui H et al.

Report Name Multitissue circadian expression of rat period homolog (rPer2) mRNA is governed by the mammalian circadian clock, the suprachiasmatic nucleus in the brain.

Publication J Biol Chem

Issue-page numbers 273:27039–27042 doi:10.1074/jbc.273.42.27039. PMID:9765215

URL http://www.jbc.org/content/273/42/27039.full

Abstract

The period (per) gene, controlling circadian rhythms in Drosophila, is expressed throughout the body in a circadian manner. A homolog ofDrosophila per was isolated from rat and designated asrPer2. The rPER2 protein showed 39 and 95% amino acid identity with mPER1 and mPER2 (mouse homologs of per) proteins, respectively. A robust circadian fluctuation ofrPer2 mRNA expression was discovered not only in the suprachiasmatic nucleus (SCN) of the hypothalamus but also in other tissues including eye, brain, heart, lung, spleen, liver, and kidney. Furthermore, the peripheral circadian expression of rPer2mRNA was abolished in SCN-lesioned rats that showed behavioral arrhythmicity. These findings suggest that the multitissue circadian expression of rPer2 mRNA was governed by the mammalian brain clock SCN and also suggest that the rPer2 gene was involved in the circadian rhythm of locomotor behavior in mammals.

Circadian rhythms in physiology and behavior are governed by the endogenous clock (1, 2). Many circadian rhythms have been described in a diverse range of species, from bacteria to human (3). However, the common molecular mechanism of the circadian clock in diverse species is totally unknown. In mammals, the suprachiasmatic nucleus (SCN)1 of the anterior hypothalamus has been shown to be the circadian pacemaker (1, 2). Much effort is being directed to identify the master genes that control the circadian rhythm in the SCN. One of the strong candidates is theclock gene, because a mutation in the clock gene results in arrhythmic locomotor behavior (4, 5). The period(per) gene in Drosophila, which is expressed throughout the body in a circadian manner, regulates the circadian locomotor rhythm (6, 7). Recently two different homologs ofDrosophila per gene were reported for mouse and human (8-11). Though the two mammalian per homologs show circadian mRNA oscillation in the mouse SCN, their functional involvement in the circadian locomotor activity has not yet been reported.

To examine whether a mammalian per homolog is involved in the circadian rhythm of locomotor behavior, we cloned a ratper homolog and monitored its circadian expression rhythms in peripheral tissues of SCN-lesioned rats that showed arrhythmic locomotor activity.

Keywords

Salgado-Delgado R, Osorio AT, Saderi N, Escobar C

Year 2011

Authors Roberto Salgado-Delgado, Araceli Tapia Osorio, Nadia Saderi, and Carolina Escobar

Report Name Disruption of Circadian Rhythms: A Crucial Factor in the Etiology of Depression

Publication Depression Research and Treatment

Issue-page numbers Volume 2011 (2011), Article ID 839743, 9 pages

URL http://www.hindawi.com/journals/drt/2011/839743/

Abstract Circadian factors might play a crucial role in the etiology of depression. It has been demonstrated that the disruption of circadian rhythms by lighting conditions and lifestyle predisposes individuals to a wide range of mood disorders, including impulsivity, mania and depression. Also, associated with depression, there is the impairment of circadian rhythmicity of behavioral, endocrine, and metabolic functions. Inspite of this close relationship between both processes, the complex relationship between the biological clock and the incidence of depressive symptoms is far from being understood. The efficiency and the timing of treatments based on chronotherapy (e.g., light treatment, sleep deprivation, and scheduled medication) indicate that the circadian system is an essential target in the therapy of depression. The aim of the present review is to analyze the biological and clinical data that link depression with the disruption of circadian rhythms, emphasizing the contribution of circadian desynchrony. Therefore, we examine the conditions that may lead to circadian disruption of physiology and behavior as described in depressive states, and, according to this approach, we discuss therapeutic strategies aimed at treating the circadian system and depression.

Keywords

Samuels MH, Lillehei K, Kleinschmidt-Demasters BK et al.

Year 1990

Authors Samuels MH, Lillehei K, Kleinschmidt-Demasters BK et al.

Report Name Patterns of pulsatile pituitary glycoprotein secretion in central hypothyroidism and hypogonadism.

Publication J Clin Endocrinol Metab

Issue-page numbers 70:391–395 doi:10.1210/jcem-70-2-391. PMID:2105331

URL http://www.ncbi.nlm.nih.gov/pubmed/2105331

Abstract Five patients with central hypothyroidism and hypogonadism due to mass or infiltrative lesions of the pituitary and hypothalamus were studied to determine pulsatile pituitary glycoprotein secretion patterns. Blood samples were obtained every 15 min over 24 h, and TSH, LH and FSH were measured by immunoradiometric assays. Hormone pulses were located by cluster analysis, and pulse patterns were compared to those in normal subjects. Three patients had unmeasurable LH levels, while two had a normal number of low amplitude pulses. In contrast, all patients had normal FSH pulse frequency, and only one had low pulse amplitude. Three patients had normal 24-h TSH pulse frequency and amplitude, while two had slightly decreased pulse parameters. However, all failed to show normal nocturnal increases in TSH pulse amplitude. Thus, anatomical hypothalamic-pituitary lesions disrupt pulsatile glycoprotein secretion in a discordant fashion. LH is most severely affected, with abnormal pulse patterns similar to those in idiopathic central hypogonadism. FSH and TSH pulses are relatively preserved, but loss of the usual nocturnal increase in TSH pulse amplitude is sufficient to cause clinical hypothyroidism. Whether these defects reflect intrinsic pituitary disease or impaired hypothalamic releasing factor function remains to be determined.

Keywords

San Martin M, Touitou Y **Year** 2000

Authors San Martin M, Touitou Y

Report Name DHEA-sulfate causes a phase-dependent increase in melatonin secretion: a study of perifused rat pineal glands

Publication Steroids

Issue-page numbers 65:491–496 doi:10.1016/S0039-128X(00)00111-2. PMID:10978727

URL http://www.sciencedirect.com/science/article/pii/S0039128X00001112

Abstract Steroid hormones affect various metabolic activities, including melatonin synthesis, in mammals and nonmammals. We report here the effects of dehydroepiandrosterone (DHEA) and DHEA-sulfate (DHEA-S), two steroids with weak androgen potency, on the levels of isoproterenol-stimulated melatonin released by perifused rat pineal glands removed in the middle of the light and dark spans [7 and 19 Hours After Light Onset (HALO), respectively] in a L/D 12:12 regimen. DHEA-S but not DHEA was found to have a direct action on β-adrenergic-stimulated melatonin release. DHEA-S increased melatonin secretion (by 50–80%) dose-dependently in pineals obtained during the light span. This effect depended on the circadian stage, because at night (19 HALO), only the highest concentration (10−3 M) of DHEA-S increased melatonin secretion (by 25%). In contrast, DHEA had no effect on melatonin release in pineals obtained during the light span. This work shows that DHEA-S but not DHEA was able to stimulate melatonin secretion by adrenergic-stimulated pineals removed during the light phase. It also suggests that the effects observed, or their intensity, or both depend on the circadian stage.

Keywords Melatonin; Pineal gland; Steroids; Dehydroepiandrosterone; Dehydroepiandrosterone sulfate; Circadian

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Sánchez de la Peña S **Year** 1993

Authors Sánchez de la Peña S

Report Name The feedsideward of cephalo-adrenal immune interactions

Publication Chronobiologia

Issue-page numbers 20:1–52. PMID:8354098

URL http://www.ncbi.nlm.nih.gov/pubmed/8354098

Abstract The feedsideward phenomenon is the interaction of three or more rhythmic physiological entities by a diversified spectrum of rhythms that constitute a rhythmic network. These rhythmic units are: a) the modulator, b) the actor, c) the reactor and d) the integrative unity. Rhythmic interactions are characterized by an alternating sequence of algorithmically predictable effects of attenuation, no effect, and stimulation occurring in different frequencies. The basis of this phenomenon was determined from experimental evidence derivec from cephalo-adrenal ex vivo studies. Internal phase-shift studies allow the demonstration ex vivo of a collateral hierarchy of rhythmic neuro-endocrine interactions as alpha, beta, gamma and delta rhythms. Linear least squares analyses describe and quantify circadian (alpha, beta and gamma) and infradian (delta) rhythms in the original series and the differences in responses [beta-alpha] and [gamma-delta]. These spontaneous and response rhythms reveal a collateral neuro-endocrine hierarchy and validate a pineal feedsideward phenomenon. Circadian-infradian murine rhythmic intermodulations are demonstrated in the epithelial corneal mitosis; brain neurosteroids and pineal melatonin content. A circadian rhythm in pineal melatonin content in female B6D2F1 mice and the chronomodulating action of melatonin + ACTH upon adrenal corticosterone production are confirmed. A chronopilot ex vivo study "suggests" that melatonin chronomodulates mouse aldosterone production. In a second chronopilot study, HrIL-2 chronomodulates rat corticosterone production ex vivo. Feedsidewards in vivo were seen in the chronomodulation of tumor-host balance occurring after melatonin, IL-2, cefodizime, and cyclosporine treatments that enhanced or delayed tumor growth and survival time of tumor-bearing mice.

Keywords

Sánchez de la Peña S, Halberg F, Halberg E et al. **Year** 1983

Authors Sánchez de la Peña S, Halberg F, Halberg E et al.

Report Name Pineal modulation of ACTH 1–17 effect upon murine corticosterone production

Publication Brain Res Bull

Issue-page numbers 11:117–125 doi:10.1016/0361-9230(83)90060-6. PMID:6313140

URL http://www.mendeley.com/research/pineal-modulation-of-acth-117-effect-upon-murine-corticosterone-production/

Abstract In tests of corticosterone production in vitro, aqueous pineal homogenate (APH) modulates the effect of a short-chain ACTH analogue, ACTH 1-17, added to adrenals from different circadian stages. Adrenal and pineal glands from female B6D2F1 mice, standardized on staggered LD 12:12 regimens, were obtained at the same clock-hour from each room, in order to cover 6 different circadian stages. Adrenals from each circadian stage were bisected and incubated with APH from the same circadian stage (isophasic incubation) or from one of the other 5 circadian stages (heterophasic incubation). ACTH 1-17 (0.05 IU) was added to each incubation medium. After 4 hours of incubation at 37 degrees C with 95% O2 and 5% CO2, the media were stored at -20 degrees C until corticosterone RIA were done. APH was found to have a statistically significant modulatory effect upon the stimulation by ACTH 1-17 of adrenal corticosterone production in vitro. This APH effect changed rhythmically as a function of circadian stage from amplification over no effect to attenuation, as a so-called feed-sideward.

Keywords

Sánchez de la Peña S, Halberg F, Ungar F et al. **Year** 1983

Authors Sánchez de la Peña S, Halberg F, Ungar F et al.

Report Name Circadian pineal modulation of pituitary effect on murine corticosterone in vitro

Publication Brain Res Bull

Issue-page numbers 10:559–565 doi:10.1016/0361-9230(83)90155-7. PMID:6860981

URL http://www.sciencedirect.com/science/article/pii/0361923083901557

Abstract An old controversy is resolved as a novel effect: In a rhythmic fashion, aqueous pineal homogenate (APH) enhances, attenuates or leaves unaffected the production of corticosterone by mouse adrenals incubated with pituitary media. All glands stem from the same circadian stage in these (isophasic) studies on 72 female CD2F1 mice, standardized for two weeks in L 0600–1800 and D 0600–1800. Every 4 hours during a 24-hour span, 12 mice were killed. Pineals were removed for the preparation of APH and stored at 4°C. Hypothalami, pituitaries and adrenals were removed, bisected and placed in wells containing 1 ml Krebs-Ringer buffer (K). at 4°C, until incubation. At each circadian stage, bisected adrenals were incubated with 95% O2 and 5% CO2 at 37 ± 1°C for 5 hours, with K only or with the addition of 0.05 IU ACTH 1–17 or APH or with isophasic pituitary or hypothalamic preincubation media with and without APH or muscle. Media were stored at −20°C until corticosterone RIA. A circadian rhythm ($p<0.05$) characterized corticosterone production after stimulation by the pituitary alone or with APH. The overall modulatory effect of APH is an increased circadian amplitude of adrenal corticosterone production, in response to the isophasic pituitary.

Keywords Pineal; Pituitary; Adrenal; Circadian; Corticosterone; Modulation; Mouse; Heterophasic sequential incubation; Isophasic sequential incubation

Authors Sánchez-Barceló EJ, Cos S, Fernández R, Mediavilla MD

Report Name Melatonin and mammary cancer: a short review

Publication Endocr Relat Cancer

Issue-page numbers 10:153–159 doi:10.1677/erc.0.0100153. PMID:12790777

URL http://www.unican.es/NR/rdonlyres/638265C7-36FF-4EBF-893B-150723B954AA/0/8MelatoninandmammarycancerashortreviewPDF

Abstract

Melatonin is an indolic hormone produced mainly by the pineal gland. The former hypothesis of its possible role in mammary cancer development was based on the evidence that melatonin down-regulates some of the pituitary and gonadal hormones that control mammary gland development and which are also responsible for the growth of hormone-dependent mammary tumors. Furthermore, melatonin could act directly on tumoral cells, as a naturally occurring antiestrogen, thereby influencing their proliferative rate. The first reports revealed a low plasmatic melatonin concentration in women with estrogen receptor (ER)-positive breast tumors. However, later studies on the possible role of melatonin on human breast cancer have been scarce and mostly of an epidemiological type. These studies described a low incidence of breast tumors in blind women as well as an inverse relationship between breast cancer incidence and the degree of visual impairment. Since light inhibits melatonin secretion, the relative increase in the melatonin circulating levels in women with a decreased light input could be interpreted as proof of the protective role of melatonin on mammary carcinogenesis. From in vivo studies on animal models of chemically induced mammary tumorigenesis, the general conclusion is that experimental manipulations activating the pineal gland or the administration of melatonin lengthens the latency and reduces the incidence and growth rate of mammary tumors, while pinealectomy usually has the opposite effects. Melatonin also reduces the incidence of spontaneous mammary tumors in different kinds of transgenic mice (c-neu and N-ras) and mice from strains with a high tumoral incidence.

In vitro experiments, carried out with the ER-positive MCF-7 human breast cancer cells, demonstrated that melatonin, at a physiological concentration (1 nM) and in the presence of serum or estradiol: (a) inhibits, in a reversible way, cell proliferation, (b) increases the expression of p53 and p21WAF1 proteins and modulates the length of the cell cycle, and (c) reduces the metastasic capacity of these cells and counteracts the stimulatory effect of estradiol on cell invasiveness; this effect is mediated, at least in part, by a melatonin-induced increase in the expression of the cell surface adhesion proteins E-cadherin and β1-integrin.

The direct oncostatic effects of melatonin depends on its interaction with the tumor cell estrogen-responsive pathway. In this sense it has been demonstrated that melatonin down-regulates the expression of ERα and inhibits the binding of the estradiol–ER complex to the estrogen response element (ERE) in the DNA. The characteristics of melatonin's oncostatic actions, comprising different aspects of tumor biology as well as the physiological doses at which the effect is accomplished, give special value to these findings and encourage clinical studies on the possible therapeutic value of melatonin on breast cancer.

Keywords

Authors Emilio J Sanchez-Barcelo, Maria D Mediavilla, Carolina Alonso-Gonzalez, Russel J Reiter

Report Name Melatonin uses in oncology: breast cancer prevention and reduction of the side effects of chemotherapy and radiation

Publication Expert Opinion on Investigational Drugs

Issue-page numbers June 2012, Vol. 21, No. 6 , Pages 819-831 (doi:10.1517/13543784.2012.681045)

URL http://informahealthcare.com/doi/abs/10.1517/13543784.2012.681045

Abstract

Introduction: The possible oncostatic properties of melatonin on different types of neoplasias have been studied especially in hormone-dependent adenocarcinomas. Despite the promising results of these experimental investigations, the use of melatonin in breast cancer treatment in humans is still uncommon.

Areas covered: This article reviews the usefulness of this indoleamine for specific aspects of breast cancer management, particularly in reference to melatonin's antiestrogenic and antioxidant properties: i) treatments oriented to breast cancer prevention, especially when the risk factors are obesity, steroid hormone treatment or chronodisruption by exposure to light at night (LAN); ii) treatment of the side effects associated with chemo- or radiotherapy.

Expert opinion: The clinical utility of melatonin depends on the appropriate identification of its actions. Because of its SERM (selective estrogen receptor modulators) and SEEM (selective estrogen enzyme modulators) properties, and its virtual absence of contraindications, melatonin could be an excellent adjuvant with the drugs currently used for breast cancer prevention (antiestrogens and antiaromatases). The antioxidant actions also make melatonin a suitable treatment to reduce oxidative stress associated with chemotherapy, especially with anthracyclines, and radiotherapy

Keywords breast cancer, chemo prevention, chemotherapy, melatonin, radiotherapy, SEEM, SERM

Sanchez-Barcelo EJ, Mediavilla MD, Alonso-Gonzalez C, Rueda N. **Year** 2012

Authors Sanchez-Barcelo EJ, Mediavilla MD, Alonso-Gonzalez C, Rueda N.

Report Name Breast Cancer Therapy Based on Melatonin.

Publication Recent Pat Endocr Metab Immune Drug Discov

Issue-page numbers 2012 Feb 20. [Epub ahead of print]

URL http://www.ncbi.nlm.nih.gov/pubmed/22369716

Abstract The usefulness of melatonin and melatoninergic drugs in breast cancer therapy is based on its Selective Estrogen Receptor Modulator (SERM) and Selective Estrogen Enzyme Modulator (SEEM) properties. Because of the oncostatic properties of melatonin, its nocturnal suppression by light-at-night (LAN) has been considered a risk-factor for breast cancer. Melatonin's SERM actions include modulation of estrogen-regulated cell proliferation, invasiveness and expression of proteins, growth factors and proto-oncogenes (hTERT, p53, p21, TGFβ, E-cadherin, etc). These actions are observable with physiologic doses of melatonin only in cells expressing ERα, and mediated by MT1 melatonin receptors. Melatonin acts like a SEEM, inhibiting expression and activity of P450 aromatase, estrogen sulfatase and type 1 17β- hydroxysteroid dehydrogenase, but stimulating that of estrogen sulfotransferase. This double action mechanism (SERM and SEEM), and the specificity for ERα bestows melatonin with potential advantages for breast cancer treatments, associated with other antiestrogenic drugs, and idea already patented. LAN enhances the growth of rat mammary tumors by decreasing or suppressing melatonin production. Epidemiologic studies have also described increased breast cancer risk in women exposed to LAN. Since the strongest suppression of nocturnal melatonin occurs with wavelength light of the blue spectral region, optical and lightening devices filtering the blue light spectrum have been proposed to avoid the risks of light-induced suppression of nocturnal melatonin.

Keywords

Sánchez-Barceló EJ, Mediavilla MD, Tan DX, Reiter RJ **Year** 0

Authors Sánchez-Barceló EJ, Mediavilla MD, Tan DX, Reiter RJ.

Report Name Scientific basis for the potential use of melatonin in bone diseases: osteoporosis and adolescent idiopathic scoliosis

Publication Journal of Osteoporosis

Issue-page numbers Volume 2010 (2010), Article ID 830231, 10 pages doi:10.4061/2010/830231

URL http://www.hindawi.com/journals/josteo/2010/830231/

Abstract The objective of this paper was to analyze the data supporting the possible role of melatonin on bone metabolism and its repercussion in the etiology and treatment of bone pathologies such as the osteoporosis and the adolescent idiopathic scoliosis (AIS). Melatonin may prevent bone degradation and promote bone formation through mechanisms involving both melatonin receptor-mediated and receptor-independent actions. The three principal mechanisms of melatonin effects on bone function could be: (a) the promotion of the osteoblast differentiation and activity; (b) an increase in the osteoprotegerin expression by osteoblasts, thereby preventing the differentiation of osteoclasts; (c) scavenging of free radicals generated by osteoclast activity and responsible for bone resorption. A variety of in vitro and in vivo experimental studies, although with some controversial results, point toward a possible role of melatonin deficits in the etiology of osteoporosis and AIS and open a new field related to the possible therapeutic use of melatonin in these bone diseases.

Keywords

Sánchez-Hidalgo M, Lee M, de la Lastra CA, et al. **Year** 2012

Authors Marina Sánchez-Hidalgo, Melanie Lee, Catalina A. de la Lastra, Juan M. Guerrero, Graham Packham

Report Name Melatonin inhibits cell proliferation and induces caspase activation and apoptosis in human malignant lymphoid cell lines

Publication Journal of Pineal Research

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2012.01006.x/abstract

Abstract Melatonin exerts strong anti-tumour activity via several mechanisms, including anti-proliferative and pro-apoptotic effects in addition to its potent antioxidant activity. Several studies have investigated the effects of melatonin on haematological malignancies. However, the previous studies investigating lymphoid malignancies have been largely restricted to a single type of malignancy, Burkitt's lymphoma (BL). Thus, we examined the actions of melatonin on the growth and apoptosis in a small panel of cell lines representing different human lymphoid malignancies including Ramos (Epstein–Barr virus–negative BL), SU-DHL-4 (diffuse large B cell lymphoma), DoHH2 (follicular B non-Hodgkin lymphoma) and JURKAT (acute T cell leukaemia). We showed that melatonin promotes cell cycle arrest and apoptosis in all these cells, although there was marked variations in responses among different cell lines (sensitivity; Ramos/DoHH2 > SU-DHL-4 > JURKAT). Melatonin-induced apoptosis was relatively rapid, with increased caspase 3 and PARP cleavage detected within 0.5–1 h following melatonin addition. Moreover, there was evidence for rapid processing of both caspase 9, as well as a breakdown of the mitochondrial inner transmembrane potential. On the contrary, caspase activation was detected only in SU-DHL-4 and Ramos cells following melatonin treatment suggesting that the extrinsic pathway does not make a consistent contribution to melatonin-induced apoptosis in malignant lymphocytes. Although all cell lines expressed the high-affinity melatonin receptors, MT1 and MT2, melatonin-induced caspase activation appeared to be independent these receptors. Our findings confirm that melatonin could be a potential chemotherapeutic/preventive agent for malignant lymphocytes. However, it is necessary to take into account that different lymphoid malignancies may differ in their response to melatonin.

Keywords apoptosis; caspase activation; leukaemia cells; lymphoma; melatonin

Sandahl B **Year** 1978

Authors Sandahl B

Report Name Seasonal birth pattern in Sweden in relation to birth order and maternal age

Publication Acta Obstet Gynecol Scand

Issue-page numbers 57:393–396 doi:10.3109/00016347809156517. PMID:726872

URL http://informahealthcare.com/doi/abs/10.3109/00016347809156517?journalCode=obs

Abstract The influence of both maternal age and parity on seasonal birth patterns in Sweden was studied, using the Swedish Medical Birth Register for 1973. The register contained reports of 109342 pregnancies. A test for seasonality, using a squared sinus function and an analysis of variance, was performed for each age and parity group. Significant differences were shown for parity irrespective of age and age groups within parity groups. There was one exception: no influence of parity could be demonstrated in women more than 35 years of age. For the lowest and the highest age groups (all parities), there was no significant seasonality in birth rate tested by the squared sinus method. This was also true for parity 3 (age group 20–24) and parity 1 (age group 30–34). The other age groups and parity classes show a significant seasonality with a maximum of births in April and May.

Keywords

Authors Sandberg MA, Pawlyk BS, Berson EL.

Report Name Acuity recovery and cone pigment regeneration after a bleach in patients with retinitis pigmentosa and rhodopsin mutations

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers September 1999 vol. 40 no. 10 2457-2461

URL http://www.iovs.org/content/40/10/2457.full

Abstract

urpose. To assess visual acuity recovery times and cone photopigment regeneration kinetics after a bleach in the fovea of patients with dominant retinitis pigmentosa due to rhodopsin mutations.

methods. The authors measured acuity recovery times by computerized photostress testing in 13 patients with dominant retinitis pigmentosa and one of eight rhodopsin mutations. The authors also measured their time constants of cone photopigment regeneration with a video imaging fundus reflectometer to determine whether acuity recovery time depended on pigment regeneration kinetics. These values were compared with those of normal subjects, by the Mann–Whitney U test. The relationship between acuity recovery time and the time constant of cone photopigment regeneration among the patients was quantified by the Spearman rank correlation.

results. The visual acuity recovery times, which averaged 22.0 seconds for the patients with retinitis pigmentosa and 11.2 seconds for the normal subjects, were significantly slower for the patient group ($P < 0.001$). The time constants of cone pigment regeneration, which averaged 172 seconds for the patients with retinitis pigmentosa and 118 seconds for the normal subjects, also were significantly slower for the patient group ($P = 0.043$). The authors also found a significant, positive correlation between the visual acuity recovery time and the time constant of pigment regeneration for the patients with retinitis pigmentosa ($r = 0.65$, $P = 0.017$).

conclusions. A slowing of foveal visual acuity recovery and cone pigment regeneration, which are related to each other, can occur in patients with retinitis pigmentosa, due to a rod-specific gene defect.

Keywords

Authors Sanders CJG, Van Weelden H, Kazzaz GA, Sigurdsson V, Toonstra J, Bruijnzeel-Koomen CA.

Report Name Photosensitivity in patients with lupus erythematosus: a clinical and photobiological study of 100 patients using a prolonged phototest protocol

Publication British Journal of Dermatology

Issue-page numbers Volume 149, Issue 1, pages 131–137, July 2003

URL http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2133.2003.05379.x/abstract?

Abstract

Background There is a clear relationship between ultraviolet (UV) radiation (UVR) and the clinical manifestations of patients with lupus erythematosus (LE). Cutaneous lesions are induced or exacerbated by exposure to UVR. Of patients with LE, 24–83% are reported to be photosensitive to UVR. LE tumidus appears to be the most photosensitive subtype of LE, followed by subacute cutaneous LE (SCLE). In general, the history of patients with LE correlates poorly with the presence or absence of photosensitivity, due to a delayed time interval between UV exposure and exacerbation of skin lesions. Phototesting using artificial UVR and visible light is a reliable way of diagnosing photosensitivity.

Objectives To investigate the photoreactivity of patients with various subtypes of LE using an individualized phototest protocol. The results of phototests were correlated with the history of photosensitivity, the subtype of LE, the presence of autoantibodies and the use of anti-inflammatory medication by these patients.

Methods Phototesting with UVA, UVB and visible light was performed in 100 patients with LE. The diagnosis of LE was established both on clinical examination and skin histology. Serological studies were also performed in all patients. The phototests were performed on large skin areas of the forearm or trunk; the first dose was twice the minimal erythema dose and the dosage was increased according to the individual reactions of the patients at the test sites. Follow-up of skin reactions at the test sites was performed for up to 2 months. Histological examination of the photoprovoked skin lesions was carried out in 57 patients.

Results Of the 100 patients included (81 women and 19 men; mean age 41 years, range 17–79), 46 had chronic discoid LE, 30 SCLE and 24 systemic LE. An abnormal reaction to UVR and visible light was found in 93% of our patients with LE. No clinical or histological evidence at the phototest sites of polymorphic light eruption was found. There was no correlation between photosensitivity and LE subtype, presence of autoantibodies or medical history. Concomitant use of anti-inflammatory medication seemed to exert only minimal influence on the results of phototesting.

Conclusions When using an extended phototesting protocol, almost all patients with LE in this study showed clinical and histological evidence of aberrant photosensitivity. Therefore, patients with LE should receive thorough advice and instruction on photoprotective measures, regardless of their history, LE subtype or presence of autoantibodies.

Keywords lupus erythematosus; photosensitivity; phototesting

Santhi N, Thorne HC, van der Veen DR, et al. **Year** 2011

Authors Santhi N, Thorne HC, van der Veen DR, Johnsen S, Mills SL, Hommes V, Schlangen LJ, Archer SN, Dijk DJ.

Report Name The spectral composition of evening light and individual differences in the suppression of melatonin and delay of sleep in humans

Publication Journal of Pineal Researc

Issue-page numbers 2011 Sep 20. doi: 10.1111/j.1600-079X.2011.00970.x

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2011.00970.x/full

Abstract The effect of light on circadian rhythms and sleep is mediated by a multi-component photoreceptive system of rods, cones and melanopsin-expressing intrinsically photosensitive retinal ganglion cells. The intensity and spectral sensitivity characteristics of this system are to be fully determined. Whether the intensity and spectral composition of light exposure at home in the evening is such that it delays circadian rhythms and sleep also remains to be established. We monitored light exposure at home during 6–8 wk and assessed light effects on sleep and circadian rhythms in the laboratory. Twenty-two women and men (23.1 ± 4.7 yr) participated in a six-way, cross-over design using polychromatic light conditions relevant to the light exposure at home, but with reduced, intermediate or enhanced efficacy with respect to the photopic and melanopsin systems. The evening rise of melatonin, sleepiness and EEG-assessed sleep onset varied significantly ($P < 0.01$) across the light conditions, and these effects appeared to be largely mediated by the melanopsin, rather than the photopic system. Moreover, there were individual differences in the sensitivity to the disruptive effect of light on melatonin, which were robust against experimental manipulations (intra-class correlation = 0.44). The data show that light at home in the evening affects circadian physiology and imply that the spectral composition of artificial light can be modified to minimize this disruptive effect on sleep and circadian rhythms. These findings have implications for our understanding of the contribution of artificial light exposure to sleep and circadian rhythm disorders such as delayed sleep phase disorder.

Keywords actigraphy; circadian; melanopsin; photopic; photoreceptors; polychromatic light

Santoro R, Marani M, Blandino G, et al. **Year** 2011

Authors R Santoro, M Marani, G Blandino, P Muti and S Strano

Report Name Melatonin triggers p53Ser phosphorylation and prevents DNA damage accumulation

Publication Oncogene

Issue-page numbers (17 October 2011) | doi:10.1038/onc.2011.469

URL http://www.nature.com/onc/journal/vaop/ncurrent/full/onc2011469a.html

Abstract Several epidemiological studies have shown that high levels of melatonin, an indolic hormone secreted mainly by the pineal gland, reduce the risks of developing cancer, thus suggesting that melatonin triggers the activation of tumor-suppressor pathways that lead to the prevention of malignant transformation. This paper illustrates that melatonin induces phosphorylation of p53 at Ser-15 inhibiting cell proliferation and preventing DNA damage accumulation of both normal and transformed cells. This activity requires p53 and promyelocytic leukemia (PML) expression and efficient phosphorylation of p53 at Ser-15 residue. Melatonin-induced p53 phosphorylation at Ser-15 residue does not require ataxia telangiectasia-mutated activity, whereas it is severely impaired upon chemical inhibition of p38 mitogen-activated protein kinase activity. By and large, these findings imply that the activation of the p53 tumor-suppressor pathway is a critical mediator of melatonin and its anticancer effects. Therefore, it provides molecular insights into increasing observational evidence for the role that melatonin has in cancer prevention.

Keywords

Authors Sappington RM, Sidorova T, Long DJ, Calkins DJ.

Report Name TRPV1: contribution to retinal ganglion cell apoptosis and increased intracellular Ca2+ with exposure to hydrostatic pressure.

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers February 2009 vol. 50 no. 2 717-728

URL http://www.iovs.org/content/50/2/717.full

Abstract

purpose. Elevated hydrostatic pressure induces retinal ganglion cell (RGC) apoptosis in culture. The authors investigated whether the transient receptor potential vanilloid 1 (TRPV1) channel, which contributes to pressure sensing and Ca2+-dependent cell death in other systems, also contributes to pressure-induced RGC death and whether this contribution involves Ca2+.

methods. trpv1 mRNA expression in RGCs was probed with the use of PCR and TRPV1 protein localization through immunocytochemistry. Subunit-specific antagonism (iodo-resiniferatoxin) and agonism (capsaicin) were used to probe how TRPV1 activation affects the survival of isolated RGCs at ambient and elevated hydrostatic pressure (+70 mm Hg). Finally, for RGCs under pressure, the authors tested whether EGTA chelation of Ca2+ improves survival and whether, with the Ca2+ dye Fluo-4 AM, TRPV1 contributes to increased intracellular Ca2+.

results. RGCs express trpv1 mRNA, with robust TRPV1 protein localization to the cell body and axon. For isolated RGCs under pressure, TRPV1 antagonism increased cell density and reduced apoptosis to ambient levels ($P \leq 0.05$), whereas for RGCs at ambient pressure, TRPV1 agonism reduced density and increased apoptosis to levels for elevated pressure ($P \leq 0.01$). Chelation of extracellular Ca2+ reduced RGC apoptosis at elevated pressure by nearly twofold ($P \leq 0.01$). Exposure to elevated hydrostatic pressure induced a fourfold increase in RGC intracellular Ca2+ that was reduced by half with TRPV1 antagonism. Finally, in the DBA/2 mouse model of glaucoma, levels of TRPV1 in RGCs increased with elevated IOP.

conclusions. RGC apoptosis induced by elevated hydrostatic pressure arises substantially through TRPV1, likely through the influx of extracellular Ca2+.

Keywords

Sasaki K, Sasaki H, Kojima M, et al. **Year** 1999

Authors Sasaki K, Sasaki H, Kojima M, Shui YB, Hockwin O, Jonasson F, Cheng HM, Ono M, Katoh N.

Report Name Epidemiological studies on UV-related cataract in climatically different countries

Publication J Epidemiol

Issue-page numbers 1999 Dec;9(6 Suppl):S33-8.

URL http://www.ncbi.nlm.nih.gov/pubmed/10709348

Abstract Cataract epidemiological surveys applying objective judgement through lens images in the climatically different places of Noto and Amami, Japan, Singapore and Reykjavik, Iceland yielded several significant results about the influence of solar UV. 1) The percentage of transparent and of lens opacification was significantly higher in the Reykjavik subjects than in the Singaporeans. 2) The percentages including early changes were higher in Amami and Singapore than in Noto and Reykjavik. 3) Progressed lens opacification was highest in Singapore. While the main type of lens opacification was cortical in Noto and Reykjavik, that of Singapore was nuclear. 4) A significant correlation between cortical opacification and the history of time spent outdoors was noticed. The UV risk for formation and/or progression of cortical opacification should be acceptable from the epidemiological standpoint.

Keywords

Sasseville A, Benhaberou-Brun D, Fontaine C, et al. **Year** 2009

Authors Alexandre Sasseville, Dalila Benhaberou-Brun, Charlotte Fontaine, Marie-Claude Charon, Marc Hébert, PhD

Report Name Wearing Blue-Blockers in the Morning Could Improve Sleep of Workers on a Permanent Night Schedule: A Pilot Study

Publication Chronobiology International

Issue-page numbers Vol. 26, No. 5 , Pages 913-925

URL http://informahealthcare.com/doi/abs/10.1080/07420520903044398

Abstract Night shiftworkers often complain of disturbed sleep during the day. This could be partly caused by morning sunlight exposure during the commute home, which tends to maintain the circadian clock on a daytime rhythm. The circadian clock is most sensitive to the blue portion of the visible spectrum, so our aim was to determine if blocking short wavelengths of light below 540 nm could improve daytime sleep quality and nighttime vigilance of night shiftworkers. Eight permanent night shiftworkers (32–56 yrs of age) of Quebec City's Canada Post distribution center were evaluated during summertime, and twenty others (24–55 yrs of age) during fall and winter. Timing, efficacy, and fragmentation of daytime sleep were analyzed over four weeks by a wrist activity monitor, and subjective vigilance was additionally assessed at the end of the night shift in the fall–winter group. The first two weeks served as baseline and the remaining two as experimental weeks when workers had to wear blue-blockers glasses, either just before leaving the workplace at the end of their shift (summer group) or 2 h before the end of the night shift (fall–winter group). They all had to wear the glasses when outside during the day until 16:00 h. When wearing the glasses, workers slept, on average ±SD, 32±29 and 34±60 more min/day, increased their sleep efficacy by 1.95±2.17% and 4.56±6.1%, and lowered their sleep fragmentation by 1.74±1.36% and 4.22±9.16% in the summer and fall–winter group, respectively. Subjective vigilance also generally improved on Fridays in the fall–winter group. Blue-blockers seem to improve daytime sleep of permanent night-shift workers.

Keywords Light wavelength, Blue-blockers, Shiftwork, Sleep, Vigilance

Authors Alexandre Sasseville, Marc Hébert

Report Name Using blue-green light at night and blue-blockers during the day to improves adaptation to night work: A pilot study

Publication Progress in Neuro-Psychopharmacology and Biological Psychiatry

Issue-page numbers Volume 34, Issue 7, 1 October 2010, Pages 1236-1242

URL http://www.sciencedirect.com/science/article/pii/S0278584610002447

Abstract

Background

Bright light at night paired with darkness during the day seem to facilitate adaptation to night work. Considering the biological clock sensitive to short wavelengths, we investigated the possibility of adaptation in shift workers exposed to blue-green light at night, combined with using blue-blockers during the day.
Methods

Four sawmill shift workers were evaluated during two weeks of night shifts (control and experimental) and one week of day shifts. Throughout the experimental week, ambient light (≈ 130 lx) was supplemented with blue-green light (200 lx) from 00:00 h to: 05:00 h on Monday and Tuesday, 06:00 h on Wednesday and 07:00 h on Thursday. Blue-blockers had to be worn outside from the end of the night shift until 16:00 h. For circadian assessment, salivary melatonin profiles were obtained between 00:00 h and 08:00 h, before and after 4 experimental night shifts. Sleep was continuously monitored with actigraphy and subjective vigilance was measured at the beginning, the middle and the end of each night and day shifts. The error percentage in wood board classification was used as an index of performance.
Results

Through experimental week, melatonin profiles of 3 participants have shifted by at least 2 hours. Improvements were observed in sleep parameters and subjective vigilance from the third night (Wednesday) as performance increased on the fourth night (Thursday) from 5.14% to 1.36% of errors ($p = 0.04$).
Conclusions

Strategic exposure to short wavelengths at night, and/or daytime use of blue-blocker glasses, seemed to improve sleep, vigilance and performance.

Keywords Melatonin; Shift work disorder; Short wavelengths; Sleep; Vigilance

Sassin JF, Frantz AG, Kapen S, Weitzman ED

Year 1973

Authors Sassin JF, Frantz AG, Kapen S, Weitzman ED

Report Name The nocturnal rise of human prolactin is dependent on sleep

Publication J Clin Endocrinol Metab

Issue-page numbers 37:436–440 doi:10.1210/jcem-37-3-436. PMID:4361974

URL http://jcem.endojournals.org/content/37/3/436.short

Abstract Four normal young adults underwent partial or complete inversion of their sleepwaking cycles to determine the relationship of the nocturnal release of human prolactin to sleep. Prolactin release shifted immediately and completely with shifts of sleep onset of 3, 6 and 12 hr. Thus, the nocturnal rise is dependent on the occurrence of sleep and is not based on an inherent rhythm related to time of day.

Keywords

Sassin JF, Frantz AG, Weitzman ED, Kapen S

Year 1972

Authors Sassin JF, Frantz AG, Weitzman ED, Kapen S

Report Name Human prolactin: 24-hour pattern with increased release during sleep

Publication Science

Issue-page numbers 177:1205–1207 doi:10.1126/science.177.4055.1205. PMID:5057627

URL http://www.sciencemag.org/content/177/4055/1205.short

Abstract Human prolactin was measured in plasma by radioimmunoassay at 20 minute intervals for a 24-hour period in each of six normal adults, whose sleep-wake cycles were monitored polygraphically. A marked diurnal variation in plasma concentrations was demonstrated, with highest values during sleep; periods of episodic release occurred throughout the 24 hours.

Keywords

Authors Sauer LA, Dauchy RT, Blask DE.

Report Name Polyunsaturated fatty acids, melatonin, and cancer prevention

Publication Biochem Pharmacol

Issue-page numbers Jun 15;61(12):1455-62.

URL http://www.ncbi.nlm.nih.gov/pubmed/11377374?dopt=Abstract

Abstract

Many nutritional, hormonal, and environmental factors affect carcinogenesis and growth of established tumors in rodents. In some cases, these factors may either enhance or attenuate the neoplastic process. Recent experiments performed in our laboratory using tissue-isolated rat hepatoma 7288CTC in vivo or during perfusion in situ have demonstrated new interactions among four of these factors. Two agents, dietary linoleic acid (C18:2n6) and "light at night," enhanced tumor growth, and two others, melatonin and n3 fatty acids, attenuated growth. Linoleic acid stimulated tumor growth because it is converted by hepatoma 7288CTC to the mitogen, 13-hydroxyoctadecadienoic acid (13-HODE). Melatonin, the neurohormone synthesized and secreted at night by the pineal gland, and dietary n3 fatty acids are potent antitumor agents. Both inhibited tumor linoleic acid uptake and 13-HODE formation. Artificial light, specifically "light at night," increased tumor growth because it suppressed melatonin synthesis and enhanced 13-HODE formation. Melatonin and n3 fatty acids acted via similar or identical G(i) protein-coupled signal transduction pathways, except that melatonin receptors and putative n3 fatty acid receptors were used. The results link the four factors in a common mechanism and provide new insights into the roles of dietary n6 and n3 polyunsaturated fatty acid intake, "light at night," and melatonin in cancer prevention in humans.

Keywords

Authors Sawchenko PE, Swanson LW

Report Name Localization, colocalization, and plasticity of corticotropinreleasing factor immunoreactivity in rat brain

Publication Fed Proc

Issue-page numbers 44:221–227. PMID:2981743

URL http://www.ncbi.nlm.nih.gov/pubmed/2981743/

Abstract The generation of antiserums against a peptide that has met the criteria predicted for corticotropin-releasing factor (CRF) has allowed the immunohistochemical localization of CRF immunoreactive neurons in the rat brain. Although CRF-stained cells have been found to be widely distributed in the central nervous system, attention has focused on neurons in the paraventricular nucleus of the hypothalamus (PVH), which is now acknowledged to be the principal source for delivery of CRF to the hypophyseal portal system. Some 2000 CRF-stained neurons can be counted in the PVH of the colchicine-treated rat, and there is evidence that enkephalin, PHI, and neurotensin coexist with CRF in subsets of parvocellular neurons. Consistent with the established negative feedback effects of adrenal steroids on CRF production and release, adrenalectomy enhances CRF immunoreactivity in parvocellular neurosecretory neurons in the PVH. In addition, immunoreactive vasopressin can be demonstrated in a majority of CRF-stained parvocellular neurons after adrenalectomy, which suggests a form of plasticity that allows for synergy of the two peptides in stimulating adrenocorticotropin secretion. The effects of adrenalectomy appear to be glucocorticoid-dependent, and specific to these peptides and this cell type. A survey of neural inputs to the hypophyseotropic zone of the PVH suggests potential substrates for the control of CRF release and/or synthesis by interoceptive stimuli, by the limbic region, and by a number of cell groups in the basal forebrain. Finally, CRF may also participate in other (nonadenohypophyseal) modes of regulation that are represented in the PVH. Thus, CRF immunoreactivity has been demonstrated in a discrete subset of oxytocinergic magnocellular neurosecretory neurons that project to the posterior pituitary, and in a small fraction of cells in the parvocellular division that project to cell groups in the brain stem and spinal cord that are associated with the control of autonomic functions.

Keywords

Sayre RM, Dowdy JC, Harris KA, et al. **Year** 2007

Authors Sayre RM, Dowdy JC, Harris KA, Berg JE, Trimble MW.

Report Name A practical UV source to induce Herpes simplex labialis lesions in the clinic

Publication Photodermatology, Photoimmunology & Photomedicine

Issue-page numbers Volume 23, Issue 1, pages 20–23, February 2007

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0781.2007.00266.x/abstract?

Abstract Background: Ultraviolet (UV) sources have been used to clinically induce herpes simplex lesions in the lips of susceptible individuals.

Methods: This study reports the optimization of a UV source for studies involving multiple clinical laboratory sites and subsequent clinical UV induction of cold sore lesions. We describe novel adaptations of a commercially available broadband UV phototherapy lamp that facilitate determination of individual's minimal erythemal dose (MED) and expose the lips with minimal risk of viral transmission to or between the volunteers and technicians.

Clinical Results: The source performed well in a clinical setting, with 171 of 386 subjects (44%) developing lesions, an induction rate similar to spectrally similar UV sources.

Conclusions: The advantages of consistent and reproducible exposure geometry, additional UV shielding and biological hygiene achieved by our method significantly enhance the execution of UV-induced herpes simplex labialis studies.

Keywords cold sore; herpes simplex labialis; sunlamp; UV; UVB; UV source

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Sayre RM, Dowdy JC, Poh-Fitzpatrick M **Year** 2004

Authors Sayre RM, Dowdy JC, Poh-Fitzpatrick M.

Report Name Dermatological risk of indoor ultraviolet exposure from contemporary lighting sources

Publication Photochem Photobiol

Issue-page numbers 2004 Jul-Aug;80:47-51.

URL http://www.ncbi.nlm.nih.gov/pubmed/15339209

Abstract Discussions of risks and implications of cutaneous exposure to indoor lighting, including hypothetical contribution to causality of melanoma, have mainly concentrated on ultraviolet (UV) A and B (UVA, UVB) spectral emissions from fluorescent bulbs. Only studies of quartz halogen lamps have suggested that users might sustain UVC-induced injury. Examination of light sources in the home and school of a child with xeroderma pigmentosum revealed that several different types emitted surprising levels of UV. Our purpose was to assess the extent of UV emissions from a variety of commonly used light sources to identify potential dermatological risks. UV and visible spectral emissions of commercially obtained lamps of several types were measured using a calibrated spectral radiometer traceable to the National Institute of Standards and Technology. Indoor light sources including fluorescent, quartz halogen and even tungsten filament incandescent lamps provided UVA, UVB and sometimes UVC emissions. Intensities of some emissions were of similar magnitude to those in sunlight. Chronic exposure to indoor lighting may deliver unexpected cumulative UV exposure to the skin and eyes. Patients with UV-exacerbated dermatoses should be cautioned about potential adverse reactions from indoor lighting.

Keywords

SCENIHR

Year 2008

Authors SCENIHR

Report Name Light Sensitivity

Publication Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)

Issue-page numbers 23 September 2008

URL http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_019.pdf

Abstract

Within the context of the promotion of wide-spread use of energy saving lamps, such as compact fluorescent lamps (CFLs), and the possible phase-out of incandescent lamps, it has been claimed that the symptoms of several diseases may be aggravated in the presence of energy saving lamps (mainly CFLs).
SCENIHR did not find suitable direct scientific data on the relationship between energy saving lamps and the symptoms in patients with various conditions (i.e xeroderma pigmentosum, lupus, migraine, epilepsy, myalgic encephalomyelitis, Irlen-Meares syndrome, fibromyalgia, electrosensitivity, AIDS/HIV, dyspraxia, and autism). Therefore, SCENIHR examined whether three lamp characteristics (flicker, electromagnetic fields, and UV/blue light emission) could act as triggers for disease symptoms. Due to lack of data on CFLs, existing data on traditional fluorescent tubes were extrapolated to situations when compact fluorescent lamps may be used.
While for some conditions either flicker and/or UV/blue light could exacerbate symptoms, there is no reliable evidence that the use of fluorescent tubes was a significant contributor. Of all compact fluorescent lamps properties, only UV/blue light radiation was identified as a potential risk factor for the aggravation of the light-sensitive symptoms in some patients with such diseases as chronic actinic dermatitis and solar urticaria.
The committee wishes to draw attention of the Commission Services to the fact that it has been observed that some single-envelope CFLs emit UVB and traces of UVC radiation. Under extreme conditions (i.e. prolonged exposures at distances <20 cm) these CFLs may lead to UV exposures approaching the current workplace limit set to protect workers from skin and retinal damage.
Due to the lack of relevant data, the number of all light-sensitive patients in the European Union, who might be at risk from the increased levels of UV/blue light radiation generated by CFL is difficult to estimate. However, a preliminary rough estimation of the worst-case scenario yields a number of around 250,000 individuals (0.05% of the population) in the EU.
The committee notes that the use of double-envelope energy saving bulbs or similar technology would largely or entirely mitigate both the risk of approaching workplace limits on UV emissions in extreme conditions and the risk of aggravating the symptoms of light-sensitive individuals.

Keywords Light sensitivity, CFL, fluorescent lamps, risk assessment, SCENIHR

SCENIHR

Year 2011

Authors SCENIHR

Report Name Health Effects of Artificial Light

Publication European Commision, Directorate-General for Health & Consumers

Issue-page numbers Bulletin

URL http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_033.pdf

Abstract

In general, the probability is low that artificial lighting for visibility purposes induces acute pathologic conditions, since expected exposure levels are much lower than those at which effects normally occur, and are also much lower than typical daylight exposures.
Certain lamp types (quartz halogen lamps, single- and double-capped fluorescent lamps as well as incandescent light bulbs) may emit UV radiation, although at low levels. However, according to a worst case scenario the highest measured UV emissions from lamps used typically in offices and schools could add to the number of squamous cell carcinomas in the EU population. Household lighting involves an illumination level which is so low that exposure to potentially problematic radiation is considered negligible.
There is no consistent evidence that long-term exposure to sunlight (specifically the blue component) may contribute to age-related macular degeneration (AMD). Whether exposure from artificial light could have effects related to AMD is uncertain.
No evidence was found indicating that blue light from artificial lighting belonging to Risk Group 0 ("exempt from risk") would have any impact on the retina graver than that of sunlight. Blue light from improperly used lamps belonging to Risk Groups 1, 2, or 3 could, in principle, induce photochemical retinal damage in certain circumstances. There is however no evidence about the extent to which this is actually occurring in practical situations.
There is mounting evidence suggesting that ill-timed exposure to light (light-at-night) may be associated with an increased risk of breast cancer, and can also cause sleep disorders, gastrointestinal, and cardiovascular disorders, and possibly affective states. Importantly, these effects are directly or indirectly due to light itself, without any specific correlation to a given lighting technology.

Keywords

Schaefer KE, Kerr CM, Buss D, Haus E

Year 1978

Authors Schaefer, KE; Kerr, CM; Buss, D; Haus, E

Report Name Effect Of 18-H Watch Schedules On Circadian Cycles Of Physiological Functions During Submarine Patrols

Publication Undersea Biomedical Research

Issue-page numbers Submarine Supplement 1979

URL http://www.dtic.mil/cgi-bin/GetTRDoc?Location=U2&doc=GetTRDoc.pdf&AD=ADA075626

Abstract Reprint: Effect of 18-h Watch Schedules on Circadian Cycles of Physiological Functions during Submarine Patrols.

Keywords

SCHÄFER E, MARCHAL B, MARMÉ D

Year 1972

Authors E. SCHÄFER, B. MARCHAL, D. MARMÉ

Report Name In vivo measurements of the phytochrome photostationary state in far red light

Publication Photochemistry and Photobiology

Issue-page numbers Volume 15, Issue 5, pages 457–464, May 1972

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.1972.tb06257.x/abstract

Abstract The in vivo photostationary state, ϕfr= ([Pfr]fr/[P]), of phytochrome in far red light has been determined in mustard seedling cotyledons by three different methods. The ϕfr is a function of the length of time of etiolation (t= 36 hr, ϕfr= 0·14; t= 72 – 120 hr, ϕfr= 0·075). The calculated ϕr= 0·8. The amount of Ptot is strongly dependent on the time of onset o far red light. These data imply that it would be almost impossible to maintain a constant level of Pfr in mustard cotyledons over a considerable period of time.

Keywords

SCHER **Year** 2010

Authors SCHER

Report Name Opinion on Mercury in Certain Energy-saving Light Bulbs

Publication Scientific Committee on Health and Environmental Risks (SCHER)

Issue-page numbers 18 May 2010

URL http://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_124.pdf

Abstract

Certain energy-saving light bulbs, namely compact fluorescent lamps (CFLs), are widely available on the market and are offered for saving electricity. They also eventually reduce carbon dioxide emissions particularly from coal-fired power plants. They fulfil the requirements of Commission Regulation (EC) No 244/2009 on ecodesign requirements for non-directional household lamps1 (Ecodesign Regulation), in contrast to traditional incandescent light bulbs which will be phased out progressively in accordance with the Regulation.
According to Directive 2002/95/EC on the restriction of hazardous substances in electrical and electronic equipment (RoHS Directive)2, a mercury content in CFLs not exceeding 5 mg per lamp is allowed (the mercury exemption for CFLs is listed as n° 1 in the Annex to the RoHS Directive). An indicative benchmark (best available technology) of 1.23 mg of mercury in energy efficient CFLs is provided in the abovementioned Ecodesign Regulation (Annex IV, n° 3 of the Ecodesign Regulation).
The above-mentioned 5 mg mercury tolerance for CFLs is being reviewed on a regular basis, in line with the four-year-review period prescribed by the RoHS Directive. Such reviews aim at assessing whether the elimination or substitution of mercury is technically possible through specific design changes or through the use of other materials, provided that the negative impacts for the environment, health and/or consumer safety generated by the substitution do not outweigh the possible benefits thereof. This is indicated in Article 5 (1.c) of the RoHS Directive.
At the end of 2007, DG Environment commissioned a technical and scientific assessment of this exemption including, among others, consultation of interested stakeholders (e.g. producers of electrical and electronic equipment, environmental organisations and consumer associations). According to this assessment (Öko-Institut and Fraunhofer IZM 2009), finalised in March 2009, the elimination of mercury in CFLs is still technically and scientifically impracticable.
On the basis of this assessment, the Commission will take a decision for the review of this mercury exemption before July 2010, after consultation with the RoHS Technical Adaptation Committee (RoHS Directive, Article 7). In support of any future review, it may further be appropriate to consider the potential risks associated with the release of mercury from a CFL when it accidentally breaks in the hands of a consumer, for example while replacing a CFL. In such a case, long-term toxicological limit values may be exceeded up to 6,000 times, and the consumer's exposure to mercury may only be 10-fold below acute intoxication. Further information can be found in annex 2. Further considerations on the risk from mercury have been published elsewhere (Groth 2008), including in the event of a CFL breakage in a consumer home.
Clean-up of the debris of a broken CFL has been described as complicated, requiring, for example, the removal of the mercury droplets with adhesive tape and their disposal as special waste. This again points to the relevance of the risk caused by the breakage of a CFL in a consumer's home.

As regards the impacts of mercury emissions related to CFLs, the life-cycle of CFLs should be considered so as to weigh the risks of a mercury escape from CFLs, be it by accidental breakage or disposal as waste (instead of an appropriate recycling) against the reduction of mercury emissions from coal-based power plants due to the lower electricity consumption of CFLs (Aucott et al. 2004). Available information indicates that the reduced electricity consumption of CFLs reduces the need for
1 OJ L 76, 24.3.2009, p. 3
2 OJ L 17, 13.2.2003, p. 19
Hg in Energy saving light bulbs
6
electricity, thus the electricity production would release less mercury, and such a decrease could, on balance, save about 10% of the mercury emissions into the environment.
Concerning disposal, Directive 2002/96/EC on waste from electrical and electronic equipment3 (WEEE Directive) requires Member States to adopt appropriate measures in order to minimise the disposal of WEEE, including CFLs, as unsorted municipal waste and to remove mercury from the collected CFLs [see article 5 and Annex II (2) of the WEEE Directive]. A proposal to recast the Directive, made by the Commission in December 2008, strengthens the requirements for separate collection, and specifies that transport of WEEE is to be carried out in a way which optimises the confinement of hazardous substances4.

Keywords

Schernhammer E, Schulmeister K — ***Year*** 2004

Authors Eva Schernhammer and Karl Schulmeister

Report Name Light at Night and Cancer Risk

Publication Photochemistry and Photobiology

Issue-page numbers 79(4):316-318. 2004 doi: 10.1562/SA-03-28.1

URL http://www.bioone.org/doi/abs/10.1562/SA-03-28.1

Abstract Environmental lighting powerfully suppresses the physiologic release of melatonin, which typically peaks in the middle of the night. This decreased melatonin production has been hypothesized to increase the risk of cancer. Evidence from experimental studies supports a link between melatonin and tumor growth. There is also fairly consistent indirect evidence from observational studies for an association between melatonin suppression, using night work as a surrogate, and breast cancer risk.

Keywords

Schernhammer ES, Berrino F, Krogh V **Year** 2010

Authors Eva S. Schernhammer, Franco Berrino, Vittorio Krogh, Giorgio Secreto, Andrea Micheli, Elisabetta Venturelli, Sara Grioni, Christopher T. Sempos, et al.

Report Name URINARY 6-SULPHATOXYMELATONIN LEVELS AND RISK OF BREAST CANCER IN PREMENOPAUSAL WOMEN: THE ORDET COHORT

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers March; 19(3): 729–737.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2837369/

Abstract

Background
Lower urinary melatonin levels are associated with a higher risk of breast cancer in postmenopausal women. Literature for premenopausal women is scant and inconsistent.
Methods
In a prospective case–control study we measured the concentration of 6-sulphatoxymelatonin (aMT6s), in the 12-hour overnight urine of 180 premenopausal women with incident breast cancer and 683 matched controls.
Results
In logistic regression models, the multivariate odds ratio (OR) of invasive breast cancer for women in the highest quartile of total overnight aMT6s output compared with the lowest was 1.43 [95% confidence interval (CI) = 0.83–2.45; Ptrend = 0.03]. Among current non-smokers no association was existent (OR, 1.00, 95% CI, 0.52–1.94; Ptrend = 0.29). We observed an OR of 0.68 between overnight urinary aMT6s level and breast cancer risk in women with invasive breast cancer diagnosed >2 years after urine collection and a significant inverse association in women with a breast cancer diagnosis >8 years after urine collection (OR, 0.17, 95% CI = 0.04–0.71; Ptrend = 0.01). There were no important variations in ORs by tumor stage or hormone receptor status of breast tumors.
Conclusion
Overall we observed a positive association between aMT6s and risk of breast cancer. However, there was some evidence to suggest that this might be driven by the influence of subclinical disease on melatonin levels, with a possible inverse association among women diagnosed further from recruitment. Thus, the influence of lagtime on the association between melatonin and breast cancer risk needs to be evaluated in further studies.

Keywords melatonin, aMT6s, premenopausal, night work, breast cancer

Year 2005

Authors Schernhammer ES, Hankinson SE

Report Name Urinary melatonin levels and breast cancer risk

Publication J Natl Cancer Inst

Issue-page numbers 97:1084–1087.doi:10.1093/jnci/dji190 PMID:16030307

URL http://jnci.oxfordjournals.org/content/97/14/1084

Abstract

Exposure to light at night suppresses melatonin production, and night-shift work (a surrogate for such exposure) has been associated with an increased risk of breast cancer. However, the association between circulating melatonin levels and breast cancer risk is unclear. In a prospective case–control study nested within the Nurses' Health Study II cohort, we measured the concentration of the major melatonin metabolite, 6-sulphatoxymelatonin (aMT6s), in the first morning urine of 147 women with invasive breast cancer and 291 matched control subjects. In logistic regression models, the relative risk (reported as the odds ratio [OR]) of invasive breast cancer for women in the highest quartile of urinary aMT6s compared with those in the lowest was 0.59 (95% confidence interval [CI] = 0.36 to 0.97). This association was essentially unchanged after adjustment for breast cancer risk factors or plasma sex hormone levels but was slightly weakened when the analysis included 43 case patients with in situ breast cancer and their 85 matched control subjects (OR = 0.70, 95% CI = 0.47 to 1.06). The exclusion of women who had a history of night-shift work left our findings largely unchanged. These prospective data support the hypothesis that higher melatonin levels, as measured in first morning urine, are associated with a lower risk of breast cancer.

Keywords

Authors Eva S. Schernhammer, MD, DrPH1,2,3 and Susan E. Hankinson

Report Name URINARY MELATONIN LEVELS AND POSTMENOPAUSAL BREAST CANCER RISK IN THE NURSES' HEALTH STUDY COHORT

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers January; 18(1): 74–79.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3036562/

Abstract

Background
Melatonin appears to play a role in breast cancer etiology, but data addressing the association between melatonin levels and breast cancer risk in postmenopausal women is sparse.
Methods
We conducted a nested case-control study in the Nurses' Health Study cohort. First spot morning urine was collected from 18,643 cancer-free women from March 2000 through December 2002. The concentration of melatonin's major metabolite, 6-sulfatoxymelatonin (aMT6s), was available for 357 postmenopausal women who developed incident breast cancer through May 31, 2006, along with 533 matched control subjects. We used multivariable conditional logistic regression models to investigate associations. All statistical tests were two-sided.
Results
An increased concentration of urinary aMT6s was statistically significantly associated with a lower risk of breast cancer (odds ratio [OR] for the highest versus lowest quartile of morning urinary 6-sulfatoxymelatonin = 0.62, 95% confidence interval [CI] = 0.41 to 0.95; P[trend] = .004). There was no apparent modification of risk by hormone receptor status of breast tumors, age, body-mass index, or smoking status.
Conclusion
Results from this prospective study add substantially to the growing literature that supports an inverse association between melatonin levels and breast cancer risk.

Keywords melatonin, aMT6s, breast cancer

Authors Schernhammer ES, Kroenke CH, Laden F, Hankinson SE

Report Name Night work and risk of breast cancer

Publication Epidemiology

Issue-page numbers 17:108–111.doi:10.1097/01.ede.0000190539.03500.c1 PMID:16357603

URL http://journals.lww.com/epidem/Abstract/2006/01000/Night_Work_and_Risk_of_Breast_Cancer.19.aspx

Abstract

Background: Melatonin shows potential oncostatic activity and is acutely suppressed by light exposure. Some evidence suggests an association between night work and breast cancer risk, possibly through the melatonin pathway.

Methods: In a cohort of premenopausal nurses, we prospectively studied the relation between rotating night shift work and breast cancer risk. Total number of months during which the nurses worked rotating night shifts was first assessed at baseline in 1989 and periodically updated thereafter. We used Cox proportional hazards models to calculate relative risks (RRs) and 95% confidence intervals (CIs).

Results: Among 115,022 women without cancer at baseline, 1,352 developed invasive breast cancer during 12 years of follow up. Women who reported more than 20 years of rotating night shift work experienced an elevated relative risk of breast cancer compared with women who did not report any rotating night shift work (multivariate RR = 1.79; 95% CI = 1.06-3.01). There was no increase in risk associated with fewer years of rotating night work.

Conclusion: Our results suggest a modestly elevated risk of breast cancer after longer periods of rotating night work. Additional studies are warranted to rule out small sample size or uncontrolled sources for confounding as alternative explanations.

Keywords

Authors Schernhammer ES, Laden F, Speizer FE et al.

Report Name Night-shift work and risk of colorectal cancer in the nurses' health study

Publication J Natl Cancer Inst

Issue-page numbers 95:825–828.doi:10.1093/jnci/95.11.825 PMID:12783938

URL http://jnci.oxfordjournals.org/content/95/11/825.short

Abstract Exposure to light at night suppresses the physiologic production of melatonin, a hormone that has antiproliferative effects on intestinal cancers. Although observational studies have associated night-shift work with an increased risk of breast cancer, the effect of night-shift work on the risk of other cancers is not known. We prospectively examined the relationship between working rotating night shifts and the risk of colorectal cancers among female participants in the Nurses' Health Study. We documented 602 incident cases of colorectal cancer among 78 586 women who were followed up from 1988 through 1998. Compared with women who never worked rotating night shifts, women who worked 1–14 years or 15 years or more on rotating night shifts had multivariate relative risks of colorectal cancer of 1.00 (95% confidence interval [CI] = 0.84 to 1.19) and 1.35 (95% CI = 1.03 to 1.77), respectively (Ptrend = .04). These data suggest that working a rotating night shift at least three nights per month for 15 or more years may increase the risk of colorectal cancer in women.

Keywords

Authors Eva S. Schernhammer, Francine Laden, Frank E. Speizer, Walter C. Willett, David J. Hunter, Ichiro Kawachi and Graham A. Colditz

Report Name Rotating Night Shifts and Risk of Breast Cancer in Women Participating in the Nurses' Health Study

Publication J Natl Cancer Inst

Issue-page numbers Volume93, Issue20 Pp. 1563-1568.

URL http://jnci.oxfordjournals.org/content/93/20/1563.full

Abstract

Background: Melatonin shows potential oncostatic action, and light exposure during night suppresses melatonin production. There is little information, however, about the direct effect of night work on the risk of cancer. We investigated the effect of night work in breast cancer. Methods: We examined the relationship between breast cancer and working on rotating night shifts during 10 years of follow-up in 78 562 women from the Nurses' Health Study. Information was ascertained in 1988 about the total number of years during which the nurses had worked rotating night shifts with at least three nights per month. From June 1988 through May 1998, we documented 2441 incident breast cancer cases. Logistic regression models were used to calculate relative risks (RRs) and 95% confidence intervals (CIs), adjusted for confounding variables and breast cancer risk factors. All statistical tests were two-sided. Results: We observed a moderate increase in breast cancer risk among the women who worked 1–14 years or 15–29 years on rotating night shifts (multivariate adjusted RR = 1.08 [95% CI = 0.99 to 1.18] and RR = 1.08 [95% CI = 0.90 to 1.30], respectively). The risk was further increased among women who worked 30 or more years on the night shift (RR = 1.36; 95% CI = 1.04 to 1.78). The test for trend was statistically significant (P = .02). Conclusions: Women who work on rotating night shifts with at least three nights per month, in addition to days and evenings in that month, appear to have a moderately increased risk of breast cancer after extended periods of working rotating night shifts.

The suprachiasmatic nucleus in the hypothalamus, one of the most important physiologic determinants of alertness and performance, drives a circadian pacemaker in mammals, with an intrinsic period averaging 24 hours. Light is the primary stimulus to disrupt and reset this pacemaker, which is expressed in changing melatonin rhythms. Light exposure at night may, therefore, be related to a variety of behavioral changes and associated health problems not yet well explored. Studies (1) have suggested an increased risk of coronary heart disease among rotating night shift workers, not fully explained by an increased prevalence of coronary risk factors. Others have linked night work to an increased breast cancer risk among women (2).

Melatonin, the “hormone of the darkness,” has only recently gained substantial attention from the scientific community with regard to its potential oncostatic actions and its possible effect on breast cancer risk (3–,10). Melatonin serum levels in humans decrease when people are exposed to light at night (11). Suppressed serum melatonin levels might enhance tumor development (12). Observational studies (2, 13–,15) are compatible with an effect of melatonin on breast cancer risk, reporting meaningful increases in breast cancer risk among postmenopausal women exposed to shiftwork. Recently, a tumor-promoting effect of light exposure was demonstrated on chemically induced tumors in rodents (16). To date, melatonin has been shown to be oncostatic for a variety of tumor cells in experimental carcinogenesis (17–,26). The evidence of a relation between melatonin and oncogenesis in humans is conflicting (27), but the majority of reports indicate protective action (28).

Several mechanisms have been hypothesized to explain an association between melatonin and breast cancer. Cohen et al. (29) proposed that loss of pineal function and the resulting decreased melatonin serum levels may increase reproductive hormone levels and, in particular, estradiol levels, thereby increasing the growth and proliferation of hormone-sensitive cells in the breast. More recent research focuses on potential mechanisms through which melatonin is directly oncostatic. Melatonin is believed to have antimitotic activity by affecting directly hormone-dependent proliferation through interaction with nuclear receptors (4). Another explanation is that melatonin increases the expression of the tumor suppressor gene p53 (3). Cells lacking p53 have been shown to be genetically unstable and thus more prone to tumors (30).

Breast cancer is the most common cancer among women in the United States. To date, the relationship between night work and breast cancer risk has not been evaluated in prospective cohort studies. A causal link between the two would be of public health importance, because small changes in shift patterns may create a substantial decrease of disease burden among women.

In this report, we evaluate the relationship between night work, as a surrogate for light exposure at night, and breast cancer risk in a large prospective cohort of premenopausal and postmenopausal women. Our analysis is based on 10 years of follow-up in 78 562 women participating in the Nurses' Health Study.

Keywords cancer, night shift

Schernhammer ES, Rosner B, Willett WC et al. **Year** 2004

Authors Schernhammer ES, Rosner B, Willett WC et al.

Report Name Epidemiology of urinary melatonin in women and its relation to other hormones and night work

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers 13:936–943. PMID:15184249

URL http://cebp.aacrjournals.org/content/13/6/936.abstract

Abstract Objective: Light exposure during night work suppresses melatonin production, and night work has been associated with an increased cancer risk. There is little information, however, about the interrelationships of night work, urinary melatonin levels, and levels of plasma steroid hormones in women. Method: We examined the reproducibility of morning urinary measurements of 6-sulfatoxymelatonin over a 3-year period in 80 premenopausal women. We assessed correlations between average urinary melatonin and plasma steroid hormone levels and evaluated potential associations between night work and hormone levels, using current and long-term shift work information from two large, prospective cohorts, the Nurses' Health Study cohorts. Results: The intraclass correlation for creatinine-adjusted 6-sulfatoxymelatonin was 0.72 (95% confidence interval, 0.65, 0.82). We found significantly increased levels of estradiol after longer durations of night work (geometric mean levels of estradiol, 8.8 pg/mL for women who never worked night shifts versus 10.1 pg/mL for women who worked 15 or more years of night shifts; P for trend = 0.03). We observed a significant inverse association between increasing number of nights worked within the 2 weeks preceding urine collection and urinary melatonin levels (r = −0.30, P = 0.008), but no association of recent night work with estradiol (r = 0.10, P = 0.41). Conclusion: A single morning urinary melatonin measurement is a reasonable marker for long-term melatonin levels among premenopausal women. Women who work on rotating night shifts seem to experience changes in hormone levels that may be associated with the increased cancer risk observed among night-shift workers.

Keywords melatonin, estrogens, night work

Schernhammer ES, Schulmeister K **Year** 2004

Authors E S Schernhammer, K Schulmeister

Report Name Melatonin and cancer risk: does light at night compromise physiologic cancer protection by lowering serum melatonin levels?

Publication British Journal of Cancer

Issue-page numbers (2004) 90, 941–943. doi:10.1038/sj.bjc.6601626

URL http://www.nature.com/bjc/journal/v90/n5/abs/6601626a.html

Abstract The suprachiasmatic nuclei in the hypothalamus, one of the most important physiological determinants of alertness and performance, drive a circadian pacemaker in mammals, with an intrinsic period averaging 24 h. Light is the primary stimulus to the disruption and resetting of this pacemaker, which is expressed in changing melatonin rhythms. Melatonin production in humans decreases when people are exposed to light at night. Since melatonin shows potential oncostatic action in a variety of tumours, it is possible that lowered serum melatonin levels caused by exposure to light at night enhance the general tumour development. Cancer is the second leading cause of death in industrialised countries like the United States, where a significant proportion of workers engage in shift work, making a hypothesised relation between light exposure at night and cancer risk relevant. Observational studies support an association between night work and cancer risk. We hypothesise that the potential primary culprit for this observed association is the lack of melatonin, a cancer-protective agent whose production is severely diminished in people exposed to light at night.

Keywords

Schernhammer ES, Stone KL

Year 2011

Authors Eva S. Schernhammer and Katie L. Stone

Report Name LIGHT POLLUTION ≠ LIGHT POLLUTION?

Publication Chronobiology International

Issue-page numbers 28:4, 378-379

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.565898

Abstract N/A

Keywords

Schernhammer ES, Thompson CA

Year 2011

Authors Eva S Schernhammer, Caroline A Thompson

Report Name Light at night and health: the perils of rotating shift work

Publication Occup Environ Med

Issue-page numbers 68:310-311 doi:10.1136/oem.2010.058222

URL http://oem.bmj.com/content/68/5/310.short?rss=1

Abstract Obesity has been on the rise in the USA and across the globe 1 and is a major public health concern. In an article in this issue of the journal, Kubo et al (see page 327) show that rotating shift work, and in particular longer term (10+ years) rotating shift work, significantly increases the risk of weight gain and obesity. 2 This is not the first study to report such an association, but is perhaps one of the most thorough and powerful examinations to date.

Keywords

Schibler U

Year 2007

Authors Ueli Schibler

Report Name The daily timing of gene expression and physiology in mammals.

Publication Dialogues in Clinical Neuroscience

Issue-page numbers (2007) Volume: 9, Issue: 3, Pages: 257-272

URL http://www.mendeley.com/research/daily-timing-gene-expression-physiology-mammals/

Abstract Mammalian behavior and physiology undergo daily rhythms that are coordinated by an endogenous circadian timing system. This system has a hierarchical structure, in that a master pacemaker, residing in the suprachiasmatic nucleus of the ventral hypothalamus, synchronizes peripheral oscillators in virtually all body cells. While the basic molecular mechanisms generating the daily rhythms are similar in all cells, most clock outputs are cell-specific. This conclusion is based on genome-wide transcriptome profiling studies in several tissues that have revealed hundreds of rhythmically expressed genes. Cyclic gene expression in the various organs governs overt rhythms in behavior and physiology, encompassing sleep-wake cycles, metabolism, xenobiotic detoxification, and cellular proliferation. As a consequence, chronic perturbation of this temporal organization may lead to increased morbidity and reduced lifespan.

Keywords

Schibler U, Brown SA

Year 2005

Authors Schibler U, Brown SA

Report Name Enlightening the adrenal gland

Publication Cell Metab

Issue-page numbers 2:278–281 doi:10.1016/j.cmet.2005.10.001. PMID:16271527

URL http://www.cell.com/cell-metabolism/abstract/S1550-4131%2805%2900295-0

Abstract * The secretion of glucocorticoid hormones is tightly regulated by the circadian clock and by negative humoral feedback loops, both acting on the hypothalamic-pituitary gland-adrenal axis. However, a new study (Ishida et al., 2005 [this issue of Cell Metabolism]) shows that light can influence the adrenal's glucocorticoid output by a more direct pathway

Keywords

Schibler U, Ripperger J, Brown SA

Year 2003

Authors Schibler U, Ripperger J, Brown SA

Report Name Peripheral circadian oscillators in mammals: time and food

Publication J Biol Rhythms

Issue-page numbers 18:250–260 doi:10.1177/0748730403018003007. PMID:12828282

URL http://jbr.sagepub.com/content/18/3/250.abstract

Abstract Peripheral cells from mammalian tissues, while perfectly capable of circadian rhythm generation, are not light sensitive and thus have to be entrained by nonphotic cues. Feeding time is the dominant zeitgeber for peripheral mammalian clocks: Daytime feeding of nocturnal laboratory rodents completely inverts the phase of circadian gene expression in many tissues, including liver, heart, kidney, and pancreas, but it has no effect on the SCN pacemaker. It is thus plausible that in intact animals, the SCN synchronizes peripheral clocks primarily through temporal feeding patterns that are imposed through behavioral restactivity cycles. In addition, body temperature rhythms, which are themselves dependent on both feeding patterns and rest-activity cycles, can sustain circadian, clock gene activity in vivo and in vitro. The SCN may also influence the phase of rhythmic gene expression in peripheral tissues through direct chemical pathways. In fact, many chemical signals induce circadian gene expression in tissue culture cells. Some of these have been shown to elicit phase shifts when injected into intact animals and are thus candidates for physiologically relevant timing cues. While the response of the SCN to light is strictly gated to respond only during the night, peripheral oscillators can be chemically phase shifted throughout the day. For example, injection of dexamethasone, a glucocorticoid receptor agonist, resets the phase of circadian liver gene expression during the entire 24-h day. Given the bewildering array of agents capable of influencing peripheral clocks, the identification of physiologically relevant agents used by the SCN to synchronize peripheral clocks will clearly be an arduous undertaking. Nevertheless, we feel that experimental systems by which this enticing problem can be tackled are now at hand.

Keywords circadian clock, peripheral oscillators, phase entrainment, synchronization, feeding time, suprachiasmatic nucleus, body temperature rhythms

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Schmidt CW

Year 2007

Authors Schmidt CW

Report Name Environmental Connections: A Deeper Look into Mental Illness

Publication Environ Health Perspect

Issue-page numbers 115:A404-A410

URL http://dx.doi.org/10.1289/ehp.115-a404

Abstract Article

Keywords melatonin

Authors Schmitt J, Seidler A, Diepgen TL, Bauer A.

Report Name Occupational UV-light exposure increases the risk for the development of cutaneous squamous cell carcinoma: A systematic review and meta-analysis

Publication British Journal of Dermatology

Issue-page numbers Volume 164, Issue 2, pages 291–307, February 2011

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.2010.10118.x/full

Abstract

Background Despite the fact that ultraviolet (UV) light exposure is the most important risk factor for cutaneous squamous cell carcinoma (SCC) there is an ongoing debate concerning the relationship between cumulative work-related UV exposure and SCC occurrence.

Objectives To analyse comprehensively the relationship between work-related UV exposure and SCC risk.

Methods We conducted a systematic electronic literature search in PubMed (up to 5 May 2010) supplemented by a hand search, which identified 18 relevant studies that were included in the review. Data abstraction and study quality assessment was done independently by two reviewers. Maximally adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) of all included studies were pooled in a random-effects meta-analysis. Sensitivity analysis included meta-regression on study-specific covariates to explore the robustness of the results and to identify sources of heterogeneity between studies. Eighteen studies (six cohort studies, 12 case–control studies) met the eligibility criteria and were included in the systematic review.

Results Sixteen studies (89%) found an increased risk of SCC in individuals with occupational UV light exposure compared with individuals without occupational UV light exposure, reaching statistical significance in 12 studies. Two studies found no association between occupational UV light exposure and SCC occurrence. The pooled OR (95% CI) was 1·77 (1·40–2·22) and did not differ significantly between cohort studies [OR (95% CI): 1·68 (1·08–2·63)] and case–control studies [OR (95% CI): 1·77 (1·37–2·30)]. Meta-regression analyses suggested an increasing strength of the association between occupational UV light exposure and SCC risk with decreasing latitude.

Conclusions In summary, there is consistent epidemiological evidence for a positive association between occupational UV light exposure and SCC risk.

Keywords

Schmoll C, Lascaratos G, Dhillon B, et al. **Year** 2011

Authors Conrad Schmoll, Gerassimos Lascaratos, Bal Dhillon, Debra Skene, Renata L. Riha

Report Name The role of retinal regulation of sleep in health and disease

Publication Sleep Medicine Reviews

Issue-page numbers Volume 15, Issue 2, April 2011, Pages 107-113

URL http://www.sciencedirect.com/science/article/pii/S1087079210000626

Abstract The process of photoentrainment, through the activation of photoreceptor transduction cascades, influences the circadian physiology of many life forms from primitive invertebrates to primates. In humans, a population of intrinsically photosensitive retinal ganglion cells (ipRGC's) is responsible for mediating the circadian rhythm and is susceptible to primary dysfunction affecting this cell population specifically, or disorders influencing light activation of retinal ganglion photoreceptors. The former may arise through cell depletion in conditions such as inherited or acquired optic neuropathies or conditions like Parkinson's disease which may alter retinal dopamine-mediated neurotransmission, and the latter, secondary to common causes of light transmission reduction associated with ageing and cataract. This review examines the current evidence linking ocular pathology and the resultant reduction in retinal phototransduction with circadian disturbances and sleep disorders, with downstream effects on our overall physiological integrity. As our understanding of the effects of light pathways on circadian biology develops, therapeutic modalities based upon the underlying pathophysiological processes are emerging, although the direct measurement, consequences and treatment of relative or absolute ipRGC dysfunction remain to be fully and clearly elucidated in man.

Keywords

Schothorst AA, Slaper H, Schouten R, Suurmond D **Year** 1985

Authors Schothorst AA, Slaper H, Schouten R, Suurmond D.

Report Name UVB doses in maintenance psoriasis phototherapy versus solar UVB exposure

Publication Photodermatol

Issue-page numbers 1985 Aug;2(4):213-20.

URL http://www.ncbi.nlm.nih.gov/pubmed/4059077/

Abstract A possible increase in the risk of skin cancer in psoriatic patients treated with long-term maintenance UVB phototherapy was assessed by comparing the cumulative doses of UVB with the amount of UVB received from sunlight by normal healthy people. The biologically-effective UVB dose (termed UVB(EE)) was measured using polysulphone film and worn as a badge by individuals with either an indoor or an outdoor occupation during 4 summer months of 1983 in The Netherlands (52 degrees N). The calculated mean annual UV-B(EE) doses were 5.9 J/cm2 for persons with an indoor occupation and 134 J/cm2 for those with an outdoor occupation. The UVB(EE) doses received by psoriasis patients during an initial course of phototherapy, as well as during maintenance treatment, were also estimated and gave a mean value of 22 J/cm2. Mean annual amounts of solar UVB(EE) exposure were calculated and compared with the administered doses of UVB(EE) during maintenance phototherapy. A dose-response model is described in order to estimate the increased incidence of non-melanoma skin cancer associated with such therapy. The cumulative incidence among patients who received maintenance phototherapy for several decades was calculated to be a factor of 2.5 to 7.5 higher than the incidence among individuals with an outdoor occupation.

Keywords

Schulmeister K, Buberl A, Weber M, Brusl H, Kitz E

Year 2011

Authors Schulmeister K, Buberl A, Weber M, Brusl H, Kitz E

Report Name Optische Strahlung: Ultraviolett-Strahlungsemission von Beleuchtungsquellen.

Publication AUVA Report Nr 55

Issue-page numbers AUVA, Vienna;

URL https://www.sozialversicherung.at/mediaDB/783330_R55b.pdf

Abstract [in German]

Keywords

Schwartzbaum J, Ahlbom A, Feychting

Year 2007

Authors Schwartzbaum J, Ahlbom A, Feychting

Report Name Cohort study of cancer risk among male and female shift workers

Publication Scand J Work Environ Health

Issue-page numbers 33:336–343. PMID:17973059

URL http://www.sjweh.fi/download.php?abstract_id=1150&file_nro=1

Abstract Objectives Melatonin, a hormone that inhibits experimentally induced cancers, is suppressed by nighttime exposure to light so that nighttime shift workers may be at an increased risk of cancer. Previous studies of shift workers found an increased risk of breast cancer among women and suggested a possible increased risk of colon cancer among women and prostate cancer. The present study was conducted to see whether these previous findings could be confirmed and whether shift workers are at elevated risk for cancer at additional sites.
Methods Altogether 2 102 126 male and 1 148 661 female workers were identified who worked in both 1960 and 1970. Their jobs were classified according to the percentage of shift workers, and they were followed from 1971 through 1989 or until they were diagnosed with cancer or died. Standardized incidence ratios (SIR) were used to compare the adjusted cancer incidence rates for shift workers with those for nonshift workers.
Results Cancer rates were not elevated for the male shift workers [all sites combined: N=6524 cases among shift workers, SIR 1.02, 95% confidence interval (95% CI) 1.00–1.05; prostate: N=1319, SIR 1.04, 95% CI 0.99–1.10] or for the female shift workers (all sites combined: N=268, SIR 1.00, 95% CI 0.89–1.13; breast: N=70 cases, SIR 0.94, 95% CI 0.74–1.18).
Conclusions No evidence was found for an association between shift work and breast or prostate cancer, or all cancer sites combined among shift workers.

Keywords cancer; melatonin.

Schwimmer H, Mursu N, Haim A — **Year** 2010

Authors Hagit Schwimmer, Netta Mursu and Abraham Haim

Report Name EFFECTS OF LIGHT AND MELATONIN TREATMENT ON BODY TEMPERATURE AND MELATONIN SECRETION DAILY RHYTHMS IN A DIURNAL RODENT, THE FAT SAN

Publication Chronobiology International

Issue-page numbers 27:7, 1401-1419

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2010.505355

Abstract Many mammals display predictable daily rhythmicity in both neuroendocrine function and behavior. The basic rest-activity cycles are usually consistent for a given species and vary from night-active (nocturnal), those mostly active at dawn and dusk (i.e., crepuscular), and to day-active (diurnal) species. A number of daily rhythms are oppositely phased with respect to the light/dark (LD) cycle in diurnal compared with nocturnal mammals, whereas others are equally phased with respect to the LD cycle, regardless of diurnality/nocturnality. Pineal produced melatonin (MLT) perfectly matches this phase-locked feature in that its production and secretion always occurs during the night in both diurnal and nocturnal mammals. As most rodents studied to date in the field of chronobiology are nocturnal, the aim in this study was to evaluate the effect of light manipulations and different photoperiods on a diurnal rodent, the fat sand rat, Psammomys obesus. The authors studied its daily rhythms of body temperature (Tb) and 6-sulphatoxymelatonin (6-SMT) under various photoperiodic regimes and light manipulations (acute and chronic exposures) while maintaining a constant ambient temperature of 30°C ± 1°C. The following protocols were used: (A) Control (CON) conditions 12L:12D; (A1) exposure to one light interference (LI) of CON-acclimated individuals for 30 min, 5 h after lights-off; (A2) short photoperiod (SP) acclimation (8L:16D) for 3 wks; (A3) 3 wks of SP acclimation with chronic LI of 15 min, three times a night at 4-h intervals; (A4) chronic exposure to constant dim blue light (470nm, 30 lux) for 24 h for 3 wks (LL). (B) The response to exogenous MLT administration, provided in drinking water, was measured under the following protocols: (B1) After chronic exposure to SP with LI, MLT was provided once, starting 1 h before the end of photophase; (B2) after a continuous exposure to dim blue light, MLT was provided at 15:00 h for 2 h for 2 wks; (B3) to CON animals, MLT was given intraperitoneally (i.p.) at 14:00 h. The results demonstrate that under CON acclimation, Psammomys obesus has robust Tb and 6-SMT daily rhythms in which the acrophase (peak time) of Tb is during the photophase, whereas that of 6-SMT is during scotophase. LI resulted in an elevation of Tb and a reduction of 6-SMT levels. A significant difference in the response was noted between acute and chronic exposure to LI, particularly in 6-SMT levels, which were lower than CON after LI and higher after chronic LI, implying an acclimation process. Constant exposure to blue light abolished Tb and 6-SMT rhythms in all the animals. MLT administration resumed the Tb daily rhythm in these animals, and had a recovery effect on the chronic LI-exposed animals, resulting in a Tb decrease. Altogether, the authors show in this study the different modifications of Tb rhythms and MLT levels in response to environmental light manipulations. These series of experiments may serve as a basis for establishing P. obesus as an animal model for further studies in chronobiology.

Keywords Animal model, Diurnal rodents, Light interference, Melatonin, Photoperiod

Sedbrook J — **Year** 2010

Authors Judy Sedbrook

Report Name The Night Shift

Publication webpage

Issue-page numbers

URL http://coopext.colostate.edu/4dmg/Flowers/night.htm

Abstract webpage

Keywords garden, night

Authors Sekaran S, Foster RG, Lucas RJ, Hankins MW

Report Name Calcium imaging reveals a network of intrinsically light-sensitive inner-retinal neurons

Publication Curr Biol

Issue-page numbers 13:1290–1298 doi:10.1016/S0960-9822(03)00510-4. PMID:12906788

URL http://www.cell.com/current-biology/retrieve/pii/S0960982203005104

Abstract Background: Mice lacking rod and cone photoreceptors (rd/rd cl) are still able to regulate a range of responses to light, including circadian photoentrainment, the pupillary light reflex, and suppression of pineal melatonin by light. These data are consistent with the presence of a novel inner-retinal photoreceptor mediating non-image-forming irradiance detection.Results: We have examined the nature and extent of intrinsic light sensitivity in rd/rd cl retinae by monitoring the effect of light stimulation (470 nm) on intracellular Ca2+ via FURA-2 imaging. Using this approach, which does not rely on pharmacological or surgical isolation of ganglion cells from the rod and cone photoreceptors, we identified a population of light-sensitive neurons in the ganglion cell layer (GCL). Retinal illumination induced an increase of intracellular Ca2+ in ~2.7% of the neurons. The light-evoked Ca2+ fluxes were dependent on the intensity and duration of the light stimulus. The light-responsive units formed an extensive network that could be uncoupled by application of the gap junction blocker carbenoxolone. Three types of light-evoked Ca2+ influx were observed: sustained, transient, and repetitive, which are suggestive of distinct functional classes of GCL photoreceptors.Conclusions: Collectively, our data reveal a heterogeneous syncytium of intrinsically photosensitive neurons in the GCL coupled to a secondary population of light-driven cells, in the absence of rod and cone inputs.

Keywords

Authors Sekine M, Yamagami T, Handa K et al.

Report Name A dose-response relationship between short sleeping hours and childhood obesity: results of the Toyama Birth Cohort Study

Publication Child Care Health Dev

Issue-page numbers 28:163–170 doi:10.1046/j.1365-2214.2002.00260.x. PMID:11952652

URL http://www.ncbi.nlm.nih.gov/pubmed/11952652

Abstract

BACKGROUND:

Short sleeping hours could cause obesity through increased sympathetic activity, elevated cortisol secretion and decreased glucose tolerance. The aim of this study was to clarify parental and lifestyle factors, particularly sleeping habits, associated with obesity in Japanese children.
METHODS:

Between June and July 1996, 8274 children (4194 males and 4080 females) aged 6-7 years living in Toyama prefecture, Japan, were investigated by questionnaire survey and the collection of anthropometric data. Subjects with a body mass index (BMI; weight in kg divided by square of height in m) greater than the age- and sex-specific cut-off points linked to adulthood overweight (BMI of 25 kg/m2 or more) were defined as obese subjects. Parental obesity was defined as a BMI of 25 kg/m2 or more. Logistic regression analysis was performed to evaluate the strength of the relationships between parental obesity or lifestyle factors and childhood obesity, adjusted for possible confounding factors.
RESULTS:

Parental obesity, long hours of TV watching and physical inactivity were significantly associated with childhood obesity. Although wake-up time was not related to obesity, there was a significant dose-response relationship between late bedtime or short sleeping hours and childhood obesity. Compared with children with 10 or more hours of sleep, the adjusted odds ratio was 1.49 (95% confidence interval 1.08-2.14) for those with 9-10 h sleep, 1.89 (1.34-2.73) for those with 8-9 h sleep and 2.87 (1.61-5.05) for those with <8 h sleep, after adjustment for age, sex, parental obesity and other lifestyle factors.
CONCLUSION:

A strong inverse association was observed in the relationship between sleeping hours and childhood obesity. Longitudinal research will be required to confirm this causality.

Keywords

Selvaag E

Year 1997

Authors E. Selvaag

Report Name Clinical drug photosensitivity. A retrospective analysis of reports to the Norwegian Adverse Drug Reactions Committee from the years 1970-1994

Publication Photodermatology, Photoimmunology & Photomedicine

Issue-page numbers Volume 13, Issue 1-2, pages 21–23, February-April 1997

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0781.1997.tb00103.x/abstract?

Abstract Adverse drug reactions reported to the Norwegian Medicine Control Authority from 1970 to 1994 were analyzed, especially with regard to cutaneous reactions and photosensitization. In the time period, almost 13,000 unwanted side effects were reported. Of these, 799 reports involved the skin and appendages, of which 64 reports (8%) were classified as photosensitivity reactions. Tetracyclines, diuretics, antihypertensive agents, and urologicals were the drugs that most often caused photosensitivity reactions. In addition, a number of uncommon photosensitizing drugs were reported. The risk for photosensitization is discussed on the basis of experimental data and the prescription rates of these substances.

Keywords cutaneous reactions; photosensitization

Sen DJ, Shishoo CJ, Lahiri A

Year 2011

Authors Dhrubo Jyoti Sen, Chamanlal J. Shishoo, Angshuman Lahiri

Report Name Three musketeers of genotoxicity: carcinogen, mutagen & teratogen

Publication NSHM Journal of Pharmacy and Healthcare Management

Issue-page numbers Vol. 02, February (2011) pp. 13-25

URL http://www.nshm.com/pdf/Three_musketeers_genotoxicity_carcinogen_mutagen_teratogen.pdf

Abstract Genotoxicity describes a deleterious action on a cell's genetic material affecting its integrity. Genotoxic substances are known to be potentially mutagenic or carcinogenic, specifically those capable of causing genetic mutation and of contributing to the development of tumors. This includes both certain chemical compounds and certain types of radiation. Typical genotoxins like aromatic amines are believed to cause mutations because they are nucleophilic and form strong covalent bonds with DNA resulting with the formation of Aromatic Amine-DNA Adducts, preventing accurate replication. Genotoxins affecting sperm and eggs can pass genetic changes down to descendants who have never been exposed to the genotoxin. A carcinogen is any substance, radionuclide or radiation that is an agent directly involved in causing cancer. This may be due to the ability to damage the genome or to the disruption of cellular metabolic processes. Several radioactive substances are considered carcinogens, but their carcinogenic activity is attributed to the radiation, for example gamma rays and alpha particles, which they emit. Carcinogens may increase the risk of cancer by altering cellular metabolism or damaging DNA directly in cells, which interferes with biological processes, and induces the uncontrolled, malignant division, ultimately leading to the formation of tumors. Usually DNA damage, if too severe to repair, leads to programmed cell death, but if the programmed cell death pathway is damaged, then the cell cannot prevent itself from becoming a cancer cell. In biology, a mutagen (Latin, literally origin of change) is a physical or chemical agent that changes the genetic material, usually DNA, of an organism and thus increases the frequency of mutations above the natural background level. As many mutations cause cancer, mutagens are typically also carcinogens. Not all mutations are caused by mutagens: so-called "spontaneous mutations" occur due to errors in DNA replication, repair and recombination. Teratology is the study of abnormalities of physiological development. It is often thought of as the study of birth defects, but it is much broader than that, taking in other developmental stages, such as puberty; and other life forms, such as plants.

Keywords Poly Aromatic Hydrocarbons (PAH), aflatoxins, biomass, radionucleotide, mutation

Serda SM, Wei ET | ***Year*** 1992

Authors Serda SM, Wei ET

Report Name Epinephrine-induced pulmonary oedema in rats is inhibited by corticotropin-releasing factor

Publication Pharmacol Res

Issue-page numbers 26:85–91 doi:10.1016/1043-6618(92)90708-J. PMID:1513751

URL http://www.sciencedirect.com/science/article/pii/104366189290708J

Abstract In various animal models of injury to skin, mucous membranes, muscle and brain, corticotropin-releasing factor (CRF) attenuated vascular leakage in the injured tissues. Here, the effects of CRF on a rat model of pulmonary oedema were examined. Male albino rats (220–290 g) received saline or CRF s.c., 30 min before pentobarbital anaesthesia, 60 mg/kg i.p., and 1 h before 1-epinephrine bitartrate (Epi), 30μg/kg i.v. Within 30 min after Epi all (n=27) saline-pretreated rats were dead from pulmonary oedema, but animals receiving human/rat CRF at doses of 7 to 57 μg/kg s.c. (n=25) were all alive. Body wt, wet and dry wt of lungs were used to calculate an oedema index. This index increased from 3.6±0.1 to 9.6±0.3 after Epi but was inhibited by 87% after CRF 28 μg/kg s.c. The ED50 of CRF for reducing pulmonary oedema was 3.2 (1.3–7.4) μg/kg s.c. Mean arterial pressure increased from 119±4 to 167±2 mmHg after Epi 10 μg/kg i.v., but was not different (118±3 to 169±4 mmHg) after CRF pretreatment, 6 μg/kg s.c., a dose which reduced lung oedema. Pharmacokinetic estimates suggest that plasma levels of CRF sufficient to attenuate lung oedema in rats approximate those seen in pregnant women at delivery, raising the possibility that endogenous CRF may protect the maternal organism during parturition.

Keywords corticotropin-releasing factor; epineprhine; pulmonary oedema

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Shady S, MacLeod DI, Fisher HS. | ***Year*** 2004

Authors Sherif Shady, Donald I. A. MacLeod , and Heidi S. Fisher

Report Name Adaptation from invisible flicker

Publication PNAS

Issue-page numbers April 6, 2004 vol. 101 no. 14 5170-5173

URL http://www.pnas.org/content/101/14/5170.abstract

Abstract Human ability to resolve temporal variation, or flicker, in the luminance (brightness) or chromaticity (color) of an image declines with increasing frequency and is limited, within the central visual field, to a critical flicker frequency of ≈50 and 25 Hz, respectively. Much remains unknown about the neural filtering that underlies this frequency-dependent attenuation of flicker sensitivity, most notably the number of filtering stages involved and their neural loci. Here we use the process of flicker adaptation, by which an observer's flicker sensitivity is attenuated after prolonged exposure to flickering lights, as a functional landmark. We show that flicker adaptation is more sensitive to high temporal frequencies than is conscious perception and that prolonged exposure to invisible flicker of either luminance or chromaticity, at frequencies above the respective critical flicker frequency, can compromise our visual sensitivity. This suggests that multiple filtering stages, distributed across retinal and cortical loci that straddle the locus for flicker adaptation, are involved in the neural filtering of high temporal frequencies by the human visual system.

Keywords

Authors Prabhaker N. Shah, Molina C. Mhatre, and Lalita S. Kothari

Report Name Effect of Melatonin on Mammary Carcinogenesis in Intact and Pinealectomized Rats in Varying Photoperiods

Publication Cancer Research

Issue-page numbers August 1984 44; 3403-3407

URL http://cancerres.aacrjournals.org/content/44/8/3403

Abstract Exposure of female Holtzman rats to constant light (24 hr/day) immediately after birth significantly increased 9,10-dimethyl-1,2-benzanthracene-induced mammary cancer. Such "functionally pinealectomized" animals also revealed significant increase in the circulating level of prolactin and exaggerated development and proliferative activity of mammary epithelium, as measured by quantitation of terminal end buds and alveolar buds from the whole mounts and by DNA synthesis, respectively. Administration of melatonin (500 μg/day/rat i.p. given from 52 to 145 days of age) completely abolished the effect of functional pinealectomy by sharply reducing 9,10-dimethyl-1,2-benzanthracene-induced cancer incidence from 95% to 25% during the post-9,10-dimethyl-1,2-benzanthracene observation period which lasted up to 180 days. On the other hand, administration of melatonin to surgically pinealectomized animals exposed to constant light reversed the effect only partially by reducing the cancer incidence from 83% to 53%. Further, melatonin treatment in intact and surgically pinealectomized animals exposed to a short photoperiod revealed qualitatively similar differences in suppression of the cancer incidence. From these results, it is concluded that, to have an impressive antitumor effect, presence of the pineal gland is essential, and the probable site of melatonin action appears to be at both the pineal gland and the hypothalamus.

Keywords

Authors Sharma A, Neekhra A, Gramajo AL, Patil J, Chwa M, Kuppermann BD, et al.

Report Name Effects of Benzo(e)Pyrene, a toxic component of cigarette smoke, on human retinal pigment epithelial cells in vitro

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers November 2008 vol. 49 no. 11 5111-5117

URL http://www.iovs.org/content/49/11/5111.full

Abstract

purpose. To better understand the cellular and molecular basis for the epidemiologic association between cigarette smoke and age-related macular degeneration (AMD), the authors examined the effects of Benzo(e)Pyrene (B(e)P), a toxic element in cigarette smoke, on human retinal pigment epithelial cells (ARPE-19).

methods. ARPE-19 cells were cultured in Dulbecco modified Eagle medium containing 10% fetal bovine serum. Cells were treated for 24 hours with 1000 μM, 400 μM, 200 μM, and 100 μM B(e)P. Cell viability was determined by a trypan blue dye-exclusion assay. Activities of caspase-3/7, caspase-8, caspase-9, and caspase-12 were measured by a fluorescence image scanner, and DNA laddering was evaluated by electrophoresis on 3% agarose gel.

results. The mean percentage of cell viabilities of ARPE-19 cells was decreased in a dose-dependent manner after exposure to B(e)P at the higher concentrations of 1000 μM (20.0 ± 0.4; $P < 0.001$), 400 μM (35.6 ± 6.4; $P < 0.001$), and 200 μM (58.7 ± 2.3; $P < 0.001$) but not at 100 μM (95.9 ± 0.7; $P > 0.05$) compared with the equivalent dimethyl sulfoxide (DMSO)-treated control cultures. There were significant increases in caspase-3/7, -8, -9, and -12 activities compared with the DMSO-treated controls ($P < 0.001$). DNA laddering revealed bands at 200-bp intervals.

conclusions. These results show that B(e)P is a toxicant to human retinal pigment epithelial cells in vitro. It causes cell death and induces apoptosis by the involvement of multiple caspase pathways.

Keywords

Sharma M, Palacios-Bois J, Schwartz G et al. **Year** 1989

Authors Sharma M, Palacios-Bois J, Schwartz G et al.

Report Name Circadian rhythms of melatonin and cortisol in aging

Publication Biol Psychiatry

Issue-page numbers 25:305–319 doi:10.1016/0006-3223(89)90178-9. PMID:2914154

URL http://www.sciencedirect.com/science/article/pii/0006322389901789

Abstract The relationship of age to the circadian rhythms of melatonin and cortisol was investigated in 44 men and 27 women (age range 19–89 years). Subjects were physically and psychiatrically normal. Four hourly serial blood samples were drawn from 8:00 am until 8:00 am the next day, with additional samples at 10:00 pm and 2:00 am. The indoor illumination was restricted to 300 lux during day and 50 lux during the night. Plasma melatonin and cortisol were estimated by radioimmunoassay. Results show that the means of melatonin and cortisol values decreased significantly with age when the subjects were divided into three age groups, i.e., 19–25 years, 42–65 years, and 66–89 years. They also showed a significant negative correlation with age. The acrophases of the two hormonal rhythms, however, showed different relationships to age. The acrophase of melatonin rhythm showed a positive correlation with age ($r = 0.38$, $p < 0.001$), and cortisol showed a negative correlation with age ($r = -0.56$, $p > 0.001$). It is suggested that this may indicate a weakened responsiveness of the circadian system in the elderly to the day-night cycle and an altered relationship between the pacemakers driving melatonin and cortisol circadian rhythms. This may thus represent a biomarker for the intrinsic process of the aging of the brain.

Keywords

Shearman LP, Zylka MJ, Weaver DR et al. **Year** 1997

Authors Shearman LP, Zylka MJ, Weaver DR et al.

Report Name Two period homologs: circadian expression and photic regulation in the suprachiasmatic nuclei

Publication Neuron

Issue-page numbers 19:1261–1269 doi:10.1016/S0896 6273(00)80417-1. PMID:9427249

URL http://www.sciencedirect.com/science/article/pii/S0896627300804171

Abstract We have characterized a mammalian homolog of the Drosophila period gene and designated it Per2. The PER2 protein shows >40% amino acid identity to the protein of another mammalian per homolog (designated Per1) that was recently cloned and characterized. Both PER1 and PER2 proteins share several regions of homology with the Drosophila PER protein, including the protein dimerization PAS domain. Phylogenetic analysis supports the existence of a family of mammalian per genes. In the mouse, Per1 and Per2 RNA levels exhibit circadian rhythms in the SCN and eyes, sites of circadian clocks. Both Per1 and Per2 RNAs in the SCN are increased by light exposure during subjective night but not during subjective day. The results advance our knowledge of candidate clock elements in mammals.

Keywords

Shellard SA, Whelan RDH, Hill BT

Year 1989

Authors S.A. Shellard, R.D.H. Whelan & B.T. Hill

Report Name Growth inhibitory and cytotoxic effects of melatonin and its metabolites on human tumour cell lines in vitro

Publication Br. J. Cancer

Issue-page numbers (1989), 60, 288-290

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2247202/pdf/brjcancer00119-0020.pdf

Abstract short communication

Keywords

Shields KM

Year 2011

Authors Shields KM.

Report Name Drug-Induced Photosensitivity

Publication Pharmacist's Letter/Prescriber's

Issue-page numbers Letter 2004; 20:200509.

URL http://www.wellnesspharmacy.net/photosensitivity.pdf

Abstract Many of the drugs listed in the proceeding table were labeled as photosensitizing based on unclear data. Unclear and incomplete reporting of adverse drug reactions lead to this confusion. Chemicals that are planar, tricyclic, or polycyclic absorb ultraviolet light, which lead them to be classified as photosensitizer drugs.

Keywords

Authors Shih M-C, Yeh K-T, Tang K-P et al.

Report Name Promoter methylation in circadian genes of endometrial cancers detected by methylation-specific PCR

Publication Mol Carcinog

Issue-page numbers 45:732–740 doi:10.1002/mc.20198. PMID:16683245

URL http://onlinelibrary.wiley.com/doi/10.1002/mc.20198/abstract?

Abstract Methylation of CpG dinucleotides in the promoter sequence of a gene can lead to deregulated and suppressed gene expression. In this study, we have developed procedures for methylation-specific polymerase chain reaction (MSP) and sequencing analysis to determine CpG methylation status of the promoter sequences of nine circadian genes in 35 endometrial cancers (EC) and paired noncancerous endometrial tissues. DNA methylation was found in the promoter sequences of PER1, PER2, and CRY1, but not of other six circadian genes in the ECs and normal tissues examined. Eleven of the 35 EC tissues showed CpG methylation in the promoter sequences of PER1, PER2, or CRY1. Of these 11 cases, 1 had promoter methylation in all the three genes, 1 in PER1 and PER2, 3 in PER1 and CRY1, and 6 in PER1, respectively. In comparison, promoter CpG methylation of PER1, PER2, or CRY1 was found in only 7 of 35 paired noncancerous tissues including 2 in PER1 and PER2, 2 in PER1, and 3 in CRY1. In summary, promoter methylation ir the PER1, PER2, or CRY1 circadian genes was detected in about one-third of EC and one-fifth of noncancerous endometrial tissues of 35 paired specimens indicating possible disruption of the circadian clock in the development of EC.

Keywords circadian genes; methylation-specific PCR; promoter; endometrial cancer

Authors Shiroma H, Higa A, Sawaguchi S, Iwase A, Tomidokoro A, Amano S, et al.

Report Name Prevalence and risk factors of pterygium in a southwestern island of Japan: the Kumejima Study.

Publication American Journal of Ophthalmology

Issue-page numbers Volume 148, Issue 5, November 2009, Pages 766-771.e1

URL http://www.sciencedirect.com/science/article/pii/S0002939409004061

Abstract

Purpose

To determine the prevalence and risk factors for pterygium in a Japanese population aged 40 years or older on Kumejima Island, Japan.
Design

Cross-sectional, population-based study.
Methods

All residents of Kumejima Island, Japan, located in Southwestern Japan (Eastern longitude 126 degrees, 48 feet and Northern latitude 26 degrees, 20 feet), aged 40 years and older were asked to undergo a comprehensive questionnaire and ocular examination.
Results

Of the 4,632 residents, 3,762 (81.2%) underwent the examination. The presence of pterygium could not be determined in 15 subjects. Of the 3,747 eligible subjects, 1,154 (30.8%; 95% confidence interval [CI], 29.3% to 32.3%) had pterygium in at least 1 eye and 491 subjects (13.1%; 95% CI, 12.1% to 14.3%) had pterygium in both eyes. In the logistic regression analysis, older age (P < .001), male gender (P = .024), hyperopic refraction (P = .001), lower intraocular pressure (P = .002), and outdoor job experience (P < .001) were independently associated with a higher risk of pterygium.
Conclusion

The prevalence of pterygium is 30.8% among adult Japanese aged 40 years and older in Kumejima. Older age, male gender, hyperopic refraction, lower intraocular pressure, and outdoor job history were independently associated with a higher risk of pterygium.

Keywords

Shochat T

Year 2012

Authors Tamar Shochat

Report Name Impact of lifestyle and technology developments on sleep

Publication Nature and Science of Sleep

Issue-page numbers Open Access Full Text Article

URL http://www.dovepress.com/impact-of-lifestyle-and-technology-developments-on-sleep-peer-reviewed-article-NSS

Abstract

Although the physiological and psychological mechanisms involved in the development of sleep disorders remain similar throughout history, factors that potentiate these mechanisms are closely related to the “zeitgeist”, ie, the sociocultural, technological and lifestyle trends which characterize an era. Technological advancements have afforded modern society with 24-hour work operations, transmeridian travel and exposure to a myriad of electronic devices such as televisions, computers and cellular phones. Growing evidence suggests that these advancements take their toll on human functioning and health via their damaging effects on sleep quality, quantity and timing. Additional behavioral lifestyle factors associated with poor sleep include weight gain, insufficient physical exercise and consumption of substances such as caffeine, alcohol and nicotine. Some of these factors have been implicated as self-help aids used to combat daytime sleepiness and impaired daytime functioning. This review aims to highlight current lifestyle trends that have been shown in scientific investigations to be associated with sleep patterns, sleep duration and sleep quality. Current understanding of the underlying mechanisms of these associations will be presented, as well as some of the reported consequences. Available therapies used to treat some lifestyle related sleep disorders will be discussed. Perspectives will be provided for further investigation of lifestyle factors that are associated with poor sleep, including developing theoretical frameworks, identifying underlying mechanisms, and establishing appropriate therapies and public health interventions aimed to improve sleep behaviors in order to enhance functioning and health in modern society.

Keywords sleep, technology, lifestyle, behavior

Shuboni D, Yan L

Year 2010

Authors D. Shuboni, L. Yan

Report Name Nighttime dim light exposure alters the responses of the circadian system

Publication Neuroscience

Issue-page numbers Volume 170, Issue 4, 10 November 2010, Pages 1172-1178

URL http://www.sciencedirect.com/science/article/pii/S0306452210011103

Abstract The daily previous termlightnext term dark cycle is the most salient entraining factor for the circadian system. However, in modern society, darkness at night is vanishing as previous termlightnext termprevious termnext termprevious termpollutionnext term steadily increases. The impact of brighter nights on wild life ecology and human physiology is just now being recognized. In the present study, we tested the possible detrimental effects of dim previous termlightnext term exposure on the regulation of circadian rhythms, using CD1 mice housed in previous termlightnext term/dim previous termlightnext term (LdimL, 300 lux:20 lux) or previous termlightnext term/dark (LD, 300 lux:1 lux) conditions. We first examined the expression of clock genes in the suprachiasmatic nucleus (SCN), the locus of the principal brain clock, in the animals of the LD and LdimL groups. Under the entrained condition, there was no difference in PER1 peak expression between the two groups, but at the trough of the PER 1 rhythm, there was an increase in PER1 in the LdimL group, indicating a decrease in the amplitude of the PER1 rhythm. After a brief previous termlightnext term exposure (30 min, 300 lux) at night, the previous termlightnext term-induced expression of mPer1 and mPer2 genes was attenuated in the SCN of LdimL group. Next, we examined the behavioral rhythms by monitoring wheel-running activity to determine whether the altered responses in the SCN of LdimL group have behavioral consequence. Compared to the LD controls, the LdimL group showed increased daytime activity. After being released into constant darkness, the LdimL group displayed shorter free-running periods. Furthermore, following the previous termlightnext term exposure, the phase shifting responses were smaller in the LdimL group. The results indicate that nighttime dim previous termlightnext term exposure can cause functional changes of the circadian system, and suggest that altered circadian function could be one of the mechanisms underlying the adverse effects of previous termlightnext termprevious termnext termprevious termpollutionnext term on wild life ecology and human physiology

Keywords Per1; Per2; circadian rhythms; suprachiasmatic nucleus; light pollution

Sigurdardottir LG, Valdimarsdóttir U, Fall K, et al.

Year 2012

Authors Lara Gudrun Sigurdardottir, Unnur Valdimarsdóttir, Katja Fall, Jennifer R. Rider, Steven W. Lockley, Schernhammer S. Eva, and Lorelei A. Mucci

Report Name Circadian Disruption, Sleep Loss and Prostate Cancer Risk: A Systematic Review of Epidemiological Studies

Publication Cancer Epidemiology, Biomarkers & Prevention

Issue-page numbers Published OnlineFirst May 7, 2012; doi: 10.1158/1055-9965.EPI-12-0116

URL http://cebp.aacrjournals.org/content/early/2012/05/05/1055-9965.EPI-12-0116.abstract

Abstract Disruption of the circadian system has been hypothesized to increase cancer risk, either due to direct disruption of the molecular machinery generating circadian rhythms or due to disruption of parameters controlled by the clock such as melatonin levels or sleep duration. This hypothesis has been studied in hormone-dependent cancers among women, but data are sparse regarding potential effects of circadian disruption on the risk of prostate cancer. This review systematically examines available data evaluating the effects of light at night, sleep patterns, and night shift work on prostate cancer risk.

Keywords

Authors Simard M, Pekary AE, Smith VP, Hershman JM

Report Name Thyroid hormones modulate thyrotropinreleasing hormone biosynthesis in tissues outside the hypothalamic-pituitary axis of male rats

Publication Endocrinology

Issue-page numbers 125:524–531 doi:10.1210/endo-125-1-524. PMID:2500333

URL Thyroid hormones modulate thyrotropinreleasing hormone biosynthesis in tissues outside the hypothalamic-pituitary axis of male rats

Abstract

In the present study we have examined the in vivo effects of thyroid hormone and TRH on secretory tissue concentrations of TRH and TRH-Gly (pGlu-His-Pro-Gly), a TRH precursor. Within secretory granules, TRH-Gly is converted to TRH through alpha-amidation of the C-terminal proline residue, using Gly as the NH2 donor. Using specific RIA, we measured the TRH-Gly immunoreactivity (TRH-Gly-IR) and TRH-IR concentrations in tissues from the reproductive and gastrointestinal systems, adrenals, and other internal organs in euthyroid, hypothyroid, and T4-treated 250-g Sprague-Dawley male rats. TRH-Gly-IR concentrations were more than 2-fold higher than TRH-IR concentrations within the adrenal, pancreas, bowel, and stomach at the time of death. Untreated hypothyroidism and exogenous TRH significantly increased adrenal TRH-Gly-IR levels. Pancreatic TRH-Gly levels increased about 2-fold in hypothyroid rats. Incubation at 60 C significantly increased TRH-Gly-IR levels in the pancreas, adrenal, bowel, stomach, and epididymis by 14-, 3-, 6-, 6-, and 6-fold, respectively. Also after 60 C incubation increases in the TRH-Gly-IR/TRH-IR ratio of 2.7-, 4-, and 1.7-fold were observed in the pancreas, epididymis, and bowel, respectively. Pooled tissue extracts were fractionated by cation exchange and reverse phase HPLC for characterization of TRH-Gly-IR. Both chromatographic methods revealed a major peak of TRH-Gly-IR coeluting with synthetic TRH-Gly. Incubation at 60 C caused 13.5-, 4.1-, 1.5-, and 5-fold increments in the TRH-Gly-IR for adrenal, pancreas, prostate, and thyroid, respectively, compared to the immediately extracted control aliquots. Cation exchange and reverse phase HPLC also revealed production of higher mol wt TRH precursor peptides after incubation at 60 C for 4 or 20 h. Only the TRH-Gly-IR peak coeluting with pGlu-His-Pro-Gly was converted into TRH by rat brain alpha-amidating enzyme. The data suggest that biosynthesis of TRH occurs in rat extrahypothalamic tissues and may be modulated by thyroid status, iv TRH, and selective thermal inactivation of enzymes that convert prepro-TRH to TRH.

Keywords

Simko F, Reiter RJ, Pechanova O, Paulis L — *Year* 2013

Authors Simko F, Reiter RJ, Pechanova O, Paulis L.

Report Name Experimental models of melatonin-deficient hypertension.

Publication Front Biosci.

Issue-page numbers 2013 Jan 1;18:616-25.

URL http://www.ncbi.nlm.nih.gov/pubmed/23276947

Abstract Melatonin secreted by the pineal gland plays an important role in the regulation of blood pressure (BP) and its administration reduces hypertension both in animals and humans. There are two experimental models of melatonin-deficient hypertension: one induced by pinealectomy and another by continuous 24 hour exposure to light. Both models cause melatonin deficiency and prevent darkness-mediated nocturnal melatonin secretion and are associated with increased BP and myocardial, vascular and renal dysfunction. These models also lead to neurohumoral activation of the renin-angiotensin system, sympathetic nervous system, adrenocorticotrophin-glucocorticoid axis and cause insulin resistance. Together, these alterations contribute to rise in blood pressure by vasoconstrictive or circulatory fluid volume overload. The light induced hypertension model mimics the melatonin deficiency in patients with insufficient nocturnal BP decline, in those who have night shift or who are exposed to environmental light pollution. For this reason, this model is useful in development of anti-hypertensive drugs.

Keywords

Simpson HW, Candlish W, Pauson AW et al. — *Year* 1988

Authors H.W. Simpson a, A.W. Pauson a, K. Griffiths b, W. Candlish a, C.S. Mcardle a, R.G. Small c

Report Name Genesis of breast cancer is in the premenopause

Publication Lancet

Issue-page numbers 332:74–76 doi:10.1016/S0140-6736(88)90007-4. PMID:2898701

URL http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2888%2990007-4/abstract

Abstract In Britain and other high-risk countries, about a third of patients with breast cancer are premenopausal at diagnosis. In the remainder, tumour initiation might have occurred in the premenopause, even though the clinical presentation was late in life. This possibility has important implications for breast cancer prevention and screening. The relations between the patient's age and tumour kinetics, prognosis, oestrogen receptors, and environmental X-ray carcinogenesis were studied, together with the age-related protection afforded by pregnancy. The findings support the hypothesis that breast cancer is initiated in the premenopause.

Keywords

Year 1989

Authors Simpson HW, Pauson A, Cornélissen G

Report Name The chronopathology of breast pre-cancer

Publication Chronobiologia

Issue-page numbers 16:365–372. PMID:2627819

URL http://www.ncbi.nlm.nih.gov/pubmed/2627819

Abstract

Breast temperatures have been measured by the automated instrumentation called the 'Chronobra' for 16 progesterone cycles in women at normal risk for breast cancer and for 15 cycles in women at high risk for breast cancer. Circatrigintan and circaseptan rhythm parameters have been examined by the single and population mean cosinor technique. In the first analysis there was strong evidence for a loss of the 28-day rhythm and its replacement by a 7-day rhythm (? frequency multiplication). In the more rigorous population mean cosinor method the presence of a phase and frequency synchronized rhythm with a period at or close to 28 days was sustained in the normal-risk subjects and it was confirmed that this rhythm is absent in the high-risk subjects. At tau = 7 days there was no rhythm detected in the normal-risk subjects and only a weak effect (p = 0.07) in the high-risk subjects. In other words, the circaseptan expression was detected in the high-risk breasts but then not in every case. The MESOR of the high-risk cases was highly significantly warmer than in the controls.

Keywords

Authors Rakhshinda Siraj, Dr. N. Ravichandran

Report Name Shift Work: Evaluation of Employee's Physical well being and its Impact on Quality of Life

Publication IJEMR

Issue-page numbers August 2012-Vol 2 Issue 8 - Online - ISSN 2249–2585 - Print - ISSN 2249-8672

URL http://www.exclusivemba.com/ijemr/App_Themes/Theme1/Images/Shift%20Work%20Evaluation%20of%20Employees%20Physical%20well%20being%20and%20its%20Impact

Abstract

Over the last a few decades, major changes have taken place in the workplace. The growth in the use of information technology, globalization , organizational restructuring, changes in work contracts and work time scheduling have radically transformed the nature of work in many organizations.

Many industrialized countries have adopted non standard work schedules and shift work system with a view to optimize utilization of human resources and to ensure continuity of operations . While a large body of research has demonstrated the positive impact of shift work practices on the financial performance of organizations, the impact on well being of employees is less well known. But the limited evidence that is available suggests that productivity gains have come at the expense of employees and the adoption of shift work has been accompanied by deterioration in the quality of life of employees. It is becoming widely recognized that shift work has significant implications for health. Hence, a greater understanding is needed of the interaction between shift work practices and well being.

The paper focuses on shift work as a work schedule in order to investigate health issues related to shift work among employees. The main purpose of paper is to systematically review the evidence in the published scientific literature that examines the association between shift work and physical well being and its impact on quality of life of employees. The paper concludes with the possible coping strategies that can be adopted in order to minimize health hazards among shift workers and thus improve their overall quality of life .

Keywords Shift work, Health, Well Being , Quality of Life.

Siu TL, Morley JW, Coroneo MT — **Year** 2008

Authors Timothy L Siu, John W Morley, Minas T Coroneo

Report Name Toxicology of the retina: advances in understanding the defence mechanisms and pathogenesis of drug- and light-induced retinopathy

Publication Clinical & Experimental Ophthalmology

Issue-page numbers Volume 36, Issue 2, pages 176–185, March 2008

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1442-9071.2008.01699.x/full

Abstract The neurosensory retina is a highly specialized sense organ that is subjected to constant exposure of systemic toxins, oxidative stress and focused light rays. Important advances have been made in recent decades in unravelling a myriad of defence mechanisms against such insults and consequently in improving the understanding of the principles underlying various drug- and light-induced disease processes. To defend against circulating toxins, the retina possesses a specialized blood–retinal barrier (BRB) that tightly regulates the transport of substances across the functional boundaries of the retina at the retinal capillaries and the retinal pigmented epithelium. An endogenous cytochrome p450 system is strategically located within the retina to neutralize agents that can diffuse through the BRB. The biooxidation effect of light is prevented by a wide array of unique antioxidant mechanisms in the retina. Nonetheless, pathological processes may evolve when these different lines of defence are overwhelmed by various xenobiotics, environmental agents such as cigarette smoke and excessive light exposure, particularly of short wavelength high frequency blue light and ultraviolet light. Latest research using transgenic models has revealed novel apoptotic pathways implicated in acute phototoxicity, in particular blue light damage, and provides important clues for further understanding the risks of high-frequency light exposure to human retinopathy. This review article summarizes the basic scientific principles of these different defence mechanisms and discuss the implications in pathophysiology and treatment.

Keywords cellular neurobiology; molecular biology; pharmacogenetics; phototoxicity; retina; toxicology

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Skene DJ, Bojkowski CJ, Currie JE et al. — **Year** 1990

Authors Skene DJ, Bojkowski CJ, Currie JE et al.

Report Name 6-sulphatoxymelatonin production in breast cancer patients

Publication J Pineal Res

Issue-page numbers 8:269–276.doi:10.1111/j.1600-079X.1990.tb00686.x PMID:2380908

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1990.tb00686.x/abstract?

Abstract The daily pattern of the major urinary metabolite of melatonin, 6-sulphatoxymelatonin (aMT6s), was determined in women prior to having a breast biopsy. Women with malignant tumors appeared to have significantly lower 24 h concentrations of aMT6s with a decrease in the amplitude of the rhythm compared to women with benign tumors. The amount of urinary aMT6s was dependent upon the age of the subject but was not affected by either menopausal status or body mass index. However, when the women with malignant tumors were compared with a large group of normal women of the same age their aMT6s levels were not outside the normal range. The results show that a large control group and very accurate age matching are essential when investigating melatonin production in different groups of subjects.

Keywords age; urinary metabolite; pineal function; melatonin secretion

Skene DJ, Lockley SW, Thapan K, Arendt J

Year 1999

Authors Skene DJ, Lockley SW, Thapan K, Arendt J

Report Name Effects of light on human circadian rhythms

Publication Reprod Nutr Dev

Issue-page numbers 39:295–304 doi:10.1051/rnd:19990302. PMID:10420432

URL http://www.ncbi.nlm.nih.gov/pubmed/10420432

Abstract Blind subjects with defective retinal processing provide a good model to study the effects of light (or absence of light) on the human circadian system. The circadian rhythms (melatonin, cortisol, timing of sleep/wake) of individuals with different degrees of light perception (n = 67) have been studied. Blind subjects with some degree of light perception (LP) mainly have normally entrained circadian rhythms, whereas subjects with no conscious light perception (NPL) are more likely to exhibit disturbed circadian rhythms. All subjects who were bilaterally enucleated showed free running melatonin and cortisol rhythms. Studies assessing the light-induced suppression of melatonin show the response to be intensity and wavelength dependent. In contrast to ocular light exposure, extraocular light failed to suppress night-time melatonin. Thus, ocular light appears to be the predominant time cue and major determinant of circadian rhythm type. Optimisation of the light for entrainment (intensity, duration, wavelength, time of administration) requires further study.

Keywords

Slaper H, Velders GJ, Daniel JS, et al.

Year 1996

Authors Slaper H, Velders GJ, Daniel JS, de Gruijl FR, van der Leun JC.

Report Name Estimates of ozone depletion and skin cancer incidence to examine the Vienna Convention achievements

Publication Nature

Issue-page numbers 384, 256 - 258 (21 November 1996); doi:10.1038/384256a0

URL http://www.nature.com/nature/journal/v384/n6606/abs/384256a0.html

Abstract DEPLETION of the ozone layer has been observed on a global scale1, and is probably related to halocarbon emissions. Ozone depletion increases the biologically harmful solar ultraviolet radiation reaching the surface of the Earth, which leads to a variety of adverse effects, including an increase in the incidence of skin cancer. The 1985 Vienna Convention provided the framework for international restrictions on the production of ozone-depleting substances. The consequences of such restrictions have not yet been assessed in terms of effects avoided. Here we present a new method of estimating future excess skin cancer risks which is used to compare effects of a 'no restrictions' scenario with two restrictive scenarios specified under the Vienna Convention: the Montreal Protocol, and the much stricter Copenhagen Amendments. The no-restrictions and Montreal Protocol scenarios produce a runaway increase in skin cancer incidence, up to a quadrupling and doubling, respectively, by the year 2100. The Copenhagen Amendments scenario leads to an ozone minimum around the year 2000, and a peak relative increase in incidence of skin cancer of almost 10% occurring 60 years later. These results demonstrate the importance of the international measures agreed upon under the Vienna Convention.

Keywords

Sliney DH

Year 2001

Authors David H Sliney

Report Name Photoprotection of the eye - UV radiation and sunglasses

Publication Journal of Photochemistry and Photobiology B: Biology

Issue-page numbers Volume 64, Issues 2-3, 15 November 2001, Pages 166-175

URL http://www.sciencedirect.com/science/article/pii/S1011134401002299

Abstract Although most health scientists now agree that health risks to the skin (e.g., skin cancer) exist from exposure to the ultraviolet radiation in sunlight, a scientific consensus has not really been achieved vis-à-vis sunlight and ocular health. A growing number of scientists warn of hazards to the eye if ultraviolet radiation — and perhaps even shorter wavelength visible radiation also — is not filtered by lenses. Despite a substantial literature on the adverse effects of ultraviolet radiation (UVR) and intense light upon ocular structures, particularly upon the retina, controversy still surrounds the question of whether the levels of natural and man-made light sources are damaging when encountered under normal viewing conditions. Although scientific evidence accumulates to indicate that chronic exposure conditions may accelerate ageing processes in ocular tissues, the quantitative question of “How much is safe?” remains to be answered conclusively.

Keywords Ultraviolet radiation; Sunglasses; Ocular exposure geometry; Cataract; Snowblindness; Polarized lenses; Squinting; Coroneo effect

Sliney DH

Year 1994

Authors Sliney, D.H.

Report Name Ocular hazards of light

Publication In: T.W.Tibbitts (ed.). International Lighting in Controlled Environments Workshop

Issue-page numbers NASA-CP-95-3309. p 183-189

URL http://www.controlledenvironments.org/Light1994Conf/4_2_Sliney/Sliney%20Text.htm

Abstract

The eye is protected against bright light by the natural aversion response to viewing bright light sources. The aversion response normally protects the sun against injury from viewing bright light sources such as the sun, arc lamps and welding arcs, since this aversion limits the duration of exposure to a fraction of a second (about 0.25 s).

There are at least five separate types of hazards to the eye and skin from optical sources:1

1. Ultraviolet photochemical injury to the skin (erythema and carcinogenic effects), and to the cornea (photokeratitis) and lens (cataract) of the eye (180 nm to 400 nm).
2. Thermal injury to the retina of the eye (400 nm to 1400 nm)
3. Blue-light photochemical injury to the retina of the eye (principally 400 nm to 550 nm; unless aphakic, 310 to 550 nm)2
4. Near-infrared thermal hazards to the lens (approximately 800 nm to 3000 nm).
5. Thermal injury (burns) of the skin (approximately 400 nm to l mm) and of the cornea of the eye (approximately 1400 nm to 1 mm).

The principal retinal hazard resulting from viewing bright light sources is photoretinitis, e.g., solar retinitis with an accompanying scotoma which results from staring at the sun. Solar retinitis was once referred to as "eclipse blindness" and associated "retinal burn." Only in recent years has it become clear that photoretinitis results from a photochemical injury mechanism following exposure of the retina to shorter wavelengths in the visible spectrum, i.e., violet and blue light. Prior to conclusive animal experiments at that time (Ham, Mueller and Sliney, 1976), it was thought to be a thermal injury mechanism. However, it has been shown conclusively that an intense exposure to short-wavelength light (hereafter referred to as "blue light") can cause retinal injury.

The product of the dose-rate and the exposure duration always must result in the same exposure dose (in joules-per-square centimeter at the retina) to produce a threshold injury. Blue-light retinal injury (photoretinitis) can result from viewing either an extremely bright light for a short time, or a less bright light for longer exposure periods. This characteristic of photochemical injury mechanisms is termed reciprocity and helps to distinguish these effects from thermal burns, where heat conduction requires a very intense exposure within seconds to cause a retinal coagulation; otherwise, surrounding tissue conducts the heat away from the retinal image. Injury thresholds for acute injury in experimental animals for both corneal and retinal effects have been corroborated for the human eye from accident data. Occupational safety limits for exposure to UVR and bright light are based upon this knowledge. As with any photochemical injury mechanism, one must consider the action spectrum, which describes the relative effectiveness of different wavelengths in causing a photobiological effect. The action spectrum for photochemical retinal injury peaks at approximately 440 nm.

Keywords

Sliney DH

Year 2002

Authors Sliney DH.

Report Name How light reaches the eye and its components

Publication International Journal of Toxicology

Issue-page numbers November 2002 vol. 21 no. 6 501-50

URL http://ijt.sagepub.com/content/21/6/501

Abstract The human eye is exquisitely sensitive to light (i.e., visible radiant energy), and when dark-adapted, the retina can detect a few photons of blue-green light. It is therefore not at all surprising that ocular tissues are also more vulnerable to ultraviolet (UV) and light damage than the skin. For this reason, humans have evolved with certain anatomical, physiological, and behavioral traits that protect this critical organ from the UV damage that would otherwise be certain from the intense bath of overhead solar ultraviolet radiation (UVR) when we are outdoors during daylight. For example, the UV exposure threshold dose for photokeratitis (“welders' flash” or “snow blindness”)—if measured as falling on a horizontal ground surface—would be reached in less than 10 minutes around midday in the summer sun. There are three critical ocular structures that could be affected by UV exposure: the cornea, the lens, and the retina. The cornea transmits radiant energy only at 295 nm and above. The crystalline lens absorbs almost all incident energy to wavelengths of nearly 400 nm. In youth, a very small amount of UV-A reaches the retina, but the lens becomes more absorbing with age. Thus there are intraocular filters that effectively filter different parts of the UV spectrum and allow only of the order of 1% or less to actually reach the retina. Nevertheless, this small fraction of energy—if phototoxic—could still be of concern. Finally, oblique rays entering the eye from the temporal side, can actually reach the equatorial (germinative) area of the lens.

Keywords Lens, Phototoxicity, Retina, Sunlight, Ultraviolet

Sliney DH

Year 1999

Authors Sliney DH

Report Name Geometrical assessment of ocular exposure to environmental UV radiation – implications for ophthalmic epidemiology

Publication J Epidemiol

Issue-page numbers 1999 Dec;9(6 Suppl):S22-32.

URL http://www.ncbi.nlm.nih.gov/pubmed/10709347

Abstract Epidemiological studies of the influence of environmental ultraviolet radiation (UVR) in the development of cataract, pterygium, droplet keratopathies and age-related macular degeneration have produced inconsistent findings. The lack of consistent results may be due largely to either incomplete or erroneous estimates of outdoor UV exposure dose. Geometrical factors dominate the determination of UVR exposure of the eye. The degree of lid opening limits ocular exposure to only those rays entering at angles near the horizon. Clouds redistribute overhead UVR to the horizon sky. Mountains, trees and building shield the eye from direct sky exposure. Most ground surfaces reflect little UVR. The result is that the highest UVR exposure occurs during light overcast where the horizon is visible and ground surface reflection is high. By contrast, exposure in a high mountain valley with green foliage results in a much lower ocular dose. Other findings of these studies show that retinal exposure to light and UVR in daylight occurs largely in the superior retina.

Keywords

Sliney DH

Year 2005

Authors David H. Sliney

Report Name Exposure geometry and spectral environment determine photobiological effects on the human eye

Publication Photochemistry and Photobiology

Issue-page numbers Volume 81, Issue 3, pages 483–489, May 2005

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2005.tb00212.x/abstract?

Abstract Photobiological effects upon the human retina, cornea and lens are highly dependent on the optical exposure geometry as well as spectral characteristics of the exposure. The organ of sight is exquisitely sensitive to light because it performs well in very low nighttime illumination levels and yet it also must adapt to extremely bright environments where light exposures are greater by many orders of magnitude. The eye has evolved to protect itself reasonably well against excessive exposure in bright environments. The retina is minimally exposed in extremely bright environments and the cornea and lens are surprisingly well protected in harsh environments. Although these protective mechanisms are good, they are not perfect and adverse changes from both acute and chronic exposures to sunlight still exist. The geometrical protective factors must be understood and appreciated whenever assessing potential adverse effects of environmental UV radiation and light on ocular structures. These natural ocular protective factors also work with the ever-changing spectrum of sunlight and the different spectral distribution of light and UV radiation across the eye's field of view. Spectral characteristics of the ocular media are also important. One can visualize a series of intraocular color filters that progressively filter shorter wavelengths and thereby aid in color vision, reduce the impact of chromatic aberrations and significantly reduce the optical radiation hazards to the lens and retina.

Keywords

Sliney DH, Bitran M

Year 0

Authors Sliney DH, Bitran M.

Report Name The ACGIH Action Spectrum for Hazard Assessment: The TLVs.

Publication In Matthes R, Sliney DH, editors. Measurements of Optical Radiation Hazards. ICNRP

Issue-page numbers ICNIRP 6/98; 1998. p.241-59.

URL http://www.icnirp.de/PubOptical.htm

Abstract N/AThe intend of this publication is to provide guidance on how to measure intense light sources (i.e. UV, visible, and infrared) and evaluate the potential hazards to the eye or skin. In addition to measurements, calculations are usually required to compare the measured exposure with optical safety limits. This determines the hazard level of the source. This reference book offers a unique source with which to catch up on the latest developments in this important field. It is aimed but not limited to : industrial hygienists, health physicists, optical physicists, photobiologists, safety engineers and lighting engineers.

Keywords

Smith EM, Morrill AC, Meyer WJ 3rd, Blalock JE **Year** 1986

Authors Smith EM, Morrill AC, Meyer WJ 3rd, Blalock JE

Report Name Corticotropin releasing factor induction of leukocyte-derived immunoreactive ACTH and endorphins

Publication Nature

Issue-page numbers 321:881–882 doi:10.1038/321881a0. PMID:3014342

URL http://www.nature.com/nature/journal/v321/n6073/abs/321881a0.html

Abstract Human peripheral leukocytes1,2 infected by virus or treated with endotoxin will, like unstimulated mouse spleen macrophages3, synthesize immunoreactive corticotrophin (ir-ACTH) and endorphins. The ir-ACTH produced appears to be identical with authentic ACTH1–6, while enough of the material has been produced in hypophysectomized mice infected with virus to demonstrate a steroidogenic reponse6. Because the production of ACTH by in vivo pituitary cells and by leukocytes is suppressed by dexamethasone both in vitro 7 and in vitro 6, suggesting8 that the production of ACTH and endorphins by leukocytes is indeed controlled, we have investigated the effects of corticotropin releas-ing-f actor (CRF), which is known9 to regulate the pituitary production of both ACTH and β-endorphin. We now report that the production of ACTH and endorphins by leukocytes is indeed induced by synthetic CRF10 and, in turn, suppressed by dexamethasone, suggesting that, as in pituitary cells, the pro-opiomelanocortin (POMC) gene may be expressed and similarly controlled in leukocytes.

Keywords

Smith KA, Schoen MW, Czeisler CA **Year** 2004

Authors Kurt A. Smith, Martin W. Schoen and Charles A. Czeisler

Report Name Adaptation of Human Pineal Melatonin Suppression by Recent Photic History

Publication The Journal of Clinical Endocrinology & Metabolism

Issue-page numbers July 1, 2004 vol. 89 no. 7 3610-3614

URL http://jcem.endojournals.org/content/89/7/3610.full

Abstract The human circadian pacemaker controls the timing of the release of the pineal hormone melatonin, which promotes sleep, decreases body temperature, and diminishes cognitive performance. Abnormal melatonin secretion has been observed in psychiatric and circadian disorders. Although melatonin secretion is directly suppressed by exposure to light in a nonlinear intensity-dependent fashion, little research has focused on the effect of prior photic history on this response. We examined eight subjects in controlled laboratory conditions using a within-subjects design. Baseline melatonin secretion was monitored under constant routine conditions and compared with two additional constant routines with a fixed light stimulus for 6.5 h of 200 lux (50 μW/cm2) after approximately 3 d of photic exposure during the subjective day of either about 200 lux (50 μW/cm2) or about 0.5 lux (0.15 μW/cm2). We found a significant increase in melatonin suppression during the stimulus after a prior photic history of approximately 0.5 lux compared with approximately 200 lux, revealing that humans exhibit adaptation of circadian photoreception. Such adaptation indicates that translation of a photic stimulus into drive on the human circadian pacemaker involves more complex temporal dynamics than previously recognized. Further elucidation of these properties could prove useful in potentiating light therapies for circadian and affective disorders.

Keywords

Smith MR, Eastman CI **Year** 2013

Authors Mark R Smith, Charmane I Eastman

Report Name Shift work: health, performance and safety problems, traditional countermeasures, and innovative management strategies to reduce circadian misalignment

Publication Nature and Science of Sleep

Issue-page numbers 2012:4 111–132

URL Shift work: health, performance and safety problems, traditional countermeasures, and innovative management strategies to reduce circadian misalignment

Abstract There are three mechanisms that may contribute to the health, performance, and safety problems associated with night-shift work: (1) circadian misalignment between the internal circadian clock and activities such as work, sleep, and eating, (2) chronic, partial sleep deprivation, and (3) melatonin suppression by light at night. The typical countermeasures, such as caffeine, naps, and melatonin (for its sleep-promoting effect), along with education about sleep and circadian rhythms, are the components of most fatigue risk-management plans. We contend that these, while better than nothing, are not enough because they do not address the underlying cause of the problems, which is circadian misalignment. We explain how to reset (phase-shift) the circadian clock to partially align with the night-work, day-sleep schedule, and thus reduce circadian misalignment while preserving sleep and functioning on days off. This involves controlling light and dark using outdoor light exposure, sunglasses, sleep in the dark, and a little bright light during night work. We present a diagram of a sleep-and-light schedule to reduce circadian misalignment in permanent night work, or a rotation between evenings and nights, and give practical advice on how to implement this type of plan.

Keywords circadian rhythms, night work, bright light, phase-shifting, sleep, melatonin

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Smolensky MH, Siegel RA, Haus E, et al. **Year** 2012

Authors Michael H. Smolensky, Ronald A. Siegel, Erhard Haus, Ramon Hermida and Francesco Portaluppi

Report Name Biological Rhythms, Drug Delivery, and Chronotherapeutics

Publication IN: Fundamentals and Applications of Controlled Release Drug Delivery,

Issue-page numbers Advances in Delivery Science and Technology, 2012, Part 5, 359-443, DOI: 10.1007/978-1-4614-0881-9_13

URL http://www.springerlink.com/content/nw752h7510271142/

Abstract Biological processes are highly structured in time as endogenously derived rhythms of short, intermediate, and long periods, with the circadian (24h) time structure most studied. Staging of key physiological and biochemical circadian rhythms gives rise to 24-h patterns in the exacerbation of chronic medical conditions, including arthritis, asthma, ulcer, and hypertension, plus manifestation of acute severe morbid and mortal events, such as myocardial infarction, stroke, and sudden cardiac death. Body rhythms may also significantly affect patient response to diagnostic tests and pharmacokinetics, pharmacodynamics, and toxicities of diverse classes of medications. This chapter reviews circadian and other period biological rhythm dependencies of the pathophysiology of disease and pharmacology of medications as the basis for chronotherapeutics and development of time-modulated drug-delivery systems.

Keywords

Soszyński P, Stowińska-Srzednicka J, Kasperlik-Zatuska A, Zgliczyński S *Year* 1989

Authors Soszyński P, Stowińska-Srzednicka J, Kasperlik-Zatuska A, Zgliczyński S

Report Name Decreased melatonin concentration in Cushing's syndrome

Publication Horm Metab Res

Issue-page numbers 21:673–674 doi:10.1055/s-2007-1009317. PMID:2559013

URL http://www.mendeley.com/research/decreased-melatonin-concentration-in-cushings-syndrome/

Abstract To determine the effect of hypercortisolaemia on the melatonin circadian secretion 12 patients with pituitary or adrenal dependent Cushing's syndrome and 5 healthy controls were studied. The melatonin circadian rhythm of secretion, observed in the control group, was abolished in the patients with hypercortisolaemia. Mean nocturnal melatonin levels and the integrated 24-hour secretion were significantly lower in the patients studied than those of the controls. Thus, in patients with Cushing's syndrome the melatonin levels are decreased and the circadian rhythm of this hormone is abolished.

Keywords

Späth-Schwalbe E, Gofferje M, Kern W et al. *Year* 1991

Authors Späth-Schwalbe E, Gofferje M, Kern W et al.

Report Name Sleep disruption alters nocturnal ACTH and cortisol secretory patterns

Publication Biol Psychiatry

Issue-page numbers 29:575–584 doi:10.1016/0006-3223(91)90093-2. PMID:1647222

URL http://www.sciencedirect.com/science/article/pii/0006322391900932

Abstract Recent studies have provided evidence that nocturnal cortisol secretion is coupled to ultradian rhythms of sleep. The present study was designed to specify how exogenous and sleep-related endogenous factors influence nocturnal adrenocorticotropin (ACTH) and cortisol secretion. We compared the influences of (1) temporary sleep deprivation, (2) arousals continuously induced during sleep and , (3) undisturbed sleep (baseline) on pituitary-adrenocortical activity in 10 healthy men. Sleep deprivation (DS) and continuous arousals during sleep (AS) were introduced at the beginning of the second rapid eye movement (REM) sleep period which is an epoch close to the first significant nocturnal rise in plasma cortisol. Compared with the baseline nights, plasma cortisol significantly increased immediately after continuous arousals were started or the subject was awakened and remained awake. Despite this exogenously provoked first cortisol peak, average cortisol release during DS and AS was no higher than during undisturbed sleep. The arousal-induced cortisol burst was followed by a temporary inhibition of cortisol secretion, suggesting that once the subject is aroused (i.e., in stage 1 sleep or awake), the hypothalamus-pituitary-adrenal (HPA) system becomes highly sensitive to negative feedback inhibition. Spontaneously occuring endogenous cortisol peaks of comparable size during undisturbed sleep did not exhibit such a temporary inhibition of cortisol secretion. We hypothesize that sleep attenuates negative feedback inhibition within the HPA system, whereas wakefulness (or stage 1 sleep) reflects increased feedback sensitivity of this system.

Keywords

Spencer CA, Greenstadt MA, Wheeler WS et al. **Year** 1980

Authors Spencer CA, Greenstadt MA, Wheeler WS et al.

Report Name The influence of long-term low dose thyrotropin-releasing hormone infusions on serum thyrotropin and prolactin concentrations in man

Publication J Clin Endocrinol Metab

Issue-page numbers 51:771–775 doi:10.1210/jcem-51-4-771. PMID:6774994

URL http://www.ncbi.nlm.nih.gov/pubmed/6774994

Abstract The purpose of the present study was to evaluate in man the relative thyrotroph and lactotroph response to a 48-h low dose constant TRH infusion. Before, during, and after the 75 ng/min TRH constant infusion, serum samples were obtained every 4 h in six euthyroid ambulating male subjects for measurements of TSH, PRL, T4, and T3. The TSH response, employing a specific and sensitive human TSH RIA, demonstrated a significant rise from the mean basal pre-TRH value of 2.35 +/- 0.64 microU/ml (+/- SEM) to 3.68 +/- 0.80 ($P < 0.005$) during the TRH infusion; this value fell below the basal level to 1.79 +/- 0.47 ($P < 0.05$) post infusion. Serum T4 values were increased above basal both during ($P < 0.025$) and after ($P < 0.025$) TRH infusion, whereas serum T3 values were not significantly changed throughout the entire study period. The daily TSH nocturnal surge was augmented in both absolute and relative terms during the first 24 h or the TRH infusion, unchanged during the second 24 h of infusion, and inhibited during the first postinfusion day. Other than a minimal increase in serum PRL during the first few hours of the infusion, no significant alteration in the mean basal concentration or circadian pattern of PRL secretion was evident during or after the low dose TRH infusion. These findings would indicate that 1) near-physiological stimulation of the pituitary with TRH produces a greater stimulation of TSH release than of PRL release and 2) the factor or factors producing the circadian TSH surge may not be mediated through fluctuations in endogenous TRH.

Keywords

Sperling HG, Harwerth RS. **Year** 1971

Authors H. G. Sperling and R. S. Harwerth

Report Name Red-green cone interactions in the increment-threshold spectral sensitivity of primates.

Publication Science

Issue-page numbers 1971; 172:180-4.

URL http://www.sciencemag.org/content/172/3979/180.abstract

Abstract Threshold spectral sensitivity of primate eyes is the upper envelope of the sensitivity of three response channels. Sensitivity in the green and red channels is modeled as linear difference functions reflecting neural interaction between cones containing photopigments with 535- and 575-nanometer peaks. Sensitivity in the blue channel seems determined by a single class of cones containing a 445-nanometer photopigment.

Keywords

Sperling HG, Johnson C, Harwerth RS

Year 1980

Authors Sperling HG, Johnson C, Harwerth RS.

Report Name Differential spectral photic damage to primate cones

Publication Vision Research

Issue-page numbers Volume 20, Issue 12, 1980, Pages 1117-1125

URL http://www.sciencedirect.com/science/article/pii/0042698980900498

Abstract Selective loss of sensitivity to blue and green parts of the spectrum following intermittent, repeated exposures to intense spectral lights persists longer than 3 yr following blue lights and between 18 and 40 days following green lights. The “blue-blindness” involves complete and sole loss of the response of the short-wavelength responsive cones. The “green-blindness” involves complete and sole loss of response of middle-wavelength sensitive cones. Histo-pathology of cones in a “blue-blinded” retina in comparison with cytochemical labeling of short-wavelength cones, reveals that they follow a similar distribution: are sparse in the foveola. reach a peak of about 16% of the cones near 1 and fall to 8–12% of the cones at 7. Continuous as distinct from intermittent exposures to similar blue lights produces a wholly different picture of gross pigment-epithelial damage with little photoreceptor degeneration.

Keywords

Spiegel K, Follenius M, Simon C et al.

Year 1994

Authors Spiegel K, Follenius M, Simon C et al.

Report Name Prolactin secretion and sleep

Publication Sleep

Issue-page numbers 17:20–27. PMID:8191199

URL http://www.ncbi.nlm.nih.gov/pubmed/8191199

Abstract To clarify the relationship between prolactin (PRL) secretion and sleep, three experimental procedures were employed and secretory rates were estimated from plasma levels using a deconvolution procedure. Eight healthy young men participated in two 24-hour studies, one using normal night sleep and one using delayed sleep, to determine the influence of sleep as a whole on the PRL rhythm. Another group of 24 subjects underwent a 1-night study to investigate the relationship between PRL secretion and the internal sleep structure. The influence of sleep quality was studied in two more groups of eight subjects. Secretory rates were calculated by deconvolution from plasma PRL measured at 10-minute intervals. Sleep was recorded polygraphically in all experiments. PRL secretory pulses occurred throughout the 24-hour cycle without significant variation in frequency, but with enhanced pulse amplitude for both night and day sleep periods. Sleep onset was rapidly followed by an increase in secretion, and awakenings coincided with an immediate offset of active secretion. Analyzing the association between secretory pulses and sleep stages demonstrated that PRL secretory rate is low at the time of rapid eye movement sleep onset. Sleep quality appeared not to affect the PRL secretory profile. These results confirmed that PRL secretion is enhanced during the whole sleep period, as inferred from plasma levels. Considering secretory pulses provides a precise determination of the temporal relations between PRL and sleep structure and demonstrates that occasionally poor sleep does not influence PRL secretion in normal humans.

Keywords

Spiegel K, Leproult R, Colecchia EF et al **Year** 2000

Authors Spiegel K, Leproult R, Colecchia EF et al

Report Name Adaptation of the 24-h growth hormone profile to a state of sleep debt

Publication Am J Physiol Regul Integr Comp Physiol

Issue-page numbers 279:R874–R883. PMID:10956244

URL http://ajpregu.physiology.org/content/279/3/R874.short

Abstract In normal men, the majority of GH secretion occurs in a single large postsleep onset pulse that is suppressed during total sleep deprivation. We examined the impact of semichronic partial sleep loss, a highly prevalent condition, on the 24-h growth hormone profile. Eleven young men were studied after six nights of restricted bedtimes (0100–0500) and after 7 nights of extended bedtimes (2100–0900). Slow-wave sleep (SWS) was estimated as the duration of stages III and IV. Slow-wave activity (SWA) was calculated as electroencephalogram power density in the 0.5- to 3-Hz frequency range. During the state of sleep debt, the GH secretory pattern was biphasic, with both a presleep onset “circadian” pulse and a postsleep onset pulse. Postsleep onset GH secretion was negatively related to presleep onset secretion and tended to be positively correlated with the amount of concomitant SWA. When sleep was restricted, both SWS and SWA were increased during early sleep. Unexpectedly, the increase in SWA affected the second, rather than the first, SWA cycle, suggesting that presleep onset GH secretion may have limited SWA in the first cycle, possibly via an inhibition of central GH-releasing hormone activity. Thus neither the GH profile nor the distribution of SWA conformed with predictions from acute sleep deprivation studies, indicating that adaptation mechanisms are operative during chronic partial sleep loss.

Keywords growth hormone secretion, slow-wave activity, sleep deprivation

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Spiegel K, Leproult R, L’hermite-Balériaux M et al. **Year** 2004

Authors Karine Spiegel, Rachel Leproult, Mireille L’Hermite-Balériaux, Georges Copinschi, Plamen D. Penev and Eve Van Cauter

Report Name Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin

Publication J Clin Endocrinol Metab

Issue-page numbers 89:5762–5771 doi:10.1210/jc.2004-1003. PMID:15531540

URL http://jcem.endojournals.org/content/89/11/5762.short

Abstract Sleep plays an important role in energy homeostasis. The present study tests the hypothesis that circulating levels of leptin, a hormone that signals energy balance to the brain, are influenced by sleep duration. We also analyzed associations between leptin and sympathovagal balance, cortisol, TSH, glucose, and insulin under different bedtime conditions. Twenty-four-hour hormonal and glucose profiles were sampled at frequent intervals, and sympathovagal balance was estimated from heart rate variability in 11 subjects studied after 6 d of 4-h bedtimes (mean ± sem of sleep duration during last 2 d: 3 h and 49 ± 2 min) and after 6 d of 12-h bedtimes (sleep: 9 h and 03 ± 15 min). A study with 8-h bedtimes was performed 1 yr later (sleep: 6 h and 52 ± 10 min). Caloric intake and activity levels were carefully controlled in all studies. Mean levels, maximal levels, and rhythm amplitude of leptin were decreased (−19%, −26%, and −20%, respectively) during sleep restriction compared with sleep extension. The decrease in leptin levels was concomitant with an elevation of sympathovagal balance. The effects of sleep duration on leptin were quantitatively associated with alterations of the cortisol and TSH profiles and were accompanied by an elevation of postbreakfast homeostasis model assessment values. Measures of perceived stress were not increased during sleep restriction. During the study with 8-h bedtimes, hormonal and metabolic parameters were intermediate between those observed with 4-h and 12-h bedtimes. In conclusion, sleep modulates a major component of the neuroendocrine control of appetite.

Keywords

Year 2003

Authors Spiegel K, Leproult R, Van Cauter E

Report Name [Impact of sleep debt on physiological rhythms.]

Publication Rev Neurol (Paris)

Issue-page numbers 159 (Suppl.11):6S11–20. PMID: 14646794

URL http://www.ncbi.nlm.nih.gov/pubmed/14646794

Abstract Sleep loss due to voluntary bedtime curtailment has become a hallmark of modern society. Even though sleep deprivation in rodents has been shown to result in death, it was until a few years ago thought that sleep loss results in increased sleepiness and decreased cognitive performance but has little or no adverse effects on human health. We measured sleep and 24-hour hormonal profiles in 11 healthy young males after 6 days of sleep restriction (4-hour bedtime) and after 6 days of sleep recovery (12-hour bedtime). At the end of sleep restriction, we observed reduced amounts of slow wave sleep (SWS) and rapid eye movement (REM) sleep and an alteration in the temporal distribution of these sleep stages, i.e. an increased pressure for REM sleep at the beginning of the sleep period and a decrease in the amount of slow wave activity (SWA) during the first sleep cycle. These later abnormalities are usually observed in depression. In addition, numerous alterations in the 24-hour hormonal profiles were observed in the state of sleep debt. The amount of melatonin secreted was reduced because of a delay in the onset of the nocturnal secretion and a reduction in the value of the acrophase. If the overall 24-hour cortisol profile was preserved, sleep restriction was associated with increased cortisol levels in late afternoon and evening hours and the duration of the quiescent period was reduced. The 24-hour mean TSH levels were reduced and the nocturnal TSH elevation was markedly dampened, most likely as a result of elevated levels of thyroid hormones. The acrophase of the 24-hour leptin profile occurred earlier, the amplitude of the rhythm and the overall mean levels were reduced. The nocturnal elevation of prolactin levels was abrupt but of short duration and the 24-hour mean levels were decreased. A pulse of growth hormone occurred prior to sleep onset, therefore affecting SWA distribution at the beginning of the sleep period. Since these alterations are qualitatively and quantitatively similar to those observed during aging and sometimes during depression, a state of sleep debt, as is experienced by a substantial fragment of the population in modern societies, is likely to increase the severity of depression and widespread age-related chronic conditions such as obesity, diabetes and hypertension.

Keywords

Authors Spiegel K, Leproult R, Van Cauter E

Report Name Impact of sleep debt on metabolic and endocrine function

Publication Lancet

Issue-page numbers 354:1435–1439 doi:10.1016/S0140-6736(99)01376-8. PMID:10543671

URL http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2899%2901376-8/abstract

Abstract

Background
Chronic sleep debt is becoming increasingly common and affects millions of people in more-developed countries. Sleep debt is currently believed to have no adverse effect on health. We investigated the effect of sleep debt on metabolic and endocrine functions.
Methods
We assessed carbohydrate metabolism, thyrotropic function, activity of the hypothalamo-pituitary-adrenal axis, and sympathovagal balance in 11 young men after time in bed had been restricted to 4 h per night for 6 nights. We compared the sleep-debt condition with measurements taken at the end of a sleep-recovery period when participants were allowed 12 h in bed per night for 6 nights.
Findings
Glucose tolerance was lower in the sleep-debt condition than in the fully rested condition ($p<0·02$), as were thyrotropin concentrations ($p<0·01$). Evening cortisol concentrations were raised ($p=0·0001$) and activity of the sympathetic nervous system was increased in the sleep-debt condition ($p<0·02$).
Interpretation
Sleep debt has a harmful impact on carbohydrate metabolism and endocrine function. The effects are similar to those seen in normal ageing and, therefore, sleep debt may increase the severity of age-related chronic disorders.

Keywords

Spiegel K, Luthringer R, Follenius M et al. **Year** 1995

Authors Spiegel K, Luthringer R, Follenius M et al.

Report Name Temporal relationship between prolactin secretion and slow-wave electroencephalic activity during sleep

Publication Sleep

Issue-page numbers 18:543–548. PMID:8552924

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24540

Abstract

It is well established that plasma prolactin (PRL) concentrations exhibit a sleep-dependent pattern, with the highest levels occurring during sleep and the lowest during waking. Still, controversy exists concerning an association between rapid eye movement (REM) and non-REM sleep cycles and plasma PRL pulses. These studies were all based on conventional scoring of sleep stages.

In the present study, plasma PRL concentrations were analyzed at 10-minute intervals in 10 subjects during the night when sleeping. PRL secretory rates were calculated by a deconvolution procedure. Spectral parameters of sleep electroencephalographic (EEG) recordings were analyzed together with PRL secretion using cross-correlation. Slow-wave activity of the EEG and PRL secretion ran parallel in all individuals. Conversely, alpha and beta bands and the EEG mean frequency were inversely proportional to PRL secretion. In 9 of the 10 subjects studied, PRL secretion was concomitant with delta waves or lagged behind by 10-20 minutes, depending on subjects, with maximum cross-correlation coefficients ranging between 0.40 and 0.67. This temporal relationship between PRL secretion and delta waves was further assessed by a pulse-by-pulse analysis based on the calculation of probability levels after computer simulations. Nine of the 10 subjects displayed significant concomitance between delta wave activity and PRL secretory oscillations. These results demonstrate that PRL secretion during sleep is coupled to delta waves in young healthy men.

Keywords

Spiegel K, Tasali E, Leproult R, Van Cauter E **Year** 2009

Authors Karine Spiegel, Esra Tasali, Rachel Leproult & Eve Van Cauter

Report Name Effects of poor and short sleep on glucose metabolism and obesity risk

Publication Nature Reviews Endocrinology

Issue-page numbers 5, 253-261 (May 2009)

URL http://www.nature.com/nrendo/journal/v5/n5/full/nrendo.2009.23.html

Abstract

The importance of sleep to hormones and glucose metabolism was first documented more than four decades ago. Since then, sleep curtailment has become an endemic behavior in modern society. In addition, the prevalence of sleep disorders, particularly obstructive sleep apnea (OSA), has increased. OSA is very common in endocrine and metabolic disorders, but often remains undiagnosed. This Review summarizes the laboratory and epidemiologic evidence that suggests how sleep loss, either behavioral or disease-related, and poor quality of sleep might promote the development of obesity and diabetes mellitus, and exacerbate existing endocrine conditions. Treatment of sleep disorders has the potential to improve glucose metabolism and energy balance. Screening for habitual sleep patterns and OSA might be critically important for patients with endocrine and metabolic disorders.

Keywords

Authors Spiegel K, Tasali E, Penev P, Van Cauter E

Report Name Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite

Publication Ann Intern Med

Issue-page numbers 141:846–850. PMID:15583226

URL http://www.annals.org/content/141/11/846.abstract

Abstract

Background: Total sleep deprivation in rodents and in humans has been associated with hyperphagia. Over the past 40 years, self-reported sleep duration in the United States has decreased by almost 2 hours.

Objective: To determine whether partial sleep curtailment, an increasingly prevalent behavior, alters appetite regulation.

Design: Randomized, 2-period, 2-condition crossover clinical study.

Setting: Clinical Research Center, University of Chicago, Chicago, Illinois.

Patients: 12 healthy men (mean age [±SD], 22 ± 2 years; mean body mass index [±SD], 23.6 ± 2.0 kg/m2).

Measurements: Daytime profiles of plasma leptin and ghrelin levels and subjective ratings of hunger and appetite.

Intervention: 2 days of sleep restriction and 2 days of sleep extension under controlled conditions of caloric intake and physical activity.

Results: Sleep restriction was associated with average reductions in the anorexigenic hormone leptin (decrease, 18%; P = 0.04), elevations in the orexigenic factor ghrelin (increase, 28%; P < 0.04), and increased hunger (increase, 24%; P < 0.01) and appetite (increase, 23%; P = 0.01), especially for calorie-dense foods with high carbohydrate content (increase, 33% to 45%; P = 0.02).

Limitations: The study included only 12 young men and did not measure energy expenditure.

Conclusions: Short sleep duration in young, healthy men is associated with decreased leptin levels, increased ghrelin levels, and increased hunger and appetite.

Keywords

Spivey A

Year 2010

Authors Angela Spivey

Report Name Lose Sleep, Gain Weight: Another Piece of the Obesity Puzzle

Publication Environ Health Perspect

Issue-page numbers 118:A28-A33.

URL http://dx.doi.org/10.1289/ehp.118-a28

Abstract Article

Keywords Light at Night, melatonin, circadian rhythm

Spivey A

Year 2011

Authors Angela Spivey

Report Name The Mixed Blessing of Phosphor-Based White LEDs

Publication Environ Health Perspect

Issue-page numbers 119:a472-a473. http://dx.doi.org/10.1289/ehp.119-a472

URL http://ehp03.niehs.nih.gov/article/info%3Adoi%2F10.1289%2Fehp.119-a472

Abstract Online Article - Light-emitting diodes (LEDs), which use less energy and last longer than even compact fluorescent lights,1 are predicted to become the leading lighting technology in the United States as incandescent bulbs are phased out.2 But Abraham Haim, director of the Israeli Center for Interdisciplinary Studies in Chronobiology, will not bring white LEDs and other so-called short-wavelength lights into his home because of his concerns about their health effects. Why? Blue light such as that emitted by LEDs has been shown to suppress production of the hormone melatonin to a greater degree than other visible wavelengths emitted at the same intensity.3,4 Melatonin suppression has been demonstrated to disrupt sleep/wake cycles and has been linked to increased risk of breast cancer.5 “Modern lights . . . that use the wavelength in the range of 460 nm to 500 nm should be considered ‘bad light,’” Haim says.

Keywords

Spivey A

Year 2010

Authors Angela Spivey

Report Name Light at Night and Breast Cancer Risk Worldwide

Publication Environ Health Perspect

Issue-page numbers 118:a525-a525

URL http://dx.doi.org/10.1289/ehp.118-a525

Abstract Several studies over the last decade have suggested that the modern practice of keeping our bodies exposed to artificial light at night, or LAN, increases cancer risk, especially for cancers (such as breast and prostate cancers) that require hormones to grow. Women who work night shifts have shown higher rates of breast cancer,1 whereas blind women, who are not likely to be exposed to or perceive LAN, have shown decreased risks.2 In 2007, the International Agency for Cancer Research declared shiftwork a probable human carcinogen.3 Now a large study of 164 countries adds another piece of evidence, implicating overall light pollution.

Keywords Light at night, breast cancer, melatonin

Stanberry LR, Das Gupta TK, Beattie CW

Year 1983

Authors Stanberry LR, Das Gupta TK, Beattie CW

Report Name Photoperiodic control of melanoma growth in hamsters: influence of pinealectomy and melatonin

Publication Endocrinology

Issue-page numbers 113:469–475 doi:10.1210/endo-113-2-469. PMID:6872938

URL http://endo.endojournals.org/content/113/2/469.short

Abstract Pinealectomy (PX) increased MM1 (melanotic melanoma no. 1) hamster melanoma growth in animals held under a 14-h light, 10-h dark (14:10) photoperiod without altering tumor latency. Hamsters maintained under a 6-h light, 18-h dark (6:18) photoperiod exhibited gonadal collapse, a longer tumor latency, and slower tumor growth rate than animals held under 14:10. PX produced a further increase in tumor latency and a decrease in growth in these animals. In contrast, acute morning injection of low doses (50 μg/day) of melatonin or delivery by Silastic capsule (35 μg/day) implanted at the time of tumor cell inoculation increased MM1 melanoma growth in hamsters held under 14:10 photocycle, without affecting testicular or adrenal function. Treatment of hamsters 11 weeks before tumor cell inoculation with 14 μg/day melatonin via Silastic capsule produced a decrease in serum PRL but no change in tumor growth or testicular or adrenal weights in animals held under 14:10. Treatment of hamsters with 17.7 μg/day melatonin (Silastic capsule) 11 weeks before tumor cell inoculation increased testes and adrenal weights as well as serum PRL and androgen levels, but significantly decreased tumor growth in hamsters held under a short daily photoperiod. These results suggest that the photoperiod under which hamsters are maintained dictates the growth rate of MM1 tumors and the effect of PX on tumor behavior. When photoperiod significantly alters gonadal and adrenal function, the quantity, time, and duration of melatonin presentation are all important variables in the effect of melatonin on tumor growth.

Keywords

Authors Staples MP, Elwood M, Burton RC, Williams JL, Marks R, Giles GG.

Report Name Non-melanoma skin cancer in Australia: the 2002 national survey and trends since 1985

Publication Med J Aust

Issue-page numbers 2006; 184:6-10.

URL http://www.mja.com.au/public/issues/184_01_020106/sta10828_fm.html

Abstract

Objectives:

To measure the incidence of treated non-melanoma skin cancer (NMSC) in Australia in 2002 and investigate trends since 1985 by histological type, sex, age group, latitude and skin type.
Design:

Face-to-face survey between 1 January and 31 December 2002 using stratified sampling of households to identify people treated for skin cancer in the previous 12 months. Self-reported diagnoses were confirmed with treatment providers. Data from similar surveys conducted in 1985, 1990 and 1995 were used to assess trends.
Setting:

Whole of Australia (population 19.6 million).
Participants:

Of 57 215 people interviewed, 4098 said they had been treated for skin cancer in the past year and 3198 gave permission for their diagnoses to be confirmed with their doctor.
Results:

817 people were confirmed as having at least one skin cancer treated in the past year. The age-standardised rate per 100 000 population for NMSC was 1170, for basal cell carcinoma (BCC) 884, and for squamous cell carcinoma (SCC) 387. The estimated number of NMSC cases in Australia for 2002 was 374 000. Cumulative risks to age 70 years of having at least one NMSC were 70% for men and 58% for women. Rates of BCC and SCC have increased since 1985, and the increases greatest for people aged 60 years and older; rates for those younger than 60 years have stabilised.
Conclusions:

The incidence of treated NMSC in Australia in 2002 was more than five times the incidence of all other cancers combined. Although the overall NMSC rates have risen since 1985, the stabilisation of rates for people younger than 60 years who were exposed to skin cancer prevention programs in their youth highlights the importance of maintaining and strengthening these programs.

Keywords

Stark H, Brown SS, Wong KW — *Year* 2011

Authors H. Stark, S. S. Brown, K. W. Wong, J. Stutz, C. D. Elvidge, I. B. Pollack, T. B. Ryerson, W. P. Dube, N. L. Wagner, D. D. Parrish

Report Name City lights and urban air

Publication Nature Geoscience, Correspondence

Issue-page numbers 4, 730–731 doi:10.1038/ngeo1300

URL http://www.nature.com/ngeo/journal/v4/n11/full/ngeo1300.html

Abstract Artificial lights are an essential part of human life at night, necessary for the safety and security of many human activities. However, the illumination of the night sky by artificial lights can adversely affect biological activities such as animal orientation1, together with human perception of the sky at night2. Here we show that city lights can also alter the concentration of nitrate radicals, an important atmospheric oxidant. These alterations have potential — albeit small — consequences for pollution levels the following day.

Keywords

Stehle J, Vanecek J, Vollrath L — *Year* 1989

Authors Stehle J, Vanecek J, Vollrath L

Report Name Effects of melatonin on spontaneous electrical activity of neurons in rat suprachiasmatic nuclei: an in vitro iontophoretic study

Publication J Neural Transm

Issue-page numbers 173–177 doi:10.1007/BF01252503. PMID:2809584

URL http://www.springerlink.com/content/r1223004775h601j/

Abstract Circadian rhythms, endogenously generated in suprachiasmatic nuclei (SCN), seem to be under the direct influence of melatonin. Therefore, the effect of iontophoretically applied melatonin on electrical activity of SCN neurons was investigated in vitro. Usually, melatonin had an inhibitory effect. In the 3-h periods before (2.00–5.00 p.m.) or after (5.00–8.00 p.m.) the light-dark transition the percentage of SCN neurons sensitive to melatonin was very high (80% and 100%, respectively). However, efficacy of melatonin was low in the periods preceeding (20%) and following (33%) this 6-h time interval.

Keywords SCN neurons - circadian rhythm - iontophoresis - melatonin receptors

Stephenson KM, Schroder CM, Bertschy G, Bourgin P **Year** 2012

Authors Kathryn M. Stephenson, Carmen M. Schroder, Gilles Bertschy, Patrice Bourgin

Report Name Complex interaction of circadian and non-circadian effects of light on mood: Shedding new light on an old story

Publication Sleep Medicine Reviews

Issue-page numbers Available online 13 January 2012

URL http://www.sciencedirect.com/science/article/pii/S1087079211000979

Abstract In addition to its role in vision, light exerts strong effects on behavior. Its powerful role in the modulation of mood is well established, yet remains poorly understood. Much research has focused on the effects of light on circadian rhythms and subsequent interaction with alertness and depression. The recent discovery of a third photoreceptor, melanopsin, expressed in a subset of retinal ganglion cells, allows major improvement of our understanding of how photic information is processed. Light affects behavior in two ways, either indirectly through the circadian timing system, or directly through mechanisms that are independent of the circadian system. These latter effects have barely been studied in regard to mood, but recent investigations on the direct effects of light on sleep and alertness suggest additional pathways through which light could influence mood. Based on our recent findings, we suggest that light, via melanopsin, may exert its antidepressant effect through a modulation of the homeostatic process of sleep. Further research is needed to understand how these mechanisms interplay and how they contribute to the photic regulation of mood. Such research could improve therapeutic management of affective disorders and influence the management of societal lighting conditions.

Keywords Mood; Light; Sleep; Circadian rhythms; Alertness; Seasonal affective disorder; Melatonin

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Stetson MH, Matt KS, Watson-Whitmyre M **Year** 1976

Authors Stetson MH, Matt KS, Watson-Whitmyre M

Report Name Photoperiodism and reproduction in golden hamsters: circadian organization and the termination of photorefractoriness

Publication Biol Reprod

Issue-page numbers 14:531–537 doi:10.1095/biolreprod14.5.531. PMID:1276317

URL http://www.biolreprod.org/content/14/5/531

Abstract The photorefractory period of the adult golden hamster is characterized by failure of the reproductive system to respond to short-day treatment with gonadal regression. The reproductive system of photorefractory hamsters remains functional irrespective of ambient photoperiod. Prolonged treatment with long days terminates photorefractoriness in hamsters, restoring the ability of the animals' hypothalamo-hypophysio-gonadal axis to respond to short daylengths. The basis of the photorefractory hamster's ability to discriminate long from short days in terminating the refractory period is a circadian oscillation of photosensitivity.

Photorefractory hamsters were treated for 22 weeks with LD 14:10 (14 h of light daily), LD 6:18, LD 6:30, LD 6:42, or LD 6:54. They were then treated for 10 weeks with LD 6:18. Exposure for 22 weeks to LD 14:10, LD 6:30 or LD 6:54 terminated photorefractoriness; when challenged with 10 weeks of short day treatment these animals underwent testicular regression. Exposure for 22 weeks to LD 6:18 or LD 6:42 did not terminate photorefractoriness; further short day treatment of these animals had no effect on their fully mature reproductive systems. Thus, whether a photoperiod is interpreted as a long day or a short day in these hamsters depends on the phase relationship between the light presented and an endogenous oscillation of photosensitivity.

Keywords

Year 1998

Authors Stevens JC, Choo KK.

Report Name Temperature sensitivity of the body surface over the life span

Publication Somatosens Mot Res

Issue-page numbers 1998;15(1):13-28.

URL http://www.ncbi.nlm.nih.gov/pubmed/9583574

Abstract

Detection thresholds to warming and cooling were measured in 13 regions of the body in 60 adults aged between 18 and 88 years. From these thresholds were constructed maps of thermal sensitivity homologous to body maps of spatial acuity (in the older literature two-point discrimination), long known to the somatosensory scientist. Maps of cold and warm sensitivity for young, middle-aged and elderly adults, show how sensitivity changes with age in the various body regions. Three characteristics emerge, irrespective of age: (1) sensitivity varies approximately 100-fold over the body surface. The face, especially near the mouth, is exquisitely sensitive, the extremities, by comparison, poor, other regions, intermediate. (2) All body regions are more sensitive to cold than to warm. (3) The better a region is at detecting cold, the better it is at detecting warm. With age, thermal sensitivity declines. The greatest changes take place in the extremities, especially the foot, where thresholds often become too large to measure. Central regions give up their sensitivity with age more slowly, and even (as in the lips) inconsequentially. Similar age-related changes have also previously been shown to characterize spatial acuity.

Keywords

Stevens RG

Year 2009

Authors Richard G Stevens

Report Name Light-at-night, circadian disruption and breast cancer: assessment of existing evidence

Publication International Journal of Epidemiology

Issue-page numbers Volume38, Issue4 Pp. 963-970

URL http://ije.oxfordjournals.org/content/38/4/963.short

Abstract Background Breast cancer incidence is increasing globally for largely unknown reasons. The possibility that a portion of the breast cancer burden might be explained by the introduction and increasing use of electricity to light the night was suggested >20 years ago.

Methods The theory is based on nocturnal light-induced disruption of circadian rhythms, notably reduction of melatonin synthesis. It has formed the basis for a series of predictions including that non-day shift work would increase risk, blind women would be at lower risk, long sleep duration would lower risk and community nighttime light level would co-distribute with breast cancer incidence on the population level.

Results Accumulation of epidemiological evidence has accelerated in recent years, reflected in an International Agency for Research on Cancer (IARC) classification of shift work as a probable human carcinogen (2A). There is also a strong rodent model in support of the light-at-night (LAN) idea.

Conclusion If a consensus eventually emerges that LAN does increase risk, then the mechanisms for the effect are important to elucidate for intervention and mitigation. The basic understanding of phototransduction for the circadian system, and of the molecular genetics of circadian rhythm generation are both advancing rapidly, and will provide for the development of lighting technologies at home and at work that minimize circadian disruption, while maintaining visual efficiency and aesthetics. In the interim, there are strategies now available to reduce the potential for circadian disruption, which include extending the daily dark period, appreciate nocturnal awakening in the dark, using dim red light for nighttime necessities, and unless recommended by a physician, not taking melatonin tablets.

Keywords Breast cancer, circadian disruption, light-at-night, melatonin, clock

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Stevens RG

Year 1987

Authors Richard G Stevens

Report Name Electric power use and breast cancer: a hypothesis.

Publication Am J Epidemiol

Issue-page numbers 1987 Apr;125(4):556-61.

URL http://www.ncbi.nlm.nih.gov/pubmed/3548332

Abstract N/A

Keywords

Stevens RG **Year** 2009

Authors Stevens RG.

Report Name Working against our endogenous circadian clock: Breast cancer and electric lighting in the modern world

Publication Mutat Res

Issue-page numbers 2009 Nov-Dec;680(1-2):106-8.

URL http://www.ncbi.nlm.nih.gov/pubmed/20336819

Abstract Breast cancer incidence increases rapidly as societies industrialize. Many changes occur during the industrialization process, one of which is a dramatic alteration in the lighted environment from a sun-based system to an electricity-based system. Increasingly, the natural dark period at night is being seriously eroded for the bulk of humanity. Based on the fact that light during the night can suppress melatonin, and also disrupt the circadian rhythm, it was proposed in 1987 that increasing use of electricity to light the night accounts in part for the rising risk of breast cancer globally. Predictions from the theory include: non-day shift work increases risk, blindness lowers risk, long sleep duration lowers risk, and population level community nighttime light level co-distributes with breast cancer incidence. Thus far, studies of these predictions are consistent in support of the theory. A new avenue of research has been on function of circadian genes and whether these are related to breast cancer risk. In particular, a length variant of Per3 (5-VNTR) has been associated with increased risk in young women, and this same 5-VNTR variant has also been found to predict morning diurnal type and shorter sleep duration compared to the 4-VNTR variant. An important question is how an effect of light-at-night (LAN) exposure on breast cancer risk might be modified by polymorphisms and/or epigenetic alterations in the circadian genes, and conversely whether light-at-night exposure (e.g., shift work) can induce deleterious epigenetic changes in these genes.

Keywords

Stevens RG **Year** 2011

Authors Richard G. Stevens

Report Name Testing the Light-at-Night (LAN) Theory for Breast Cancer Causation

Publication Chronobiology International

Issue-page numbers 2011 28:8, 653-656

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.606945

Abstract N/A

Keywords Light at night, breast cancer

Stevens RG

Year 2006

Authors Stevens RG

Report Name Artificial lighting in the industrialized world: circadian disruption and breast cancer

Publication Cancer Causes Control

Issue-page numbers 17:501–507 doi:10.1007/s10552-005-9001-x. PMID:16596303

URL Artificial lighting in the industrialized world: circadian disruption and breast cancer

Abstract

Breast cancer risk is high in industrialized societies, and increases as developing countries become more Westernized. The reasons are poorly understood. One possibility is circadian disruption from aspects of modern life, in particular the increasing use of electric power to light the night, and provide a sun-free environment during the day inside buildings. Circadian disruption could lead to alterations in melatonin production and in changing the molecular time of the circadian clock in the suprachiasmatic nuclei (SCN). There is evidence in humans that the endogenous melatonin rhythm is stronger for persons in a bright-day environment than in a dim-day environment; and the light intensity necessary to suppress melatonin at night continues to decline as new experiments are done. Melatonin suppression can increase breast tumorigenesis in experimental animals, and altering the endogenous clock mechanism may have downstream effects on cell cycle regulatory genes pertinent to breast tissue development and susceptibility. Therefore, maintenance of a solar day-aligned circadian rhythm in endogenous melatonin and in clock gene expression by exposure to a bright day and a dark night, may be a worthy goal. However, exogenous administration of melatonin in an attempt to achieve this goal may have an untoward effect given that pharmacologic dosing with melatonin has been shown to phase shift humans depending on the time of day it's given. Exogenous melatonin may therefore contribute to circadian disruption rather than alleviate it.

Keywords

Authors Richard G. Stevens, David E. Blask, George C. Brainard, Johnni Hansen, Steven W. Lockley, Ignacio Provencio, Mark S. Rea, and Leslie Reinlib

Report Name Meeting Report: The Role of Environmental Lighting and Circadian Disruption in Cancer and Other Diseases

Publication Environ Health Perspect

Issue-page numbers 115(9): 1357-1362

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1964886/

Abstract Light, including artificial light, has a range of effects on human physiology and behavior and can therefore alter human physiology when inappropriately timed. One example of potential light-induced disruption is the effect of light on circadian organization, including the production of several hormone rhythms. Changes in light–dark exposure (e.g., by nonday occupation or transmeridian travel) shift the timing of the circadian system such that internal rhythms can become desynchronized from both the external environment and internally with each other, impairing our ability to sleep and wake at the appropriate times and compromising physiologic and metabolic processes. Light can also have direct acute effects on neuroendocrine systems, for example, in suppressing melatonin synthesis or elevating cortisol production that may have untoward long-term consequences. For these reasons, the National Institute of Environmental Health Sciences convened a workshop of a diverse group of scientists to consider how best to conduct research on possible connections between lighting and health. According to the participants in the workshop, there are three broad areas of research effort that need to be addressed. First are the basic biophysical and molecular genetic mechanisms for phototransduction for circadian, neuroendocrine, and neurobehavioral regulation. Second are the possible physiologic consequences of disrupting these circadian regulatory processes such as on hormone production, particularly melatonin, and normal and neoplastic tissue growth dynamics. Third are effects of light-induced physiologic disruption on disease occurrence and prognosis, and how prevention and treatment could be improved by application of this knowledge.

Keywords breast cancer, circadian rhythms, clock genes, lighting, melatonin, phototransduction, pineal gland

Year 1996

Authors Stevens RG, Davis S

Report Name The melatonin hypothesis: electric power and breast cancer

Publication Environ Health Perspect

Issue-page numbers 104:135-140

URL http://dx.doi.org/10.1289/ehp.96104s1135

Abstract Breast cancer is a disease of modern life. As societies industrialize, risk increases, yet it is unclear which of the myriad changes coming with industrialization drives this increase. One important hallmark of modern life is the pervasive use of electric power. Electric power produces light at night (LAN) and electric and magnetic fields (EMF), either or both of which may alter pineal function and its primary hormone melatonin, thereby, perhaps increasing the risk of breast cancer. This hypothesis, stated a decade ago, is now receiving considerable experimental and epidemiological attention. The circumstantial case for the hypothesis has three aspects: light effects on melatonin, EMF effects on melatonin, and melatonin effects on breast cancer. The strongest of these aspects is the effects of light on melatonin. It is clear that the normal nocturnal melatonin rise in humans can be suppressed by light of sufficient intensity. The evidence for an effect of melatonin on breast cancer in experimental animals is strong, but the evidence in humans is scant and difficult to gather. The weakest aspect of the circumstantial case is EMF effects on melatonin. Whereas a half dozen independent laboratories have published findings of suppression in animals, there are inconsistencies, and there are no published data on humans. The direct evidence bearing on the hypothesis is sparse but provocative. Two laboratories have published data showing substantial increases in chemically induced breast cancer in rats by a weak AC (alternating current) magnetic field. The epidemiological evidence is very limited but has offered some support as well. An effect of electric power on breast cancer would have profound implications, and this possibility deserves continued investigation.

Keywords EMF, breast cancer, light at night

Stevens RG, Hansen J, Costa G, et al. **Year** 2011

Authors Richard G Stevens, Johnni Hansen, Giovanni Costa, Erhard Haus, Timo Kauppinen, Kristan J Aronson, Gemma Castaño-Vinyals, Scott Davis, Monique H W Frings-Dresen, Lin

Report Name Considerations of circadian impact for defining 'shift work' in cancer studies: IARC Working Group Report

Publication Occup Environ Med

Issue-page numbers 2011;68:154-162

URL http://oem.bmj.com/content/68/2/154.abstract

Abstract Based on the idea that electric light at night might account for a portion of the high and rising risk of breast cancer worldwide, it was predicted long ago that women working a non-day shift would be at higher risk compared with day-working women. This hypothesis has been extended more recently to prostate cancer. On the basis of limited human evidence and sufficient evidence in experimental animals, in 2007 the International Agency for Research on Cancer (IARC) classified 'shift work that involves circadian disruption' as a probable human carcinogen, group 2A. A limitation of the epidemiological studies carried out to date is in the definition of 'shift work.' IARC convened a workshop in April 2009 to consider how 'shift work' should be assessed and what domains of occupational history need to be quantified for more valid studies of shift work and cancer in the future. The working group identified several major domains of non-day shifts and shift schedules that should be captured in future studies: (1) shift system (start time of shift, number of hours per day, rotating or permanent, speed and direction of a rotating system, regular or irregular); (2) years on a particular non-day shift schedule (and cumulative exposure to the shift system over the subject's working life); and (3) shift intensity (time off between successive work days on the shift schedule). The group also recognised that for further domains to be identified, more research needs to be conducted on the impact of various shift schedules and routines on physiological and circadian rhythms of workers in real-world environments.

Keywords

Stevens RG, Rea MS **Year** 2001

Authors Richard G. Stevens and Mark S. Rea

Report Name Light in the built environment: potential role of circadian disruption in endocrine disruption and breast cancer

Publication Cancer Causes and Control

Issue-page numbers Volume 12, Number 3, 279-287, DOI: 10.1023/A:1011237000609

URL http://www.springerlink.com/content/p1u276v654234w08/

Abstract Life in industrialized societies is primarily life inside buildings. Illumination from electric lighting in the built environment is quite different from solar radiation in intensity, spectral content, and timing during the 24-hour daily period. Humans evolved over millions of years with the day–night pattern of solar radiation as the primary circadian cue. This pattern maintained a 24-hour rhythm of melatonin release, as well as a host of other physiological rhythms including the sleep–wake cycle. Electric lighting in the built environment is generally more than sufficient for visual performance, but may be inappropriate for the maintenance of normal neuroendocrine rhythms in humans; e.g., insufficient during the day and too much at night. Lighting standards and engineering stress visual performance, whereas circadian function is not currently emphasized. The molecular biological research on the circadian clock and on mechanisms of phototransduction makes it clear that light for vision and light for circadian function are not identical systems. In particular, if electric lighting as currently employed contributes to `circadian disruption' it may be an important cause of `endocrine disruption' and thereby contribute to a high risk of breast cancer in industrialized societies.

Keywords breast cancer - buildings - circadian disruption - endocrine disruption - light

Stokkan K-A, Yamazaki S, Tei H et al. **Year** 2001

Authors Stokkan K-A, Yamazaki S, Tei H et al.

Report Name Entrainment of the circadian clock in the liver by feeding

Publication Science

Issue-page numbers 291:490–493 doi:10.1126/science.291.5503.490. PMID:11161204

URL http://www.sciencemag.org/content/291/5503/490.abstract

Abstract Circadian rhythms of behavior are driven by oscillators in the brain that are coupled to the environmental light cycle. Circadian rhythms of gene expression occur widely in peripheral organs. It is unclear how these multiple rhythms are coupled together to form a coherent system. To study such coupling, we investigated the effects of cycles of food availability (which exert powerful entraining effects on behavior) on the rhythms of gene expression in the liver, lung, and suprachiasmatic nucleus (SCN). We used a transgenic rat model whose tissues express luciferase in vitro. Although rhythmicity in the SCN remained phase-locked to the light-dark cycle, restricted feeding rapidly entrained the liver, shifting its rhythm by 10 hours within 2 days. Our results demonstrate that feeding cycles can entrain the liver independently of the SCN and the light cycle, and they suggest the need to reexamine the mammalian circadian hierarchy. They also raise the possibility that peripheral circadian oscillators like those in the liver may be coupled to the SCN primarily through rhythmic behavior, such as feeding.

Keywords

Storch K-F, Lipan O, Leykin I et al. **Year** 2002

Authors Storch K-F, Lipan O, Leykin I et al.

Report Name Extensive and divergent circadian gene expression in liver and heart

Publication Nature

Issue-page numbers 417:78–83 doi:10.1038/nature744. PMID:11967526

URL http://www.nature.com/nature/journal/v417/n6884/full/nature744.html

Abstract Many mammalian peripheral tissues have circadian clocks1, 2, 3, 4; endogenous oscillators that generate transcriptional rhythms thought to be important for the daily timing of physiological processes5, 6. The extent of circadian gene regulation in peripheral tissues is unclear, and to what degree circadian regulation in different tissues involves common or specialized pathways is unknown. Here we report a comparative analysis of circadian gene expression in vivo in mouse liver and heart using oligonucleotide arrays representing 12,488 genes. We find that peripheral circadian gene regulation is extensive (greater than or equal to8–10% of the genes expressed in each tissue), that the distributions of circadian phases in the two tissues are markedly different, and that very few genes show circadian regulation in both tissues. This specificity of circadian regulation cannot be accounted for by tissue-specific gene expression. Despite this divergence, the clock-regulated genes in liver and heart participate in overlapping, extremely diverse processes. A core set of 37 genes with similar circadian regulation in both tissues includes candidates for new clock genes and output genes, and it contains genes responsive to circulating factors with circadian or diurnal rhythms.

Keywords

Stossi F, Likhite VS, Katzenellenbogen JA, Katzenellenbogen BS **Year** 2006

Authors Stossi F, Likhite VS, Katzenellenbogen JA, Katzenellenbogen BS

Report Name Estrogen-occupied estrogen receptor represses cyclin G2 gene expression and recruits a repressor complex at the cyclin G2 promoter

Publication J Biol Chem

Issue-page numbers 281:16272–16278 doi:10.1074/jbc.M513405200. PMID:16608856

URL http://www.jbc.org/content/281/24/16272

Abstract Estrogens, acting through their nuclear receptors have a broad impact on target cells, eliciting a transcriptional response program that involves gene repression as well as gene stimulation. While much is known about the mechanisms by which the estrogen-occupied estrogen receptor (ER) stimulates gene expression, the molecular events that lead to gene repression by the hormone-ER complex are largely unknown. Because estradiol represses expression of the cyclin G2 gene, which encodes a negative regulator of the cell cycle, our aim was to understand the mechanism by which cyclin G2 is repressed by estrogen. We show that cyclin G2 is a primary ER target gene in MCF-7 breast cancer cells that is rapidly and robustly down-regulated by estrogen. Promoter analysis reveals a responsive region containing a half-estrogen response element and GC-rich region that interact with ER and Sp1 proteins. Mutation of the half-ERE abrogates hormone-mediated repression. Mutational mapping of receptor reveals a requirement for its N-terminal region and DNA binding domain to support cyclin G2 repression. Following estradiol treatment of cells, chromatin immunoprecipitation analyses reveal recruitment of ER to the cyclin G2 regulatory region, dismissal of RNA polymerase II, and recruitment of a complex containing N-CoR and histone deacetylases, leading to a hypoacetylated chromatin state. Our study provides evidence for a mechanism by which the estrogen-occupied ER is able to actively repress gene expression in vivo and indicates a role for nuclear receptor corepressors and associated histone deacetylase activity in mediating negative gene regulation by this hormone-occupied nuclear receptor.

Keywords

Straif K, Baan R, Grosse Y, et al. **Year** 2008

Authors Kurt Straif , Robert Baan , Yann Grosse , Béatrice Secretan , Fatiha El Ghissassi , Véronique Bouvard , Andrea Altieri , Lamia Benbrahim-Tallaa , Vincent Cogliano

Report Name Carcinogenicity of shift-work, painting, and fire-fighting

Publication The Lancet Oncology

Issue-page numbers Volume 8, Issue 12, Pages 1065 - 1066, December 2007

URL http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2807%2970373-X/fulltext

Abstract N/A

Keywords

Authors Strong RE, Marchant BK, Reimherr FW, Williams E, Soni P, Mestas R.

Report Name Narrow-band blue-light treatment of seasonal affective disorder in adults and the influence of additional nonseasonal symptoms

Publication Depression and Anxiety

Issue-page numbers Volume: 26, Issue: 3, Publisher: Wiley Subscription Services, Inc., A Wiley Company, Pages: 273-8

URL http://www.mendeley.com/research/seasonal-affective-disorder-adults/

Abstract

BACKGROUND: Bright visible-spectrum light therapy has proven effective in the treatment of seasonal affective disorder (SAD) and recent basic research suggests that blue wavelengths approximately 470 nm account for that effectiveness. To more stringently test the importance of these wavelengths, bright red-light was used for the placebo (control) condition. METHODS: Thirty subjects meeting DSM-IV criteria for SAD were randomized to narrow-band light-emitting diode panels emitting blue- or red-light in this 3-week, parallel, double-blind trial. Twenty-five subjects participated in an open-label blue-light follow-up. Subjects were divided in a blinded, post hoc manner into two groups: SAD only and those experiencing depression with seasonal intensification. The outcome was assessed using Hamilton Depression Rating Scale-17 item version (HAMD-17) and the Structured Interview Guide for the Hamilton Depression Rating Scale-SAD version. Responders were defined by Clinical Global Impression-Improvement scale. RESULTS: HAMD-17 scores improved more under the blue-light condition (51%) than under the red-light condition (32%) (P=.05). Further, in the blue arm 60% of subjects responded compared with 13% in the red arm (P=.01). During the open-label phase, subjects from both double-blind arms improved over baseline. SAD alone patients responded numerically better to treatment than those experiencing depression with seasonal intensification during both treatment periods. CONCLUSIONS: Narrow bandwidth blue-light therapy proved superior to red-light therapy. Blue-light therapy produced results similar to both previous 10,000 lux visible-spectrum light studies and many medication studies. The use of bright red panels supported claims that wavelengths of approximately 470 nm account for the documented effectiveness of light therapy.

Keywords

Sturgeon SR, Luisi N, Balasubramanian R, Reeves KW **Year** 2012

Authors Susan R. Sturgeon, Nicole Luisi, Raji Balasubramanian and Katherine W. Reeves

Report Name Sleep duration and endometrial cancer risk

Publication Cancer Causes and Control

Issue-page numbers DOI: 10.1007/s10552-012-9912-2

URL http://www.springerlink.com/content/a43vt375426n3436/

Abstract

Purpose
Recent data indicate that night shift work is associated with increased endometrial cancer risk, perhaps through a pathway involving lower melatonin production. Melatonin is an antiestrogenic hormone, with production in a circadian pattern that is dependent on presence of dark at night. Sleep duration is positively associated with melatonin production and may be an indicator of melatonin levels in epidemiologic studies.
Methods
We evaluated associations between self-reported sleep duration and endometrial cancer risk using publicly available prospective data on 48,725 participants in the Women's Health Initiative Observational Study, among whom 452 adjudicated incident cases of endometrial cancer were diagnosed over approximately 7.5 years of follow-up. Sleep duration was self-reported at baseline. Cox proportional hazards regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for endometrial cancer risk with adjustment for potential confounders.
Results
Most women reported sleeping ≤6 (33.3%) or 7 (38.5%) h each night; fewer reported sleeping 8 (23.4%) or ≥9 (4.8%) h each night. In adjusted analyses, there was an indication of reduced risk associated with longer sleep duration, though no statistically significant association was observed. Women who slept ≥9 h had a nonsignificant reduced risk of endometrial cancer compared with women who slept ≤6 h (HR = 0.87; 95% CI = 0.51–1.46).
Conclusions
We found weak evidence of an association between sleep duration and endometrial cancer risk. Self-reported sleep duration may not adequately represent melatonin levels, thus further studies utilizing urinary melatonin levels are necessary to establish the mechanism by which night shift work increases endometrial cancer risk.

Keywords Endometrial cancer incidence – Sleep duration – Cohort study

Subramanian A, Kothari L **Year** 1991

Authors Subramanian A, Kothari L

Report Name Suppressive effect by melatonin on different phases of 9,10-dimethyl-1,2-benzanthracene (DMBA)-induced rat mammary gland carcinogenesis

Publication Anticancer Drugs

Issue-page numbers 2:297–303 doi:10.1097/00001813-199106000-00013. PMID:1802026

URL http://www.ncbi.nlm.nih.gov/pubmed/1802026

Abstract This comprehensive study examines the influence of oral melatonin on the initiation and promotion phases of DMBA-induced mammary tumorigenesis in intact and pinealectomized female Holtzman rats reared in short (light:dark schedule L:D 10:14) and long (L:D 24:0) photoperiods. Melatonin administration in the initiation phase significantly suppressed tumor incidence only in intact animals reared in both photoperiods, indicating that the presence of the pineal was obligatory. On the other hand, during the promotion phase, irrespective of the presence or absence of the pineal, the tumor-suppressive effect of exogenous melatonin was pronounced.

Keywords

Suh BY, Liu JH, Berga SL et al. **Year** 1988

Authors Suh BY, Liu JH, Berga SL et al.

Report Name Hypercortisolism in patients with functional hypothalamicamenorrhea

Publication J Clin Endocrinol Metab

Issue-page numbers 66:733–739 doi:10.1210/jcem-66-4-733. PMID:3346352

URL http://jcem.endojournals.org/content/66/4/733.short

Abstract Hypercortisolism was found in patients with functional hypothalamic amenorrhea (HA) in preliminary short term studies conducted during the morning hours (0800–1100 h). This observation prompted us to characterize the circadian and pulsatile patterns of serum cortisol and LH levels at 15-min intervals for 24 h in 10 women with functional HA and in 7 normal women during the early follicular phase of their cycles. The mean integrated 24-h serum cortisol levels (area under the curve) were significantly ($P < 0.01$) higher in the HA patients than in normal women. The mean cortisol levels in the HA patients were elevated ($P < 0.005$) compared to those in the normal women during the daytime hours (0800–1600 h), but not during the evening (1600–2400 h) and sleeping hours (2400–0800 h). This selective hypercortisolism during the waking period of the day was almost entirely related to increased duration and amplitude of secretory episodes (peak area) rather than a change in pulse frequency. The serum cortisol increments in response to a noon meal that occurred in normal women were markedly impaired ($P < 0.01$) in the HA patients.

Compared with that in the normal women, mean LH pulse frequency was reduced by 30% in the HA patients. The 24-h mean LH levels and mean LH pulse amplitude were not significantly different from those in the normal women. However, among the HA patients there were marked individual differences in LH pulse frequency and amplitude, with prolonged interpulse quiescent periods, indicative of dysfunction of the hypothalamic GnRH pulse generator.

We conclude that neuroendocrine activation of the ACTH-adrenal axis and inhibition of the GnRH pulse generator in women are associated with HA. Further, spontaneous resumption of normal cyclicity occurred in the majority (8 of 10) of the HA patients with no medical treatment, suggesting that this syndrome is a reversible hypothalamic disorder of a functional nature.

Keywords

Sun J, Yaga K, Reiter RJ

Year 1993

Authors Jih-Hsing Sun, Ken Yaga, Russel J. Reiter , Mario Garza, Lucien C. Manchester, Dun-Xian Tan, Burkhard Poeggeler

Report Name Reduction in pineal N-acetyltransferase activity and pineal and serum melatonin levels in rats after their exposure to red light at night

Publication Neuroscience Letters

Issue-page numbers Volume 149, Issue 1, 4 January 1993, Pages 56-58

URL http://www.sciencedirect.com/science/article/pii/030439409390346M

Abstract Pineal gland N-acetyltransferase (NAT) activity and pineal and serum levels of melatonin declined linearly in albino rats exposed to different irradiances (low, 170 μW/cm2; moderate, 420 μW/cm2; high, 1040 μW/cm2) red light during the middle of the night. High intensity red light (1040 μW/cm2) was as effective as white light (670 μW/cm2) in suppressing pineal NAT activity and pineal and serum melatonin levels. The lowered melatonin levels and the reduction in NAT activity following exposure to red light suggest that red light cannot be regarded as 'safe' light when studying circadian melatonin production in the albino rat, at least at the intensities used in this experiment.

Keywords Red light; Pineal gland; Melatonin; N-Acetyltransferase activity

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Suvanto S, Partinen M, Härmä M, Ilmarinen J

Year 1990

Authors Suvanto S, Partinen M, Härmä M, Ilmarinen J

Report Name Flight attendants' desynchronosis after rapid time zone changes

Publication Aviat Space Environ Med

Issue-page numbers 61:543–547. PMID:2369394

URL http://www.mendeley.com/research/flight-attendants-desynchronosis-after-rapid-time-zone-changes/

Abstract The aim of the present study was to measure perceived effects of rapid time zone changes on flight attendants' sleep length, quality, adaptation, and recovery time, and to clarify the individual factors related to perceived desynchronosis after time zone changes. The mean age of 285 female subjects was 35.0 years and that of 57 men was 34.1 years. The data were gathered by means of a questionnaire filled out by all Finnish flight attendants who worked on transmeridian routes. The quality of sleep, perceived adjustment, and recovery times were dependent on the flight direction and on the number of time zones crossed. The effects of age, neuroticism, and sex partly explained the variation of perceived desynchronosis, which increased linearly with increasing age and neuroticism.

Keywords

Authors Joanna Szular, Hana Sehadova, Carla Gentile, Gisela Szabo, Wen-Hai Chou, Steven G. Britt, Ralf Stanewsky

Report Name Rhodopsin 5– and Rhodopsin 6–Mediated Clock Synchronization in Drosophila melanogaster Is Independent of Retinal Phospholipase C-β Signaling

Publication J Biol Rhythms

Issue-page numbers February 2012 vol. 27 no. 1 25-36

URL http://jbr.sagepub.com/content/27/1/25.abstract

Abstract Circadian clocks of most organisms are synchronized with the 24-hour solar day by the changes of light and dark. In Drosophila, both the visual photoreceptors in the compound eyes as well as the blue-light photoreceptor Cryptochrome expressed within the brain clock neurons contribute to this clock synchronization. A specialized photoreceptive structure located between the retina and the optic lobes, the Hofbauer-Buchner (H-B) eyelet, projects to the clock neurons in the brain and also participates in light synchronization. The compound eye photoreceptors and the H-B eyelet contain Rhodopsin photopigments, which activate the canonical invertebrate phototransduction cascade after being excited by light. We show here that 2 of the photopigments present in these photoreceptors, Rhodopsin 5 (Rh5) and Rhodopsin 6 (Rh6), contribute to light synchronization in a mutant (norpAP41) that disrupts canonical phototransduction due to the absence of Phospholipase C-β (PLC-β). We reveal that norpAP41 is a true loss-of-function allele, resulting in a truncated PLC-β protein that lacks the catalytic domain. Light reception mediated by Rh5 and Rh6 must therefore utilize either a different (nonretinal) PLC-β enzyme or alternative signaling mechanisms, at least in terms of clock-relevant photoreception. This novel signaling mode may distinguish Rhodopsin-mediated irradiance detection from image-forming vision in Drosophila.

Keywords Rhodopsin 5, Rhodopsin 6, Phospholipase C, Cryptochrome, Drosophila melanogaster, Hofbauer-Buchner eyelet

Authors Taheri S

Report Name The link between short sleep duration and obesity: we should recommend more sleep to prevent obesity

Publication Arch Dis Child

Issue-page numbers 91:881–884 doi:10.1136/adc.2005.093013. PMID:17056861

URL http://adc.bmj.com/content/91/11/881

Abstract

Sleep may affect energy balance. Sleep may not be the only answer to the obesity pandemic, but its effect should be considered seriously, as even small changes in the energy balance are beneficial. Good sleep could be part of the obesity prevention approach.

We are currently facing a major obesity pandemic. Most alarming is the accelerated increase in overweight and obesity in children, with childhood obesity tracking into adulthood. Although there is a strong genetic contribution to obesity, the current pandemic has been driven by environmental factors. Unfortunately, interventions aiming to alter food selection (eg, less fat and sugar) and calorie intake (eg, smaller portions) and to increase physical activity have not been able to result in long-term weight loss and maintenance. These approaches are confounded by the fact that only an insignificant daily energy surplus could result in obesity over time. Although changes in the basic balance between energy intake (food calories) and expenditure (physical activity) are obviously responsible for the current obesity pandemic, our understanding of the factors that alter this balance remains incomplete. Intriguingly, sleep may be a factor that alters both sides of the energy balance equation. The precise physiological functions of sleep are unknown, but the contribution of sleep to physical and psychological health, and its social and economic significance, is increasingly recognised. 1 Sleep research has mainly concentrated on the cognitive consequences of sleep loss, on the basis of the belief that sleep is for the brain alone. Recently, however, there has been a shift in interest in the consequences of sleep loss for other organs and several physiological systems. Also, more laboratory studies on sleep are now concentrating on investigating the health and performance effects of chronic partial sleep restriction, which is truer of real life, rather than acute total sleep deprivation. On

Keywords

Authors Shahrad Taheri, Ling Lin, Diane Austin, Terry Young, Emmanuel Mignot

Report Name Short Sleep Duration Is Associated with Reduced Leptin, Elevated Ghrelin, and Increased Body Mass Index

Publication PLoS Med

Issue-page numbers 1(3): e62

URL http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0010062

Abstract

Background

Sleep duration may be an important regulator of body weight and metabolism. An association between short habitual sleep time and increased body mass index (BMI) has been reported in large population samples. The potential role of metabolic hormones in this association is unknown.

Methods and Findings

Study participants were 1,024 volunteers from the Wisconsin Sleep Cohort Study, a population-based longitudinal study of sleep disorders. Participants underwent nocturnal polysomnography and reported on their sleep habits through questionnaires and sleep diaries. Following polysomnography, morning, fasted blood samples were evaluated for serum leptin and ghrelin (two key opposing hormones in appetite regulation), adiponectin, insulin, glucose, and lipid profile. Relationships among these measures, BMI, and sleep duration (habitual and immediately prior to blood sampling) were examined using multiple variable regressions with control for confounding factors.

A U-shaped curvilinear association between sleep duration and BMI was observed. In persons sleeping less than 8 h (74.4% of the sample), increased BMI was proportional to decreased sleep. Short sleep was associated with low leptin (p for slope = 0.01), with a predicted 15.5% lower leptin for habitual sleep of 5 h versus 8 h, and high ghrelin (p for slope = 0.008), with a predicted 14.9% higher ghrelin for nocturnal (polysomnographic) sleep of 5 h versus 8 h, independent of BMI.

Conclusion

Participants with short sleep had reduced leptin and elevated ghrelin. These differences in leptin and ghrelin are likely to increase appetite, possibly explaining the increased BMI observed with short sleep duration. In Western societies, where chronic sleep restriction is common and food is widely available, changes in appetite regulatory hormones with sleep curtailment may contribute to obesity.

Keywords

Takahashi JS, Hong H, Ko CH, McDearmon EL **Year** 2008

Authors Joseph S. Takahashi, Hee-Kyung Hong, Caroline H. Ko & Erin L. McDearmon

Report Name The genetics of mammalian circadian order and disorder: implications for physiology and disease

Publication Nature Reviews Genetics

Issue-page numbers 9, 764-775 (October 2008)

URL http://www.nature.com/nrg/journal/v9/n10/abs/nrg2430.html

Abstract

Circadian cycles affect a variety of physiological processes, and disruptions of normal circadian biology therefore have the potential to influence a range of disease-related pathways. The genetic basis of circadian rhythms is well studied in model organisms and, more recently, studies of the genetic basis of circadian disorders has confirmed the conservation of key players in circadian biology from invertebrates to humans. In addition, important advances have been made in understanding how these molecules influence physiological functions in tissues throughout the body. Together, these studies set the scene for applying our knowledge of circadian biology to the understanding and treatment of a range of human diseases, including cancer and metabolic and behavioural disorders.

Keywords

Takahashi M

Year 2012

Authors Masaya Takahashi

Report Name Prioritizing sleep for healthy work schedules

Publication Journal of Physiological

Issue-page numbers 2012, 31:6 doi:10.1186/1880-6805-31-6

URL http://www.biomedcentral.com/content/pdf/1880-6805-31-6.pdf

Abstract

Good sleep is advantageous to the quality of life. Sleep-related benefits are particularly helpful for the working class, since poor or inadequate amounts of sleep degrade work productivity and overall health. This review paper explores the essential role of sleep in healthy work schedules and primarily focuses on the timing of sleep in relation to the work period (that is, before, during and after work). Data from laboratory, field and modeling studies indicate that consistent amounts of sleep prior to work are fundamental to improved performance and alertness in the workplace. In addition, planned naps taken during work maintain appropriate levels of waking function for both daytime and night-time work. Clearly, sufficient sleep after work is vital in promoting recovery from fatigue. Recent data also suggest that the time interval between shifts should be adjusted according to the biological timing of sleep. Although sleep is more likely to be replaced by job and other activities in the real life, research shows that it is worthwhile to revise the work schedules in order to optimize sleep before, sometime during and after the work period. Therefore, we suggest establishing work-sleep balance, similar to work-life balance, as a principle for designing and improving work schedules.

Keywords Alertness; napping; productivity; recovery; sleep

Takahashi Y, Katsuura T, Shimomura Y, Iwangaga K

Year 2011

Authors Yoshika TAKAHASHI, Tetsuo KATSUURA, Yoshihiro SHIMOMURA and Koichi IWANAGA

Report Name Prediction Model of Light-induced Melatonin Suppression

Publication Journal of Light & Visual Environment

Issue-page numbers Vol. 35 (2011) , No. 2 123

URL http://www.jstage.jst.go.jp/article/jlve/35/2/35_123/_article

Abstract The prediction method of melatonin suppression values was based on previous studies related to melatonin suppression and pupil constriction. Estimated values that considered pupil constriction were larger than the actual suppression values. We focused on the pupil constriction and its correction factor to interpret the action spectrum for the properties of the melatonin suppression model. When the correction factor was used to modify the model, actual suppression values were almost completely predictable. These factors suggest that it might be possible to explain the indescribable results.

Keywords circadian, melatonin, action spectrum, pupil, photoreceptor, suprachiasmatic nucleus

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Takano A, Shimizu K, Kani S et al.

Year 2000

Authors Takano A, Shimizu K, Kani S et al.

Report Name Cloning and characterization of rat casein kinase 1epsilon

Publication FEBS Lett

Issue-page numbers 477:106–112 doi:10.1016/S0014-5793(00)01755-5. PMID:10899319

URL http://www.uniprot.org/citations/10899319

Abstract Genes differentially expressed in the subjective day and night in the rat suprachiasmatic nucleus (SCN) were surveyed by differential display. A gene homologous to human casein kinase 1epsilon (CK1epsilon) was isolated, which initially appeared to be expressed in the suprachiasmatic nucleus (SCN) in a circadian manner. We here describe the cDNA cloning of the rat CK1epsilon and characterization of the protein products. The rCK1epsilon is predominantly expressed in the brain including the SCN, binds and phosphorylates mPer1, mPer2, and mPer3 in vitro, and translocates mPer1 and mPer3, but not mPer2, to the cell nucleus depending on its kinase activity when coexpressed with these Per proteins in COS-7 cells.

Keywords

Takasu NN, Hashimoto S, Yamanaka Y, et al. **Year** 0

Authors Nana N. Takasu, Satoko Hashimoto, Yujiro Yamanaka, Yusuke Tanahashi, Ayano Yamazaki, Sato Honma, and Ken-ichi Honma

Report Name Repeated exposures to daytime bright light increase nocturnal melatonin rise and maintain circadian phase in young subjects under fixed sleep schedule

Publication AJP - Regu Physiol

Issue-page numbers December 2006 vol. 291 no. 6 R1799-R1807

URL http://ajpregu.physiology.org/content/291/6/R1799.abstract

Abstract Effects of two different light intensities during daytime were examined on human circadian rhythms in plasma melatonin, core body temperature, and wrist activity under a fixed sleep schedule. Sleep qualities as indicated by polysomnography and subjective sleepiness were also measured. In the first week, under dim light conditions (~10 lx), the onset and peak of nocturnal melatonin rise were significantly delayed, whereas the end of melatonin rise was not changed. The peak level of melatonin rise was not affected. As a result, the width of nocturnal melatonin rise was significantly shortened. In the second week, under bright light conditions (~5,000 lx), the phases of nocturnal melatonin rise were not changed further, but the peak level was significantly increased. Core body temperature at the initial sleep phase was progressively elevated during the course of dim light exposure and reached the maximum level at the first night of bright light conditions. Subjective sleepiness gradually declined in the course of dim light exposure and reached the minimum level at the first day of bright light. These findings indicate that repeated exposures to daytime bright light are effective in controlling the circadian phase and increasing the peak level of nocturnal melatonin rise in plasma and suggest a close correlation between phase-delay shifts of the onset of nocturnal melatonin rise or body temperature rhythm and daytime sleepiness.

Keywords light intensity; core temperature; sleepiness; polysomnography; entrainment

Tamarkin L, Baird CJ, Almeida OFX **Year** 1985

Authors Tamarkin L, Baird CJ, Almeida OFX

Report Name Melatonin: a coordinating signal for mammalian reproduction?

Publication Science

Issue-page numbers 227:714–720 doi:10.1126/science.3881822. PMID:3881822

URL http://www.sciencemag.org/content/227/4688/714.abstract

Abstract There is a daily rhythm in the production of the pineal hormone melatonin in all mammalian species. Production is stimulated by darkness and inhibited by light. This provides a signal reflecting the changing environmental lighting cycle. In seasonally breeding mammals that use changes in the photoperiod to time their reproductive cycles, temporal signals to the reproductive system are controlled by the daily rhythm in melatonin production.

Keywords

Authors Tamarkin L, Cohen M, Roselle D et al.

Report Name Melatonin inhibition and pinealectomy enhancement of 7,12-dimethylbenz(a)anthracene-induced mammary tumors in the rat

Publication Cancer Res

Issue-page numbers 41:4432–4436. PMID:6796259

URL http://cancerres.aacrjournals.org/content/41/11_Part_1/4432

Abstract The effects of the pineal hormone, melatonin, and of pinealectomy on the incidence of mammary adenocarcinoma in Sprague-Dawley rats treated with 7,12-dimethylbenz(α)-anthracene (DMBA) were investigated. Melatonin (2.5 mg/kg), begun on the same day as DMBA (15 mg) treatment and given daily in the afternoon for 90 days, significantly reduced the incidence of mammary tumors from 79% (control) to 20% (treated) ($p < 0.002$). Rats pinealectomized at 20 days of age and treated with 7 mg of DMBA at 50 days of age had a higher incidence of tumors (88%) compared to control animals (22%). Fifteen mg of DMBA, which resulted in a higher incidence of tumors, reduced the difference between pinealectomized and control animals. Melatonin only partially reversed the effects of pinealectomy, reducing the incidence from 87% (pinealectomy alone) to 63% (pinealectomy plus melatonin); however, the tumor incidence was still lower (27%) in nonpinealectomized, melatonin-treated animals. Assessment of plasma prolactin, luteinizing hormone, follicle-stimulating hormone, estradiol, and cortisol in DMBA-treated tumor-free and tumor-bearing animals revealed a significantly lower plasma prolactin concentration [27 ± 5 (S.E.) ng/ml] in melatonin-treated animals as compared to vehicle-treated animals [65 ± 8 ng/ml]. The concentration of plasma prolactin was less in melatonin-treated, pinealectomized rats (55 ± 10 ng/ml) as compared to vehicle-treated, pinealectomized animals (101 ± 13 ng/ml). Other hormones were not affected by melatonin treatment. These data support the hypothesis that melatonin inhibits the development of DMBA-induced mammary tumors in the rat while removal of the pineal gland stimulates development of such tumors. Additionally, these experiments provide evidence that these effects may be mediated by a suppression of plasma prolactin levels.

Keywords

Tan D, Hardeland R, Manchester LC, ***Year*** 2012

Authors Dun-Xian Tan, Ruediger Hardeland, Lucien C. Manchester, Sergio Rosales-Corral, Ana Coto-Montes, Jose Antonio Boga, Russel J. Reiter

Report Name The emergence of naturally-occurring melatonin isomers and their proposed nomenclature

Publication Journal of Pineal Research

Issue-page numbers Accepted Article (Accepted, unedited articles published online for future issues)

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2012.00979.x/abstract

Abstract Melatonin was considered to be the sole member of this natural family. The emergence of naturally-occurring melatonin isomers has opened an exciting new research area. Currently, several melatonin isomers have been identified in wine and these molecules are believed to be synthesized by either yeasts or bacteria. A tentative nomenclature for the melatonin isomers is proposed in this article. It will be important to explore whether all organisms have the capacity to synthesize melatonin isomers, especially under the conditions of environmental stress. These isomers probably share many of biological functions of melatonin, but their activities seem to exceed those of melatonin. Based on limited available information, it seems that melatonin isomers differ in their biosynthetic pathways from melatonin. Especially in those compounds in which the aliphatic side chair is not attached to ring atom 3, the starting material may not be tryptophan. Also, the metabolic pathways of melatonin isomers remain unknown. This therefore is another promising area of research to explore. It is our hypothesis that melatonin isomers would increase the performance of yeasts and probiotic bacteria during the processes of fermentation. Therefore, yeasts producing elevated levels of these isomers might have a superior alcohol tolerance and be able to produce higher levels of alcohol. This can be tested by comparing existing yeast strains differing in alcohol tolerance. Selection for melatonin isomers may become a strategy for isolating more resistant yeast and Lactobacillus strains, which can be of interest for industrial alcohol production and quality improvements in bacterially fermented foods such as kimchi.

Keywords melatonin; melatonin isomer; antioxidant; nomenclature; fermentation; kimchi; beer; wine

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Tannenbaum MG, Reiter RJ, Vaughan MK et al. ***Year*** 1987

Authors Tannenbaum MG, Reiter RJ, Vaughan MK et al.

Report Name Adrenalectomy prevents changes in rat pineal melatonin content and N-acetyltransferase activity induced by acute insulin stress

Publication J Pineal Res

Issue-page numbers 4:395–402 doi:10.1111/j.1600-079X.1987.tb00879.x. PMID:3312570

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1987.tb00879.x/abstract?

Abstract The activity of N-acetyltransferase (NAT) the content of melatonin (MEL) in the rat pineal have been shown to be sensitive to several types of stressors. This study was designed to assess the role of the adrenals in mediating the effect of one such stressor, insulin-induced hypoglycemia, on pineal synthetic activity. Intact bilaterally adrenalectomized (ADX) adult male rats were kept under light:dark cycles of 14:10 (lights on 0600 h) injected intraperitoneally with 10 IU insulin at 1300 h, groups (n = 8) were killed 2, 3, or 4 h postinjection. Plasma catecholamines were assayed by means of high performance liquid chromatography radioimmunoassay was used to assess pineal NAT activity MEL content. All injected groups were rendered hypoglycemic by insulin administration. Compared to uninjected controls, plasma epinephrine in hypoglycemic intact rats rose after 2 h, whereas epinephrine did not change in hypoglycemic ADX animals. The increase in epinephrine in intact animals was correlated with a rise in NAT activity at 2 h. Moreover, pineal MEL content at 2, 3, 4 h was significantly greater than control values. In contrast, no changes in pineal biosynthetic function were found in ADX rats. This differential response by intact ADX rats suggests that an adrenal product (possibly epinephrine) is responsible for mediating the stimulatory effects of acute insulin-induced hypoglycemic stress on the rat pineal.

Keywords pineal gland; adrenal gland; hypoglycemia

Tapia-Osorioa A, Salgado-Delgadob R, Angeles-Castellanosa M, Escobar C **Year** 2013

Authors Araceli Tapia-Osorioa, Roberto Salgado-Delgadob, Manuel Angeles-Castellanosa, Carolina Escobar

Report Name Disruption of circadian rhythms due to chronic constant light leads to depressive and anxiety-like behaviors in the rat

Publication Behavioural Brain Research

Issue-page numbers Volume 252, 1 September 2013, Pages 1–9

URL http://www.sciencedirect.com/science/article/pii/S0166432813003070

Abstract Depression is strongly associated with the circadian system, disruption of the circadian system leads to increased propensity to disease and to mood disorders including depression. The present study explored in rats the effects of circadian disruption by constant light on behavioral and hormonal indicators of a depressive-like condition and on the biological clock, the suprachiasmatic nucleus (SCN). Exposure to constant light for 8 weeks resulted in loss of circadian patterns of spontaneous general activity, melatonin and corticosterone. Moreover these rats exhibited anhedonia in a sucrose consumption test, and increased grooming in the open-field test, which reflects an anxiety-like condition. In the SCN decreased cellular activation was observed by c-Fos immunohistochemistry. In rats exposed to constant darkness, circadian behavioral and hormonal patterns remained conserved, however mild depresive-like indicators were observed in the anhedonia test and mild anxiety-like behaviors were observed in the open field test. Data indicate that chronic conditions of LL or DD are both disruptive for the activity of the SCN leading to depression- and anxiety-like behavior. Present results point out the main role played by the biological clock and the risk of altered photoperiods on affective behavior.

Keywords Circadian disruption; Depression; Suprachiasmatic nucleus; Constant darkness; Light pollution; Melatonin

Taylor HR, West S, Muñoz B, et al. **Year** 1992

Authors Taylor HR, West S, Muñoz B, Rosenthal FS, Bressler SB, Bressler NM.

Report Name The long-term effects of visible light on the eye

Publication Arch Ophthalmol

Issue-page numbers 1992;110(1):99-104.

URL http://archopht.ama-assn.org/cgi/content/abstract/110/1/99

Abstract The relationship between exposure to sunlight and senile cataract, age-related macular degeneration, pterygium, and climatic droplet keratopathy was examined in 838 watermen who work on the Chesapeake Bay. The presence and severity of lenticular, corneal, and macular changes were assessed by either clinical examination or from stereo macular photographs. From detailed exposure histories, ocular exposure was estimated for three bands of visible radiation—violet (400 to 450 nm), blue (400 to 500 nm), or all visible (400 to 700 nm)—as well as for UV-A (320 to 340 nm) and UV-B (290 to 320 nm). The results with each band of visible radiation were similar. Neither cortical nor nuclear cataract was associated with ocular exposure to blue or all visible radiation, but pterygium and climatic droplet keratopathy were more common with higher exposures. Compared with age-matched controls, patients with advanced age-related macular degeneration (geographic atrophy or disciform scarring) had significantly higher exposure to blue or visible light over the preceding 20 years (odds ratio, 1.36 [1.00 to 1.85]) but were not different in respect to exposure to UV-A or UV-B. These data suggest that high levels of exposure to blue or visible light may cause ocular damage, especially later in life, and may be related to the development of age-related macular degeneration.

Keywords

Authors Taylor HR, West SK, Rosenthal FS, Muñoz B, Newland HS, Abbey H, et al.

Report Name Effect of ultraviolet radiation on cataract formation

Publication N Engl J Med

Issue-page numbers 319:1429-1433December 1, 1988

URL http://www.nejm.org/doi/pdf/10.1056/NEJM198812013192201

Abstract

To investigate the relation of ultraviolet radiation and cataract formation, we undertook an epidemiologc survey of 838 watermen (mean age, 53 years) who worked on Chesapeake Bay. The annual ocular exposure was calculated from the age of 16 for each waterman by combining a detailed occupational history with laboratory and field measurements of sun exposure. Cataracts were graded by ophthalmologic examination for both type and severity.

Some degree of cortical cataract was found in 111 of the watermen (13 percent), and some degree of nuclear cataract in 229 (27 percent). Logistic regression analysis showed that high cumulative levels of ultraviolet B exposure significantly increased the risk of cortical cataract (regression coefficient, 0.70; P = 0.04). A doubling of cumulative exposure increased the risk of cortical cataract by a factor of 1.60 (95 percent confidence interval, 1.01 to 2.64). Those whose annual average exposure was in the upper quartile had a risk increased by 3.30 (confidence interval, 0.90 to 9.97) as compared with those in the lowest quartile. Analysis using a serially additive expected-dose model showed that watermen with cortical lens opacities had a 21 percent higher average annual exposure to ultraviolet B (t-test, 2.23; P = 0.03). No association was found between nuclear cataracts and ultraviolet B exposure or between cataracts and ultraviolet A exposure.

We conclude that there is an association between exposure to ultraviolet B radiation and cataract formation, which supports the need for ocular protection from ultraviolet B.

Keywords

Taylor PJ, Pocock SJ

Year 1972

Authors Taylor PJ, Pocock SJ

Report Name Mortality of shift and day workers 1956–68

Publication Br J Ind Med

Issue-page numbers 29:201–207. PMID:5021999

URL http://oem.bmj.com/content/29/2/201.abstract

Abstract Little research has been reported about the long-term effects of shift work. An investigation is described on 8 603 male manual workers from 10 organizations in England and Wales designed to assess the mortality experience of day, shift, and ex-shift workers. Three major types of shift system were involved. All had been employed by the same organization for not less than 10 years and the follow-up period was between 1956 and 1968. Only 22 men could not be completely traced and the cause of death was obtained for all but eight of the 1 578 deaths. Man-years at risk for each group were calculated in order to compare observed deaths with those expected from national mortality rates. The overall number of deaths was very close to that expected and no significant excess mortality was found in either the shift or ex-shift groups. Shift workers in some age groups had higher mortality than expected but this was not consistent between either organizations or types of shift work. A study of 14 main causes of death revealed some differences from national experience in both day and shift workers but these can be attributed to regional and occupational differences. To eliminate any occupational factor the mortality of skilled craftsmen and their mates was compared for day and shift work with no evidence of any shift work effect. The results lead to the conclusion that shift work would appear tc have no adverse effect upon mortality.

Keywords

Tei H, Okamura H, Shigeyoshi Y et al.

Year 1997

Authors Tei H, Okamura H, Shigeyoshi Y et al.

Report Name Circadian oscillation of a mammalian homologue of the Drosophila period gene

Publication Nature

Issue-page numbers 389:512–516 doi:10.1038/39086. PMID:9333243

URL http://www.nature.com/nature/journal/v389/n6650/abs/389512a0.html

Abstract Many biochemical, physiological and behavioural processes in organisms ranging from microorganisms to vertebrates exhibit circadian rhythms1. In Drosophila, the gene period (per) is required for the circadian rhythms of locomotor activity and eclosion behaviour2. Oscillation in the levels of per mRNA and Period (dPer) protein in the fly brain is thought to be responsible for the rhythmicity3,4. However, no per homologues in animals other than insects have been identified. Here we identify the human and mouse genes (hPER and mPer, respectively) encoding PAS-domain (PAS, a dimerization domain present in Per, Amt and Sim)-containing polypeptides that are highly homologous to dPer. Besides this structural resemblance, mPer shows autonomous circadian oscillation in its expression in the suprachiasmatic nucleus, which is the primary circadian pacemaker in the mammalian brain5,6. Clock, a mammalian clock gene encoding a PAS-containing polypeptide7,8, has now been cloned: it is likely that the Per homologues dimerize with other molecule(s) such as Clock through PAS–PAS interaction in the circadian clock system.

Keywords

Authors Tenkanen L, Sjöblom T, Härmä M

Report Name Joint effect of shift work and adverse life-style factors on the risk of coronary heart disease

Publication Scand J Work Environ Health

Issue-page numbers 24:351–357. PMID:9869306

URL http://www.sjweh.fi/download.php?abstract_id=355&file_nro=1

Abstract

Objectives The joint effect of shift work and certain adverse life-style factors on coronary heart disease (CHD) was studied.
Methods Base-line measurements were obtained for a 6-year follow-up of an industrially employed cohort (N=1806), whose shiftwork status was recorded from a questionnaire filled out by a sample of the cohort. The CHD end points (codes 410414 of the 9th revision of the International Classification of Diseases) were obtained from official Finnish registers. In order that the joint effects of shift work and life-style factors on the risk of CHD could be studied, dichotomized variables and their combinations as a dummy variable system in Cox's proportional hazards models were used.
Results The relative risks were 1, 1.6 [95% confidence interval (95% CI) 1.1-2.51, 1.3 (95% CI 0.9-2.1), and 2.7 (95% CI 1 . 8 4 . 1) for the following combinations of shift work (SW) and smoking (SM): SW-&SM-, SW-&SM+, SW+&SM-, and SW+&SM+, respectively; and the corresponding figures for shift work and obesity (BMI 228 kg/m2) were 1,1.2 (95% CI0.8-1.9), 1.3 (95% CI0.9-1.9), and 2.3 (95% CI 1.5-3.6), respectively. Inboth cases the effect was at least multiplicative. For the shift workers the relative risk for CHD rose gradually with increasing numbers of adverse life-style factors, but for the day workers there was no clear dose-response pattern. C O ~ C ~ U SS~hOift~ wSo rk seems to trigger the effect of other, lifestyle-related risk factors of CHD and therefore calls for active prevention among shift workers.

Keywords circadian rhythm, interaction, obesity, physical activity, smoking, thrombosis

Terman M, Terman JS **Year** 2005

Authors Michael Terman, Jiuan Su Terman

Report Name Light Therapy

Publication In: Principles and Practice of Sleep Medicine, 4th edition, Edited by Kryger MH, Roth T, Dement WC

Issue-page numbers Philadelphia, Elsevier, 2005, pp 1424-1442

URL http://www.day-lights.com/light-therapy-news/downloads/light-therapy-wp.pdf

Abstract

The susceptibility of the circadian system to selective phase shifting by timed light exposure has broad implications for the treatment of sleep-phase and depressive disorders. Light therapies have been devised that can normalize the patterns of delayed sleep phase syndrome (through circadian phase advances) and advanced sleep phase syndrome (through circadian phase delays). Doctors and patients need to become cognizant of the daily intervals when light exposure—and darkness—can facilitate or hamper adjustment. The primary intervals lie at the edges of the “subjective night,” which coincide with the tails of the nocturnal melatonin cycle, but they can be inferred clinically through a chronotype questionnaire. The lighting schedule may have to be continually adjusted as the subjective night shifts gradually in the desired direction. The treatment strategy for seasonal and nonseasonal depressive disorders is similar. In winter depression, the magnitude of phase advances correlates with the degree of mood improvement, and the optimum timing of light therapy must be specified relative to circadian rather than solar time. Apart from its use as a monotherapy, light therapy in both outpatient and inpatient trials indicates that light therapy accelerates remission of nonseasonal depression in conjunction with medication. Exploratory applications for treatment of antepartum and premenstrual depression, bulimia nervosa, sleep disruption of senile dementia, and shift work and jet lag disturbance are considered. The chapter provides the clinician with guidelines for selecting lighting apparatus based on safety, efficacy, and comfort factors; summarizes adverse effects of light overdose; and offers a straightforward protocol for selecting treatment time of day.

Keywords

Authors Terzolo M, Piovesan A, Puligheddu B et al.

Report Name Effects of long-term, low-dose, time-specified melatonin administration on endocrine and cardiovascular variables in adult men

Publication J Pineal Res

Issue-page numbers 9:113–124 doi:10.1111/j.1600-079X.1990.tb00699.x. PMID:2177501

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1990.tb00699.x/abstract

Abstract Six healthy adult male volunteers underwent serial blood drawings at 4-hour intervals over 24 hours for the definition of melatonin (MT), prolactin (PRL), cortisol, and testosterone circadian patterns. Serum levels of triiodotironine (T3) and thyroxine (T4) were determined at 0800. Systolic and diastolic blood pressure and heart rate were automatically recorded every 30 minutes for 24 hours. The responses of luteinizing hormone (LH), follicle stimulating hormone (FSH), PRL, thyroid stimulating hormone (TSH), cortisol, and aldosterone to a stimulation test with gonadotrophinreleasing hormone (Gn-RH), thyrotrophin-releasing hormone (TRH), adrenocorticotrophin (ACTH), and testosterone to human chorionic gonadotrophin (HCG) were also evaluated. The same protocol was repeated after a two-month course of treatment with MT, 2 mg per os daily at 1800. After treatment, we recorded a marked elevation of mean serum MT levels with a significant phase-advance of its circadian rhythm. The 24-hour patterns of cortisol and testosterone displayed an anticipation of the morning acrophase of about 1.5 hour (not significant) for cortisol and three hours ($P < 0.05$) for testosterone. PRL pattern was unchanged as well as serum levels of thyroid hormones. The circadian organization of the cardiovascular variables did not show any changes after MT supplementation; the pituitary, adrenal, and testicular responses to specific stimuli were comparable before and after treatment. These results are compatible with the view that the MT signal may provide temporal cues to the neuroendocrine network for the organization of testicular circadian periodicity.

Keywords adrenal; blood pressure; circadian rhythms; heart rate; hormonal responses; melatonin; pituitary; testes

Terzolo M, Revelli A, Guidetti D et al. **Year** 1993

Authors Terzolo M, Revelli A, Guidetti D et al.

Report Name Evening administration of melatonin enhances the pulsatile secretion of prolactin but not of LH and TSH in normally cycling women

Publication Clin Endocrinol (Oxf)

Issue-page numbers 39:185–191 doi:10.1111/j.1365-2265.1993.tb01772.x. PMID:8370131

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1993.tb01772.x/abstract

Abstract

OBJECTIVE The aim of the study was to evaluate the effects of exogenous melatonin on the spontaneous pulsatile release of PRL, TSH and LH in normal women.

DESIGN A double blind placebo-controlled protocol was designed to study seven subjects in the mid follicular phase of two non-consecutive cycles. Two mg of exogenous melatonin or placebo were given at 1600 and 2000 h, and blood samples were collected every 10 minutes from 1800 to 2400 h for hormone determination.

RESULTS Melatonin treatment caused a significant upward resetting of the pulsatile pattern of PRL in six out of seven subjects. Average maximal peak height was significantly increased (median 716 mIU/l (range 198-1433) on melatonin vs 324 mIU/l (212-688) on placebo, P<0.001), nadir value (572 mIU/l (148-1084) vs 216 mIU/l (54-580), P < 0 001) and area under the peak (26352 mIU/l min (5904-93672) vs 12096 mIU/l min (2340-33552), P<0 001), whereas peak number, amplitude and interpeak interval did not change significantly. TSH pulsatility was unaffected by melatonin administration in four out of six subjects. Distribution of LH patterns after melatonin was inhomoge-neous: level of pulsatility was higher in two cases and reduced in three; group analysis did not therefore show significant variation of pulsatility parameters.

CONCLUSIONS Exogenous melatonin has a stimulatory effect on PRL release without affecting the temporal pattern of its pulsatile secretion in normal women. Melatonin has minor, if any, effect on TSH secretion whereas the effect on LH may depend on individual sensitivity.

Keywords

Tetsuo M, Poth M, Markey SP **Year** 1982

Authors Tetsuo M, Poth M, Markey SP

Report Name Melatonin metabolite excretion during childhood and puberty

Publication J Clin Endocrinol Metab

Issue-page numbers 55:311–313 doi:10.1210/jcem-55-2-311. PMID:7085857

URL http://dx.doi.org/10.1210/jcem-55-2-311

Abstract

Daily urinary excretion of conjugated 6-hydroxymelatonin, the major metabolite of the pineal hormone melatonin, has been determined in 54 boys and 47 girls (aged 3–16 yr) and 20 normal adults to determine whether a change in melatonin production is seen during the maturation of reproductive function in humans. There was no correlation between daily excretion rates and age in children, and the excretion rates were similar to those in adults. In addition, children of all ages had normal circadian patterns of 6-hydroxymelatonin excretion from the earliest age tested. A significant increase in 6-hydroxymelatonin excretion was observed at the time of the onset of breast development (Tanner stage II) in girls. No similar difference was seen during puberty in males. The significance of this difference in Tanner II girls is not known.

Keywords

Authors Pooja Thakurdas, Shweta Sharma, Boynao Sinam, Meenakshi Chib and Dilip Joshi

Report Name NOCTURNAL ILLUMINATION DIMMER THAN STARLIGHT ALTERED THE CIRCADIAN RHYTHM OF ADULT LOCOMOTOR ACTIVITY OF A FRUIT FLY

Publication Chronobiology International

Issue-page numbers 27:1, 83-94

URL http://informahealthcare.com/doi/abs/10.3109/07420520903398567

Abstract The effects of nocturnal irradiance tenfold dimmer than starlight intensity on the locomotor activity rhythm of Drosophila jambulina were investigated in two types of light-dark (12 h:12 h) cycles, in which light intensity of the photophase was 10 lux while that of the scotophase was either 0 lux for control flies or 0.0006 lux for experimental flies. Activity onset in the experimental flies was 5.4 h prior to lights-on, so it occurred around midnight. However, activity onset of the control flies coincided almost with the lights-on. Nevertheless, activity offset was the same in both groups, occurring at lights-off. Duration of the active phase (α) and activity passes/fly/cycle (APC) in the experimental flies was far greater than in controls. After-effects of the nocturnal illumination of the light-dark cycles when the flies were transferred to constant darkness were evident as the period of the free-running rhythm was shortened, α was lengthened, and APC was enhanced in the experimental compared to control flies. Thus, very low photic sensitivity of these flies appears to be a physiological adaptation to dim-light ambiance in its natural breeding site in the field.

Keywords Drosophila jambulina, Light entrainment, Nocturnal illumination, Circadian activity rhythm

Authors Pooja Thakurdas, Shweta Sharma, Keny Vanlalhriatpuia, Boynao Sinam, Meenakshi Chib, Ashok Shivagaje and Dilip Joshi

Report Name LIGHT AT NIGHT ALTERS THE PARAMETERS OF THE ECLOSION RHYTHM IN A TROPICAL FRUIT FLY, DROSOPHILA JAMBULINA

Publication Chronobiology International

Issue-page numbers 26:8, 1575-1586

URL http://informahealthcare.com/doi/abs/10.3109/07420520903529765

Abstract We investigated the effects of natural light at night (LAN) in the field and artificial LAN in the laboratory on the circadian rhythm of pupal eclosion in a tropical wild type strain of Drosophila jambulina captured at Galle, Sri Lanka (6.1oN, 80.2oE). The influence of natural LAN, varying in intensity from 0.004 lux (starlight intensity) to 0.45 lux (moonlight intensity), on the entrainment pattern of the circadian rhythm of eclosion at 25o ± 0.5oC was examined by subjecting the mixed-aged pupae to natural cycles of light and darkness at the breeding site of this strain in the field. The eclosion peak was 2 h prior to sunrise, and the 24 h rhythmicity was the most robust. Effects of artificial LAN at 25o ± 0.5oC were determined in the laboratory by subjecting pupae to LD 12:12 cycles in which the light intensity of the photophase was 500 lux in all LD cycles, while that of the scotophase was either 0 lux (complete darkness, DD), 0.5, 5, or 50 lux. In the 0 lux LAN condition (i.e., the control experiment), the eclosion peak was 2 h after lights-on, and the 24 h eclosion rhythm was not as strong as in the 0.5 lux LAN condition. The entrainment pattern in 0.5 lux LAN was strikingly similar to that in the field, as the 0.5 lux LAN condition is comparable to the full moonlight intensity in the tropics. LAN at 0.5 lux dramatically altered both parameters of entrainment, as the eclosion peak was advanced by 4 h and the 24 h eclosion rhythm was better than that of the control experiment. LAN at 5 lux, however, resulted in a weak eclosion rhythm that peaked in the subjective forenoon. Interestingly, the 50 lux LAN condition rendered the eclosion events unambiguously arrhythmic. After-effects of LAN on the period (τ) of the free-running rhythm and the nature of eclosion rhythm were also determined in DD by a single LD 12:12 to DD transfer. After-effects of the LAN intensity were observed on both the τ and nature of the eclosion rhythm in all four experiments. Pupae raised in 0.5 lux LAN exhibited the shortest τ (20.6 ± 0.2 h, N = 11 for this and subsequent values) and the most robust rhythm, while pupae raised in 50 lux LAN had the longest τ (29.5 ± 0.2 h) and weakest rhythm in DD. Thus, these results demonstrate the intensity of LAN, varying from 0 to 50 lux, profoundly influences the parameters of entrainment as well as free-running rhythmicity of D. jambulina. Moreover, the observed arrhythmicity in LD 12:12 cycles caused by the 50 lux LAN condition appeared to be the masking effect of relatively bright light at night, as the LD 12:12 to DD transfer restored the rhythmicity, although it was rather weak.

Keywords Circadian rhythm, Drosophila jambulina, Eclosion, LAN, Light at night

Authors Kavita Thapan, Josephine Arendt and Debra J Skene

Report Name An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans

Publication The Journal of Physiology

Issue-page numbers 535, 261-267.

URL http://jp.physoc.org/content/535/1/261.full

Abstract

1.

Non-image forming, irradiance-dependent responses mediated by the human eye include synchronisation of the circadian axis and suppression of pineal melatonin production. The retinal photopigment(s) transducing these light responses in humans have not been characterised.

2.

Using the ability of light to suppress nocturnal melatonin production, we aimed to investigate its spectral sensitivity and produce an action spectrum. Melatonin suppression was quantified in 22 volunteers in 215 light exposure trials using monochromatic light (30 min pulse administered at circadian time (CT) 16-18) of different wavelengths (λmax 424, 456, 472, 496, 520 and 548 nm) and irradiances (0.7-65.0 μW cm−2).

3.

At each wavelength, suppression of plasma melatonin increased with increasing irradiance. Irradiance-response curves (IRCs) were fitted and the generated half-maximal responses (IR50) were corrected for lens filtering and used to construct an action spectrum.

4.

The resulting action spectrum showed unique short-wavelength sensitivity very different from the classical scotopic and photopic visual systems. The lack of fit ($r^2 < 0.1$) of our action spectrum with the published rod and cone absorption spectra precluded these photoreceptors from having a major role. Cryptochromes 1 and 2 also had a poor fit to the data. Fitting a series of Dartnall nomograms generated for rhodopsin-based photopigments over the λmax range 420-480 nm showed that rhodopsin templates between λmax 457 and 462 nm fitted the data well ($r^2 \geq 0.73$). Of these, the best fit was to the rhodopsin template with λmax 459 nm ($r^2 = 0.74$).

5.

Our data strongly support a primary role for a novel short-wavelength photopigment in light-induced melatonin suppression and provide the first direct evidence of a non-rod, non-cone photoreceptive system in humans.

In addition to image generation, the mammalian eye is capable of detecting changes in environmental light irradiance resulting in non-image forming light responses. Non-image forming, irradiance-dependent responses in humans include synchronisation of the circadian clock (Arendt & Broadway, 1986; Czeisler et al. 1986; Boivin et al. 1996; Zeitzer et al. 2000), suppression of pineal melatonin production (Lewy et al. 1980; Bojkowski et al. 1987; McIntyre et al. 1989; Brainard et al. 1997; Zeitzer et al. 2000), elevation of core body temperature (Badia et al. 1991), pupil constriction, reduced slow eye movements and enhanced alertness (Badia et al. 1991; Cajochen et al. 2000). Current evidence points to these responses being mediated by the eyes. For example, melatonin suppression cannot be induced in blindfolded or bilaterally enucleated subjects (Czeisler et al. 1995) or by extraocular light exposure (Lockley et al. 1998). In addition, only non-24 h (free running) circadian rhythms were observed in bilaterally enucleated people (Lockley et al. 1997; Skene et al. 1999), suggesting that, in the absence of eyes, the light-dark cycle is unable to synchronise the human circadian clock to the 24-h day.

The neural pathways mediating some non-image forming responses are anatomically distinct from the classical visual pathways. Circadian (phase shifting) and acute (melatonin suppression) responses to ocular light are transmitted from a discrete subset of retinal ganglion cells via the retinohypothalamic tract (RHT) to the hypothalamic suprachiasmatic nuclei (SCN), the site of the human circadian pacemaker (Moore et al. 1995). Efferent signals from the SCN are transmitted through a multisynaptic pathway (hypothalamic subparaventricular nuclei, thoracic intermediolateral cell column, superior cervical ganglia) to the pineal gland and acute suppression of melatonin occurs (Klein & Moore, 1979; Larsen et al. 1998).

Although the retinal rod and cone cells are vital for image formation, their role in non-image forming light responses may not be as essential. Recent studies using rodless/coneless mice have shown that novel non-rod, non-cone photoreceptor(s) may mediate circadian photoentrainment (Freedman et al. 1999), acute light responses (melatonin suppression) (Lucas et al. 1999) and pupil constriction (Lucas et al. 2001). Several candidate opsin-based photopigments have been identified including vertebrate

ancient opsin (Soni & Foster, 1997), melanopsin (Provencio et al. 2000) and OP479 (Lucas et al. 2001). A role for a retinal vitamin B2-based photopigment, cryptochrome, in mammalian circadian photoentrainment has also been proposed (Miyamoto & Sancar, 1998). A recent report, however, has shown the classical opsins and cryptochromes to be functionally redundant in mediating light masking of behaviour in mice (Selby et al. 2000). Whether these photoreceptors are functionally redundant in circadian photoentrainment and melatonin suppression remains to be determined.

The retinal photopigment(s) mediating non-image forming light responses in humans have not been characterised. Identification of a photopigment requires investigation of the spectral sensitivity of the light-dependent response and construction of an action spectrum. Here we report the first complete action spectrum conducted in humans. Suppression of night-time melatonin production was used as the light-dependent response. Although previous research has shown wavelength dependence of melatonin suppression (Brainard et al. 1985, 2001; Skene et al. 1999) and suggested that an intact trichromatic visual system was not essential (Ruberg et al. 1986), these studies have fallen short of producing an action spectrum to characterise the photopigment. Our action spectrum data describe a novel opsin-based, non-rod, non-cone photoreceptor system in the human retina.

Keywords

Thieden E, Philipsen PA, Sandby-Møller J, et al. ***Year*** 2004

Authors Thieden E, Philipsen PA, Sandby-Møller J, Heydenreich J, Wulf HC.

Report Name Proportion of lifetime UV dose received by children, teenagers and adults based on time stamped personal dosimetry.

Publication Journal of Investigative Dermatology

Issue-page numbers (2004) 123, 1147–1150; doi:10.1111/j.0022-202X.2004.23466.x

URL http://www.nature.com/jid/journal/v123/n6/full/5602607a.html

Abstract

Ultraviolet (UV) reduction campaigns since 1986 were based on the estimation that individuals get 80% of their cumulative lifetime UV dose by the age of 18. To investigate if this estimation is true, we compared annual UV doses received during life in 164 Danish volunteers: children, teenagers, indoor workers, and golfers (age range 4–67 y) who recorded sun exposure behavior in diaries and carried personal UV dosimeters, measuring time-stamped UV doses. The annual UV dose did not significantly correlate with age but the variation in annual UV dose was high (median 166 SED (standard erythema dose), 95% range: 37–551 SED). The annual UV dose did correlate with days with risk behavior (sunbathing/exposing upper body) ($r=0.51$, $p<0.001$) and in adults also with hours performing outdoor sports ($r=0.39$, $p<0.001$), gardening, and sun-bed sessions ($r=0.26$, $p=0.02$). Teenagers had significantly more days with risk behavior than adults (21 vs 13 d, $p=0.006$) but not than children (15 d). No differences in UV dose among the age groups were found on workdays. Only 25% of the lifetime UV dose was received before the age of 20 and the annual UV dose was thus independent of age. Reduction of cumulative lifetime UV dose could be obtained by minimizing risk behavior.

Keywords children, diary, risk, skin cancer, UV dosimeter

Thieden E, Philipsen PA, Wulf HC **Year** 2006

Authors Thieden E, Philipsen PA, Wulf HC.

Report Name Ultraviolet radiation exposure pattern in winter compared with summer based on time-stamped personal dosimeter readings

Publication The British journal of dermatology

Issue-page numbers Volume: 154, Issue: 1, Pages: 133-138

URL http://www.mendeley.com/research/ultraviolet-radiation-exposure-pattern-winter-compared-summer-based-timestamped-personal-dosimeter-readings/

Abstract BACKGROUND: Personal annual ultraviolet (UV) radiation data based on daily records are needed to develop protective strategies. OBJECTIVES: To compare UV radiation exposure patterns in the winter half-year (October-March) and the summer half-year (April-September) for Danish indoor workers. METHODS: Nineteen indoor workers (age range 17-56 years) wore personal UV dosimeters, measuring time-stamped UV doses continuously during a year. The corresponding sun exposure behaviour was recorded in diaries. Similar data were collected for 28 volunteers during sun holidays in the winter half-year. The relationship between UV dose and sun exposure behaviour was analysed. RESULTS: The ambient UV dose during the winter in Denmark (at 56 degrees N) was 394 standard erythema doses (SED) or 10.5% of the annual ambient UV dose. In winter compared with summer the subjects had: (i) a lower percentage of ambient UV radiation, 0.82% vs. 3.4%; (ii) a lower solar UV dose in Denmark, 3.1 SED (range 0.2-52) vs. 133 SED (range 69-363); (iii) less time outdoors per day with positive dosimeter measurements, 10 min vs. 2 h; and (iv) no exposure (0 SED) per day on 77% vs. 19% of the days. Sun holidays outside Denmark in winter gave a median 4.3 SED per day (range 0.6-7.6) and 26 SED (range 3-71) per trip. CONCLUSIONS: In the winter half-year indoor workers received a negligible UV dose from solar exposure in Denmark and needed no UV precautions. No UV precautions are needed from November to February during holidays to latitudes above 45 degrees N, while precautions are needed the whole year around at lower latitudes.

Keywords

Ticher A, Haus E, Ron IG et al. **Year** 1996

Authors Ticher A, Haus E, Ron IG et al.

Report Name The pattern of hormonal circadian time structure (acrophase) as an assessor of breast-cancer risk

Publication Int J Cancer

Issue-page numbers 65:591–593 doi:10.1002/(SICI)1097-0215(19960301)65:5<591::AID-IJC6>3.0.CO;2-Y. PMID:8598308

URL http://www.ncbi.nlm.nih.gov/pubmed/8598308

Abstract Through many hormones are secreted in a pulsatile manner, their secretion pattern can be superimposed by a 24-hour sinusoidal curve. The sinusoidal curve is then characterized by the estimated peak clock time location (acrophase), the adjusted mean (mesor) and the amplitude. When the distribution of the acrophases of 12 hormones was compared among women with regard to their age and to the level of risk of developing breast cancer, statistically significant differences were revealed between distribution patterns of acrophases of women with high (n = 12 and 45 circadian profiles) or low (n = 12 and 41 circadian profiles) risk of developing breast cancer. However, when the amplitude/mesor ratios of the corresponding hormonal rhythms were analyzed, significant differences occurred between age groups rather than between risk levels. These observations suggest that the endocrine time structure between individual women can be used as an assessor of breast-cancer risk.

Keywords

Tillett T

Year 2006

Authors Tillett T

Report Name Headliners: Breast Cancer: Decreased Melatonin Production Linked to Light Exposure

Publication Environ Health Perspect

Issue-page numbers 114:A99-A99

URL http://dx.doi.org/10.1289/ehp.114-a99

Abstract article

Keywords light at night, breast cancer, melatonin

Timonen S, Franzas B, Wichmann K

Year 1964

Authors Timonen S, Franzas B, Wichmann K

Report Name Photosensibility of the human pituitary

Publication Ann Chir Gynaecol Fenn

Issue-page numbers 53:165–172. PMID:14163867

URL http://www.ncbi.nlm.nih.gov/pubmed/14163867

Abstract N/A

Keywords

Tischkau SA

Year 0

Authors Shelley A. Tischkau

Report Name AHR and the Circadian Clock

Publication in: The AH Receptor in Biology and Toxicology (ed R. Pohjanvirta)

Issue-page numbers John Wiley & Sons, Inc., Hoboken, NJ, USA. DOI: 10.1002/9781118140574.ch35

URL http://onlinelibrary.wiley.com/doi/10.1002/9781118140574.ch35/summary

Abstract

Summary

This chapter contains sections titled:

* Introduction
* The bHLH-PAS Domain Family
* Molecular Control of Circadian Rhythms
* Clock-Controlled Regulation of AHR Signaling
* Effects of AHR on Endogenous Rhythmicity
* Crosstalk between AHR Signaling and Light Signaling in the Circadian Clock
* Molecular Interactions of AHR and Circadian Clock Components
* Conclusions
* References

Keywords AHR, and circadian clock; circadian rhythms, molecular control; clock-controlled AHR signaling

Authors Toma JG, Amerongen HM, Hennes SC et al.

Report Name Effects of olfactory bulbectomy, melatonin, and/or pinealectomy on three sublines of the Dunning R3327 rat prostatic adenocarcinoma

Publication J Pineal Res

Issue-page numbers 4:321–338 doi:10.1111/j.1600-079X.1987.tb00870.x. PMID:3625464

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1987.tb00870.x/abstract?

Abstract Conventional antiandrogen therapy for prostatic cancer generally results in the death of androgen-dependent cells, resulting in shrinkage of the tumor, followed by regrowth of the tumor as androgen-insensitive cells take over. Because of reported antigonadotropic antineoplastic effects of the pineal hormone melatonin (MEL), we hypothesized that this indole might provide an effective therapy for prostate cancer, as it would be effective against both populations of tumor cells. We used three sublines of the Dunning R3327 rat prostatic adenocarcinoma to determine whether MEL could suppress the growth of these tumors and, if so, by what mechanisms this occurs. In one experiment, we compared the growth of a well-differentiated slow-growing Dunning tumor in rats given MEL combined with the potentiating procedure olfactory bulbectomy (BULBX), with that in rats pinealectomized (PINX) or untreated. Tumor growth in BULBX-MEL rats was significantly suppressed over that in the other two groups, as were the weights of the gonads accessory sex glands. Tumor morphology, DNA concentration, androgen receptor concentration distribution were identical in untreated controls in BULBX-MEL rats, suggesting that the treatment affected all populations of tumor cells equally. With another strain of well-differentiated slow-growing Dunning tumor, we examined the effects of MEL in rats with without BULBX. Reproductive parameters were not suppressed in BULBX-MEL rats and, while there was a trend toward slower tumor growth in this group, this was not significant. Intact rats given MEL grew larger tumors than did control rats but, again, differences were not significant. In a third experiment, we examined a fast-growing androgen insensitive anaplastic Dunning tumor. PINX was without effect on this tumor, but BULBX-MEL resulted in a significant suppression of one of the constants in the logistic equation fitted to the growth curves. This indicates that there were some direct antitumor effects of BULBX-MEL on this tumor strain. We conclude that MEL suppresses growth of some Dunning tumor strains.

Keywords pineal; prostate cancer; Dunning tumors

Authors Tomany SC, Cruickshanks KJ, Klein R, Klein BE, Knudtson MD.

Report Name Sunlight and the 10-year incidence of age-related maculopathy: the Beaver Dam Eye Study

Publication Arch Ophthalmol

Issue-page numbers 2004;122:750-757.

URL http://archopht.ama-assn.org/cgi/content/abstract/122/5/750

Abstract

Objective To examine the association of sunlight exposure and indicators of sun sensitivity with the 10-year incidence of age-related maculopathy (ARM).

Design Population-based cohort study.

Participants We included persons aged 43 to 86 years at the baseline examination from 1988 to 1990, living in Beaver Dam, Wis, of whom 3684 persons underwent 5-year follow-up and 2764 underwent 10-year follow-up.

Methods Data on sun exposure and indicators of sun sensitivity were obtained from a standardized questionnaire administered at baseline and/or follow-up. We determined ARM status by grading stereoscopic color fundus photographs using the Wisconsin Age-Related Maculopathy Grading System.

Main Outcome Measures Incidence and progression of ARM.

Results While controlling for age and sex, we found that participants exposed to the summer sun for more than 5 hours a day during their teens, in their 30s, and at the baseline examination were at a higher risk of developing increased retinal pigment (risk ratio [RR], 3.17; 95% confidence interval [CI], 1.24-8.11; P = .01) and early ARM (RR, 2.14; 95% CI, 0.99-4.61; P = .05) by 10 years than those exposed less than 2 hours per day during the same periods. In participants reporting the highest summer sun exposure levels in their teens and 30s, the use of hats and sunglasses at least half the time during the same periods was associated with a decreased risk of developing soft indistinct drusen (RR, 0.55; 95% CI, 0.33-0.90; P = .02) and retinal pigment epithelial depigmentation (RR, 0.51; 95% CI, 0.29-0.91; P = .02). Participants who experienced more than 10 severe sunburns during their youth were more likely than those who experienced 1 or no burn to develop drusen with a 250-μm diameter or larger (RR, 2.52; 95% CI, 1.29-1.71; P = .01) by the 10-year examination. No relationships were found between UV-B exposure, winter leisure time spent outdoors, skin sun sensitivity, or number of bad sunburns experienced by the time of the baseline examination and the 10-year incidence and progression of ARM or its associated lesions.

Conclusions Few significant relationships between environmental exposure to light and the 10-year incidence and progression of ARM were found in the Beaver Dam Eye Study. Consistent with results from the baseline and 5-year follow-up examinations, significant associations were found between extended exposure to the summer sun and the 10-year incidence of early ARM and increased retinal pigment. A protective effect of hat and sunglasses use by participants while in their teens and 30s against the 10-year incidence of soft indistinct drusen and retinal pigment epithelial depigmentation was also found, but only in those who reported the highest amount of sun exposure during the same periods.

Keywords

Authors Tomany SC, Klein R, Klein BE

Report Name Beaver Dam Eye Study. The relationship between iris color, hair color, and skin sun sensitivity and the 10-year incidence of age-related maculopathy: the Beaver Dam Eye Study

Publication Ophthalmology

Issue-page numbers Volume: 110, Issue: 8, Pages: 1526-1533

URL http://www.mendeley.com/research/relationship-between-iris-color-hair-color-skin-sun-sensitivity-10year-incidence-agerelated-maculopathy-beaver-dam-eye-study/

Abstract PURPOSE: To examine the association between iris color, hair color, and skin sun sensitivity and the 10-year incidence of age-related maculopathy (ARM). DESIGN: Population-based cohort study. PARTICIPANTS: A population of 4926 adults (range, 43-86 years of age at baseline) living in Beaver Dam, Wisconsin, was studied at baseline (1988-1990); of these, 3684 and 2764 subjects, respectively, participated in 5-year and 10-year follow-up examinations. METHODS: Data on hair color at age 15 years and skin responsiveness to sun exposure were obtained from a standardized questionnaire administered at the baseline examination. Iris color was determined with penlight illumination during the baseline examination by using photographic standards. Age-related maculopathy status was determined by grading stereoscopic color fundus photos with the Wisconsin Age-Related Maculopathy Grading System. MAIN OUTCOME MEASURES: Incidence and progression of ARM. RESULTS: When controlling for age and gender, people with brown eyes were significantly more likely to develop soft indistinct drusen (risk ratio RR, 1.53; 95% confidence interval CI, 1.19-1.97; P < 0.01) than were people with blue eyes. However, people with brown eyes were significantly less likely to develop retinal pigment epithelial depigmentation (RR, 0.58; 95% CI, 0.41-0.82; P < 0.01) than were people with blue eyes. When compared with persons with blond hair, persons with brown hair were at decreased risk of developing pigmentary abnormalities (RR, 0.73; 95% CI, 0.53-1.00; P = 0.05). Iris color, hair color, and skin sun sensitivity were not associated with the development of late ARM. CONCLUSION: Iris color and hair color were found to be associated with the 10-year incidence of pigmentary abnormalities. Iris color seems to be inconsistently related to the 10-year incidence of early ARM lesions and the progression of ARM.

Keywords

Torres-Farfan C, Richter HG, Rojas-García P et al. **Year** 2003

Authors Torres-Farfan C, Richter HG, Rojas-García P et al.

Report Name mt1 Melatonin receptor in the primate adrenal gland: inhibition of adrenocorticotropin-stimulated cortisol production by melatonin

Publication J Clin Endocrinol Metab

Issue-page numbers 88:450–458 doi:10.1210/jc.2002-021048. PMID:12519889

URL http://jcem.endojournals.org/content/88/1/450.full.pdf

Abstract Breast cancer risk is high in industrialized societies, and increases as developing countries become more Westernized. The reasons are poorly understood. One possibility is circadian disruption from aspects of modern life, in particular the increasing use of electric power to light the night, and provide a sun-free environment during the day inside buildings. Circadian disruption could lead to alterations in melatonin production and in changing the molecular time of the circadian clock in the suprachiasmatic nuclei (SCN). There is evidence in humans that the endogenous melatonin rhythm is stronger for persons in a bright-day environment than in a dim-day environment; and the light intensity necessary to suppress melatonin at night continues to decline as new experiments are done. Melatonin suppression can increase breast tumorigenesis in experimental animals, and altering the endogenous clock mechanism may have downstream effects on cell cycle regulatory genes pertinent to breast tissue development and susceptibility. Therefore, maintenance of a solar day-aligned circadian rhythm in endogenous melatonin and in clock gene expression by exposure to a bright day and a dark night, may be a worthy goal. However, exogenous administration of melatonin in an attempt to achieve this goal may have an untoward effect given that pharmacologic dosing with melatonin has been shown to phase shift humans depending on the time of day it's given. Exogenous melatonin may therefore contribute to circadian disruption rather than alleviate it.

Keywords

Torres-Farfan C, Rocco V, Monsó C et al. **Year** 2006

Authors Torres-Farfan C, Rocco V, Monsó C et al.

Report Name Maternal melatonin effects on clock gene expression in a nonhuman primate fetus

Publication Endocrinology

Issue-page numbers 147:4618–4626 doi:10.1210/en.2006-0628. PMID:16840546

URL http://endo.endojournals.org/content/147/10/4618.full

Abstract In the adult mammal the circadian system, which allows predictive adaptation to daily environmental changes, comprises peripheral oscillators in most tissues, commanded by the suprachiasmatic nucleus (SCN) of the hypothalamus. The external environment of the fetus is provided by its mother. In primates, maternal melatonin is a candidate to entrain fetal circadian rhythms, including the SCN rhythms of metabolic activity. We found in the 90% of gestation capuchin monkey fetus expression of the clock genes Bmal-1, Per-2, Cry-2, and Clock in the SCN, adrenal, pituitary, brown fat, and pineal. Bmal-1, Per-2, and the melatonin 1 receptor (MT1) showed a robust oscillatory expression in SCN and adrenal gland, whereas a circadian rhythm of dehydroepiandrosterone sulphate was found in plasma. Maternal melatonin suppression changed the expression of Bmal-1, Per-2, and MT1 in the fetal SCN. These effects were reversed by maternal melatonin replacement. In contrast, neither maternal melatonin suppression nor its replacement had effects on the expression of Per-2 and Bmal-1 or MT1 in the fetal adrenal gland or the circadian rhythm of fetal plasma dehydroepiandrosterone sulphate. Our data suggest that maternal melatonin is a Zeitgeber for the fetal SCN but probably not for the adrenal gland.

Keywords

Tortosa F, Puig-Domingo M, Peinado MA et al. *Year* 1989

Authors Tortosa F, Puig-Domingo M, Peinado MA et al.

Report Name Enhanced circadian rhythm of melatonin in anorexia nervosa

Publication Acta Endocrinol (Copenh)

Issue-page numbers 120:574–578. PMID:2728803

URL http://www.eje-online.org/content/120/5/574.abstract

Abstract Abstract. Plasma melatonin circadian profiles were investigated in a group of 4 patients with anorexia nervosa and 4 healthy regularly cycling women. There were no differences in the mean age of both groups, whereas the anorexia nervosa patients had lower mean body weight (37.8 ± 2.0 vs 57.0 ± 4.9 kg) and body mass index (13.9 ± 1.1 vs 20.8 ± 2.0). Samples were collected every 2 h and plasma melatonin was measured by using a RIA with an iodinated tracer. Anorexia nervosa patients exhibited higher diurnal (60.7 ± 1.8 vs 25.4 ± 1.72 pmol/l, P< 0.02) and nocturnal (419.2 ± 37.4 vs 108.0 ± 33.6 pmol/l), P< 0.001) mean plasma melatonin concentrations. There were no differences in the time peak for nocturnal melatonin secretion in both groups, detected at 02.00 h. In anorexia nervosa, the melatonin circadian profile paralleled that observed in the control group, indicating that the increased melatonin values for anorexia nervosa were probably due to an enhanced secretory pineal function rather than an impaired melatonin metabolism. These results suggest a participation of the pineal gland in the pathophysiology of anorexia nervosa.

Keywords

Touitou Y, Fèvre M, Bogdan A et al. *Year* 1984

Authors Touitou Y, Fèvre M, Bogdan A et al.

Report Name Patterns of plasma melatonin with ageing and mental condition: stability of nyctohemeral rhythms and differences in seasonal variations

Publication Acta Endocrinol (Copenh)

Issue-page numbers 106:145–151. PMID:6539550

URL http://www.eje-online.org/content/106/2/145.abstract

Abstract Abstract. Effects of ageing and mental condition on the nyctohemeral and seasonal rhythms of plasma melatonin in human subjects were investigated. Four groups of subjects were formed for a transverse study: 7 healthy young men (24 years), 6 elderly women, 6 elderly men and 6 elderly patients (2 men and 4 women) suffering from senile dementia (70–80 years). The subjects were synchronized. Blood samples were taken every 4 h during 24 h in January, March, June and October. In comparison to young men, the plasma levels of melatonin were markedly decreased (by about one half) in elderly subjects without any difference according to sex or mental condition. Nyctohemeral rhythms of the hormone were validated in all groups and at all sampling sessions. The nyctohemeral acrophases were remarkably stable (around 03.00 h) whatever the season, age or sex. A seasonal variation was found in all groups (except elderly women) with differences between young and elderly subjects: plasma melatonin levels were significantly lower in January than in June in young men, whereas in elderly subjects they were significantly lower in October than in January/March. No significant difference was observed in mesor, amplitude or acrophase of nyctohemeral and seasonal rhythms of plasma melatonin in patients with senile dementia when compared with healthy elderly subjects. The stability of the nyctohemeral peak time whatever the age group or season as opposed to the differences in the seasonal pattern of plasma melatonin according to the age groups raises the problems of both outdoor photoperiod and ageing in ruling the secretion of melatonin in man.

Keywords

Touitou Y, Haus E **Year** 1992

Authors Touitou Y, Haus E

Report Name Biological rhythms and aging

Publication In: Touitou Y & Haus E, Eds. Biologic Rhythms in Clinical and Laboratory Medicine

Issue-page numbers Berling, Heidelberg: Springer-Verlag. pp. 188–207.

URL N/A

Abstract N/A

Keywords

Touitou Y, Motohashi Y, Reinberg A et al. **Year** 1990

Authors Touitou Y, Motohashi Y, Reinberg A et al.

Report Name Effect of shift work on the night-time secretory patterns of melatonin, prolactin, cortisol and testosterone

Publication Eur J Appl Physiol Occup Physiol

Issue-page numbers 60:288–292 doi:10.1007/BF00379398. PMID:2357985

URL http://www.springerlink.com/content/w4633732864463r3/

Abstract In a study of the internal desynchronization of circadian rhythms in 12 shift workers, 4 of them, aged 25–34 years, agreed to be sampled every 2 h during their night shift (0000 hours to 0800 hours). They were oil refinery operators with a fast rotating shift system (every 3–4 days). We found marked changes in the secretory profiles of melatonin, prolactin and testosterone. Melatonin had higher peak-values resulting in a four-times higher amplitude than in controls. With respect to prolactin and testosterone, peak and trough times were erratic and the serum concentrations were significantly decreased in shift workers. Serum cortisol presented a decreased rhythm amplitude together with higher concentrations at 0000 hours in shift workers. This study clearly shows that fast rotating shift-work modifies peak or trough values and rhythm amplitudes of melatonin, prolactin, testosterone and cortisol without any apparent phase shift of these hormones. Whether the large rhythm amplitude of melatonin may be considered as a marker of tolerance to shift work, as reported for body temperature and hand grip strength, since it would help the subjects to maintain their internal synchronization, needs further investigation.

Keywords Shift work - Melatonin - Cortisol - Testosterone - Prolactin - Circadian rhythm

Travis RC, Allen DS, Fentiman IS, Key TJ

Year 2004

Authors Travis RC, Allen DS, Fentiman IS, Key TJ

Report Name Melatonin and breast cancer: a prospective study

Publication J Natl Cancer Inst

Issue-page numbers 96:475–482.doi:10.1093/jnci/djh077 PMID:15026473

URL http://jnci.oxfordjournals.org/content/96/6/475.short

Abstract Background: Experimental data from animals suggest a protective role for the pineal hormone melatonin in the etiology of breast cancer, but results from the few retrospective case–control studies that examined the association in humans have been inconsistent. To determine whether low levels of endogenous melatonin are associated with an increased risk for developing breast cancer, we conducted a prospective nested case–control study among British women. Methods: Concentrations of 6-sulfatoxymelatonin, the main metabolite of melatonin in urine and a validated marker of circulating melatonin levels, were measured by radioimmunoassay in 24-hour urine samples collected from women shortly after enrollment in the prospective Guernsey III Study. Levels of 6-sulfatoxymelatonin were compared among 127 patients diagnosed with breast cancer during follow-up and among 353 control subjects, matched for age, recruitment date, menopausal status, and day of menstrual cycle for premenopausal women or number of years postmenopausal for postmenopausal women. Associations were examined by analyses of covariance and conditional logistic regression. All tests of statistical significance were two-sided. Results: No statistically significant differences in urinary 6-sulfatoxymelatonin concentrations were observed between women who developed breast cancer and control subjects among premenopausal or postmenopausal women (P= .8 and P= .9, respectively). When data from premenopausal and postmenopausal women were combined in a multivariable analysis adjusted for potential confounders and grouped into three categories defined by 6-sulfatoxymelatonin tertiles of control subjects, the level of 6-sulfatoxymelatonin excreted was not statistically significantly associated with the risk of breast cancer (odds ratio [OR] for breast cancer = 0.95, 95% confidence interval [CI] = 0.55 to 1.65, comparing the middle category with the lowest category of 6-sulfatoxymelatonin concentration, and OR = 0.99, 95% CI = 0.58 to 1.70, comparing the highest category with the lowest category). Conclusion: We found no evidence that the level of melatonin is strongly associated with the risk for breast cancer.

Keywords

Travis RC, Allen NE, Peeters PH et al.

Year 2003

Authors Travis RC, Allen NE, Peeters PH et al.

Report Name Reproducibility over 5 years of measurements of 6-sulphatoxymelatonin in urine samples from postmenopausal women

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers 12:806–808. PMID:12917214

URL http://cebp.aacrjournals.org/content/12/8/806.full

Abstract To assess the appropriateness of a single measurement of urinary 6-sulfatoxymelatonin (aMT6S) as a marker for long-term exposure to endogenous melatonin in epidemiological studies, we examined the reproducibility of aMT6S in first morning urine voids collected from 40 postmenopausal women. Urine specimens were collected on three different occasions, and the mean time between the first and the third urine sample was 5.1 years. Urinary aMT6S levels were measured by radioimmunoassay and adjusted for creatinine. The intraclass correlation for aMT6S adjusted for creatinine was 0.56 (95% confidence interval, 0.39–0.73). The classification of aMT6S concentrations in first morning voids from postmenopausal women appears to be sufficiently reproducible to justify its use as a marker for long-term exposure to melatonin in epidemiological studies.

Keywords

Authors Gregory S. Travlos, Ralph E. Wilson, James A. Murrell, Colin F. Chignell, Gary A. Boorman

Report Name The Effect of Short Intermittent Light Exposures on the Melatonin Circadian Rhythm and NMU-Induced Breast Cancer in Female F344/N Rats

Publication Toxicol Pathol

Issue-page numbers January 2001 vol. 29 no. 1 126-136

URL http://tpx.sagepub.com/content/29/1/126.abstract

Abstract We investigated the effects of altered endogenous nighttime melatonin concentrations on mammary tumor production in an N-nitroso-N-methylurea (NMU)-induced breast cancer model in female Fischer 344 (F344)/N rats. Experiments were designed 1) to evaluate whether short-duration intermittent exposures to light at night would affect the nocturnal rise of melatonin, resulting in a decrease in nighttime serum melatonin concentrations, 2) to evaluate whether any suppression of nighttime serum melatonin concentrations could be maintained for a period of weeks, and 3) to determine the effects of suppressed serum melatonin concentrations on the incidence and progression of NMU-induced breast cancer. In vivo studies were used to assess serum melatonin concentrations after 1 day and 2 and 10 weeks of nightly administration of short-duration intermittent light exposure at night and incidence of NMU-induced tumors. Five 1-minute exposures to incandescent light every 2 hours after the start of the dark phase of the light: dark cycle decreased the magnitude of the nocturnal rise of serum melatonin concentrations in rats by approximately 65%. After 2 weeks of nightly intermittent light exposures, an average decrease of the peak nighttime serum melatonin concentrations of approximately 35% occurred. The amelioration continued and, at 10 weeks, peak nighttime serum melatonin concentrations were still decreased, by approximately 25%. Because peak endogenous nighttime serum melatonin values could be moderately suppressed for at least 10 weeks, a 26-week NMU mammary tumor study was conducted. Serum melatonin concentrations and incidence, multiplicity, and weight of NMU-induced mammary tumors were assessed. A group of pinealectomized (Px) animals was also included in the tumor study. No effect on the development of mammary tumors in an NMU-induced tumor model in rats occurred when endogenous nighttime serum melatonin concentrations were moderately suppressed by short-duration intermittent light exposures at night. At necropsy, there were no alterations in mammary tumor incidence (28/40 NMU controls, 28/40 NMU + light, 31/40 NMU + Px), multiplicity (2.18 tumors/tumor-bearing NMU control, 1.89 NMU + light, 2.39 NMU + Px), or average tumor weight (1.20 g NMU control, 1.19 g NMU + light, 0.74 g NMU + Px). Tumor burden had no effect on the serum melatonin cycle. At 26 weeks, however, animals exposed to intermittent light at night exhibited approximately 3-fold higher serum melatonin concentrations as compared with controls. Additionally, rats that had been pinealectomized at 4 weeks of age had serum melatonin concentrations that were markedly higher than the expected baseline concentrations for pinealectomized rats (<15 pg/ml), suggesting the reestablishment of a melatonin cycle. This finding was unexpected and suggests that melatonin can be produced by an organ or tissue other than the pineal gland.

Keywords Light, melatonin, N-nitroso-N-methylurea, circadian, Fischer 344/N, rats

Tricoire H, Møller M, Chemineau P, Malpaux B **Year** 2003

Authors Tricoire H, Møller M, Chemineau P, Malpaux B

Report Name Origin of cerebrospinal fluid melatonin and possible function in the integration of photoperiod

Publication Reprod Suppl

Issue-page numbers 61:311–321. PMID:14635944

URL http://www.ncbi.nlm.nih.gov/pubmed/14635944

Abstract Melatonin, which is synthesized at night by the pineal gland, is present in the cerebrospinal fluid (CSF), but its entry site and its role in this compartment are not known. Using several approaches, we tested the hypothesis that melatonin enters the CSF through the pineal recess, an evagination of the third ventricle. CSF melatonin concentrations are higher near the pineal gland than in the anterior part of the third ventricle, and decrease markedly (80%) after sealing off the pineal recess. Moreover, ultrastructure and permeability analyses of the pineal-CSF interface showed that melatonin could reach the CSF either via delivery in situ by protruding pinealocytes that make direct contact with the CSF or via extracellular secretion and interstitial fluid draining into the ventricular lumen. These data indicate that melatonin in the CSF probably originates from a few pinealocytes of the basal part of the pineal gland neighbouring the pineal recess. Melatonin carried to the brain by the blood appears to be able to mediate the effects of photoperiod on reproduction, but it is unclear whether melatonin in CSF may fine-tune this response both in terms of timing and amplitude. It is critical to determine which pathway, blood or CSF, allows melatonin to reach its central targets more efficiently.

Keywords

Tsai SY, Thomas KA, Lentz MJ, Barnard KE. **Year** 2011

Authors Tsai SY, Thomas KA, Lentz MJ, Barnard KE.

Report Name Light is beneficial for infant circadian entrainment: an actigraphic study.

Publication J Adv Nurs.

Issue-page numbers 2011 Nov 1. doi: 10.1111/j.1365-2648.2011.05857.x.

URL http://www.ncbi.nlm.nih.gov/pubmed/22043963

Abstract tsai s.-y., thomas k.a., lentz m.j. & barnard k.e. (2011) Light is beneficial for infant circadian entrainment: an actigraphic study. Journal of Advanced Nursing ABSTRACT: Aim. This article is a report of an exploratory study of the relation between light exposure and circadian rest-activity patterns in infants. Background. Ambient light is a major environmental stimulus for regulation of circadian rhythm of sleep and wake in adults, but few studies have been conducted to examine environmental light exposure in relation to rest-activity circadian rhythm parameters of infants. Methods. An intensive within-subject design was used with a convenience sample of 22 infants (mean postnatal age 49·8 days) who wore a combined light and activity monitoring device for seven consecutive days at home. For each infant, light data (lux) were aggregated over the 7 days into categories of illumination and expressed in mean minutes/day. Circadian light and activity parameters, including mesor, amplitude, acrophase and R(2) cosinor fit, were determined using cosinor analysis. Associations between light exposure and circadian rest-activity rhythm parameters were examined using correlation and regression analyses. Data were collected between 2006 and 2007. Results. Infants spent only one-eighth of their daytime hours in an environment with >100 lux light level. There was a relatively large statistically significant relation between the acrophase of light exposure and the acrophase of activity. Increased duration of daily exposure to >100 lux of illumination, and increased amplitude of circadian rhythm of light were associated with stronger circadian patterns of infant activity. Conclusion. Results suggest an association between light and activity patterns and that increasing duration of exposure to moderate light levels may be a simple and economical nursing intervention during the early postnatal weeks.

Keywords

Tsao JY, Saunders HD, Creighton JR, et al. **Year** 2010

Authors J Y Tsao, H D Saunders, J R Creighton, M E Coltrin and J A Simmons

Report Name Solid-state lighting: an energy-economics perspective

Publication J. Phys. D: Appl. Phys.

Issue-page numbers 43 354001 doi:10.1088/0022-3727/43/35/354001

URL http://iopscience.iop.org/0022-3727/43/35/354001

Abstract Artificial light has long been a significant factor contributing to the quality and productivity of human life. As a consequence, we are willing to use huge amounts of energy to produce it. Solid-state lighting (SSL) is an emerging technology that promises performance features and efficiencies well beyond those of traditional artificial lighting, accompanied by potentially massive shifts in (a) the consumption of light, (b) the human productivity and energy use associated with that consumption and (c) the semiconductor chip area inventory and turnover required to support that consumption. In this paper, we provide estimates of the baseline magnitudes of these shifts using simple extrapolations of past behaviour into the future. For past behaviour, we use recent studies of historical and contemporary consumption patterns analysed within a simple energy-economics framework (a Cobb–Douglas production function and profit maximization). For extrapolations into the future, we use recent reviews of believed-achievable long-term performance targets for SSL. We also discuss ways in which the actual magnitudes could differ from the baseline magnitudes of these shifts. These include: changes in human societal demand for light; possible demand for features beyond lumens; and guidelines and regulations aimed at economizing on consumption of light and associated energy.

Keywords solid state lighting, light at night

Tso MO, La Piana FG **Year** 1975

Authors Tso MO, La Piana FG.

Report Name The human fovea after sungazing

Publication Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol

Issue-page numbers 1975 Nov-Dec;79(6):OP788-95.

URL http://www.ncbi.nlm.nih.gov/pubmed/1209815

Abstract Three patients who had malignant melanomas of the uvea and normal foveas agreed to look at the sun for one hour before enucleation of the eyes. Two of the patients sungazed with an undilated pupil, and 24 hours later, recovered their preexposure visual acuity with no detectable scotoma. One of the patients looked at the sun with a partially dilated pupil, and 24 hours later her visual acuity dropped from 20/20 to 20/25. After sungazing, all three eyes exhibited a prolonged recovery time from the photostress test. Fluorescein angiography in two patients showed that there was leakage of dye in the fovea. Fluorescein angiography done two days earlier had revealed no abnormalities. The foveas of all patients were studied by light and electron microscopy. Two patients showed sloughing of necrotic RPE into the subretinal space at the fovea. Degenerative changes and loss of melanin granules were obsered in the RPE in the fovea of the third patient. This study shows that in spite of the minimal subjective visual impairment, leakage of fluorescein from the choroidal vasculature and histologic changes in the fovea could be demonstrated after exposure to the sunlight.

Keywords

Authors Turek FW, Joshu C, Kohsaka A, Lin E, Ivanova G, McDearmon E, Laposky A, Losee-Olson S, Easton A, Jensen DR, Eckel RH, Takahashi JS, Bass J

Report Name Obesity and metabolic syndrome in circadian Clock mutant mice

Publication Science

Issue-page numbers 308:1043–5. doi: 10.1126/science.1108750

URL http://www.ncbi.nlm.nih.gov/pubmed/15845877

Abstract

The CLOCK transcription factor is a key component of the molecular circadian clock within pacemaker neurons of the hypothalamic suprachiasmatic nucleus. We found that homozygous Clock mutant mice have a greatly attenuated diurnal feeding rhythm, are hyperphagic and obese, and develop a metabolic syndrome of hyperleptinemia, hyperlipidemia, hepatic steatosis, hyperglycemia, and hypoinsulinemia. Expression of transcripts encoding selected hypothalamic peptides associated with energy balance was attenuated in the Clock mutant mice. These results suggest that the circadian clock gene network plays an important role in mammalian energy balance.

Keywords

Turner PL, Mainster MA

Year 2008

Authors P L Turner and M A Mainster

Report Name Circadian photoreception: ageing and the eye's important role in systemic health

Publication Br J Ophthalmol

Issue-page numbers 2008 November; 92(11): 1439–1444

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2582340/

Abstract

Aim:
To analyse how age-related losses in crystalline lens transmittance and pupillary area affect circadian photoreception and compare the circadian performance of phakic and pseudophakic individuals of the same age.
Methods:
The spectral sensitivity of circadian photoreception peaks in the blue part of the spectrum at approximately 460 nm. Photosensitive retinal ganglion cells send unconscious information about environmental illumination to non-visual brain centres including the human body's master biological clock in the suprachiasmatic nuclei. This information permits human physiology to be optimised and aligned with geophysical day–night cycles using neural and hormonal messengers including melatonin. Age-related transmittance spectra of crystalline lenses and photopic pupil diameter are used with the spectral sensitivity of melatonin suppression and the transmittance spectra of intraocular lenses (IOLs) to analyse how ageing and IOL chromophores affect circadian photoreception.
Results:
Ageing increases crystalline lens light absorption and decreases pupil area resulting in progressive loss of circadian photoreception. A 10-year-old child has circadian photoreception 10-fold greater than a 95-year-old phakic adult. A 45-year-old adult retains only half the circadian photoreception of early youth. Pseudophakia improves circadian photoreception at all ages, particularly with UV-only blocking IOLs which transmit blue wavelengths optimal for non-visual photoreception.
Conclusions:
Non-visual retinal ganglion photoreceptor responses to bright, properly timed light exposures help assure effective circadian photoentrainment and optimal diurnal physiological processes. Circadian photoreception can persist in visually blind individuals if retinal ganglion cell photoreceptors and their suprachiasmatic connections are intact. Retinal illumination decreases with ageing due to pupillary miosis and reduced crystalline lens light transmission especially of short wavelengths. Inadequate environmental light and/or ganglion photoreception can cause circadian disruption, increasing the risk of insomnia, depression, numerous systemic disorders and possibly early mortality. Artificial lighting is dimmer and less blue-weighted than natural daylight, contributing to age-related losses in unconscious circadian photoreception. Optimal intraocular lens design should consider the spectral requirements of both conscious and unconscious retinal photoreception.

Keywords

Turner PL, Van Someren EJW, Mainster MA **Year** 0

Authors Patricia L. Turner, Eus J.W. Van Someren, Martin A. Mainster

Report Name The role of environmental light in sleep and health: Effects of ocular aging and cataract surgery

Publication Sleep Medicine Reviews

Issue-page numbers Volume 14, Issue 4, August 2010, Pages 269-280

URL http://www.sciencedirect.com/science/article/pii/S1087079209001233

Abstract Environmental illumination profoundly influences human health and well-being. Recently discovered photoreceptive retinal ganglion cells (pRGCs) are primary mediators of numerous circadian, neuroendocrine and neurobehavioral responses. pRGCs provide lighting information to diverse nonvisual (non-image-forming) brain centers including the suprachiasmatic nuclei (SCN) which serve as the body's master biological clock. The SCN exert functional control over circadian aspects of physiology. The timing and strength (amplitude) of SCN rhythmic signals are affected by light exposure. Light deficiency may attenuate SCN function and its control of physiological and hormonal rhythms which in turn can result in a cascade of adverse events. Inadequate pRGC photoreception cannot be perceived consciously, but may aggravate many common age-associated problems including insomnia, depression and impaired cognition. In this review we (1) summarize circadian physiology, emphasizing light's critical role as the most important geophysical timing cue in humans; (2) analyze evidence that typical residential lighting is insufficient for optimal pRGC requirements in youth and even more so with advancing age; (3) show how ocular aging and cataract surgery impact circadian photoreception; and (4) review some of the diverse morbidities associated with chronodisruption in general and those which may be caused by light deficiency in particular.

Keywords Aging; Circadian; Chronodisruption; Crystalline lens; Hypothalamic–pituitary–adrenal axis; Insomnia;

Tynes T, Hannevik M, Andersen A et al. **Year** 1996

Authors Tynes T, Hannevik M, Andersen A et al.

Report Name Incidence of breast cancer in Norwegian female radio and telegraph operators

Publication Cancer Causes Control

Issue-page numbers 7:197–204.doi:10.1007/BF00051295 PMID:8740732

URL http://www.springerlink.com/content/x157k50107289894/

Abstract Exposure to electromagnetic fields may cause breast cancer in women if it increases susceptibility to sex-hormone-related cancer by diminishing the pineal gland's production of melatonin. We have studied breast cancer incidence in female radio and telegraph operators with potential exposure to light at night, radio frequency (405 kHz-25 MHz), and, to some extent, extremely low frequency fields (50 Hz). We linked the Norwegian Telecom cohort of female radio and telegraph operators working at sea to the Cancer Registry of Norway to study incident cases of breast cancer. The cohort consisted of 2,619 women who were certified to work as radio and telegraph operators between 1920 and 1980. Cancer incidence was analyzed on the basis of the standardized incidence ratio (SIR), with the Norwegian female population as the comparison group. The incidence of all cancers was close to unity (SIR=1.2). An excess risk was seen for breast cancer (SIR=1.5). Analysis of a nested case-control study within the cohort showed an association between breast cancer in women aged 50 + years and shift work. In a model with adjustment for age, calendar year, and year of first birth, the rate ratio for breast cancer associated with being a radio and telegraph operator-in comparison with all Norwegian women born 1935 or later-analyzed with Poisson regression, was 1.5 after adjustment for fertility factors. These results support a possible association between work as a radio and telegraph operator and breast cancer. Future epidemiologic studies on breast cancer in women aged 50 and over, should address possible disturbances of chronobiological parameters by environmental factors.

Keywords cancer - case-control - cohort - electromagnetic - Norway - radiofrequency - seamen - wome

Uchiyama M, Lockley SW

Year 2009

Authors Makoto Uchiyama, Steven W Lockley

Report Name Non-24-Hour Sleep-Wake Syndrome in Sighted and Blind Patients

Publication Sleep Medicine Clinics

Issue-page numbers Volume: 4, Issue: 2, Pages: 195-211

URL http://www.sleep.theclinics.com/article/S1556-407X%2809%2900016-2/abstract

Abstract Non–24-hour sleep–wake syndrome is a cyclic debilitating circadian rhythm sleep disorder characterized by an inability to sleep on a 24-hour schedule. Individuals who are physically or biologically isolated from a normal 24-hour light/dark cycle exhibit a sleep/wake cycle that is different from, and usually longer than, 24 hours. It is relatively rare in sighted patients and in some cases may be associated with delayed sleep phase disorder or psychiatric disorders. It is more common in individuals who are totally blind. This article reviews the clinical characteristics of patients who have non–24-hour sleep–wake syndrome, discusses the biologic mechanisms that may underlie its development, and describes potential treatment strategies.

Keywords Circadian rhythm sleep disorders, Non–24-hour sleep–wake disorder, Free-running type, Non-entrained type, Blindness, Melatonin

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Uguz AC, Cig B, Espino J, et al.

Year 2012

Authors A. Cihangir Uguz, Bilal Cig, Javier Espino, Ignacio Bejarano, Mustafa Naziroglu, Ana B. Rodríguez, José A. Pariente

Report Name Melatonin Potentiates Chemotherapy-Induced Cytotoxicity and Apoptosis in Rat Pancreatic Tumor Cells

Publication Journal of Pineal Research

Issue-page numbers Accepted Article (Accepted, unedited articles published online for future issues)

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2012.00974.x/abstract

Abstract Melatonin has antitumor activity via several mechanisms including its antiproliferative and proapoptotic effects in addition to its potent antioxidant action. Thus, melatonin has proven useful in the treatment of tumors in association with chemotherapeutic drugs. The present study was performed to evaluate the effect of melatonin on the cytotoxicity and apoptosis induced by three different chemotherapeutic agents, namely, 5-fluorouracil (5-FU), cisplatin and doxorubicin in the rat pancreatic tumor cell line AR42J., We found that both melatonin and the three chemotherapeutic drugs induce a time-dependent decrease of AR42J cell viability, reaching the highest cytotoxic effect after 48 hours of incubation. Furthermore, melatonin significantly augmented the cytotoxicity of the chemotherapeutic agents. Consistently, cotreatment of AR42J cells with each of the chemotherapeutic agents in the presence of melatonin increased the population of apoptotic cells, elevated mitochondrial membrane depolarization and augmented intracellular reactive oxygen species (ROS) production compared to treatment with each chemotherapeutic agent alone. These results provide evidence that in vitro melatonin enhances chemotherapy-induced cytotoxicity and apoptosis in rat pancreatic tumor AR42J cells and, therefore, melatonin may be potentially applied to pancreatic tumor treatment as a powerful synergistic agent in combination with chemotherapeutic drugs.

Keywords Melatonin; chemotherapy; cytotoxicity; apoptosis; AR42J cells

Ungar F, Halberg F **Year** 1962

Authors Ungar F, Halberg F

Report Name Circadian rhythm in the in vitro response of mouse adrenal to adrenocorticotropic hormone

Publication Science

Issue-page numbers 137:1058–1060 doi:10.1126/science.137.3535.1058. PMID:13923797

URL http://www.sciencemag.org/content/137/3535/1058.abstract

Abstract Adrenal corticosterone production resulting from adrenocorticotropic hormone (ACTH) stimulation in vitro depends upon the time of gland removal. This rhythm in adrenal reactivity to ACTH is out of phase with the corticosterone rhythm in serum of the mice used as donors of adrenals. The responsiveness of the gland to exogenous ACTH is highest when serum corticosterone levels are lowest.

Keywords

US Bureau of Labor Statistics **Year** 2007

Authors US Bureau of Labor Statistics

Report Name Occupational Outlook Handbook, 2006–07 Edition Aircraft Pilots and Flight Engineers

Publication Department of Labor. www.bls.gov/oco/ocos107.htm

Issue-page numbers

URL http://www.bls.gov/oco/ocos107.htm

Abstract * Regional and low-cost airlines offer the best opportunities; pilots face strong competition for jobs at the major airlines, which offer better pay and benefits.
* Many pilots have learned to fly in the military, but growing numbers have college degrees with flight training from civilian flying schools that are certified by the Federal Aviation Administration (FAA).
* Newly hired pilots at major airlines typically have about 4,000 hours of flight experience.

Keywords

US Bureau of Labor Statistics

Year 2005

Authors US Bureau of Labor Statistics

Report Name Occupational Outlook Handbook

Publication Department of Labor http://www.bls.org

Issue-page numbers

URL http://www.bls.gov/oco/

Abstract The Occupational Outlook Handbook is a nationally recognized source of career information, designed to provide valuable assistance to individuals making decisions about their future work lives. The Handbook is revised every two years.

Keywords

Year 2002

Authors Vajdic CM, Kricker A, Giblin M, McKenzie J, Aitken J, Giles GG, et al.

Report Name Sun exposure predicts risk of ocular melanoma in Australia

Publication Int. J. Cancer

Issue-page numbers 101, 175–182 (2002)

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.10579/pdf

Abstract

Previous studies examining sun exposure and ocular melanoma have produced inconsistent results. We investigated this association in a population-based case-control study in Australia. Cases (n 290) aged 18–79 years were diagnosed between January 1996 and July 1998. Controls (n 893) were randomly selected from the electoral rolls and frequencymatched to cases by age, sex and state. A self-administered questionnaire and a telephone interview measured sun exposure on weekdays and weekends at 10, 20, 30 and 40 years of age and over the whole of life for specific jobs and recreations. Multivariate logistic regression models of ocular melanoma and sun exposure contained age, sex, region of birth, eye color and measures of ocular and cutaneous sun sensitivity as covariates. Choroid and ciliary body melanoma (n 246) was positively associated with time outdoors on weekdays and, less persuasively, total time outdoors but not ambient solar irradiance. Odds ratios increased with increasing exposure to OR 1.8 (95% confidence interval 1.1–2.8) for the highest quarter of sun exposure on weekdays up to 40 years of age for men and women together. The strongest positive associations were for total exposure up to 40 years of age, lifetime occupational exposure and total exposure at about 20 years of age in men; all had odds ratios between 2 and 3 in the highest exposure categories. There was inconclusive evidence for an association between sun exposure and iris (n 25) or conjunctival (n 19) melanomas. Sun exposure is an independent risk factor for choroidal and ciliary body melanoma in Australia.

Keywords ocular melanoma; aetiology; sun exposure; UV radiation;

Authors van Amelsvoort LG, Jansen NW, Kant I

Report Name Smoking among shift workers: More than a confounding factor

Publication Chronobiol Int

Issue-page numbers 23:1105–1113 doi:10.1080/07420520601089539. PMID:17190698

URL http://www.mendeley.com/research/smoking-among-shift-workers-more-confounding-factor/

Abstract In studies on the cardiovascular disease risk among shift workers, smoking is considered to be a confounding factor. In a study of 239 shift and 157 daytime workers, it was found that shift work was prospectively related to increased cigarette consumption, indicating that smoking might be in the causative pathway; however, the number of study subjects was too low to warrant sound conclusions. Therefore, data from the Maastricht Cohort study were used to investigate the longitudinal relation between smoking and shift work in a much larger population. In this study, a total of 12,140 employees were followed for two years by means of self-administered questionnaires. The authors compared workers who normally worked during daytime hours only (74%) with those who worked other than day shifts (26%). Logistic regression analyses were performed, adjusting for demographic factors of age, gender, and educational level to evaluate the risk of starting to smoke (n = 25) in the group of non-smoking workers and the risk of quitting (n = 318) in the group of smoking workers. Logistic regression analysis showed a significant association between shift work and taking up smoking during the two-year follow-up (odds ratio: 1.46, p = 0.03). The risk to stop smoking was somewhat lower in shift workers (odds ratio: 0.91) but not statistically significant (p = 0.5). To conclude, this study showed that, independent of educational level, shift workers are more prone to start smoking. This finding might have important implications for studies on the health effects of shift workers and for possible interventions aimed at the reduction of the excess health risk among shift workers.

Keywords

Authors van Amelsvoort LG, Schouten EG, Kok FJ

Report Name Duration of shiftwork related to body mass index and waist to hip ratio

Publication Int J Obes Relat Metab Disord

Issue-page numbers 23:973–978 doi:10.1038/sj.ijo.0801028. PMID:10490804

URL http://www.ncbi.nlm.nih.gov/pubmed/10490804

Abstract

OBJECTIVE:

An elevated cardiovascular disease risk for shiftworkers has frequently been reported, however, the mechanism is still unknown. Changes in eating habits, in physical activity or metabolic factors could be involved. In this study we assessed the relationship between body mass index (BMI) as a possible indicator of changed eating habits or metabolic involvement and duration of shiftwork.
DESIGN:

Data from an ongoing cohort study among 377 shiftworkers and non-shiftworking controls, all starting in a new job were used. Anthropometric measurements were carried out at the start of the assignment. Job history was obtained by a questionnaire.
RESULTS:

A positive relationship was observed between BMI and waist to hip ratio (WHR) and duration of shiftwork experience, with an adjustment for age. The linear regression coefficients, with additional adjustments for sex, smoking status, physical activity and educational level were 0.12 kg/m2 per y in shiftwork for BMI (P<0.05) and 0.0016 per y in shiftwork for WHR (P<0.05).
CONCLUSIONS:

These results suggest a relationship between years worked in shifts with BMI and WHR for both males and females. Whether this might reflect an effect of changed dietary habits or a metabolic effect is not yet clear.

Keywords

Year 2000

Authors Van Cauter E, Copinschi G

Report Name Interrelationships between growth hormone and sleep

Publication Growth Horm IGF Res

Issue-page numbers 10 Suppl B;S57–S62 doi:10.1016/S1096-6374(00)80011-8. PMID:10984255

URL http://www.sciencedirect.com/science/article/pii/S1096637400800118

Abstract In healthy young adults, the 24-hour profile of plasma growth hormone (GH) levels consists of stable low levels abruptly interrupted by bursts of secretion. In normal women, daytime GH secretory pulses are frequent. However, in normal men, a sleep-onset-associated pulse is generally the major or even the only daily episode of active secretion. Extensive evidence indicates the existence of a consistent relationship between slow-wave (SW) sleep and increased GH secretion. There is a linear relationship between the amount of SW sleep (measured by either visual scoring or spectral analysis of the EEG) and the amount of concomitant GH secretion. During ageing, SW sleep and GH secretion decrease exponentially and with the same chronology. Pharmacological stimulation of SW sleep results in increased GH release, and compounds that increase SW sleep may therefore represent a novel class of GH secretagogues.

Keywords Ageing; growth hormone; growth hormone-releasing hormone; rapid-eye-movement sleep; slow-wavesleep; somatostatin

Authors Van Cauter E, Kerkhofs M, Caufriez A et al.

Report Name A quantitative estimation of growth hormone secretion in normal man: reproducibility and relation to sleep and time of day

Publication J Clin Endocrinol Metab

Issue-page numbers 74:1441–1450 doi:10.1210/jc.74.6.1441. PMID:1592892

URL http://www.ncbi.nlm.nih.gov/pubmed/1592892

Abstract Recent reports, based on measurements of plasma GH levels, have challenged the concept that GH secretion is dependent on sleep and not modulated by circadian rythmicity. Because plasma levels reflect not only the secretory process, but also the effects of distribution and degradation, temporal limits of active secretion and, consequently, synchrony with other physiological events cannot be accurately estimated from circulating concentrations. The present study was undertaken to examine the roles of sleep and time of day in modulating pulsatile GH secretion, using a mathematical procedure (deconvolution) allowing secretory rates to be estimated from peripheral levels. Eight young nonobese healthy men participated each in six separate 16-h studies involving either normal or delayed sleep. Plasma GH levels were measured at 15-min intervals, and GH secretory rates were calculated by deconvolution. Each individual study was preceded by one night of habituation, and sleep was polygraphically recorded in all studies. Repeated measurements of plasma insulin-like growth factor-I (IGF-I) were performed in all subjects. Deconvolution revealed the existence of approximately 20% more GH pulses than detected in the plasma profiles. Large peaks of plasma GH concentrations often reflected the occurrence of a succession of secretory pulses. The total amount of GH secreted varied 10-fold across individual studies, but the within-subject variability (32%) was less than half the across-subject variability (65%). IGF-I levels were also more reproducible for a given subject than across subjects (11% vs. 36% variability) and did not correlate with the amount of GH secreted. During normal waking hours, the GH secretory rate was similar in the evening and the morning. This secretory rate was doubled during wakefulness at times of habitual sleep and tripled during sleep, even when sleep was delayed until 0400 h. A pulse starting within 30 min after sleep onset was present in all profiles with normal sleep and in 13 of 16 profiles with delayed sleep. The amount of GH secreted in response to sleep onset was tightly correlated with the level of secretion during wakefulness (r = 0.92). Almost 70% (57 of 83) of the pulses occurring during sleep were associated with slow wave (SW) stages. The amount of GH secreted in SW-associated pulses was correlated with the amount of SW occurring during the pulse, even when sleep-onset pulses were not considered. We conclude that in normal adult men, the amount of GH secretion and the levels of IGF-I are more reproducible within than across individuals.(ABSTRACT TRUNCATED AT 400 WORDS)

Keywords

Van Cauter E, Plat L, Copinschi G

Year 1998

Authors Van Cauter E, Plat L, Copinschi G

Report Name Interrelations between sleep and the somatotropic axis

Publication Sleep

Issue-page numbers 21:553–566. PMID:9779515

URL http://ukpmc.ac.uk/abstract/MED/9779515

Abstract

In the human as in other mammals, growth hormone (GH) is secreted as a series of pulses. In normal young adults, a major secretory episode occurs shortly after sleep onset, ir temporal association with the first period of slow-wave (SW) sleep. In men, approximately 70% of the daily GH output occurs during early sleep throughout adulthood. In women, the contribution of sleep-dependent GH release to the daily output is lower and more variable. Studies involving shifts of the sleep-wake cycle have consistently shown that sleep wake homeostasis is the primary determinant of the temporal organization of human GH release. Effects of circadian rhythmicity may occasionally be detected. During nocturnal sleep, the sleep-onset GH pulse is caused by a surge of hypothalamic GHRH release which coincides with a circadian-dependent period of relative somatostatin disinhibition. Extensive evidence indicates the existence of a consistent relationship between SW sleep and increased GH secretion and, conversely, between awakenings and decreased GH release. There is a linear relationship between amounts of SW sleep--whether measured by visual scoring or by delta activity--and amounts of concomitant GH secretion, although dissociations may occur, most likely because of variable levels of somatostatin inhibition. Pharmacological stimulation of SW sleep results in increased GH release, and compounds which increase SW sleep may therefore represent a novel class of GH secretagogues. During aging, SW sleep and GH secretion decrease with the same chronology, raising the possibility that the peripheral effects of the hyposomatotropism of the elderly may partially reflect age-related alterations in sleep-wake homeostasis. While the association between sleep and GH release has been well documented, there is also evidence indicating that components of the somatotropic axis are involved in regulating sleep. The studies are most consistent in indicating a role for GHRH in promoting NREM and/or SW sleep via central, rather than peripheral, mechanisms. A role for GH in sleep regulation is less well-documented but seems to involve REM, rather than NREM, sleep. It has been proposed that the stimulation of GH release and the promotion of NREM sleep by GHRH are two separate processes which involve GHRH neurons located in two distinct areas of the hypothalamus. Somatostatinergic control of GH release appears to be weaker during sleep than during wake, suggesting that somatostatinergic tone is lower in the hypothalamic area(s) involved in sleep regulation and sleep-related GH release than in the area controlling daytime GH secretion. While the concept of a dual control of daytime and sleep-related GH secretion remains to be directly demonstrated, it allows for the reconciliation of a number of experimental observations.

Keywords

Van Cauter E, Plat L, Scharf MB et al. **Year** 1997

Authors Van Cauter E, Plat L, Scharf MB et al.

Report Name Simultaneous stimulation of slow-wave sleep and growth hormone secretion by gamma-hydroxybutyrate in normal young Men

Publication J Clin Invest

Issue-page numbers 100:745–753 doi:10.1172/JCI119587. PMID:9239423

URL http://www.jci.org/articles/view/119587/pdf

Abstract T he aim of this study was to investigate, in normal young men, whether gamma-hydroxybutyrate (GHB), a reliable stimulant of slow-wave (SW) sleep in normal subjects, would simultaneously enhance sleep related growth hormone (GH) secretion. Eight healthy young men participated each in four experiments involving bedtime oral administration of placebo, 2.5, 3.0, and 3.5 g of GHB. Polygraphic sleep recordings were performed every night, and blood samples were obtained at 15-min intervals from 2000 to 0800. GHB effects were mainly observed during the first 2 h after sleep onset. There was a doubling of GH secretion, resulting from an increase of the amplitude and the duration of the first GH pulse after sleep onset. This stimulation of GH secretion was significantly correlated to a simultaneous increase in the amount of sleep stage IV. Abrupt but transient elevations of prolactin and cortisol were also observed, but did not appear to be associated with the concomitant stimulation of SW sleep. Thyrotropin and melatonin profiles were not altered by GHB administration. These data suggest that pharmacological agents that reliably stimulate SW sleep, such as GHB, may represent a novel class of powerful GH secretagogues.

Keywords

Van Cauter E, Spiegel K, Tasali E, Leproult R **Year** 2008

Authors Eve Van Cauter, Karine Spiegel, Esra Tasali, Rachel Leproult

Report Name Metabolic consequences of sleep and sleep loss

Publication Sleep Medicine

Issue-page numbers Volume 9, Supplement 1 , Pages S23-S28, September 2008

URL http://www.sleep-journal.com/article/S1389-9457%2808%2970013-3/abstract

Abstract Reduced sleep duration and quality appear to be endemic in modern society. Curtailment of the bedtime period to minimum tolerability is thought to be efficient and harmless by many. It has been known for several decades that sleep is a major modulator of hormonal release, glucose regulation and cardiovascular function. In particular, slow wave sleep (SWS), thought to be the most restorative sleep stage, is associated with decreased heart rate, blood pressure, sympathetic nervous activity and cerebral glucose utilization, compared with wakefulness. During SWS, the anabolic growth hormone is released while the stress hormone cortisol is inhibited. In recent years, laboratory and epidemiologic evidence have converged to indicate that sleep loss may be a novel risk factor for obesity and type 2 diabetes. The increased risk of obesity is possibly linked to the effect of sleep loss on hormones that play a major role in the central control of appetite and energy expenditure, such as leptin and ghrelin. Reduced leptin and increased ghrelin levels correlate with increases in subjective hunger when individuals are sleep restricted rather than well rested. Given the evidence, sleep curtailment appears to be an important, yet modifiable, risk factor for the metabolic syndrome, diabetes and obesity. The marked decrease in average sleep duration in the last 50 years coinciding with the increased prevalence of obesity, together with the observed adverse effects of recurrent partial sleep deprivation on metabolism and hormonal processes, may have important implications for public health.

Keywords Sleep deprivation , Glucose metabolism , Diabetes , Appetite regulation , Leptin , Ghrelin , Obesity

Van Cauter E, Sturis J, Byrne MM et al. **Year** 1993

Authors Van Cauter E, Sturis J, Byrne MM et al.

Report Name Preliminary studies on the immediate phase-shifting effects of light and exercise on the human circadian clock

Publication J Biol Rhythms

Issue-page numbers 8 Suppl;S99–S108. PMID:8274769

URL http://www.ncbi.nlm.nih.gov/pubmed/8274769

Abstract The aim of the present research was to determine the magnitude and direction of immediate phase shifts of human rhythms following a single exposure to a 3-hr pulse of bright light or physical activity. The pulse of light or activity was presented under "constant-routine" conditions, and measurements of the resultant phase shifts were performed under the same constant-routine conditions on the first day following pulse presentation. Four overt rhythms that are strongly dependent on circadian timing--namely, the rhythms of plasma cortisol, plasma thyroid-stimulating hormone (TSH), plasma melatonin, and body temperature--were monitored. The analysis of the TSH profiles indicated that exposure to light at about the time of the minimum of body temperature resulted in phase advances averaging less than 1 hr in magnitude. Exposure to light approximately 3 hr before the time of the minimum of body temperature resulted in phase delays of 1-2 hr. Preliminary analyses of the melatonin profiles have confirmed these observations. Our findings regarding the effects of exercise are still inconclusive.

Keywords

Van Cauter E, Sturis J, Byrne MM et al. **Year** 1994

Authors Van Cauter E, Sturis J, Byrne MM et al.

Report Name Demonstration of rapid light-induced advances and delays of the human circadian clock using hormonal phase markers

Publication Am J Physiol

Issue-page numbers 266:E953–E963. PMID:8023927

URL http://ajpendo.physiology.org/content/266/6/E953.abstract

Abstract To determine the magnitude and direction of phase shifts of human circadian rhythms occurring within 1 day after a single exposure to bright light, plasma thyrotropin, melatonin, and cortisol levels and body temperature were monitored for 38 h in 17 men who were each studied two times, once during continuous dim light conditions and once with light exposure. After a period of entrainment to a fixed sleep-wake cycle, a 3-h light pulse (5,000 lux) was presented under constant routine conditions, and the resultant phase shifts were measured, also under constant routine conditions, on the 1st day after pulse presentation. The phase shifts in response to light occurred within 24 h and were in the delaying direction for most of the nocturnal period, with the crossover to phase advances occurring approximately 1 h after the temperature minimum. Phase shifts averaged 1 h, with delays being larger than advances, and were achieved without significant changes in rhythm amplitude. The immediate response of the human circadian clock to a single 3-h light pulse is thus characteristic of "type 1" resetting.

Keywords

van Coevorden A, Mockel J, Laurent E et al. **Year** 1991

Authors A. van Coevorden, J. Mockel, E. Laurent, M. Kerkhofs, M. L'Hermite-Baleriaux, C. Decoster, P. Neve, and

Report Name Neuroendocrine rhythms and sleep in aging men

Publication Am J Physiol

Issue-page numbers 260:E651–E661. PMID:2018128

URL http://ajpendo.physiology.org/content/260/4/E651.short

Abstract

To delineate the physiological effects of aging on basal levels and temporal patterns of neuroendocrine secretions, the 24-h profiles of cortisol, thyroid-stimulating hormone (TSH), melatonin, prolactin, and growth hormone (GH) levels were simultaneously obtained at frequent intervals in eight healthy, active elderly men, age 67-84 yr and in eight young male adults, age 20-27 yr. The study was preceded by an extended period of habituation to laboratory conditions, and sleep was polygraphically recorded. Mean cortisol levels in the elderly were normal, but the amplitude of the circadian rhythm was reduced. Circulating levels of daytime and nighttime levels of both TSH and GH were greatly diminished in old age. In contrast, prolactin and melatonin concentrations were decreased during the nighttime only. The circadian rises of cortisol, TSH, and melatonin occurred 1-1.5 h earlier in elderly subjects, and the distribution of rapid-eye-movement stages during sleep was similarly advanced, suggesting that circadian timekeeping is modified during normal senescence. Despite perturbations of sleep, sleep-related release of GH and prolactin occurred in all elderly men. Age-related decreases in hormonal levels were associated with a decrease in the amplitude, but not the frequency, of secretory pulses. These findings demonstrate that the normal process of aging involves alterations in the central mechanisms controlling the temporal organization of endocrine release in addition to a reduction of secretory outputs.

Keywords

van de Werken M, Giménez MC, de Vries B, et al. | ***Year*** 2013

Authors Maan van de Werken, Marina C. Giménez, Bonnie de Vries, Domien G. M. Beersma, and Marijke C. M. Gordijn

Report Name Short-wavelength attenuated polychromatic white light during work at night: limited melatonin suppression without substantial decline of alertness

Publication Chronobiology International

Issue-page numbers Posted online on May 24, 2013. (doi:10.3109/07420528.2013.773440)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2013.773440

Abstract Exposure to light at night increases alertness, but light at night (especially short-wavelength light) also disrupts nocturnal physiology. Such disruption is thought to underlie medical problems for which shiftworkers have increased risk. In 33 male subjects we investigated whether short-wavelength attenuated polychromatic white light (<530 nm filtered out) at night preserves dim light melatonin levels and whether it induces similar skin temperature, alertness, and performance levels as under full-spectrum light. All 33 subjects participated in random order during three nights (at least 1 wk apart) either under dim light (3 lux), short-wavelength attenuated polychromatic white light (193 lux), or full spectrum light (256 lux). Hourly saliva samples for melatonin analysis were collected along with continuous measurements of skin temperature. Subjective sleepiness and activation were assessed via repeated questionnaires and performance was assessed by the accuracy and speed of an addition task. Our results show that short-wavelength attenuated polychromatic white light only marginally (6%) suppressed salivary melatonin. Average distal-to-proximal skin temperature gradient (DPG) and its pattern over time remained similar under short-wavelength attenuated polychromatic white light compared with dim light. Subjects performed equally well on an addition task under short-wavelength attenuated polychromatic white light compared with full-spectrum light. Although subjective ratings of activation were lower under short-wavelength attenuated polychromatic white light compared with full-spectrum light, subjective sleepiness was not increased. Short-wavelength attenuated polychromatic white light at night has some advantages over bright light. It hardly suppresses melatonin concentrations, whereas performance is similar to the bright light condition. Yet, alertness is slightly reduced as compared with bright light, and DPG shows similarity to the dim light condition, which is a physiological sign of reduced alertness. Short-wavelength attenuated polychromatic white light might therefore not be advisable in work settings that require high levels of alertness.

Keywords Health, humans, light at night, performance, skin temperature, sleepiness

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van de Wetering M, de Lau W, Clevers H | ***Year*** 2002

Authors van de Wetering M, de Lau W, Clevers H

Report Name WNT signaling and lymphocyte development

Publication Cell

Issue-page numbers 109 Suppl;S13–S19 doi:10.1016/S0092-8674(02)00709-2. PMID:11983149

URL http://www.cell.com/abstract/S0092-8674%2802%2900709-2

Abstract Developmental studies in model organisms have revealed that cell fate decisions are governed by only a handful of highly conserved signal transduction cascades. Recent data indicate that at least two of these, the Wnt and the Notch cascades, have been recruited by the vertebrate immune system to control early lymphopoiesis.

Keywords

Van den Heiligenberg S, Deprés-Brummer P, Barbason H, et al. ***Year*** 1999

Authors Simone van den Heiligenberg1, Petra Deprés-Brummer1, Hervé Barbason4, Bruno Claustrat3, Michel Reynes2, Francis Lévi

Report Name The tumor promoting effect of constant light exposure on diethylnitrosamine-induced hepatocarcinogenesis in rats

Publication Life Sciences

Issue-page numbers Volume 64, Issue 26, 21 May 1999, Pages 2523-2534

URL http://www.sciencedirect.com/science/article/pii/S0024320599002106

Abstract The hypothesis that light-induced circadian clock suppression exerts a promoting effect on liver carcinogenesis was investigated in rats.

Sixty-five male Wistar rats were given diethylnitrosamine (DEN, 10 mg/kg/day p.o.) for 6 weeks and were randomized into 3 groups. Rats from group 1 (N = 20) received DEN only. Rats from group 2 (N = 22) also received phenobarbital (pheno, 30 mg/rat/day p.o.) for 4 weeks as a promoting agent and rats from group 3 (N = 23) were exposed to continuous light. Three months after starting DEN treatment, urinary 6-sulfatoxymelatonin (αMT6s) excretion, a marker of circadian clock function, had lost its circadian rhythmicity in the LL group, with a 4-fold lower 24h mean than that found in the LDpheno and LD groups (8.0 ± 3.2 View the MathML source, 33.6 ± 3.1 View the MathML source and 34.3 ± 2.4 View the MathML source respectively; p from ANOVA < 0.001). Laparotomy was then performed. The proportion of rats with macroscopic nodules on liver surface was 72% (LD group), 89% (LDpheno group) and 95% (LL group) (p from $\chi 2 = 0.1$). Nodules were more numerous and larger both in the LL group and in the LDpheno one as compared to the LD group (p from $\chi 2 < 0.05$). All the rats died with hepatocellular carcinomas, with a median survival of 5 months, similar in all 3 groups. Light-induced circadian clock suppression exerted a promoting effect similar to that caused by phenobarbital in this model, yet through different effects on circadian system function.

Keywords circadian rhythms; continuous light; hepatocarcinogenesis; diethylnitrosamine; 6-sulfatoxymelatonin

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van der Leun JC, de Gruijl FR ***Year*** 2002

Authors van der Leun JC, de Gruijl FR.

Report Name Climate change and skin cancer

Publication Photochem. Photobiol. Sci.

Issue-page numbers 2002, 1, 324-326 DOI: 10.1039/B201025A

URL http://pubs.rsc.org/en/Content/ArticleLanding/2002/PP/b201025a

Abstract Depletion of the ozone layer and climate change by the increasing greenhouse effect are distinctly different processes. It is becoming quite clear, however, that the two global environmental problems are interlinked in several ways [D. L. Albritton, P. J. Aucamp, G. Mégie, R. T. Watson, Scientific Assessment of Ozone Depletion, 1998, World Meteorological Organization, Global Ozone Research and Monitoring Project, Report No. 44 (WMO, Geneva, 1998)]. In the present analysis we deal with the possibility of such an interlinkage within one effect on human health, namely, skin cancer. The increase in the incidence of skin cancer is one of the most extensively studied effects of increasing ultraviolet radiation by ozone depletion (F. R. de Gruijl, Skin cancer and solar radiation, Eur. J. Cancer, 1999, 35, 2003–2009). We wondered if this impact could also be influenced by increasing environmental temperatures. Here we show that it is likely that such an influence will occur. For the same reason, it is likely that the baseline incidence of skin cancer will be augmented by rising temperatures, which may become significant in magnitude.

Keywords

van der Leun JC, Piacentini RD, de Gruijl FR

Year 2008

Authors van der Leun JC, Piacentini RD, de Gruijl FR.

Report Name Climate change and human skin cancer

Publication Photochem Photobiol Sci.

Issue-page numbers 2008 Jun;7(6):730-3. Epub 2008 Apr 18.

URL http://www.ncbi.nlm.nih.gov/pubmed/18528559

Abstract As part of an inventory of potential interactions between effects of ozone depletion and climate change, a possible effect of ambient temperature on sun-induced skin cancers was suggested. Mouse experiments had shown that increased room temperature enhanced ultraviolet (UV) radiation-induced carcinogenesis; the effective UV dose was increased by 3-7% per degrees C. The present investigation was aimed at studying a possible temperature effect on human skin cancer. Existing data on the incidence of human skin cancer were analyzed, as available from two special surveys of non-melanoma skin cancer in the United States. The incidence of non-melanoma skin cancer in the ten regions surveyed not only correlated significantly with the ambient UV dose but also with the average daily maximum temperature in summer. For squamous cell carcinoma the incidence was higher by 5.5% (SE 1.6%) per degrees C and for basal cell carcinoma by 2.9% (SE 1.4%) per degrees C. These values correspond to an increase of the effective UV dose by about 2% per degrees C. Although the precise nature of this correlation with temperature requires further studies, it can be concluded that the temperature rises coming with climate change can indeed amplify the induction of non-melanoma skin cancers by UV radiation in human populations.

Keywords

Van Der Tweel L.

Year 1964

Authors VAN DER TWEEL L.

Report Name Relation between psychophysics and electrophysiology of flicker

Publication Documenta Ophthalmologica

Issue-page numbers Volume 18, Number 1, 287-304, DOI: 10.1007/BF00160581

URL http://www.springerlink.com/content/wn657151v1643r30/

Abstract Experiments are described measuring ERG's and occipital EEG's and de Lange curves under identical conditions. There is little correspondence between the responses and the psychophysical results. ERG responses as found by Gouras & Gunkel give second harmonics at about 10 cps. Curves are shown in which the h.f. attenuation is smaller for the ERG and EEG responses than for the de Lange curves. The EEG responses with large field illumination show a linear and highly variable character with different subjects between 9–15 cps. A sharp resonance at 10 cps is reported in one subject. Strong essential second harmonics are found in the EEG below 9 cps and with small fields and high intensities round 27 cps. Opposite phase stimulation cancels fundamental frequency responses and does not influence second harmonics. Also here little relation is found with psychophysical results.

Keywords

Authors Annette van Maanen, Anne Marie Meijer, Marcel G. Smits, Frans J. Oort

Report Name Termination of short term melatonin treatment in children with delayed Dim Light Melatonin Onset: Effects on sleep, health, behavior problems, and parenting stress

Publication Sleep Medicine

Issue-page numbers In Press, Corrected Proof

URL http://www.sciencedirect.com/science/article/pii/S1389945711002358

Abstract Objective

To investigate the effects of termination of short term melatonin treatment on sleep, health, behavior, and parenting stress in children with delayed previous termDimnext termprevious termLightnext term Melatonin Onset.
Methods

Forty-one children (24 boys, 17 girls; mean age = 9.43 years) entered melatonin treatment for 3 weeks and then discontinued treatment by first taking a half dose for 1 week and then stopping completely for another week. Sleep was measured with sleep diaries filled in by parents and with actometers worn by children. Analyses were conducted with linear mixed models.
Results

Sleep latency was longer during the stop week compared to the treatment weeks. Sleep start was later and actual sleep time was shorter during the half dose and stop weeks compared to the treatment weeks. Sleep efficiency deteriorated in the stop week. previous termDimprevious termLight Melatonin Onset was earlier after treatment, but this effect disappeared after the stop week. In addition to the effects on sleep, results from questionnaires completed by parents showed that melatonin treatment also had positive effects on children's health and behavior problems and parenting stress. While health deteriorated after treatment discontinuation, the effects on behavior problems and parenting stress remained. Behavior problems at baseline did not influence the effect of melatonin treatment.
Conclusions

This study showed that complete termination of treatment after 4 weeks of melatonin use was too early. However, clinicians may advise a lower dose after a successful treatmen trial of several weeks.

Keywords Melatonin; Termination; Children; Sleep; Health; Behavior problems; Parenting stress

van Norren D, Gorgels TGMF

Year 2011

Authors Dirk van Norren, Theo G.M.F. Gorgels

Report Name The Action Spectrum of Photochemical Damage to the Retina: A Review of Monochromatic Threshold Data

Publication Photochemistry and Photobiology

Issue-page numbers Volume 87, Issue 4, pages 747–753, July/August 2011

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2011.00921.x/abstract

Abstract Photochemical damage to the retina occurs for prolonged exposures of intense light. Two action spectra exist for this phenomenon. In rat an action spectrum matching the absorption spectrum of rhodopsin was found. In macaque, the susceptibility for photochemical damage decreased continuously from the UV to long visible wavelengths. Later, such a spectrum was also found in rat. In search for critical parameters that determine the shape of the spectrum we gathered all available data on the damage threshold dose for monochromatic radiation and noted the experimental conditions. The rhodopsin action spectrum was found in two sources; the other 16 sources adhered to the short wavelength spectrum. Comparing the conditions we conclude that the critical parameters for the generation of either action spectrum remain elusive. Experiments are suggested to resolve this issue and fill a few gaps in our knowledge.

Keywords

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van Norren D, Schellekens P

Year 1990

Authors van Norren D, Schellekens P.

Report Name Blue light hazard in rat

Publication Vision Res.

Issue-page numbers 1990;30(10):1517-20.

URL http://www.ncbi.nlm.nih.gov/pubmed/2247961

Abstract Rats have been extensively used in light damage studies. Retinal damage threshold for white light were found at 1-10 J/cm2, and the action spectrum resembled the absorption spectrum of visual pigment. We wished to answer the question whether a different class of light damage, the "blue light hazard", with white light damage thresholds at about 300 J/cm2, and an action spectrum peaking in the ultra-violet, could also be demonstrated in rat. To that purpose 5 deg patches of retina were exposed to white xenon light with exposure times between 10 sec and 1 hr. We found that for funduscopic threshold damage the product of irradiance and exposure time was constant at a level of 315 J/cm2. Thereafter, the action spectrum was measured by exposing rat eyes to narrow band spectral lights. Threshold irradiant dose ranged from 4 J/cm2 at 379 nm to 2000 J/cm2 at 559 nm. Thus, susceptibility for damage sharply increased towards the ultra-violet, just like in earlier monkey studies. We conclude that in similar experimental conditions susceptibility to photic injury in rat is comparable to that in primates. Rat is the first species for which two different action spectra of photochemical damage have been established.

Keywords

Authors Vandewalle G, Balteau E, Phillips C, Degueldre C, Moreau V, Sterpenich V, et al.

Report Name Daytime light exposure dynamically enhances brain responses

Publication Current Biology

Issue-page numbers 16, 1616–1621, August 22, 2006

URL http://dev.ulb.ac.be/ur2nf/reprints/Vandewallle_CurrBiol_16%2815%2906.pdf

Abstract

In humans, light enhances both alertness and performance during nighttime and daytime [1–4] and influences regional brain function [5]. These effects do not correspond to classical visual responses but involve a non-image forming (NIF) system, which elicits greater endocrine, physiological, neurophysiological, and behavioral responses to shorter light wavelengths than to wavelengths geared toward the visual system [6–11]. During daytime, the neural changes induced by light exposure, and their time courses, are largely unknown. With functional magnetic resonance imaging (fMRI), we characterized the neural correlates of the alerting effect of daytime light by assessing the responses to an auditory oddball task [12–15], before and after a short exposure to a bright white light. Light-induced improvement in subjective alertness was linearly related to responses in the posterior thalamus. In addition, light enhanced responses in a set of cortical areas supporting attentional oddball effects, and it prevented decreases of activity otherwise observed during continuous darkness. Responses to light were remarkably dynamic. They declined within minutes after the end of the light stimulus, following various region-specific time courses. These findings suggest that light can modulate activity of subcortical structures involved in alertness, thereby dynamically promoting cortical activity in networks involved in ongoing nonvisual cognitive processes.

Keywords

Vandewalle G, Gais S, Schabus M, et al. **Year** 2007

Authors Vandewalle G, Gais S, Schabus M, Balteau E, Carrier J, Darsaud A, et al.

Report Name Wavelength-dependent modulation of brain responses to a working memory task by daytime light exposure

Publication Cereb. Cortex

Issue-page numbers 17 (12): 2788-2795. doi: 10.1093/cercor/bhm007

URL http://cercor.oxfordjournals.org/content/17/12/2788.short

Abstract In addition to classical visual effects, light elicits nonvisual brain responses, which profoundly influence physiology and behavior. These effects are mediated in part by melanopsin-expressing light-sensitive ganglion cells that, in contrast to the classical photopic system that is maximally sensitive to green light (550 nm), is very sensitive to blue light (470–480 nm). At present, there is no evidence that blue light exposure is effective in modulating nonvisual brain activity related to complex cognitive tasks. Using functional magnetic resonance imaging, we show that, while participants perform an auditory working memory task, a short (18 min) daytime exposure to blue (470 nm) or green (550 nm) monochromatic light (3 × 1013 photons/cm2/s) differentially modulates regional brain responses. Blue light typically enhanced brain responses or at least prevented the decline otherwise observed following green light exposure in frontal and parietal cortices implicated in working memory, and in the thalamus involved in the modulation of cognition by arousal. Our results imply that monochromatic light can affect cognitive functions almost instantaneously and suggest that these effects are mediated by a melanopsin-based photoreceptor system.

Keywords

Vandewalle G, Maquet P, Dijk DJ **Year** 2009

Authors Vandewalle G, Maquet P, Dijk DJ.

Report Name Light as a modulator of cognitive brain function

Publication Trends in Cognitive Sciences

Issue-page numbers Volume 13, Issue 10, 429-438, 14 September 2009

URL http://www.cell.com/trends/cognitive-sciences/abstract/S1364-6613%2809%2900168-5

Abstract Humans are a diurnal species usually exposed to light while engaged in cognitive tasks. Light not only guides performance on these tasks through vision but also exerts non-visual effects that are mediated in part by recently discovered retinal ganglion cells maximally sensitive to blue light. We review recent neuroimaging studies which demonstrate that the wavelength, duration and intensity of light exposure modulate brain responses to (non-visual) cognitive tasks. These responses to light are initially observed in alertness-related subcortical structures (hypothalamus, brainstem, thalamus) and limbic areas (amygdala and hippocampus), followed by modulations of activity in cortical areas, which can ultimately affect behaviour. Light emerges as an important modulator of brain function and cognition.

Keywords

Authors Vandewalle G, Schmidt C, Albouy G, Sterpenich V, Darsaud A, Rauchs G, et al.

Report Name Brain responses to violet, blue, and green monochromatic light exposures in humans: prominent role of blue light and the brainstem

Publication PLoS ONE

Issue-page numbers 2(11): e1247. doi:10.1371/journal.pone.0001247

URL http://www.plosone.org/article/info:doi/10.1371/journal.pone.0001247

Abstract

Background

Relatively long duration retinal light exposure elicits nonvisual responses in humans, including modulation of alertness and cognition. These responses are thought to be mediated in part by melanopsin-expressing retinal ganglion cells which are more sensitive to blue light than violet or green light. The contribution of the melanopsin system and the brain mechanisms involved in the establishment of such responses to light remain to be established.
Methodology/Principal Findings

We exposed 15 participants to short duration (50 s) monochromatic violet (430 nm), blue (473 nm), and green (527 nm) light exposures of equal photon flux (1013ph/cm2/s) while they were performing a working memory task in fMRI. At light onset, blue light, as compared to green light, increased activity in the left hippocampus, left thalamus, and right amygdala. During the task, blue light, as compared to violet light, increased activity in the left middle frontal gyrus, left thalamus and a bilateral area of the brainstem consistent with activation of the locus coeruleus.
Conclusion/Significance

These results support a prominent contribution of melanopsin-expressing retinal ganglion cells to brain responses to light within the very first seconds of an exposure. The results also demonstrate the implication of the brainstem in mediating these responses in humans and speak for a broad involvement of light in the regulation of brain function.

Keywords

Vandewalle G, Schwartz S, Grandjean D, et al. **Year** 2010

Authors Vandewalle G, Schwartz S, Grandjean D, Wuillaume C, Balteau E, Degueldre C, et al.

Report Name Spectral quality of light modulates emotional brain responses in humans.

Publication PNAS

Issue-page numbers October 25, 2010, doi: 10.1073/pnas.1010180107

URL http://www.pnas.org/content/early/2010/10/14/1010180107

Abstract Light therapy can be an effective treatment for mood disorders, suggesting that light is able to affect mood state in the long term. As a first step to understand this effect, we hypothesized that light might also acutely influence emotion and tested whether short exposures to light modulate emotional brain responses. During functional magnetic resonance imaging, 17 healthy volunteers listened to emotional and neutral vocal stimuli while being exposed to alternating 40-s periods of blue or green ambient light. Blue (relative to green) light increased responses to emotional stimuli in the voice area of the temporal cortex and in the hippocampus. During emotional processing, the functional connectivity between the voice area, the amygdala, and the hypothalamus was selectively enhanced in the context of blue illumination, which shows that responses to emotional stimulation in the hypothalamus and amygdala are influenced by both the decoding of vocal information in the voice area and the spectral quality of ambient light. These results demonstrate the acute influence of light and its spectral quality on emotional brain processing and identify a unique network merging affective and ambient light information.

Keywords

Vanecek J **Year** 1995

Authors Vanecek J

Report Name Melatonin inhibits increase of intracellular calcium and cyclic AMP in neonatal rat pituitary via independent pathways

Publication Mol Cell Endocrinol

Issue-page numbers 107:149–153 doi:10.1016/0303-7207(94)03437-X. PMID:7768326

URL http://www.mendeley.com/research/melatonin-inhibits-increase-intracellular-calcium-cyclic-amp-neonatal-rat-pituitary-via-independent-pathways/

Abstract In neonatal rat pituitary, melatonin inhibits GnRH-induced increase of cAMP and Ca2+i. Both effects are transduced by specific high-affinity melatonin receptors coupled with pertussis toxin-sensitive G-protein. We have attempted to determine whether melatonin acts via independent pathways on both messengers or whether the indole directly inhibits only one of the messengers and the second is decreased as a secondary consequence. Melatonin inhibition of cAMP accumulation was not prevented by agents known to block melatonin effect on Ca2+i such as Na(+)- or Ca2(+)-free medium, Bay K, nifedipine, KCl or gramicidin. Melatonin effect on Ca2+i was not prevented by forskolin or 8-bromo-cAMP. We therefore conclude that melatonin inhibits cAMP accumulation and Ca2+i increase independently by separate pathways.

Keywords

Vaněcek J

Year 1988

Authors Vaněcek J

Report Name Melatonin binding sites

Publication J Neurochem

Issue-page numbers 51:1436–1440 doi:10.1111/j.1471-4159.1988.tb01108.x. PMID:3171587

URL http://www.ncbi.nlm.nih.gov/pubmed/3171587

Abstract The distribution and characterization of specific melatonin binding sites were studied using 125I-melatonin. Autoradiography revealed only three sites of specific melatonin binding in brain: the suprachiasmatic nuclei, the median eminence, and the small part of choroid plexus at the caudal end of the fourth ventricle. Two other sites were detected outside the CNS: the anterior pituitary and the retina. The specific binding of 125I-melatonin was saturable and reversible. The dissociation constant (KD) of the binding sites was 60 pM. The concentration of the binding sites (Bmax) in the median eminence was 26 fmol/mg protein, and in the pituitary 3 fmol/mg protein. Specificity of the binding sites was tested by displacement of 125I-melatonin. The order of potency--melatonin much less than N-acetyl-5-hydroxytryptamine less than 5-methoxytryptamine much less than 5-hydroxytryptamine = 3,4-dihydroxyphenylethylamine = noradrenaline--shows high specificity of the binding sites for melatonin.

Keywords

Vaněček J, Illnerová H

Year 1981

Authors J. Vaněček and Helena Illnerová

Report Name Effect of light at night on the pineal rhythm in N-acetyltransferase activity in the Syrian hamster Mesocricetus auratus

Publication Cellular and Molecular Life Sciences

Issue-page numbers Volume 38, Number 4, 513-514, DOI: 10.1007/BF01952669

URL http://www.springerlink.com/content/qr70287737j73722/

Abstract Pineal N-acetyltransferase activity in the male Syrian hamster exhibited a daily rhythm; the maximal night-time value was 3.5-fold higher than the day-time value. When hamsters were exposed to light at night N-acetyltransferase declined within 30 min to 1/5 of its former activity. These results indicate that in the Syrian hamster the pineal melatonin rhythm may be regulated at least partly via changes in N-acetyltransferase activity.

Keywords

Vanecek J, Klein DC

Year 1995

Authors Vanecek J, Klein DC

Report Name Melatonin inhibition of GnRH-induced LH release from neonatal rat gonadotroph: involvement of Ca2+ not cAMP

Publication Am J Physiol

Issue-page numbers 269:E85–E90. PMID:7631782

URL http://ajpendo.physiology.org/content/269/1/E85.abstract

Abstract Melatonin inhibits gonadotropin-releasing hormone-induced release of luteinizing hormone (LH) from the neonatal rat gonadotrophs. The second messenger involved is not known, although there are several candidates, including adenosine 3',5'-cyclic monophosphate (cAMP) and intracellular free Ca2+. The present study addresses the question of which second messenger mediates melatonin inhibition of LH release. We found that the effect of melatonin was not prevented by cAMP protagonists, including 8-bromo-cAMP, dibutyryl cAMP, 3-isobutyl-1-methylxanthine, and forskolin. However, treatments that enhanced Ca2+ influx masked the effects of melatonin, and treatments that blocked Ca2+ influx mimicked the effects of melatonin. Moreover, melatonin decreased K(+)-induced LH release, which is dependent on Ca2+ influx but did not block release of LH due to thapsigargin-induced mobilization of Ca2+ from intracellular stores. These findings indicate that melatonin inhibits gonadotropin-releasing hormone-induced LH release, primarily through an action involving inhibition of Ca2+ influx, and that cAMP does not seem to be involved in this effect of melatonin.

Keywords

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various

Year 2006

Authors various

Report Name Abstracts from the 17th annual meeting of the society for light treatment and biological rhythms (Eindhoven, the Netherlands)

Publication Chronobiology International

Issue-page numbers Vol. 23, No. 3 , Pages 695-746 (doi:10.1080/07420520600767622)

URL http://informahealthcare.com/doi/abs/10.1080/07420520600767622

Abstract various

Keywords

Vaughan GM, Reiter RJ **Year** 1986

Authors Vaughan GM, Reiter RJ

Report Name Pineal dependence of the Syrian hamster's nocturnal serum melatonin surge

Publication J Pineal Res

Issue-page numbers 3:9–14 doi:10.1111/j.1600-079X.1986.tb00721.x. PMID:3958897

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.1986.tb00721.x/abstract

Abstract The usual nocturnal surge of pineal melatonin content was blocked by bilateral superior cervical ganglionectomy in male Syrian hamsters. Ganglionectomy and pinealectomy each prevented the nocturnal rise of serum melatonin concentration seen in control animals. The normal nocturnal surge of circulating inelatonin in this species appears to depend on the pineal gland and its sympathetic innervation.

Keywords * pineal;

Vaughan MK, Hubbard GB, Champney TH et al. **Year** 1987

Authors Vaughan MK, Hubbard GB, Champney TH et al.

Report Name Splenic hypertrophy and extramedullary hematopoiesis induced in male Syrian hamsters by short photoperiod or melatonin injections and reversed by melatonin pellets or pineal

Publication Am J Anat

Issue-page numbers 179:131–136 doi:10.1002/aja.1001790205. PMID:3618524

URL http://onlinelibrary.wiley.com/doi/10.1002/aja.1001790205/abstract?

Abstract Adult male Syrian hamsters either placed in a short photoperiod alone or kept in a long photoperiod and given daily afternoon injections of the pineal indole melatonin (25 μg) exhibited splenic hypertrophy and extramedullary hematopoiesis in addition to a marked regression in testicular weight. The testicular regression as well as the changes in spleen weight and histology could be prevented if the animals in short photoperiod were either pinealectomized or implanted subcutaneously with a pellet containing 1 mg melatonin. Female Syrian hamsters given afternoon injections of melatonin for 7 or 12 weeks had ovaries devoid of corpora lutea; additionally, these animals had reduced relative spleen weights compared to the control animals. In conclusion, it is apparent that spleen weight varies with the functional status of the gonads. Splenic hypertrophy accompanied by pineal-induced testicular regression in males may be related to splenic extramedullary hematopoiesis.

Keywords

Vaughan MK, Reiter RJ **Year** 1971

Authors Vaughan MK, Reiter RJ

Report Name Transient hypertrophy of the ventral prostate and coagulating glands and accelerated thymic involution following pinealectomy in the mouse

Publication Tex Rep Biol Med, 29:579–586. PMID:4113015

Issue-page numbers 1971 Winter;29(4):579-86.

URL http://www.ncbi.nlm.nih.gov/pubmed/4113015

Abstract N/A

Keywords

Veldhuis JD, Evans WS, Demers LM et al. **Year** 1985

Authors J. D. VELDHUIS, W. S. EVANS,, L. M. DEMERS,, M.O. THORNER, D. WAKAT and A. D. ROGOL

Report Name Altered neuroendocrine regulation of gonadotropin secretion in women distance runners

Publication J Clin Endocrinol Metab

Issue-page numbers 61:557–563 doi:10.1210/jcem-61-3-557. PMID:3926810

URL http://jcem.endojournals.org/content/61/3/557.short

Abstract We tested the hypothesis that the neuroendocrine control of gonadotropin secretion is altered in certain women distance runners with secondary amenorrhea. To this end, we quantitated the frequency and amplitude of spontaneous pulsatile LH secretion during a 24–h interval in nine such women. The ability of the pituitary gland to release LH normally was assessed by administration of graded bolus doses of GnRH during the subsequent 8 h. Compared to normally menstruating women, six of nine amenorrheic distance runners had a distinct reduction i spontaneous LH pulse frequency, with one, three, six, five, four, or two pulses per 24 h (normal, 8–15 pulses/24 h). This reduction in LH pulse frequency occurred without any significant alterations in plasma concentrations of estradiol and free testosterone or 24–h integrated serum concentrations of LH, FSH, or PRL. Moreover, in long-distance runners, the capacity of the pituitarygland to release LH was normal or accentuated in response to exogenous pulses of GnRH. In the six women athletes with diminished spontaneous LH pulsatility, acut ovarian responsiveness also was normal, since serum estradiol concentrations increased normally in response to the GnRH-induced LH pulses. Although long-distance runners had significantly lower estimated percent body fat compared to control women, specific changes in pulsatile gonadotropin release did not correlate with degree of body leanness. In summary, certain long-distance runners with secondary amenorrhea or severe oligomenorrhea have unambiguously decreased spontaneous LH pulse frequency with intact pituitary responsiveness to GnRH. This neuroendocrine disturbance may be relevant to exercise-associated amenorrhea, since pulsatile LH release is a prerequisite for cyclic ovarian function. We speculate that such alterations in pulsatile LH release in exercising women reflect an adaptive respons of the hypothalamic pulse generator controlling the intermittent GnRH signal to the pituitary gland. The basis for amenorrhea in the remaining runners who have normal pulsatile properties of LH release is not known.

Keywords

Veldhuis JD, Johnson ML, Lizarralde G, Iranmanesh A **Year** 1992

Authors Veldhuis JD, Johnson ML, Lizarralde G, Iranmanesh A

Report Name Rhythmic and nonrhythmic modes of anterior pituitary gland secretion

Publication Chronobiol Int

Issue-page numbers 9:371–379 doi:10.3109/07420529209064549. PMID:1394609

URL http://www.mendeley.com/research/rhythmic-nonrhythmic-modes-anterior-pituitary-gland-secretion/

Abstract Because of confounding effects of subject-specific and hormone-specific metabolic clearance, the nature of anterior pituitary secretory events in vivo is difficult to ascertain. We review an approach to this problem, in which deconvolution analysis is used to dissect the underlying secretory behavior of an endocrine gland quantitatively from available serial plasma hormone concentration measurements assuming one- or two-compartment elimination kinetics. This analytical tool allows one to ask the following physiological questions: (a) does the anterior pituitary gland secrete exclusively in randomly dispersed bursts, and/or does a tonic (constitutive) mode of interburst hormone secretion exist? and (b) what secretory mechanisms generate the circadian or nyctohemeral rhythms in blood concentrations of pituitary hormones?

Keywords

Verkasalo PK, Pukkala E, Stevens RG et al. **Year** 1999

Authors Verkasalo PK, Pukkala E, Stevens RG et al.

Report Name Inverse association between breast cancer incidence and degree of visual impairment in Finland

Publication Br J Cancer

Issue-page numbers 80:1459–1460 doi:10.1038/sj.bjc.6690544. PMID:10424751

URL http://www.mendeley.com/research/inverse-association-between-breast-cancer-incidence-and-degree-of-visual-impairment-in-finland/

Abstract A total of 10935 women with visual impairment were identified from the Finnish Register of Visual Impairment and followed up for cancer through the Finnish Cancer Registry for years 1983-1996. Breast cancer risk decreased by degree of visual impairment (P for trend 0.04) which suggests a dose-response relationship between visible light and breast cancer risk.

Keywords

Authors Vermeulen M, Palermo M, Giordano M

Report Name Neonatal pinealectomy impairs murine antibodydependent cellular cytotoxicity

Publication J Neuroimmunol

Issue-page numbers 43:97–101 doi:10.1016/0165-5728(93)90079-E. PMID:8458988

URL http://www.sciencedirect.com/science/article/pii/016557289390079E

Abstract The pineal gland, through its principal hormone melatonin, is able to modulate different immune functions. We have previously demonstrated that exogenous melatonin induces a significant enhancement of murine antibody-dependent cellular cytotoxicity (ADCC). In order to determine whether the pineal gland plays a physiological role in ADCC regulation, we studied the influence of neonatal pinealectomy on this activity. The results presented here indicate that ablation of the pineal gland during the first week of life significantly reduces ADCC levels in adult mice. This impairment appears around 60 days of age, suggesting that sexual hormones may be involved in the pineal effect. Moreover, the administration of melatonin to pinealectomized mice restores ADCC levels regardless of the hour and seasonal time of injection. On the basis of the data reported here, a physiological regulation of ADCC by the pineal gland can be assumed.

Keywords Pineal gland; Pinealectomy; Melatonin; Cytotoxicity; Fcγ receptors

Authors Vgontzas AN, Bixler EO, Lin HM et al

Report Name Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: clinical implications

Publication J Clin Endocrinol Metab

Issue-page numbers 86:3787–3794 doi:10.1210/jc.86.8.3787. PMID:11502812

URL http://jcem.endojournals.org/content/86/8/3787.abstract

Abstract Although insomnia is, by far, the most commonly encountered sleep disorder in medical practice, our knowledge in regard to its neurobiology and medical significance is limited. Activation of the hypothalamic-pituitary-adrenal axis leads to arousal and sleeplessness in animals and humans; however, there is a paucity of data regarding the activity of the hypothalamic-pituitary-adrenal axis in insomniacs. We hypothesized that chronic insomnia is associated with increased plasma levels of ACTH and cortisol. Eleven young insomniacs (6 men and 5 women) and 13 healthy controls (9 men and 4 women) without sleep disturbances, matched for age and body mass index, were monitored in the sleep laboratory for 4 consecutive nights, whereas serial 24-h plasma measures of ACTH and cortisol were obtained during the fourth day. Insomniacs, compared with controls, slept poorly (significantly higher sleep latency and wake during baseline nights). The 24-h ACTH and cortisol secretions were significantly higher in insomniacs, compared with normal controls (4.2 ± 0.3 vs. 3.3 ± 0.3 pm, P = 0.04; and 218.0 ± 11.0 vs. 190.4 ± 8.3 nm, P = 0.07). Within the 24-h period, the greatest elevations were observed in the evening and first half of the night. Also, insomniacs with a high degree of objective sleep disturbance (% sleep time < 70), compared with those with a low degree of sleep disturbance, secreted a higher amount of cortisol. Pulsatile analysis revealed a significantly higher number of peaks per 24 h in insomniacs than in controls (P < 0.05), whereas cosinor analysis showed no differences in the temporal pattern of ACTH or cortisol secretion between insomniacs and controls. We conclude that insomnia is associated with an overall increase of ACTH and cortisol secretion, which, however, retains a normal circadian pattern. These findings are consistent with a disorder of central nervous system hyperarousal rather than one of sleep loss, which is usually associated with no change or decrease in cortisol secretion or a circadian disturbance. Chronic activation of the hypothalamic-pituitary-adrenal axis in insomnia suggests that insomniacs are at risk not only for mental disorders, i.e. chronic anxiety and depression, but also for significant medical morbidity associated with such activation. The therapeutic goal in insomnia should be to decrease the overall level of physiologic and emotional arousal, and not just to improve the nighttime sleep.

Keywords

Vgontzas AN, Chrousos GP **Year** 2002

Authors Vgontzas AN, Chrousos GP

Report Name Sleep, the hypothalamic-pituitary-adrenal axis, and cytokines: multiple interactions and disturbances in sleep disorders

Publication Endocrinol Metab Clin North Am

Issue-page numbers 31:15–36 doi:10.1016/S0889-8529(01)00005-6. PMID:12055986

URL http://www.mendeley.com/research/sleep-hypothalamicpituitaryadrenal-axis-cytokines-multiple-interactions-disturbances-sleep-disorders-2/

Abstract Sleep is an important component of mammalian homeostasis, vital for survival. Sleep disorders are common in the general population and are associated with significant medical, psychologic, and social disturbances. Sleep, in particular deep sleep, has an inhibitory influence on the HPA axis, whereas activation of the HPA axis or administration of glucocorticoids can lead to arousal and sleeplessness. Insomnia, the most common sleep disorder, is associated with a 24-hour increase of ACTH and cortisol secretion, consistent with a disorder of central nervous system hyperarousal. Sleepiness and fatigue are very prevalent in the general population, and recent studies have demonstrated that the proinflammatory cytokines IL-6 and/or TNF-alpha are elevated in disorders associated with excessive daytime sleepiness, such as sleep apnea, narcolepsy, and idiopathic hypersomnia. Sleep deprivation leads to sleepiness and daytime hypersecretion of IL-6. Combined, these findings suggest that the HPA axis stimulates arousal, while IL-6 and TNF-alpha are possible mediators of excessive daytime sleepiness in humans.

Keywords

Vgontzas AN, Zoumakis E, Bixler EO et al. **Year** 2004

Authors Vgontzas AN, Zoumakis E, Bixler EO et al.

Report Name Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines

Publication J Clin Endocrinol Metab

Issue-page numbers 89:2119–2126 doi:10.1210/jc.2003-031562. PMID:15126529

URL http://jcem.endojournals.org/content/89/5/2119.abstract

Abstract Total sleep restriction in humans is associated with increased daytime sleepiness, decreased performance, and hormonal/metabolic disturbances. The effects of mild chronic sleep restriction that mimic real life are not known. To assess the effects of modest sleep restriction from 8 to 6 h/night for 1 wk, 25 young, healthy, normal sleepers (12 men and 13 women) were studied for 12 consecutive nights in the sleep laboratory. After 1 wk of sleep restriction, although subjects' nighttime sleep was deeper, subjects were significantly sleepier (multiple sleep latency test) and performed worse in four primary variables of psychomotor vigilance test (both $P < 0.01$). Furthermore, 24-h secretion of IL-6 was increased by 0.8 ± 0.3 pg/ml ($P < 0.05$) in both sexes, whereas TNFα was increased only in men. Also, the peak cortisol secretion was lower after sleep restriction than at baseline, and this difference was stronger in men (55.18 ± 24.83 nmol/liter; $P < 0.05$) than in women (35.87 ± 24.83 nmol/liter; $P < 0.16$). We conclude that in young men and women, modest sleep loss is associated with significant sleepiness, impairment of psychomotor performance, and increased secretion of proinflammatory cytokines. Given the potential association of these behavioral and physical alterations with health, well-being, and public safety, the idea that sleep or parts of it are optional should be regarded with caution.

Keywords

Vidaller A, Guadarrama F, Llorente L et al. ***Year*** 1992

Authors Vidaller A, Guadarrama F, Llorente L, Méndez JB, Larrea F, Villa AR, Alarcón-Segovia D.

Report Name Hyperprolactinemia inhibits natural killer (NK) cell function in vivo and its bromocriptine treatment not only corrects it but makes it more efficient

Publication J Clin Immunol

Issue-page numbers 12:210–215 doi:10.1007/BF00918091. PMID:1400902

URL http://www.springerlink.com/content/l76881663q267klq/

Abstract We studied NK cell function in eight patients with pathological hyperprolactinemia by measuring 51Cr release by K562 cells exposed to their mononuclear cells and found it decreased compared to normal controls (P less than 0.01). Bromocriptine (BrC) treatment corrected NK function but also made it more efficient at 12:1 than at 25:1 or 50:1 effector:target ratios (ANOVA; P = 0.01). The study of NK cell function in agarose revealed that its decrease in hyperprolactinemia is due to their low active binding to target cells active killing, and recycling capacity. BrC tended to correct them but also increased recycling capacity to levels higher than those of controls (P less than 0.05). Sequential studies in three hyperprolactinemic patients before and after BrC showed correction of NK function within 1 week but its increased efficiency at the 12:1 effector:target ratio required 8 weeks. We conclude that hyperprolactinemia decreases NK cell function. BrC corrects this by decreasing prolactin levels but also makes NK function more efficient by increasing the capacity of NK cells to recycle after killing.

Keywords

Vidaller A, Llorente L, Larrea F et al ***Year*** 1986

Authors Vidaller A, Llorente L, Larrea F, Mendez JP, Alcocer-Varela J, Alarcon-Segovia D.

Report Name T-cell dysregulation in patients with hyperprolactinemia: effect of bromocriptine treatment

Publication Clin Immunol Immunopathol

Issue-page numbers 38:337–343 doi:10.1016/0090-1229(86)90243-6. PMID:2935343

URL http://www.sciencedirect.com/science/article/pii/0090122986902436

Abstract We studied four patients with tumoral hyperprolactinemia and normal ovarian function before and after prolactine levels had become normal with treatment with bromocriptine (BrC), a dopamine agonist that inhibits prolactin release. Their proliferative responses to concanavalin A, pokeweed mitogen, and, to a lesser extent, phytohemagglutinin, their spontaneous and concanavalin A-induced suppression, and their production of interleukin 2 were found to be decreased and to correct partially or completely after bromocriptine treatment. The T-cell response to interleukin 2 was low in two patients in whom it increased after BrC treatment. These findings give insight on the immunomodulatory role of prolactin in vivo.

Keywords

Vinciguerra M, Tevy MF, Mazzoccoli G **Year** 2013

Authors Manlio Vinciguerra, Maria Florencia Tevy, Gianluigi Mazzoccoli

Report Name A ticking clock links metabolic pathways and organ systems function in health and disease

Publication Clinical and Experimental Medicine

Issue-page numbers April 2013

URL http://link.springer.com/article/10.1007/s10238-013-0235-8

Abstract Rhythmic variations with 24-h periodicity hallmark homeostatic regulation, metabolic processes and organ systems function, driven by a circadian timing system composed of central and peripheral oscillators. Recent reports suggest that disrupted circadian rhythmicity of physiology and behavior severely alters body homeostasis. Nuclear receptors and transcriptional regulators sense hormonal and metabolic cues and manage the rhythmic patterns of chromatin remodelling and gene expression, playing a key role in the cross talk between the circadian clock circuitry, the metabolic pathways and the organ systems. The alteration of this cross talk contributes to the pathophysiology of metabolic, degenerative, immune-related and neoplastic diseases.

Keywords

Vinogradova I, Anisimov V **Year** 2013

Authors Irina Vinogradova,

Report Name Melatonin prevents the development of the metabolic syndrome in male rats exposed to different light/dark regimens

Publication Biogerontology

Issue-page numbers June 2013

URL http://link.springer.com/article/10.1007/s10522-013-9437-4

Abstract Effect of light regimens (standard 12:12 light/dark, constant light, natural lightning of the north-west of Russia) and that of melatonin on the development of metabolic syndrome during aging of rats was studied. It was found out that during the process of aging of rats kept in the conditions of the broken rhythm of day and night, different disturbances of metabolism in the form of abdominal obesity, hyperinsulinemia, hypercholesterolemia, hyperglycemia, hyperbetalipoproteinemia and glycosuria occurred. These disturbances can be considered to be metabolic syndrome or the syndrome of insulin resistance. The use of melatonin at night time starting in the rats of 4 month old allowed to decrease the age metabolism disorders in the rats. This fact indirectly proves the insufficiency of this hormone in human in the conditions of natural lighting of the north-west of Russia.

Keywords

Vinogradova IA, Anisimov VN, Bukalev AV, et al. **Year** 2009

Authors Irina A. Vinogradova, Vladimir N. Anisimov, Andrey V. Bukalev, Anna V. Semenchenko, and Mark A. Zabezhinski

Report Name Circadian disruption induced by light-at-night accelerates aging and promotes tumorigenesis in rats

Publication Aging (Albany NY)

Issue-page numbers 2009 October; 1(10): 855–865.

URL http://www.impactaging.com/papers/v1/n10/full/100092.html

Abstract We evaluated the effect of various light/dark regimens on the survival, life span and tumorigenesis in rats. Two hundred eight male and 203 females LIO rats were subdivided into 4 groups and kept at various light/dark regimens: standard 12:12 light/dark (LD); natural lighting of the North-West of Russia (NL); constant light (LL), and constant darkness (DD) since the age of 25 days until natural death. We found that exposure to NL and LL regimens accelerated development of metabolic syndrome and spontaneous tumorigenesis, shortened life span both in male and females rats as compared to the standard LD regimen. We conclude that circadian disruption induced by light-at-night accelerates aging and promotes tumorigenesis in rats. This observation supports the conclusion of the International Agency Research on Cancer that shift-work that involves circadian disruption is probably carcinogenic to humans.

Keywords light-at-night, life span, tumorigenesis, rats

Vinogradova IA, Anisimov VN, Bukalev AV, et al. **Year** 2010

Authors Irina A. Vinogradova, Vladimir N. Anisimov, Andrey V. Bukalev, Viktor A. Ilyukha, Evgeniy A. Khizhkin, Tatiana A. Lotosh, Anna V. Semenchenko, and Mark A. Zabezhinski

Report Name Circadian disruption induced by light-at-night accelerates aging and promotes tumorigenesis in young but not in old rats

Publication Aging (Albany NY)

Issue-page numbers 2010 February; 2(2): 82–92.

URL https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2850144/

Abstract We evaluated the effect of exposure to constant light started at the age of 1 month and at the age of 14 months on the survival, life span, tumorigenesis and age-related dynamics of antioxidant enzymes activity in various organs in comparison to the rats maintained at the standard (12:12 light/dark) light/dark regimen. We found that exposure to constant light started at the age of 1 month accelerated spontaneous tumorigenesis and shortened life span both in male and female rats as compared to the standard regimen. At the same time, the exposure to constant light started at the age of 14 months failed to influence survival of male and female rats. While delaying tumors in males, constant light accelerated tumors in females. We conclude that circadian disruption induced by light-at-night started at the age of 1 month accelerates aging and promotes tumorigenesis in rats, however failed affect survival when started at the age of 14 months.

Keywords Light-at-night, life span, tumorigenesis, rats

Authors Viola AU, Archer SN, James LM, Groeger JA, Lo JC, Skene DJ, von Schantz M, Dijk DJ.

Report Name PER3 polymorphism predicts sleep structure and waking performance

Publication Curr Biol

Issue-page numbers 17:613–618 doi:10.1016/j.cub.2007.01.073. PMID:17346965

URL http://www.mendeley.com/research/per3-polymorphism-predicts-sleep-structure-and-waking-performance/

Abstract Circadian rhythmicity and sleep homeostasis interact to regulate sleep-wake cycles [1-4], but the genetic basis of individual differences in sleep-wake regulation remains largely unknown [5]. PERIOD genes are thought to contribute to individual differences in sleep timing by affecting circadian rhythmicity [6], but not sleep homeostasis [7, 8]. We quantified the contribution of a variable-number tandem-repeat polymorphism in the coding region of the circadian clock gene PERIOD3 (PER3) [9, 10] to sleep-wake regulation in a prospective study, in which 24 healthy participants were selected only on the basis of their PER3 genotype. Homozygosity for the longer allele (PER3(5/5)) had a considerable effect on sleep structure, including several markers of sleep homeostasis: slow-wave sleep (SWS) and electroencephalogram (EEG) slow-wave activity in non-rapid eye movement (non-REM) sleep and theta and alpha activity during wakefulness and REM sleep were all increased in PER3(5/5) compared to PER3(4/4) individuals. In addition, the decrement of cognitive performance in response to sleep loss was significantly greater in the PER3(5/5) individuals. By contrast, the circadian rhythms of melatonin, cortisol, and peripheral PER3 mRNA expression were not affected. The data show that this polymorphism in PER3 predicts individual differences in the sleep-loss-induced decrement in performance and that this differential susceptibility may be mediated by its effects on sleep homeostasis.

Keywords

Viola AU, James LM, Schlangen LJ, Dijk DJ. **Year** 0

Authors Viola AU, James LM, Schlangen LJ, Dijk DJ.

Report Name Blue-enriched white light in the workplace improves self-reported alertness, performance and sleep quality

Publication Scandinavian journal of work environment health

Issue-page numbers Volume: 34, Issue: 4, Publisher: Scandinavian journal of work, environment & health, Pages: 297-306

URL http://www.mendeley.com/research/blueenriched-white-light-in-the-workplace-improves-selfreported-alertness-performance-and-sleep-quality/

Abstract OBJECTIVES: Specifications and standards for lighting installations in occupational settings are based on the spectral sensitivity of the classical visual system and do not take into account the recently discovered melanopsin-based, blue-light-sensitive photoreceptive system. The authors investigated the effects of exposure to blue-enriched white light during daytime workhours in an office setting. METHODS: The experiment was conducted on 104 white-collar workers on two office floors. After baseline assessments under existing lighting conditions, every participant was exposed to two new lighting conditions, each lasting 4 weeks. One consisted of blue-enriched white light (17 000 K) and the other of white light (4000 K). The order was balanced between the floors. Questionnaire and rating scales were used to assess alertness, mood, sleep quality, performance, mental effort, headache and eye strain, and mood throughout the 8-week intervention. RESULTS: Altogether 94 participants mean age 36.4 (SD 10.2) years were included in the analysis. Compared with white light (4000 K), blue-enriched white light (17 000 K) improved the subjective measures of alertness (P<0.0001), positive mood (P=0.0001), performance (P<0.0001), evening fatigue (P=0.0001), irritability (P=0.004), concentration (P<0.0001), and eye discomfort (P=0.002). Daytime sleepiness was reduced (P=0.0001), and the quality of subjective nocturnal sleep (P=0.016) was improved under blue-enriched white light. When the participants' expectation about the effect of the light treatments was entered into the analysis as a covariate, significant effects persisted for performance, alertness, evening fatigue, irritability, difficulty focusing, concentrating, and blurred vision. CONCLUSIONS: Exposure to blue-enriched white light during daytime workhours improves subjective alertness, performance, and evening fatigue.

Keywords

Authors Vioque J, Torres A, Quiles J

Report Name Time spent watching television, sleep duration and obesity in adults living in Valencia, Spain

Publication Int J Obes Relat Metab Disord

Issue-page numbers 24:1683–1688 doi:10.1038/sj.ijo.0801434. PMID:11126224

URL http://www.nature.com/ijo/journal/v24/n12/abs/0801434a.html

Abstract

OBJECTIVE: To analyse the association of time watching television (TV) and physical activity with obesity in the Mediterranean area of Spain with the highest prevalence of obesity.

DESIGN: Cross-sectional study.

SETTING: Valencia Region in Spain.

PARTICIPANTS: A representative sample of 814 men and 958 women, aged 15 y and older, participating in a Health and Nutrition Survey conducted in 1994.

MEASUREMENTS: Height and weight were directly measured during home interviews. The outcome measure was obesity, defined as a body mass index 30 kg/m2. Covariates were self-reported hours of TV viewing, physical activity habits, sleeping duration, age, gender, educational level, smoking and marital status. Prevalence odds ratios (POR) estimated by logistic regression were used as effect measures.

RESULTS: Obese people reported to spend more time watching TV (mean±s.d.: 3.6±1.5 h/day) than non-obese ones (3.0±1.4 h/day), and less sleeping time. In multivariate analysis, obesity was associated with TV viewing, sleeping time and physical activity at work. People watching TV 4 h/day showed a higher adjusted prevalence odds ratio of obesity, POR=2.38 (95% confidence interval, 1.54-3. 69), compared with those watching TV £1 h/day. People who reported to sleep 9 h/day presented a lower POR of obesity than those sleeping £6 h/day, POR=0.43 (0.27-0.67). Statistically significant dose-responses were observed for both associations, so that the prevalence odds ratio of obesity was 30% higher for each hour of increased TV viewing and 24% lower for each additional hour of sleeping time. In addition, the prevalence of obesity was lowest among single people, those more physically active at work, and those with a high educational level.

CONCLUSION: Time spent watching television and a low physical activity at work were related to obesity in adults. The inverse association between obesity and sleep duration deserves further research.

Keywords

Visser J, van Boxel-Dezaire A, Methorst D et al. **Year** 1998

Authors Visser J, van Boxel-Dezaire A, Methorst D et al.

Report Name Differential regulation of interleukin-10 (IL-10) and IL-12 by glucocorticoids in vitro

Publication Blood

Issue-page numbers 91:4255–4264. PMID:9596674

URL Differential regulation of interleukin-10 (IL-10) and IL-12 by glucocorticoids in vitro

Abstract Antigen-presenting cells are thought to modulate the development of Th1 and Th2 cells by the secretion of interleukin-10 (IL-10) and IL-12. Because glucocorticoids (GC) favor the development of Th2 responses, we determined whether dexamethasone (DEX) and hydrocortisone (HC) have differential effects on lipopolysaccharide-induced IL-10 and IL-12 production in whole-blood cultures. Significant inhibition of IL-12(p40) and IL-12(p70) was found with 10−8 mol/L and 10−9 mol/L DEX respectively, whereas IL-10 was relatively insensitive or even stimulated. Accordingly, the expression of IL-12(p40) and IL-12(p35) mRNA was more sensitive to DEX than IL-10 mRNA. The glucocorticoid receptor (GR) antagonist RU486 enhanced IL-12 production and largely abrogated the inhibition of IL-12 by GC, indicating that this suppression was mainly GR-mediated. High concentrations of RU486 were inhibitory for IL-10, suggesting that GC may exert a positive effect on IL-10. In the presence of neutralizing anti–IL-10 antibodies, DEX was still capable of IL-12 suppression whereas RU486 still enhanced IL-12 production, indicating that GC do not modulate IL-12 via IL-10 exclusively. Taken together these results indicate that GC may favor Th2 development by differential regulation of IL-10 and IL-12.

Keywords

Viswanathan AN, Hankinson SE, Schernhammer ES **Year** 2007

Authors Viswanathan AN, Hankinson SE, Schernhammer ES

Report Name Night shift work and the risk of endometrial cancer

Publication Cancer Res

Issue-page numbers 67:10618–10622.doi:10.1158/0008-5472.CAN-07-2485 PMID:17975006

URL http://cancerres.aacrjournals.org/content/67/21/10618.abstract

Abstract Melatonin has several oncostatic properties, including possible anti-estrogenic and anti-aromatase activity, and seems to be linked with fat metabolism. Night workers have lower levels of melatonin, which may predispose them to develop cancer. Endometrial cancer risk is influenced significantly by hormonal and metabolic factors; therefore, we hypothesize that night workers may have an increased risk of endometrial cancer. Of the 121,701 women enrolled in a prospective cohort study, 53,487 women provided data on rotating night shift work in 1988 and were followed through on June 1, 2004. A total of 515 women developed medical record–confirmed invasive endometrial cancer. We used Cox regression models to calculate multivariate relative risks (MVRRs), controlling for endometrial cancer risk factors. Women who worked 20+ years of rotating night shifts had a significantly increased risk of endometrial cancer [MVRR, 1.47; 95% confidence interval (95% CI), 1.03–1.14]. In stratified analyses, obese women working rotating night shifts doubled their baseline risk of endometrial cancer (MVRR, 2.09; 95% CI, 1.24–3.52) compared with obese women who did no night work, whereas a nonsignificant increase was seen among non-obese women (MVRR, 1.07; 95% CI, 0.60–1.92). Women working rotating night shifts for a long duration have a significantly increased risk of endometrial cancer, particularly if they are obese. We speculate that this increased risk is attributable to the effects of melatonin on hormonal and metabolic factors. Our results add to growing literature that suggests women who work at night may benefit from cancer prevention strategies.

Keywords endometrial cancer, light exposure, melatonin, night work

Viswanathan AN, Schernhammer ES. ***Year*** 2009

Authors Viswanathan AN, Schernhammer ES.

Report Name Circulating melatonin and the risk of breast and endometrial cancer in women

Publication Cancer Lett

Issue-page numbers 2009 Aug 18;281(1):1-7. Epub 2008 Dec 12.

URL http://www.ncbi.nlm.nih.gov/pubmed/19070424

Abstract Several decades of observational data have accumulated to implicate a potential role for melatonin in cancer prevention. Experimental studies suggest that the antineoplastic action of melatonin arises through many different mechanisms, including melatonin's antioxidant, antimitotic, and antiangiogenic activity, as well as its ability to modulate the immune system and alter fat metabolism. Melatonin interacts with membrane and nuclear receptors, and may be linked to the regulation of tumor growth. Of particular relevance to breast cancer risk, melatonin may also block the estrogen receptor ERalpha and impact the enzyme aromatase, which produces estradiol. A growing number of epidemiologic studies have evaluated the relationship between night shift work as well as how varying duration of sleep affects peak melatonin secretion at night. While the studies demonstrate lower nightly melatonin levels in night workers, the evidence for an association between sleep duration and melatonin production is less clear. Similarly, both case-control and prospective cohort studies have consistently linked night shift work with breast cancer risk and, more recently, endometrial cancer - another tumor highly sensitive to estrogens. While, to date, the evidence for an association between sleep duration and breast cancer risk is less convincing, overall, there is increasing support for a potentially important link between melatonin and breast cancer risk and perhaps the risk of other tumors. As evidence increases, modifiable factors that have been shown to affect melatonin production, such as night shift work, are likely to gain increasing recognition as potential public health hazards. Additional studies are needed to delineate further the potential of melatonin in cancer prevention.

Keywords

Vitaterna MH, King DP, Chang AM et al. ***Year*** 1994

Authors Vitaterna MH, King DP, Chang AM et al.

Report Name Mutagenesis and mapping of a mouse gene, Clock, essential for circadian behavior

Publication Science

Issue-page numbers 264:719–725 doi:10.1126/science.8171325. PMID:8171325

URL http://www.sciencemag.org/content/264/5159/719.short

Abstract In a search for genes that regulate circadian rhythms in mammals, the progeny of mice treated with N-ethyl-N-nitrosourea (ENU) were screened for circadian clock mutations. A semidominant mutation, Clock, that lengthens circadian period and abolishes persistence of rhythmicity was identified. Clock segregated as a single gene that mapped to the midportion of mouse chromosome 5, a region syntenic to human chromosome 4. The power of ENU mutagenesis combined with the ability to clone murine genes by map position provides a generally applicable approach to study complex behavior in mammals.

Keywords

Vivien-Roels B, Pévet P, Claustrat B

Year 1988

Authors B. Vivien-Roels, P. Pévet, B. Claustrat

Report Name Pineal and circulating melatonin rhythms in the box turtle, Terrapene carolina triunguis: Effect of photoperiod, light pulse, and environmental temperature

Publication General and Comparative Endocrinology

Issue-page numbers Volume 69, Issue 2, February 1988, Pages 163-173

URL http://www.sciencedirect.com/science/article/pii/0016648088900020

Abstract Pineal and circulating melatonin concentrations have been measured throughout the 24-hr cycle in the box turtle, Terrapene carolina triunguis, under different conditions of photoperiod and temperature. An obvious effect of photoperiod on the duration of the night rise of pineal and circulating melatonin is observed; the period of elevated melatonin is 4.30 hr in long photoperiod (18L:6D) and 11.00 hr in short photoperiod (8L:16D). A single pulse of 1 hr illumination beginning 1.30 hr after the onset of darkness, in a 16L:8D cycle, has no effect on pineal or circulating melatonin levels. A clear effect of environmental temperature on the amplitude of the day-night rhythm of melatonin production is observed. A possible role of the pineal of poikilotherms in the transduction of several environmental factors, via the daily pattern of melatonin secretion, is hypothesized.

Keywords

Vollmer C, Michel U, Randler C

Year 2012

Authors Christian Vollmer, Ulrich Michel, and Christoph Randler

Report Name Outdoor Light at Night (LAN) Is Correlated With Eveningness in Adolescents

Publication Chronobiology International

Issue-page numbers Posted online on January 3, 2012. (doi:10.3109/07420528.2011.635232)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.635232

Abstract External zeitgebers synchronize the human circadian rhythm of sleep and wakefulness. Humans adapt their chronotype to the day-night cycle, the strongest external zeitgeber. The human circadian rhythm shifts to evening-type orientation when daylight is prolonged into the evening and night hours by artificial light sources. Data from a survey of 1507 German adolescents covering questions about chronotype and electronic screen media use combined with nocturnal satellite image data suggest a relationship between chronotype and artificial nocturnal light. Adolescents living in brightly illuminated urban districts had a stronger evening-type orientation than adolescents living in darker and more rural municipalities. This result persisted when controlling for time use of electronic screen media, intake of stimulants, type of school, age, puberty status, time of sunrise, sex, and population density. Time spent on electronic screen media use—a source of indoor light at night—is also correlated with eveningness, as well as intake of stimulants, age, and puberty status, and, to a lesser degree, type of school and time of sunrise. Adequate urban development design and parents limiting adolescents' electronic screen media use in the evening could help to adjust adolescents' zeitgeber to early school schedules when they provide appropriate lighting conditions for daytime and for nighttime.

Keywords Adolescents, Chronotype, CSM, Electronic screen media, Intake of stimulants, Light at night (LAN), Light pollution, Midpoint of sleep, Remote sensing

von Gall C, Weaver DR, Moek J et al. **Year** 2005

Authors von Gall C, Weaver DR, Moek J et al.

Report Name Melatonin plays a crucial role in the regulation of rhythmic clock gene expression in the mouse pars tuberalis

Publication Ann N Y Acad Sci

Issue-page numbers 1040:508–511 doi:10.1196/annals.1327.105. PMID:15891103

URL http://onlinelibrary.wiley.com/doi/10.1196/annals.1327.105/abstract?

Abstract Circadian rhythms in physiology and behavior are driven by a central clock residing within the hypothalamic suprachiasmatic nucleus (SCN). Molecularly, the biological clock is based on the transcriptional/translational feedback loop of clock genes (mPer, mCry, Clock, and Bmal1). Circadian expression of clock genes is not limited to the SCN, but is found in many peripheral tissues. Peripheral rhythms depend on neuroendocrine/neuronal output from the SCN. Melatonin, the hormone of darkness, represents an important neuroendocrine output of the circadian clock. The hypophyseal pars tuberalis (PT) is one of the main target regions for melatonin. The aim of the study was to test whether mPer mCry, Clock, and Bmal1 are rhythmically expressed in the mouse PT and how the absence of melatonin receptors affects clock gene expression. We analyzed clock gene expression by in situ hybridization and compared wild-type (WT), melatonin 1 receptor knockout (MT1 ko), and melatonin 2 receptor knockout (MT2 ko) mice. mPer1, mCry1, Clock, and Bmal1, but not mPer2 and mCry2, were rhythmically expressed in the PT of WT and MT2 ko mice. In the PT of MT1 ko mice, expression of mPer1, mCry1, Clock, and Bmal1 was dramatically reduced. We conclude that melatonin, acting through the MT1 receptor, is an important regulator of rhythmic clock gene expression in the mouse PT.

Keywords circadian rhythms; clock genes; mice; melatonin; pars tuberalis; prolactin; photoperiod; seasonality

Vondrasová D, Hájek I, Illnerová H **Year** 1997

Authors Vondrasová D, Hájek I, Illnerová H

Report Name Exposure to long summer days affects the human melatonin and cortisol rhythms

Publication Brain Res

Issue-page numbers 759:166–170 doi:10.1016/S0006-8993(97)00358-2. PMID:9219878

URL http://www.mendeley.com/research/exposure-long-summer-days-affects-human-melatonin-cortisol-rhythms/

Abstract Exposure of 8 human subjects in summer to a natural 16 h bright light photoperiod phase advanced the morning salivary melatonin decline and cortisol rise and shortened the nocturnal melatonin signal by 2 h relative to the winter patterns of the same subjects followed under a combined artificial and natural light 16 h photoperiod. The data suggest that summer days experienced from sunrise till sunset and not winter days with a combined artificial and natural light long photoperiod evoke a true long day response of the human circadian system.

Keywords

Voordouw BC, Euser R, Verdonk RE et al. **Year** 1992

Authors B C Voordouw, R Euser, R E Verdonk, B T Alberda, F H de Jong, A C Drogendijk, B C Fauser and M Cohen

Report Name Melatonin and melatonin-progestin combinations alter pituitary-ovarian function in women and can inhibit ovulation

Publication J Clin Endocrinol Metab

Issue-page numbers 74:108–117 doi:10.1210/jc.74.1.108. PMID:1727807

URL http://jcem.endojournals.org/content/74/1/108.short

Abstract Although melatonin (MEL) controls seasonal reproductive cyclicity in some mammalian species, its role in women is controversial. In this study data are presented related to the influence of MEL or MEL-progestin combinations on the pituitary-ovarian axis and ovulation in 32 women. MEL was administered in a dosage of 300 mg to 12 women for 4 months [to 8 women daily (days 1-30) and to 4 women on days 5-17 of the cycle]. MEL was also combined with the synthetic progestin norethisterone (NET) in an attempt to evaluate MEL's effect on a partially suppressed pituitary-ovarian axis. In 16 women, 4 combinations were tested on 4 women each on days 1-21: dosages of 300 mg MEL/0.75 mg NET, 75 mg MEL/0.75 mg NET, 7.5 mg MEL/0.75 mg NET, and 75 mg MEL/0.30 mg NET. In addition, 2 women were medicated with 300 mg MEL alone, and 2 were medicated with 300 mg MEL/0.15 mg NET on days 1-21 for 2 months. During the study, LH, FSH, estradiol (E2), and progesterone (P4) blood levels were determined at regular intervals. After a period of 4 months, daily administration of 300 mg MEL (days 1-30) caused significantly decreased mean LH levels compared to those in 8 nonmedicated controls (P less than 0.001). Also compared to nonmedicated control data, a significant inhibition of P4 in the first and fourth medication months (P less than 0.001) was observed. LH and E2 inhibition reached significance in the fourth medication month (P less than 0.005). Also, the treatments of 300 mg MEL (days 5-17) and 75 mg MEL combined with 0.3 mg NET caused a significant decrease in LH, E2, and P4 levels compared to those in the nonmedicated control group in the first and fourth medication months (P less than 0.05). The data further suggest an additive or synergistic effect between MEL and NET. The medications did not alter sleep-wake rhythms and were not complicated by any side-effects. The presented data suggest that MEL and MEL/NET combinations inhibit ovarian function in women, and that MEL/NET combinations can emerge as effective oral contraceptives.

Keywords

Vos JJ, Bouman MA **Year** 1964

Authors Vos J. J., and M.A. Bouman

Report Name Contribution of the Retina to Entropic Scatter

Publication J. Opt. Soc. Am.

Issue-page numbers 54 (1964) pp 95-100

URL N/A

Abstract N/A

Keywords glare

Authors Wada K, Nagata C, Nakamura K, Iwasa S, Shiraki M, Shimizu H

Report Name Light exposure at night, sleep duration and sex hormone levels in pregnant Japanese women.

Publication Endocr J.

Issue-page numbers 2012 Feb 15. [Epub ahead of print]

URL http://www.ncbi.nlm.nih.gov/pubmed/22333297

Abstract

The association between light exposure at night and sex hormone levels in utero has scarcely reported. We assessed the associations between sleep duration or being awake in the late evening hours, which can be as indicator of light exposure at night, and the maternal and umbilical blood hormone levels during pregnancy and at delivery among Japanese women. The data for 236 women and their newborns who visited a maternal clinic in Gifu, Japan, between May 2000 and October 2001 were analyzed. Maternal blood samples were obtained at approximately the 10th weeks, 29th weeks of gestation, and at delivery. Umbilical cord artery blood was immediately drawn after birth. Information for sleep during pregnancy was obtained by a self-administered questionnaire. The levels of estradiol and testosterone were measured using radioimmunoassay. Maternal serum testosterone level in the 10th week was higher among those who were awake at or after 1:00 a.m. than among those who were asleep at that time (P = 0.032). Maternal estradiol level in the 29th week was inversely associated with sleep duration on weekends (P = 0.043). Umbilical testosterone level at delivery inversely correlated with sleep duration on weekdays (P = 0.030). These associations were somewhat stronger among mothers with female offspring than those with male offspring. These results suggested that exposure to light at night might increase sex hormone levels during pregnancy.

Keywords

Authors Amely Wahnschaffe, Sven Haedel, Andrea Rodenbeck, Claudia Stoll, Horst Rudolph,

Report Name Out of the Lab and into the Bathroom: Evening Short-Term Exposure to Conventional Light Suppresses Melatonin and Increases Alertness Perception

Publication International Journal of Molecular Sciences

Issue-page numbers 2013, 14, 2573-2589; doi:10.3390/ijms14022573

URL http://www.mdpi.com/1422-0067/14/2/2573/pdf

Abstract

Life in 24-h society relies on the use of artificial light at night that might disrupt synchronization of the endogenous circadian timing system to the solar day. This could have a negative impact on sleep–wake patterns and psychiatric symptoms. The aim of the study was to investigate the influence of evening light emitted by domestic and work place lamps in a naturalistic setting on melatonin levels and alertness in humans. Healthy subjects (6 male, 3 female, 22–33 years) were exposed to constant dim light (<10 lx) for six evenings from 7:00 p.m. to midnight. On evenings 2 through 6, 1 h before habitual bedtime, they were also exposed to light emitted by 5 different conventional lamps for 30 min. Exposure to yellow light did not alter the increase of melatonin in saliva compared to dim light baseline during (38 ± 27 pg/mL vs. 39 ± 23 pg/mL) and after light exposure (39 ± 22 pg/mL vs. 44 ± 26 pg/mL). In contrast, lighting conditions including blue components reduced melatonin increase significantly both during (office daylight white: 25 ± 16 pg/mL, bathroom daylight white: 24 ± 10 pg/mL, Planon warm white: 26 ± 14 pg/mL, hall daylight white: 22 ± 14 pg/mL) and after light exposure (office daylight white: 25 ± 15 pg/mL, bathroom daylight white: 23 ± 9 pg/mL, Planon warm white: 24 ± 13 pg/mL, hall daylight white: 22 ± 26 pg/mL). Subjective alertness was significantly increased after exposure to three of the lighting conditions which included blue spectral components in their spectra. Evening exposure to conventional lamps in an everyday setting influences melatonin excretion and alertness perception within 30 min.

Keywords

Waldhauser F, Boepple PA, Crowley WF Jr *Year* 1993

Authors Waldhauser F, Boepple PA, Crowley WF Jr

Report Name Changes of serum melatonin levels during human sexual maturation. In: Grave GD & Cutler GB, Jr, Eds

Publication Sexual Precocity

Issue-page numbers New York: Raven Press. pp. 181–192.

URL N/A

Abstract N/A

Keywords

Waldhauser F, Boepple PA, Schemper M et al. *Year* 1991

Authors F. WALDHAUSER, P. A. BOEPPLE, M. SCHEMPER, M. J. MANSFIELD and W. F. CROWLEY JR.

Report Name Serum melatonin in central precocious puberty is lower than in age-matched prepubertal children

Publication J Clin Endocrinol Metab

Issue-page numbers 73:793–796 doi:10.1210/jcem-73-4-793. PMID:1909703

URL http://jcem.endojournals.org/content/73/4/793.short

Abstract

In children a progressive decrease in nocturnal serum melatonin (MT) has been shown with advancing age, suggesting a reduction in the amplitude of the circadian MT curve with maturation. Whether this alteration of MT levels is related to human sexual maturation or occurs independently remains to be elucidated. Also, the impact of gonadal steroids on the MT rhythm remains an open question.

We examined 56 patients (51 females and 5 males) with central precocious puberty (52 idiopathic and 4 neurogenic). Patients were studied before and 3, 6, and 12 months after initiation of GnRH analog treatment. Three hundred and thirty-seven endocrinologically normal subjects (190 males and 147 females) served as controls. In all subjects nocturnal serum MT (blood collection between 2300 and 0100 h) was measured with a highly specific RIA.

In young patients, aged 1–5 yr, we found significantly lower MT levels than in age-matched controls. Pubertal patients, aged 5–9 yr, displayed nocturnal MT levels in the same range as control subjects approaching normal pubertal age. In contrast to endocrinologically normal children, there was no age-dependent decrease in nocturnal MT in untreated precocious puberty; rather, it appeared that serum MT had already declined in association with the onset of sexual maturation. Although there was a significant difference in weight between patients and agematched controls, the low MT values in patients 1–5 yr old were only partly explained by the weight difference ($P < 0.0009$); their pubertal status also contributed significantly ($P < 0.006$). Pituitary-gonadal suppression induced by long term GnRH analog treatment did not result in a return to prepubertal MT levels; rather, nocturnal MT decreased during therapy.

The collected data indicate that nocturnal serum MT levels are related to sexual maturation, since serum MT is similar in precocious puberty and normal pubertal children. Since suppression of the pituitary-gonadal axis did not result in increases in nocturnal MT levels in young patients with precocity (i.e. return to age-appropriate levels), the reduction of nocturnal MT with normal puberty is not likely to be dependent on pubertal gonadotropin or sex steroid milieu.

Keywords

Waldhauser F, Dietzel M | ***Year*** 1985

Authors Waldhauser F, Dietzel M

Report Name Daily and annual rhythms in human melatonin secretion: role in puberty control

Publication Ann N Y Acad Sci

Issue-page numbers 453:205–214 doi:10.1111/j.1749-6632.1985.tb11811.x. PMID:3865581

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1985.tb11811.x/abstract

Abstract N/A

Keywords

Waldhauser F, Steger H, Vorkapic P | ***Year*** 1987

Authors Waldhauser F, Steger H, Vorkapic P

Report Name Melatonin secretion in man and the influence of exogenous melatonin on some physiological and behavioral variables

Publication Adv Pineal Res

Issue-page numbers 2:207–223

URL N/A

Abstract N/A

Keywords

Authors Waldhauser F, Weiszenbacher G, Frisch H et al.

Report Name Fall in nocturnal serum melatonin during prepuberty and pubescence

Publication Lancet

Issue-page numbers 323:362–365 doi:10.1016/S0140-6736(84)90412-4. PMID:6141425

URL http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2884%2990412-4/abstract

Abstract Morning (7:30 AM to 10:00 AM) and nighttime (11:00 PM to 1:00 AM) serum melatonin concentrations were measured in 89 children, adolescents, and young adults. Morning levels (generally 0-20 pg/ml) did not change with sexual maturation or with age. Nighttime levels decreased significantly both with sexual maturation and with age. Nighttime serum melatonin fell from 195±24 pg/ml (mean±SEM) in prepubertal children younger than 7 years of age, to 119±23 pg/ml in prepubertal children aged 7 years or older, to 49±4 pg/ml in young adults (puberty stage v). Similarly, nocturnal serum melatonin levels fell from 210±35 pg/ml in the youngest age group (ages 1-5) to 133±17 in children aged 5-11 years and to 46±4 in young adults. Nocturnal plasma concentrations of luteinising hormone measured at various stages of puberty tended to vary inversely with those of melatonin (r=-0·35). Past difficulties in demonstrating a relation between gonadal maturation and human pineal function may have reflected the use of insufficiently sensitive or specific melatonin assays, or serum sampling only during daytime, or the initiation of sample collection when subjects were already too old.

Keywords

Authors Waldhauser F, Weiszenbacher G, Tatzer E et al.

Report Name Alterations in nocturnal serum melatonin levels in humans with growth and aging

Publication J Clin Endocrinol Metab

Issue-page numbers 66:648–652 doi:10.1210/jcem-66-3-648. PMID:3350912

URL http://jcem.endojournals.org/content/66/3/648.short

Abstract

The available data on potential alterations in serum melatonin (MLT) levels during a human lifetime are fragmentary and inconsistent. We, therefore, measured day- and nighttime serum MLT concentrations in 367 subjects (210 males and 157 females), aged 3 days to 90 yr. Blood samples were collected between 0730 and 1000 h and between 2300 and 0100 h. Serum MLT levels were measured by RIA.

The mean nighttime serum MLT concentration was low during the first 6 months of life, i.e. 27.3 ± 5.4 (±se) pg/mL (0.12 ± 0.02 nmol/L). It then increased to a peak value at 1–3 yr of age [329.5 ± 42.0 pg/mL; (1.43 ± 0.18 nmol/L)], and it was considerably lower [62.5 ± 9.0 pg/mL; (0.27 ± 0.04 nmol/L)] in individuals aged 15–20 yr. During the following decades serum MLT declined moderately until old age (70–90 yr of age), i.e. 29.2 ± 6.1 pg/mL (0.13 ± 0.03 nmol/L). This biphasic MLT decline follows 2 exponential functions with different slopes (from age 1–20 yr: $r = -0.56$; $P < 0.001$; $y = 278.7 \times e - 0.09x$; from age 20–90 yr: $r = -0.44$; $P < 0.001$; $y = 84.8 \times e - 0.017x$). The decrease in nocturnal serum MLT in children and adolescents (1–20 yr) correlated with the increase in body weight ($r = -0.54$; $P < 0.001$) and body surface area ($r = -0.71$; $P < 0.001$). At a later age (20–90 yr) there was no correlation among these variables. Daytime serum MLT levels were low and no agerelated alterations were found.

This study revealed major age-related alterations in nocturnal serum MLT levels. The negative correlation between serum MLT and body weight in childhood and adolescence is evidence that expansion of body size is responsible for the huge MLT decrease during that period. The moderate decline at older ages must derive from other factors.

Keywords

Waldstreicher J, Duffy JF, Brown EN et al. **Year** 1996

Authors Waldstreicher J, Duffy JF, Brown EN et al.

Report Name Gender differences in the temporal organization of proclactin (PRL) secretion: evidence for a sleep-independent circadian rhythm of circulating PRL levels- a clinical research cer

Publication J Clin Endocrinol Metab

Issue-page numbers 81:1483–1487 doi:10.1210/jc.81.4.1483. PMID:8636355

URL http://www.ncbi.nlm.nih.gov/pubmed/8636355

Abstract Although a nocturnal rise in PRL secretion is well known, it has long been presumed to be evoked by sleep. To determine whether PRL secretion was driven by a sleep-independent circadian rhythm, we studied 12 men and 10 women using a constant routine protocol. Under the constant routine conditions of continuous semirecumbent wakefulness in constant indoor room light with hourly meals distributed throughout the day and night, a persistent circadian rhythm of PRL secretion was present in men and in women at the follicular and luteal phases of the menstrual cycle. Furthermore, the amplitude of this rhythm in women was significantly greater than that in men. The present data demonstrate the presence of a robust sleep-independent endogenous circadian rhythm of PRL secretion in humans. We hypothesize that this endogenous component of the circadian rhythm of PRL secretion together with those of body temperature, urine production, and cortisol, TSH, and melatonin secretion are driven by the central circadian pacemaker located in the suprachiasmatic nucleus of the hypothalamus.

Keywords

Walters JF, Hampton SM, Ferns GA, Skene DJ **Year** 2005

Authors Walters JF, Hampton SM, Ferns GA, Skene DJ

Report Name Effect of menopause on melatonin and alertness rhythms investigated in constant routine conditions

Publication Chronobiol Int

Issue-page numbers 22:859–872 doi:10.1080/07420520500263193. PMID:16298772

URL http://www.mendeley.com/research/effect-menopause-melatonin-alertness-rhythms-investigated-constant-routine-conditions/

Abstract Although studies have reported the effects of the menstrual cycle on melatonin rhythmicity, none has investigated the effects of menopause on the melatonin rhythm. The circadian rhythm in melatonin and its relationship to subjective alertness was investigated in pre- and postmenopausal women under constant routine conditions (controlled posture, dim lighting, calorie intake, temperature, and prolonged wakefulness). Eleven healthy pre-menopausal (42+/-4 yr) and 10 postmenopausal women (55+/-2 yr) participated in the study. Salivary melatonin samples and subjective measures of alertness and sleepiness were assessed hourly during the 22 h constant routine protocol. Postmenopausal women had a significantly earlier melatonin acrophase (1.1+/-0.5 h clock time in decimal h; mean+/-SEM, $p<0.05$) compared to the pre-menopausal women (2.3+/-0.3 h). There was no significant difference between melatonin onset and amplitude between the pre-menopausal and postmenopausal women. Self-rated alertness declined in both study groups as the length of sleep deprivation increased. Melatonin onset preceded the onset of self-rated sleepiness in both groups. The time interval between melatonin onset and the onset of sleepiness and alertness offset was significantly greater in the postmenopausal women compared to the pre-menopausal women. In conclusion, under controlled experimental conditions the timing of the melatonin rhythm was advanced in postmenopausal women altering its phase relationship to subjective alertness and sleepiness.

Keywords

Wang AL, Lukas TJ, Yuan M, et al. **Year** 2009

Authors Wang AL, Lukas TJ, Yuan M, Du N, Handa JT, Neufeld AH.

Report Name Changes in retinal pigment epithelium related to cigarette smoke: possible relevance to smoking as a risk factor for age-related macular degeneration

Publication PLoS ONE

Issue-page numbers 4(4): e5304. doi:10.1371/journal.pone.0005304

URL http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0005304

Abstract Age-related Macular Degeneration (AMD) is a major cause of central vision loss in the elderly and smoking is a primary risk factor associated with the prevalence and incidence of AMD. To better understand the cellular and molecular bases for the association between smoking and AMD, we determined the effects of Benzo(a)Pyrene (B(a)P), a toxic element in cigarette smoke, on cultured retinal pigment epithelia (RPE) and we examined the RPE/choroid from mice exposed to chronic cigarette smoke. We measured: mitochondrial DNA (mtDNA) damage, phagocytic activity, lysosomal enzymes, exosome markers and selected complement pathway components. In the presence of a non-cytotoxic dose of B(a)P, there was extensive mtDNA damage but no nuclear DNA damage. RPE phagocytic activity was not altered but there were increased lysosomal activity, exocytotic activity and complement pathway components. Retinas from mice exposed to cigarette smoke contained markers for mtDNA damage, exosomes and complement pathway components surrounding Bruch's membrane. Markers for these processes are found in drusen from AMD patients. Thus, smoking may cause damage to mtDNA and increased degradative processes in the RPE. These altered cell biological processes in the RPE may contribute to the formation of drusen in individuals who are cigarette smokers and underlie susceptibility to genetic mutations associated with AMD.

Keywords

Wang C, Fan S, Li Z et al. **Year** 2005

Authors Chenguang Wang, Saijun Fan, Zhiping Li, Maofu Fu, Mahadev Rao, Yongxian Ma, Michael P. Lisanti, Chris Albanese, Benita S. Katzenellenbogen, et al.

Report Name Cyclin D1 antagonizes BRCA1 repression of estrogen receptor alpha activity

Publication Cancer Res

Issue-page numbers 65:6557–6567 doi:10.1158/0008-5472.CAN-05-0486. PMID:16061635

URL http://cancerres.aacrjournals.org/content/65/15/6557

Abstract The cyclin D1 gene is frequently overexpressed in human breast cancer and is capable of inducing mammary tumorigenesis when overexpressed in transgenic mice. The BRCA1 breast tumor susceptibility gene product inhibits breast cancer cellular growth and the activity of several transcription factors. Herein, cyclin D1 antagonized BRCA1-mediated repression of estrogen receptor α (ERα)–dependent gene expression. Cyclin D1 repression of BRCA1 function was mediated independently of its cyclin-dependent kinase, retinoblastoma protein, or p160 (SRC-1) functions in human breast and prostate cancer cells. In vitro, cyclin D1 competed with BRCA1 for ERα binding. Cyclin D1 and BRCA1 were both capable of binding ERα in a common region of the ERα hinge domain. A novel domain of cyclin D1, predicted to form a helix-loop-helix structure, was required for binding to ERα and for rescue of BRCA1-mediated ERα transcriptional repression. In chromatin immunoprecipitation assays, 17β-estradiol (E2) enhanced ERα and cyclin D1 recruitment to an estrogen response element (ERE). Cyclin D1 expression enhanced ERα recruitment to an ERE. E2 reduced BRCA1 recruitment and BRCA1 expression inhibited E2-induced ERα recruitment at 12 hours. Cyclin D1 expression antagonized BRCA1 inhibition of ERα recruitment to an ERE, providing a mechanism by which cyclin D1 antagonizes BRCA1 function at an ERE. As cyclin D1 abundance is regulated by oncogenic and mitogenic signals, the antagonism of the BRCA1-mediated ERα repression by cyclin D1 may contribute to the selective induction of BRCA1-regulated target genes.

Keywords

Wang W, Shi F

Year 2012

Authors Wei WANG, Fangxiong SHI

Report Name Induction of abnormal oocyte division under the constant light in the

Publication Asian Pacific Journal of Reproduction

Issue-page numbers (2012)-

URL http://apjr.net/Paper/12-0039.pdf

Abstract Objective: In order to study the effect of constant light on the ovary, 12 young adult female eraxtasm wineareti oenx paonsde dth teo ocvoanrsietas nwt elrieg hetx faomr i3n7e dd ahyisst oalnodg itchaelliyr . eTshtreo uress cuyltcsl essh owweerde trheacto rcdoends tabnyt dliagihlyt induced in an abnormal and uncontrolled division of oocytes. In these divided-oocyte follicles (fDolOliFcsu)l, atrw aon otrru mmo. re divided-oocytes shared one zona pellucida and usually floated freely in the from multioocyte fTohlliisc lfeasn tastic phenomenon was discovered for the first time, and it was different mice and dogs.

Keywords

Wang X

Year 2009

Authors Wang X.

Report Name The antiapoptotic activity of melatonin in neurodegenerative diseases

Publication CNS Neurosci Ther

Issue-page numbers 2009 Winter;15(4):345-57. Epub 2009 Oct 10.

URL http://www.ncbi.nlm.nih.gov/pubmed/19818070

Abstract Melatonin plays a neuroprotective role in models of neurodegenerative diseases. However, the molecular mechanisms underlying neuroprotection by melatonin are not well understood. Apoptotic cell death in the central nervous system is a feature of neurodegenerative diseases. The intrinsic and extrinsic apoptotic pathways and the antiapoptotic survival signal pathways play critical roles in neurodegeneration. This review summarizes the reports to date showing inhibition by melatonin of the intrinsic apoptotic pathways in neurodegenerative diseases including stroke, Alzheimer disease, Parkinson disease, Huntington disease, and amyotrophic lateral sclerosis. Furthermore, the activation of survival signal pathways by melatonin in neurodegenerative diseases is discussed.

Keywords

Wang X-S, Armstrong MEG, Cairns BJ, et al. ***Year*** 2011

Authors X-S. Wang,corresponding author M. E. G. Armstrong, B. J. Cairns, T. J. Key, and R. C. Travis

Report Name Shift work and chronic disease: the epidemiological evidence

Publication Occup Med (Lond)

Issue-page numbers March; 61(2): 78–89.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3045028/

Abstract

Background Shift work, including night work, has been hypothesized to increase the risk of chronic diseases, including cancer, cardiovascular disease (CVD), metabolic syndrome and diabetes. Recent reviews of evidence relating to these hypotheses have focussed on specific diseases or potential mechanisms, but no general summary of the current data on shift work and chronic disease has been published.
Methods Systematic and critical reviews and recent original studies indexed in PubMed prior to 31 December 2009 were retrieved, aided by manual searches of reference lists. The main conclusions from reviews and principle results from recent studies are presented in text and tables.
Results Published evidence is suggestive but not conclusive for an adverse association between night work and breast cancer but limited and inconsistent for cancers at other sites and all cancers combined. Findings on shift work, in relation to risks of CVD, metabolic syndrome and diabetes are also suggestive but not conclusive for an adverse relationship.
Conclusions Heterogeneity of study exposures and outcomes and emphasis on positive but non-significant results make it difficult to draw general conclusions. Further data are needed for additional disease endpoints and study populations.

Keywords Cancer, cardiovascular disease, circadian disruption, diabetes, light at night, melatonin, metabolic syndrome, night work, shift work

Authors Wang XS, Travis RC, Reeves G, Green J, Allen NE, Key TJ, Roddam AW, Beral V.

Report Name Characteristics of the Million Women Study participants who have and have not worked at night

Publication Scand J Work Environ Health

Issue-page numbers 2012 Jul 9. pii: 3313. doi: 10.5271/sjweh.3313. [Epub ahead of print]

URL http://www.ncbi.nlm.nih.gov/pubmed/22772745

Abstract

OBJECTIVES:

The aim of this study was to compare the characteristics of women who had and had not worked at night in terms of their risk factors for common disease, indicators of general health, social activities, employment, and sleep behavior.
METHODS:

The Million Women Study is a large prospective cohort study of women's health in the United Kingdom with 1.3 million women recruited during 1996-2001 (aged 50-64 years) through 66 National Health Service breast screening centers. We analyzed the data from a random sample of 41 652 participants who, in 2009-2010, reported their history of night work.
RESULTS:

Of the participants, 1 in 8 women (13%) reported that they had ever worked at night and 1 in 50 (2%) reported working at night for ≥20 years. For 33 sociodemographic, behavioral, reproductive, and hormonal factors examined, 20 showed highly significant differences between "ever" and "never" night workers (P<0.0001); 12 showed significant trends by duration of night work (P<0.01). In particular, compared to women who had never worked at night, women who had worked at night were more likely to (i) be of lower socioeconomic status [the odds ratio (OR) for ever versus never night workers of being in the lowest third of socioeconomic status was 1.15, 99% confidence interval (95% CI) 1.06-1.25]; (ii) have ever used hormone replacement therapy (HRT) for the menopause (OR 1.43, 99% CI 1.33-1.55); (iii) be current smokers (OR 1.37, 99% CI 1.19-1.58); and (iv) be obese (OR 1.26, 99% CI 1.15-1.37). Compared to women who had never worked at night, women who had worked at night for ≥20 years were more likely to be (i) of lower socioeconomic status (OR 1.28, 99% CI 1.04-1.57); (ii) nulliparous (OR 1.47, 99% CI 1.12-1.91); (iii) current smokers (OR 1.63, 99% CI 1.18-2.25); and (iv) obese (OR 1.55, 99% CI 1.25-1.93). Former night workers were more likely than never night workers to report a range of sleep disturbances, including poor quality of sleep (OR 1.15, 99% CI 1.01-1.31) and having to take medication to sleep (OR 1.35, 99% CI 1.15-1.60).
CONCLUSIONS:

Women who reported having worked at night were substantially different from those who reporting never having worked at night and many of the differences would put "ever night workers" at increased risks of cancer, vascular disease, and many other common conditions.

Keywords cancer; cohort; Million Women Study; night work; risk factor; shift work; sleep; vascular disease

Authors Wang Z, Keller LM, Dillon J, Gaillard ER.

Report Name Oxidation of A2E results in the formation of highly reactive aldehydes and ketones

Publication Photochemistry and Photobiology

Issue-page numbers Volume 82, Issue 5, pages 1251–1257, September 2006

URL http://onlinelibrary.wiley.com/doi/10.1562/2006-04-01-RA-864/full

Abstract It has been reported that the photo-oxidation of A2E, a component of human retinal lipofuscin, leads to products that are toxic to cells via dark reactions. Because these compounds have been implicated in the development of various maculopathies such as age-related macular degeneration (AMD), it is important to determine the structures of those deleterious compounds. Both the photo-oxidation and auto-oxidation of A2E lead to the same complex mixture of products, some of which have lower molecular weights than the staring material. Because A2E is homologous to β-carotene, it was hypothesized that its oxidation would lead to products analogous to those found in oxidized β-carotene, namely, a series of cleavage products along the acyclic chain with the concomitant formation of aldehydes. This was found to be the case based upon 1) the formation of all of the aldehydes predicted from the oxidation of β-carotene, 2) the loss of 28 amu (carbonyl moiety) from the molecular ion, 3) the facile reaction of the aldehydes with nitrophenylhydrazines to form nitrophenylhydrazones and 4) the subsequent MS/MS cleavage of those derivatives at the N-N bond. If formed in vivo, these aldehydes would have toxic effects on any cell. Finally, the similarity in product mixtures from both the photo-oxidation and auto-oxidation strongly suggests that the intermolecular photo-oxidation of A2E results primarily from a radical process without the involvement of singlet oxygen. Any formation of singlet oxygen most likely arises from sensitization by the aldehyde oxidation products, as this process is well known for aldehydes, in general, and retinal, specifically.

Keywords

Authors Ward EM, Schulte PA, Straif K, Hopf NB, Caldwell JC, Carreón T, et al.

Report Name Research Recommendations for Selected IARC-Classified Agents

Publication Environ Health Perspect

Issue-page numbers 118:1355-1362.

URL http://dx.doi.org/10.1289/ehp.0901828

Abstract

Objectives: There are some common occupational agents and exposure circumstances for which evidence of carcinogenicity is substantial but not yet conclusive for humans. Our objectives were to identify research gaps and needs for 20 agents prioritized for review based on evidence of widespread human exposures and potential carcinogenicity in animals or humans.

Data sources: For each chemical agent (or category of agents), a systematic review was conducted of new data published since the most recent pertinent International Agency for Research on Cancer (IARC) Monograph meeting on that agent.

Data extraction: Reviewers were charged with identifying data gaps and general and specific approaches to address them, focusing on research that would be important in resolving classification uncertainties. An expert meeting brought reviewers together to discuss each agent and the identified data gaps and approaches.

Data synthesis: Several overarching issues were identified that pertained to multiple agents; these included the importance of recognizing that carcinogenic agents can act through multiple toxicity pathways and mechanisms, including epigenetic mechanisms, oxidative stress, and immuno- and hormonal modulation.

Conclusions: Studies in occupational populations provide important opportunities to understand the mechanisms through which exogenous agents cause cancer and intervene to prevent human exposure and/or prevent or detect cancer among those already exposed. Scientific developments are likely to increase the challenges and complexities of carcinogen testing and evaluation in the future, and epidemiologic studies will be particularly critical to inform carcinogen classification and risk assessment processes.

Keywords animal, carcinogen, carcinogenesis, epidemiology, human, IARC, mechanisms of carcinogenicity, occupational.

Warman VL, Dijk D, Warman GR, et al. **Year** 2003

Authors Victoria L. Warman, Derk-Jan Dijk, Guy R. Warman, Josephine Arendt, Debra J. Skene

Report Name Phase advancing human circadian rhythms with short wavelength light

Publication Neuroscience Letters

Issue-page numbers 342 (2003) 37-40

URL http://www.jigsawhealth.com/document_manager/HighSensitivityShortWavelengths.pdf

Abstract The photoreceptor(s) responsible for photoresetting of the human circadian system have not been identified. The aim of the present study was to assess the ability of short wavelength light to alter the timing of circadian rhythms. Eleven male subjects were studied in 15 4-day trials with a single 4 h light pulse administered on day 3, immediately after habitual wake time. The magnitude of the phase shifts in the melatonin acrophase and offset were similar after white (4300 mW/cm2) and short wavelength (28 mW/cm2) light exposure even though the white light pulse contained 185-fold more photons than the short wavelength light. This finding suggests short wavelength sensitivity of the photoreceptors mediating synchronization of human circadian rhythms.

Keywords Circadian rhythms; Light; Wavelength; Phase shifts; Melatonin; Temperature; Photoreception

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Wartenberg D, Stapleton CP **Year** 1998

Authors Wartenberg D, Stapleton CP

Report Name Risk of breast cancer is also increased among retired US female airline cabin attendants

Publication BMJ

Issue-page numbers 316:1902. PMID:9632420

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1113371/

Abstract N/A

Keywords

Warthen DM, Provencio I

Year 2012

Authors Daniel M Warthen, Ignacio Provencio

Report Name The role of intrinsically photosensitive retinal ganglion cells in nonimage-forming responses to light

Publication Eye and Brain

Issue-page numbers 2012:4

URL http://scholar.google.com/scholar_url?hl=en&q=https://www.dovepress.com/getfile.php%3FfileID%3D13868&sa=X&scisig=AAGBfm2BEdC2BfoXqIA1NBNTl497QUUakw&oi=sch

Abstract Light exerts many effects on behavior and physiology. These effects can be characterized
as either image-forming or nonimage-forming (NIF) visual processes. Image-
forming vision refers to the process of detecting objects and organisms in the environment and distinguishing their physical characteristics, such as size, shape, and direction of motion. NIF vision, in contrast, refers to effects of light that are independent of fine spatiotemporal vision. NIF effects are many and varied, ranging from modulation of basal physiology, such as heart rate and body temperature, to changes in higher functions, such as mood and cognitive
performance. In mammals, many NIF effects of light are dependent upon the inner retinal photopigment melanopsin and the cells in which melanopsin is expressed, the intrinsically photosensitive retinal ganglion cells (ipRGCs). The ipRGCs project broadly throughout the brain. Many of these projections terminate in areas known to mediate NIF effects, while others
terminate in regions whose link to photoreception remains to be established. Additionally, the presence of ipRGC projections to areas of the brain with no known link to photoreception suggests the existence of additional ipRGC-mediated NIF effects. This review summarizes the known NIF effects of light and the role of melanopsin and ipRGCs in driving these effects, with an eye toward stimulating further investigation of the many and varied effects of light on physiology and behavior.

Keywords amygdala, bed nucleus of the stria terminalis, melanopsin, opsin, optic nerve, retina

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Wassell J, Davies S, Bardsley W, Boulton M.

Year 1999

Authors Wassell J, Davies S, Bardsley W, Boulton M.

Report Name The photoreactivity of the retinal age pigment lipofuscin

Publication Journal of Biological Chemistry

Issue-page numbers 274, 23828-23832.

URL http://www.jbc.org/content/274/34/23828.abstract

Abstract The presence of the age pigment lipofuscin is associated with numerous age-related diseases. In the retina lipofuscin is located within the pigment epithelium where it is exposed to high oxygen and visible light, a prime environment for the generation of reactive oxygen species. Although we, and others, have demonstrated that retinal lipofuscin is a photoinducible generator of reactive oxygen species it is unclear how this may translate into cell damage. The position of lipofuscin within the lysosome infers that irradiated lipofuscin is liable to cause oxidative damage to either the lysosomal membrane or the lysosomal enzymes. We have found that illumination of lipofuscin with visible light is capable of extragranular lipid peroxidation, enzyme inactivation, and protein oxidation. These effects, which were pH-dependent, were significantly reduced by the addition of the antioxidants, superoxide dismutase and 1,4-diazabicyclo(2,2,2)-octane, confirming a role for both the superoxide anion and singlet oxygen. We postulate that lipofuscin may compromise retinal cell function by causing loss of lysosomal integrity and that this may be a major contributory factor to the pathology associated with retinal light damage and diseases such as age-related macular degeneration.

Keywords

Waterhouse JM, Folkard S, Minors DS | ***Year*** 1992

Authors Waterhouse JM, Folkard S, Minors DS

Report Name Shiftwork, health and safety. An overview of the scientific literature 1978–1990

Publication London: HMSO

Issue-page numbers

URL http://www.worldcat.org/title/shiftwork-health-and-safety-an-overview-of-the-scientific-literature-1978-1990/oclc/26087876

Abstract N/A

Keywords

Weaver DR, Rivkees SA, Reppert SM | ***Year*** 1989

Authors Weaver DR, Rivkees SA, Reppert SM

Report Name Localization and characterization of melatonin receptors in rodent brain by in vitro autoradiography

Publication J Neurosci

Issue-page numbers 9:2581–2590. PMID:2545841

URL http://www.jneurosci.org/content/9/7/2581

Abstract Little is known of the neural sites of action for the pineal hormone, melatonin. Thus, we developed an in vitro autoradiographic method using 125I-labeled melatonin (I-MEL) to study putative melatonin receptors in rodent brain. We first determined optimal in vitro labeling conditions for autoradiographic detection of I-MEL binding sites in rat median eminence, the most intensely labeled area in the rat brain. We then assessed the pharmacologic and kinetic properties of I-MEL binding sites in rat median eminence by quantitative autoradiography. These sites have high affinity for I-MEL (equilibrium dissociation constant = 43 pM). I-MEL binding was inhibited by nanomolar concentrations of melatonin or 6-chloromelatonin, but was not inhibited by serotonin, dopamine, or norepinephrine (100 microM). These results suggest that I- MEL binding sites identified by in vitro autoradiography represent specific, high-affinity melatonin receptors. Studies of the distribution of I-MEL binding in rat, Syrian hamster, and Djungarian hamster brain confirm that the median eminence and suprachiasmatic nucleus are major sites of I-MEL binding in rodent brain; other brain areas labeled in one or more of these species were the thalamus (paraventricular, anteroventral, and reuniens nuclei, nucleus of the stria medullaris, and medial part of the lateral habenular nucleus), hypothalamus (dorsomedial nucleus), subiculum, and area postrema. The presence of putative melatonin receptors in the suprachiasmatic nuclei and median eminence of these rodent species suggests that these brain regions are important loci for melatonin effects on circadian rhythms and reproduction.

Keywords

Authors Webb AR, DeCosta BR, Holick MF.

Report Name Sunlight regulates the cutaneous production of vitamin D3 by causing its photodegradation

Publication The Journal of Clinical Endocrinology & Metabolism

Issue-page numbers May 1, 1989 vol. 68 no. 5 882-887

URL http://jcem.endojournals.org/content/68/5/882.short

Abstract

Exposure to sunlight initiates the formation of vitamin D3 in skin as the UV B radiation in the solar spectrum causes the photoconversion of 7-dehydrocholesterol to previtamin D3. A heat-induced isomerization then converts previtamin D3 to vitamin D3 over a period of days. A number of irradiation products of vitamin D3 are known to form upon irradiation with high intensity UV radiation, but the effect of subsequent exposures to sunlight on the vitamin D3 formed in skin is not known. To investigate this phenomenon, human skin containing vitamin D3 was exposed to sunlight in Boston. A model system of [3H]vitamin D3 in methanol was also used to study the effects of sunlight on vitamin D3 throughout the year. Vitamin D3 proved to be exquisitely sensitive to sunlight, and once formed in the skin, exposure to sunlight resulted in its rapid photodegradation to a variety of photoproducts, including 5,6-transvitamin D3, suprasterol I, and suprasterol II.

Keywords

Authors Webb AR, Kift R, Durkin MT, O'Brien SJ, Vail A, Berry JL, et al.

Report Name The role of sunlight exposure in determining the vitamin D status of the U.K. white adult population

Publication British Journal of Dermatology

Issue-page numbers Volume 163, Issue 5, pages 1050–1055, November 2010

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.2010.09975.x/abstract

Abstract

Background Vitamin D is necessary for bone health and is potentially protective against a range of malignancies. Opinions are divided on whether the proposed optimal circulating 25-hydroxyvitamin D [25(OH)D] level (≥ 32 ng mL−1) is an appropriate and feasible target at population level.

Objectives We examined whether personal sunlight exposure levels can provide vitamin D sufficient (≥ 20 ng mL−1) and optimal status in the U.K. public.

Methods This prospective cohort study measured circulating 25(OH)D monthly for 12 months in 125 white adults aged 20–60 years in Greater Manchester. Dietary vitamin D and personal ultraviolet radiation (UVR) exposure were assessed over 1–2 weeks in each season. The primary analysis determined the post-summer peak 25(OH)D required to maintain sufficiency in wintertime.

Results Dietary vitamin D remained low in all seasons (median 3·27 μg daily, range 2·76–4·15) while personal UVR exposure levels were high in spring and summer, low in autumn and negligible in winter. Mean 25(OH)D levels were highest in September [28·4 ng mL−1; 28% optimal, zero deficient (<5 ng mL−1)], and lowest in February (18·3 ng mL−1; 7% optimal, 5% deficient). A February 25(OH)D level of 20 ng mL−1 was achieved following a mean (95% confidence interval) late summer level of 30·4 (25·6–35·2) and 34·9 (27·9–41·9) ng mL−1 in women and men, respectively, with 62% of variance explained by gender and September levels.

Conclusions Late summer 25(OH)D levels approximating the optimal range are required to retain sufficiency throughout the U.K. winter. Currently the majority of the population fails to reach this post-summer level and becomes vitamin D insufficient during the winter.

Keywords cancer; diet; osteomalacia; rickets; ultraviolet radiation; vitamin D

Webb SM, Champney TH, Lewiński AK, Reiter RJ

Year 1985

Authors Susan M. Webb, Thomas H. Champney, Andrzej K. Lewiński, Russel J. Reiter

Report Name Photoreceptor Damage and Eye Pigmentation: Influence on the Sensitivity of Rat Pineal N-Acetyltransferase Activity and Melatonin Levels to Light at Night

Publication Neuroendocrinology

Issue-page numbers Vol. 40, No. 3, 1985

URL http://content.karger.com/ProdukteDB/produkte.asp?Doi=124076

Abstract The threshold of light irradiance capable of inhibiting nighttime pineal serotonin N-acetyltransferase (NAT) activity and melatonin content, and the importance of intact photoreceptors and eye pigmentation on these changes, were investigated in the rat. Groups of intact albino and black-eyed rats and albino animals with light-induced photoreceptor damage were studied in the dark period before, and after 15 and 30 min of exposure to either 0.0005, 0.175 or 3.33 μW/cm2 irradiance of light. In animals with photoreceptor damage, the sensitivity of the pineal gland to light decreased so that only the highest irradiance tested (3.33 μW/cm2) was capable of totally inhibiting pineal NAT activity and melatonin levels. In one study, pineal NAT and melatonin levels in intact albino rats were inhibited by all three irradiances studied. In a second experiment, albino and black-eyed animals behaved identically, only responding with a depression in pineal NAT and melatonin after exposure to light irradiances of either 0.175 or 3.33 μW/cm2. In conclusion, the lowest irradiance of cool white light capable of inhibiting pineal NAT and melatonin in albino rats is around 0.0005 μW/cm2. At the irradiances studied, photoreceptor damage influences the response of pineal NAT and melatonin to acute light exposure at night. On the other hand, eye pigmentation does not seem to have a major effect on the nighttime inhibition of the pineal by light.

Keywords

Webley GE, Leidenberger F

Year 1986

Authors Webley GE, Leidenberger F

Report Name The circadian pattern of melatonin and its positive relationship with progesterone in women

Publication J Clin Endocrinol Metab

Issue-page numbers 63:323–328 doi:10.1210/jcem-63-2-323. PMID:3722324

URL http://jcem.endojournals.org/content/63/2/323.short

Abstract To investigate the possible role of melatonin in the regulation of the human menstrual cycle, the circadian pattern of melatonin was determined in the follicular and luteal phases of 10 normal women. Four-hourly sampling was used to derive a melatonin index which described the total exposure to melatonin for 24 h. This sampling procedure adequately represented the circadian melatonin output and demonstrated that pulses of melatonin secretion, inconsistent with a measured half-life of 47 min, did not exist. A significant increase ($P < 0.001$) i n the melatonin index was found in the luteal phase compared to that in the follicular phase. To investigate the influence of exogenous progestins on the melatonin pattern, repeated 24-h profiles were measured in 8 women taking the 3-phase contraceptive pill. There was a significant increase ($P < 0.01$) in the melatonin index associated with an increase in the dose of progestin. These results are consistent with a positive relationship between melatonin and progesterone and suggest that changes in the circadian pattern of melatonin secretion, rising during the luteal phase with a fall before ovulation, may act as a modulator of cyclicity.

Keywords

Webley GE, Luck MR **Year** 1986

Authors Webley GE, Luck MR

Report Name Melatonin directly stimulates the secretion of progesterone by human and bovine granulosa cells in vitro

Publication J Reprod Fertil

Issue-page numbers 78:711–717 doi:10.1530/jrf.0.0780711. PMID:3806524

URL http://www.reproduction-online.org/content/78/2/711.full.pdf

Abstract Melatonin, at concentrations and periods of exposure reflecting those present during the circadian cycle, was investigated for its influence on steroid production by granulosa cells cultured in serum-supplemented medium. At high (200 pg/ml) but not low (20 pg/ml) physiological concentrations, melatonin significantly stimulated progesterone production by human granulosa cells. This response was independent of the overall level of cell activity and was seen under the different culture conditions associated with different culture media. Exposure to melatonin for 8 h significantly stimulated progesterone secretion to a level similar to that achieved under continuous exposure, and the effect was reduced to control levels during subsequent periods in which no melatonin was added. Melatonin had no consistent effect on aromatase activity in the conversion of stored or serum-available androgen to oestradiol. Melatonin significantly stimulated progesterone production by bovine granulosa cells in vitro, at concentrations similar to those present during the endogenous nocturnal rise (100\p=n-\400pg/ml). This response to physiological conditions by human and bovine cells suggests a role for melatonin in the regulation of progesterone production by the ovary.

Keywords

Wedderburn A **Year** 1994

Authors Wedderburn A

Report Name Instruments for designing, implementing and assessing working time arrangements

Publication Bulletin of European Studies on Time

Issue-page numbers 7

URL http://openlibrary.org/books/OL16498270M/Instruments_for_designing_implementing_and_assessing_working_time_arrangements

Abstract N/A

Keywords

Wegmann HM, Klein KE

Year 1985

Authors Wegmann HM, Klein KE

Report Name Jet-lag and aircrew scheduling

Publication In: Folkard S and Monk TH, ed., Hours of work. Temporal factors in work scheduling.

Issue-page numbers Chichester, John Wiley & Sons, pp. 263–276

URL N/A

Abstract N/A

Keywords

Wehr TA

Year 1996

Authors Wehr TA

Report Name A ‘clock for all seasons’ in the human brain

Publication Prog Brain Res

Issue-page numbers 111:321–342 doi:10.1016/S0079-6123(08)60416-1. PMID:8990923

URL http://www.sciencedirect.com/science/article/pii/S0079612308604161

Abstract N/A

Keywords

Wehr TA **Year** 2001

Authors Wehr TA

Report Name Photoperiodism in humans and other primates: evidence and implications

Publication J Biol Rhythms

Issue-page numbers 16:348–364 doi:10.1177/074873001129002060. PMID:11506380

URL http://jbr.sagepub.com/content/16/4/348.abstract

Abstract Most of the anatomical and molecular substrates of the system that encodes changes in photoperiod in the duration of melatonin secretion, and the receptor molecules that read this signal, have been shown to be conserved in monkeys and humans, and the functions of this system appear to be intact from the level of the retina to the level of the melatonin-duration signal of change of season. While photoperiodic seasonal breeding has been shown to occur in monkeys, it remains unclear whether photoperiod and mediation of photoperiod's effects by melatonin influence human reproduction. Epidemiological evidence suggests that inhibition of fertility by heat in men in summer contributes to seasonal variation in human reproduction at lower latitudes and that stimulation of fertility by lengthening of the photoperiod in spring contributes to the variation at higher latitudes. Parallels between the seasonality of human reproduction and seasonal affective disorder suggest that they may be governed by common biological processes. Historical and experimental evidence indicates that human responses to seasonal changes in the natural photoperiod may have been more robust prior to the Industrial Revolution and that subsequently they have been increasingly suppressed by alterations of the physical environment.

Keywords melatonin, light, seasons, reproduction, depression

Wehr TA **Year** 1991

Authors THOMAS A. WEHR

Report Name The durations of human melatonin secretion and sleep respond to changes in daylength (photoperiod)

Publication J Clin Endocrinol Metab

Issue-page numbers 73:1276–1280 doi:10.1210/jcem-73-6-1276. PMID:1955509

URL http://jcem.endojournals.org/content/73/6/1276

Abstract Seasonal changes in daylength (photoperiod) modify the duration of nocturnal melatonin (MT) secretion in many vertebrates. In some cases the changes in MT act as chemical signals that trigger photoperiodic induction of breeding and other seasonal phenomena. It is unclear whether, and to what extent changes in daylength modify the duration of human MT secretion. To address this question, I investigated whether the duration of human MT secretion could be altered by artificial photoperiods. I exposed eight healthy volunteers to a conventional “summer” photoperiod of 16 h light and 8 h darkness for 1 week and to a “winter” photoperiod of 10 h light and 14 h darkness for 4 weeks. As occurs in animals, the duration of nocturnal MT secretion in human beings was longer after exposure to the short photoperiod (12.5 ± 1.8 vs. 10.3 ± 0.8 h, t = 3.778, P < 0.01). The duration of the sleep-phase (recorded by electroencephalogram) was also longer (11.0 ± 0.8 vs. 7.7 ± 0.2 h, t = 11.754, P < 0.001). Whether such changes would lead to significant seasonal changes in human physiology and behavior under natural lighting conditions may be worthy of further investigation.

Keywords

Wehr TA

Year 2009

Authors THOMAS A. WEHR

Report Name In short photoperiods, human sleep is biphasic

Publication Journal of Sleep Research

Issue-page numbers Volume 1, Issue 2, pages 103-107, June 1992

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2869.1992.tb00019.x/abstract

Abstract Results of a photoperiod experiment show that human sleep can be unconsolidated and polyphasic, like the sleep of other animals. When normal individuals were transferred from a conventional 16-h photoperiod to an experimental 10-h photo-period, their sleep episodes expanded and usually divided into two symmetrical bouts, several hours in duration, with a 1–3 h waking interval between them. The durations of nocturnal melatonin secretion and of the nocturnal phase of rising sleepiness (measured in a constant routine protocol) also expanded, indicating that the timing of internal processes that control sleep and melatonin, such as circadian rhythms, had been modified by the change in photoperiod. Previous work suggests that the experimental results could be simulated with dual-oscillators, entrained separately to dawn and dusk, or with a two-process model, having a lowered threshold for sleep-onset during the scotoperiod.

Keywords circadian rhythms; comparative physiology; light; melatonin; models; photoperiodism; sleep

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Wehr TA, Giesen HA, Moul DE

Year 1995

Authors T. A. Wehr, H. A. Giesen, D. E. Moul, E. H. Turner, and P. J. Schwartz

Report Name Suppression of men's responses to seasonal changes in day length by modern artificial lighting

Publication American Journal of Physiology - Regulatory, Integrative and Comparative Physiology

Issue-page numbers July 1995 vol. 269 no. 1 R173-R178

URL http://ajpregu.physiology.org/content/269/1/R173.abstract

Abstract We recently reported that humans have conserved mechanisms, like those that exist in other animals, which detect changes in day length and make corresponding adjustments in the duration of nocturnal periods of secretion of melatonin and of other functions. We detected these responses in individuals who were exposed to artificial "days" of different durations. The purpose of the present study was to determine whether men who are exposed to natural and artificial light in an urban environment at 39 degrees N are still able to detect and respond to seasonal changes in duration of the natural photoperiod. We measured profiles of circadian rhythms during 24-h periods of constant darkness (< 1 lx) and found no summer-winter differences in durations of nocturnal periods of active secretion of melatonin, rising levels of cortisol, high levels of thyrotropin, and low levels of rectal temperature. The results of this and our previous study suggest that modern men's use of artificial light suppresses responses to seasonal changes in the natural photoperiod that might otherwise occur at this latitude.

Keywords

Authors T. A. Wehr, D. E. Moul, G. Barbato, H. A. Giesen, J. A. Seidel, C. Barker, and C. Bender

Report Name Conservation of photoperiod-responsive mechanisms in humans

Publication AJP - Regu Physio

Issue-page numbers October 1993 vol. 265 no. 4 R846-R857

URL http://ajpregu.physiology.org/content/265/4/R846.abstract

Abstract

In animals, circadian pacemakers respond to seasonal changes in day length by making corresponding adjustments in the durations of diurnal and nocturnal periods of circadian rhythms; these adjustments mediate effects of photoperiod on breeding and other seasonally recurring phenomena. Little is known about photoperiod responses of human circadian pacemakers. To investigate this question, we recorded and compared circadian rhythm profiles of 15 individuals after chronic exposures to short (8 h) and long (14 h) nights. As occurs in animals, durations of nocturnal periods of active melatonin secretion (11.9 +/- 1.6 vs. 10.3 +/- 1.3 h, df = 14, t = 4.583, P < 0.0005, paired t test), high prolactin secretion (12.9 +/- 2.1 vs. 9.9 +/- 2.2 h, df = 11, t = 2.917, P < 0.01), and sleep (10.6 +/- 0.8 vs. 7.6 +/- 0.4 h, df = 14, t = 17.122, P < 0.0005) were longer after exposure to long nights than after short ones. Durations of nocturnal periods of low rectal temperature (11.6 +/- 2.3 vs. 9.5 +/- 1.6 h, df = 12, t = 3.912, P < 0.001) and rising cortisol secretion (10.8 +/- 1.6 vs. 9.3 +/- 1.9 h, df = 14, t = 3.130, P < 0.005) were also longer. Some of these differences persisted during 24-h periods of enforced wakefulness in constant dim light, indicating that prior exposure to the two regimes induced abiding changes in the timing of internal processes, such as circadian pacemaker oscillations, that control the durations of nocturnal and diurnal periods of the rhythms.

Keywords

Authors Wei ET, Gao GC

Report Name Corticotropin-releasing factor: an inhibitor of vascular leakage in rat skeletal muscle and brain cortex after injury

Publication Regul Pept

Issue-page numbers 33:93–104 doi:10.1016/0167-0115(91)90205- U. PMID:1882088

URL http://www.sciencedirect.com/science/article/pii/016701159190205U

Abstract Corticotropin-releasing factor (CRF) and other peptides of the corticoliberin superfamily inhibit development of edema in skin and mucosa after noxious stimuli. Here, the breadth of CRFs protective activity on small blood vessels was examined after injury to skeletal muscle or to brain cortex. Male rats (View the MathML source) were anesthetized with sodium pentobarbital 60 mg/kg i.p. and Monastral blue 60 mg/kg i.v. was injected 3 min before mechanical injury to muscle produced by a 4 cm midline surgical incision in the rectus abdominis or before freeze injury to the cortex produced by applying a cold probe (− 50°C) to the skull for 4 min. Vascular leakage, measured as area of dye staining multiplied by its light intensity, was quantified with an image-analysis system. CRF, having the human/rat sequence, 30 μg/kg s.c., injected once (30 min) or twice (30 min and 10 min) before injury to muscle or to brain, inhibited the lesion size by 58% and 55%, respectively (tissues taken at 0.5 and 1 h). Microscopy showed that CRF inhibited Monastral blue labeling of small blood vessels. The ED50 (95% C.L.) of CRF for reducing vascular leakage in muscle after celiotomy was 24 (9 to 64) μg/kg s.c. h/rCRF injected 30 μg/kg s.c. 2 h before celiotomy inhibited vascular leakage by 41%, indicating its long duration of action. CRF inhibited vascular leakage after celiotomy in adrenalectomized rats and this effect was not obtained with dexamethasone phosphate, 1 mg/kg s.c. α-Helical CRF (9–41), a CRF receptor antagonist, attenuated the actions of CRF on celiotomy. Laser-Doppler flowmeter measurements of skeletal muscle showed that the anti-inflammatory effects of CRF occurred when there were no significant concurrent changes in blood flow. From these results, we surmise that CRF has a versatile protective effect on small blood vessels when it inhibits leakage within different vascular beds.

Keywords CRF, corticotropin-releasing factor; Muscle; Brain; Edema; Anti-inflammatory; Monastral blue; Adrenalectomy; Dexamethasone

Year 1997

Authors Weibel L, Follenius M, Spiegel K et al.

Report Name Growth hormone secretion in night workers

Publication Chronobiol Int

Issue-page numbers 14:49–60 doi:10.3109/07420529709040541. PMID:9042551

URL http://informahealthcare.com/doi/abs/10.3109/07420529709040541

Abstract We previously reported that, in night workers, cortisol and TSH rhythms, known to have a high endogenous component, adapted only partially to the nocturnal schedule. The aim of the present study was to investigate the degree of adaptation of the growth hormone (GH) rhythm, considered to be mainly sleep-dependent, but for which a weak circadian drive has also been suggested. Eleven night workers were studied during their usual sleep-wake cycle, and two groups of 11 normally day-active subjects, sleeping once during the night and once after an 8-h sleep delay, were used as control groups. GH secretory rates were calculated by deconvolution of the plasma concentrations analyzed at 10-min intervals. The total amount of GH secreted during the 24 h did not differ between the three groups and the main secretory episode occurred, in most cases, during the first half of the sleep period. In night sleepers and night workers the enhanced amount of GH secreted at that time was followed by a significantly lower amount secreted during the second part of the sleep period ($p < 0.001$ and $p < 0.05$, respectively). For night sleepers, an enhanced GH pulse frequency was found at the beginning of sleep, whereas for night workers and day sleepers the pulses were distributed more randomly throughout the nychthemeron. After an abrupt sleep shift, all the subjects displayed a GH pulse at the usual time of early sleep, but such a pulse was present in only 8 of 11 night workers. Thus the amount of GH secreted between 23:00 h and 03:00 h in day sleepers did not differ significantly from that observed in night sleepers, whereas it differed for night workers. These results confirm the considerable influence of sleep in driving the GH rhythm and the existence of a circadian influence revealed by an acute shift in the sleep period. They also provide evidence of an incomplete adjustment of GH rhythms in night workers.

Keywords

Weibel L, Follenius M, Spiegel K et al. *Year* 1995

Authors Weibel L, Follenius M, Spiegel K et al.

Report Name Comparative effect of night and daytime sleep on the 24-hour cortisol secretory profile

Publication Sleep

Issue-page numbers 18:549–556. PMID:8552925

URL http://www.journalsleep.org/ViewAbstract.aspx?pid=24539

Abstract To determine whether cortisol secretion interacts with daytime sleep in a similar manner to that reported for night sleep, 14 healthy young men were studied during two 24-hour cycles. During one cycle they slept during the night, during the other the sleep period was delayed by 8 hours. Secretory rates were calculated by a deconvolution procedure from plasma cortisol, measured at 10-minute intervals. The amount of cortisol secreted during night sleep was lower than during the corresponding period of sleep deprivation (12.7 ± 1.1 vs. 16.3 ± 1.6 mg; $p < 0.05$), but daytime sleep beginning at the habitual time of morning awakening failed to inhibit cortisol secretion significantly. There was no difference between the amount of cortisol secreted from 0700 to 1500 hours in sleeping subjects and in subjects who were awake during the same period of time (24.2 ± 1.5 vs. 22.5 ± 1.4 mg). Even if the comparison between sleeping and waking subjects was restricted to the period 0700-1100 hours or 0700-0900 hours, no significant difference was found. Neither secretory pulse amplitude nor frequency differed significantly in either period. However, detailed analysis of the secretory rates in daysleepers demonstrated a transient decrease in cortisol secretion at about the time of sleep onset, which began 10 minutes before and lasted 20 minutes after falling asleep. Spontaneous or provoked awakenings had a determining influence on the secretory profiles. Ten to 20 minutes after awakening from either night or day sleep cortisol secretion increased significantly. The main secretory episode in the early morning, which reflects the interaction between circadian processes and awakenings, did not differ in its timing between night and day sleepers, providing evidence of the strength of the circadian rhythm. These findings demonstrate that daytime sleep beginning at the circadian cortisol acrophase, when compared to wakefulness, did not induce a significant decrease in the amount of cortisol secreted during the subsequent 2- or 4-hour period, despite a transient decrease in secretion around the time of sleep onset.

Keywords

Weinberg U, Weitzman ED, Fukushima DK et al. *Year* 1980

Authors Weinberg U, Weitzman ED, Fukushima DK et al.

Report Name Melatonin does not suppress the pituitary luteinizing hormone response to luteinizing hormone-releasing hormone in men

Publication J Clin Endocrinol Metab

Issue-page numbers 51:161–162 doi:10.1210/jcem-51-1-161. PMID:6991518

URL http://www.ncbi.nlm.nih.gov/pubmed/6991518

Abstract The effect of an iv melatonin infusion on the pituitary LH response to LHRH was studied in five young men. Melatonin (30 micrograms/min; total dose, 7.2 mg) was infused for a 4-h period, 2 h before and 2 h after a LRH stimulation (single iv 150-microgram dose). Each subject's control response to LRH was obtained previously. During the melatonin infusion, supraphysiological concentrations of melatonin (20 times) were documented using a specific RIA. All five subjects had a LH rise after LRH stimulation, and this response was not affected by the melatonin infusion. These results indicate that an acute constant infusion of a pharmacological amount of melatonin does not suppress LRH-induced LH release from the pituitary in men. In addition, no change in sleepiness and behavior was found.

Keywords

Weinzirl J, Wolf M, Nelle M, et al. **Year** 2012

Authors J. Weinzirl, M. Wolf, M. Nelle, P. Heusser and U. Wolf

Report Name Colored Light and Brain and Muscle Oxygenation

Publication Oxygen Transport to Tissue XXXIII

Issue-page numbers 2012, Volume 737, Part 1, 33-36, DOI: 10.1007/978-1-4614-1566-4_5

URL http://www.springerlink.com/content/g274005788183713/

Abstract Colored light is applied in medicine in the treatment of various diseases. The aim of this study was to investigate potential effects of exposure to blue and red light on brain and muscle blood volume ([tHb]) and tissue oxygenation (StO2) measured by noninvasive near-infrared spectrophotometry (NIRS). Ten healthy volunteers were included in a randomized crossover study. Blue light exposure leads to decreased oxygen consumption in the brain and the skeletal muscle. Blue and red light have significantly different effects on [tHb] and StO2.

Keywords

Welsh DK, Logothetis DE, Meister M, Reppert SM **Year** 1995

Authors Welsh DK, Logothetis DE, Meister M, Reppert SM

Report Name Individual neurons dissociated from rat suprachiasmatic nucleus express independently phased circadian firing rhythms

Publication Neuron

Issue-page numbers 14:697–706 doi:10.1016/0896-6273(95)90214-7. PMID:7718233

URL http://www.sciencedirect.com/science/article/pii/0896627395902147

Abstract Within the mammalian hypothalamus, the suprachiasmatic nucleus (SCN) contains a circadian clock for timing of diverse neuronal, endocrine, and behavioral rhythms. By culturing cells from neonatal rat SCN on fixed microelectrode arrays, we have been able to record spontaneous action potentials from individual SCN neurons for days or weeks, revealing prominent circadian rhythms in firing rate. Despite abundant functional synapses, circadian rhythms expressed by neurons in the same culture are not synchronized. After reversible blockade of neuronal firing lasting 2.5 days, circadian firing rhythms re-emerge with unaltered phases. These data suggest that the SCN contains a large population of autonomous, single-cell circadian oscillators, and that synapses formed in vitro are neither necessary for operation of these oscillators nor sufficient for synchronizing them.

Keywords

Werner S, Brismar K, Wetterberg L, Eneroth P | ***Year*** 1981

Authors Werner S, Brismar K, Wetterberg L, Eneroth P

Report Name Circadian rhythms of melatonin, prolactin, growth hormone and cortisol in patients with pituitary adenomas, empty sella syndrome, and Cushing's syndrome due to adrenal tumou

Publication In: Birau N & Schloot W, Eds. Melatonin: Current Status and Perspectives

Issue-page numbers Oxford: Pergamon Press Ltd. pp 357–364

URL N/A

Abstract N/A

Keywords

Werth VP, Honigsmann H | ***Year*** 0

Authors Werth VP, Honigsmann H.

Report Name Photoaggravated dermatoses

Publication In: Lim HW, Honigsmann H, Hawk JLM, editors. Photodermatology

Issue-page numbers New York: Informa; 2007. p.251-66.

URL book

Abstract book

Keywords

Authors Kathleen E. West, Michael R. Jablonski, Benjamin Warfield, Kate S. Cecil, Mary James, Melissa A. Ayers, James Maida, et al.

Report Name Blue light from light-emitting diodes elicits a dose-dependent suppression of melatonin in humans

Publication Journal of Applied Physiology

Issue-page numbers March 2011 vol. 110 no. 3 619-626

URL http://jap.physiology.org/content/110/3/619.abstract

Abstract

Light suppresses melatonin in humans, with the strongest response occurring in the short-wavelength portion of the spectrum between 446 and 477 nm that appears blue. Blue monochromatic light has also been shown to be more effective than longer-wavelength light for enhancing alertness. Disturbed circadian rhythms and sleep loss have been described as risk factors for astronauts and NASA ground control workers, as well as civilians. Such disturbances can result in impaired alertness and diminished performance. Prior to exposing subjects to short-wavelength light from light-emitting diodes (LEDs) (peak λ = 469 nm; ½ peak bandwidth = 26 nm), the ocular safety exposure to the blue LED light was confirmed by an independent hazard analysis using the American Conference of Governmental Industrial Hygienists exposure limits. Subsequently, a fluence-response curve was developed for plasma melatonin suppression in healthy subjects (n = 8; mean age of 23.9 ± 0.5 years) exposed to a range of irradiances of blue LED light. Subjects with freely reactive pupils were exposed to light between 2:00 and 3:30 AM. Blood samples were collected before and after light exposures and quantified for melatonin. The results demonstrate that increasing irradiances of narrowband blue-appearing light can elicit increasing plasma melatonin suppression in healthy subjects ($P < 0.0001$). The data were fit to a sigmoidal fluence-response curve ($R2 = 0.99$; $ED50 = 14.19$ μW/cm2). A comparison of mean melatonin suppression with 40 μW/cm2 from 4,000 K broadband white fluorescent light, currently used in most general lighting fixtures, suggests that narrow bandwidth blue LED light may be stronger than 4,000 K white fluorescent light for suppressing melatonin.

Keywords pineal, light-emitting diode

Westrin A, Lam RW. ***Year*** 2007

Authors Asa Westrin, Raymond W Lam

Report Name Seasonal affective disorder: a clinical update

Publication Annals of clinical psychiatry official journal of the American Academy of Clinical Psychiatrists

Issue-page numbers Volume: 19, Issue: 4, Pages: 239-246

URL http://www.mendeley.com/research/seasonal-affective-disorder-a-clinical-update/

Abstract BACKGROUND: Seasonal affective disorder (SAD) consists of recurrent major depressive episodes in the fall/winter with remissions in spring/summer. METHOD: A Medline search was conducted to identify studies relating to clinical management of SAD using the Medical Subject Heading, seasonal affective disorder, and key words, depress and season, focusing on studies published in the past 10 years. The Cochrane library of systematic reviews was also searched for relevant studies. RESULTS: A careful history is important to make the diagnosis and differentiate SAD from other similar conditions such as subsyndromal SAD and atypical depression. Seasonal patterns with winter worsening are also recognized in "nonseasonal" depression as well as many other psychiatric conditions, and comorbidity with SAD is common. The pathophysiology of SAD seems to be heterogeneous as research on circadian, neurotransmitter function and genetic hypotheses have shown discrepant results. A dual vulnerability model with differential loading on separate seasonal and depression factors has been proposed to explain these findings. Recent systematic reviews have shown that light therapy is an efficacious and well-tolerated treatment for SAD. There is also evidence for efficacy of pharmacotherapy to treat and prevent SAD. Clinical studies show equal effectiveness with light and antidepressants, so patient preference should be considered in the selection of initial treatment. Dawn stimulation, negative air ions, exercise and cognitve behaviour therapy are under investigation and may also be helpful treatments for SAD. CONCLUSIONS: SAD is a common condition with significant psychosocial impairment. Clinicians should be vigilant in recognizing seasonal patterns of depressive episodes because there are effective, evidence-based treatments for SAD.

Keywords

Wetterberg L, Arendt J, Paunier L et al. ***Year*** 1976

Authors Wetterberg L, Arendt J, Paunier L et al.

Report Name Human serum melatonin changes during the menstrual cycle

Publication J Clin Endocrinol Metab

Issue-page numbers 42:185–188 doi:10.1210/jcem-42-1-185. PMID:1249188

URL http://jcem.endojournals.org/content/42/1/185.short

Abstract Serum melatonin concentration in early morning during the menstrual cycle, studied in five healthy women, showed that melatonin was elevated at the time of menstrual bleeding and had its nadir at the time of ovulation. It is possible that melatonin is involved in the regulation of the menstrual cycling in humans.

Keywords

Whitehead AJ, Mares JA, Danis RP

Year 2006

Authors Whitehead AJ, Mares JA, Danis RP.

Report Name Macular pigment: a review of current knowledge

Publication Arch Ophthalmol

Issue-page numbers 2006;124:1038-1045.

URL http://archopht.ama-assn.org/cgi/content/full/124/7/1038

Abstract The existence of the macula lutea of the human retina has been known for more than 200 years. It is established that the xanthophylls lutein and zeaxanthin are responsible for the yellow color. The effect of macular photopigments on blue-light filtration and color perception is well established. It has been postulated that the pigment might serve to reduce chromatic aberration and to improve visual acuity. The antioxidant capabilities of these xanthophylls combined with their ability to trap short-wavelength light may serve to protect the outer retina, retinal pigment epithelium, and choriocapillaris from oxidative damage. Current ideas on the pathophysiology of age-related macular degeneration may be compatible with the proposed function of lutein and zeaxanthin. This review will summarize our knowledge about macular pigment regarding current efforts in research and the epidemiology of age-related eye disease.

Keywords

Wielgus AR, Chignell CF, Ceger P, Roberts JE

Year 2010

Authors Wielgus AR, Chignell CF, Ceger P, Roberts JE.

Report Name Comparison of A2E cytotoxicity and phototoxicity with all-trans-retinal in human retinal pigment epithelial cells

Publication Photochemistry and Photobiology

Issue-page numbers Volume 86, Issue 4, pages 781–791, July/August 2010

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1751-1097.2010.00750.x/abstract

Abstract All-trans-retinal is the precursor of A2E, a fluorophore within lipofuscin, which accumulates in human retinal pigment epithelial (hRPE) cells and contributes to age-related macular degeneration. Here we have compared the in vitro dark cytotoxicity and visible-light-mediated photoreactivity of all-trans-retinal and A2E in hRPE cells. All-trans-retinal caused distinct cytotoxicity in hRPE cells measured with cell metabolic activity (MTS) and lactate dehydrogenase release assays. Significant increases in intracellular oxidized glutathione (GSSG), extracellular GSH and GSSG levels and lipid hydroperoxide production were observed in cells incubated in the dark with 25 and 50 μm all-trans-retinal. Light modified all-trans-retinal's harmful action and decreased extracellular glutathione and hydroperoxide levels. A2E (<25 μm) did not affect cell metabolism or cytoplasmic membrane integrity in the dark or when irradiated. 25 μm A2E raised the intracellular GSSG level in hRPE cells to a much smaller extent than 25 μm all-trans-retinal. A2E did not induce glutathione efflux or hydroperoxide generation in the dark or after irradiation. These studies support our previous conclusions that although A2E may be harmful at high concentrations or when oxidized, its phototoxic properties are insignificant compared to those of all-trans-retinal. The endogenous production of A2E may serve as a protective mechanism to prevent damage to the retina by free all-trans-retinal.

Keywords

Wielgus AR, Zhao B, Chignell CF, et al. **Year** 2010

Authors Albert R. Wielgus, Baozhong Zhao, Colin F. Chignell, Dan-Ning Hu, Joan E. Roberts

Report Name Phototoxicity and cytotoxicity of fullerol in human retinal pigment epithelial cells

Publication Toxicology and Applied Pharmacology

Issue-page numbers Volume 242, Issue 1, 1 January 2010, Pages 79-90

URL http://www.sciencedirect.com/science/article/pii/S0041008X0900413X

Abstract The water-soluble nanoparticle hydroxylated fullerene [fullerol, nano-C60(OH)22–26] has several clinical applications including use as a drug carrier to bypass the blood ocular barriers. We have previously found that fullerol is both cytotoxic and phototoxic to human lens epithelial cells (HLE B-3) and that the endogenous antioxidant lutein blocked some of this phototoxicity. In the present study we have found that fullerol induces cytotoxic and phototoxic damage to human retinal pigment epithelial cells. Accumulation of nano-C60(OH)22–26 in the cells was confirmed spectrophotometrically at 405 nm, and cell viability, cell metabolism and membrane permeability were estimated using trypan blue, MTS and LDH assays, respectively. Fullerol was cytotoxic toward hRPE cells maintained in the dark at concentrations higher than 10 μM. Exposure to an 8.5 J·cm− 2 dose of visible light in the presence of > 5 μM fullerol induced TBARS formation and early apoptosis, indicating phototoxic damage in the form of lipid peroxidation. Pretreatment with 10 and 20 μM lutein offered some protection against fullerol photodamage. Using time resolved photophysical techniques, we have now confirmed that fullerol produces singlet oxygen with a quantum yield of Φ = 0.05 in D2O and with a range of 0.002–0.139 in various solvents. As our previous studies have shown that fullerol also produces superoxide in the presence of light, retinal phototoxic damage may occur through both type I (free radical) and type II (singlet oxygen) mechanisms. In conclusion, ocular exposure to fullerol, particularly in the presence of sunlight, may lead to retinal damage.

Keywords Nanoparticles; Fullerenes; Fullerol; Ocular toxicology; Ocular phototoxicity; Human retinal pigment epithelial cells;

Wille JJ Jr **Year** 2003

Authors Wille JJ Jr

Report Name Circadian rhythm of tumor promotion in the two-stage model of mouse tumorigenesis

Publication Cancer Lett

Issue-page numbers 190:143–149 doi:10.1016/S0304-3835(02)00594-3. PMID:12565168

URL http://www.sciencedirect.com/science/article/pii/S0304383502005943

Abstract The question of whether cancer risk is influenced by time-of-day exposure to potentially carcinogenic agents was approached in this study by exposing mouse skin to a single initiating dose of 7,12-dimethylbenz [∀-]anthracene, followed by a 12 week regime of bi-weekly skin treatments with the tumor promoter, 12-0-tetradecanoyl-phorbol acetate (TPA), given at four different circadian clock times (CCTs). Tumor incidence, average number of tumors per mouse and tumor size showed a dominant circadian component with an acrophase occurring at 23:00 h CCT. Pre-treatment with all trans-retinoic acid, prior to bi-weekly TPA promotion, reduced tumor incidence, average number and size of tumors per animal by greater than 80%, but did not suppress the underlying circadian rhythm of sensitivity to TPA-induced tumor formation.

Keywords Carcinogenesis; Circadian rhythms; Retinoic acid; Tumor promotion; 12-0-tetradecanoyl-phorbol acetate

Authors Williams RA, Howard AG, Williams TP.

Report Name Retinal damage in pigmented and albino rats exposed to low levels of cyclic light following a single mydriatic treatment

Publication Current Eye Research

Issue-page numbers 1985, Vol. 4, No. 2 , Pages 97-102

URL http://informahealthcare.com/doi/abs/10.3109/02713688508999974?journalCode=cey

Abstract The present study demonstrated that less than three days of exposure to low levels of normally cycled ambient illumination are sufficient to cause death to photoreceptor cells in adult pigmented and albino rat. Cyclic light levels as low as 133 and 320 lux were found to destroy photoreceptor cells. A single mydriatic treatment with atropine immediately preceding the three-day exposure was sufficient to permit the effect in pigmented rats. No mydriasis was required for albino rats. When pigmented rats were reared in either 3 lux or 100 lux, it was found that these different light histories did not significantly affect the rats' subsequent susceptibility, during mydriasis, to retinal damage by cyclic illumination.

Keywords

Authors Wilson DW, Griffiths K, Halberg F et al.

Report Name Breast skin temperature rhythms in relation to ovulation

Publication Chronobiologia

Issue-page numbers 10:231–243. PMID:6641367

URL http://www.ncbi.nlm.nih.gov/pubmed/6641367

Abstract

Breast skin temperatures have been monitored at 30-min intervals throughout wake-span for the whole or part of the menstrual cycle of women aged 20-37 years using both manual and automatic (chronobra) methods of measurement. Circadian breast skin temperature rhythms have been mathematically characterized and rhythm parameters assessed in relation to the estimated time of ovulation. Data generally indicate that there is a peri-ovulatory rise in breast temperature. Computer simulation and practical experiments, based on changes in the residual sums of squares from target values obtained for days in the cycle prior to ovulation, have indicated that this peri-ovulatory increase in temperature is possibly detectable within 24 h. The use of the chronobra and associated statistics may be of value in signalling the onset of the infertile phase of the menstrual cycle.

Time series analysis was used to characterize circadian breast skin temperature rhythms and to assess their potential in natural family planning. Study subjects were premenopausal women volunteers who were drawn mainly from research staff at the Tenovus Institute and from a group of women in Cardiff practicing natural family planning. These women had no palpable signs of any breast abnormality and 2 women from the Institute were taking oral contraceptives (OCs). These chronophysiological studies of the breast also indluded data from a clinically healthy 9-year-old premenarcheal girl. All measurements of breast skin temperature were generally taken at 30 minute intervals from 0700 to 2300 during wake span for each day of the study. The extremely good linear response of all series to temperature changes, irrespective of the instrument, meant that when calibration data have been applied to observations made during these studies, it is unlikely that the absolute accuracy falls outside 0.10 degrees Centigrade. Prior to the statistical analysis of temperature changes during the menstrual cycle, cosinor analysis was used to investigate the existence of circadian rhythms in women with clinically health breasts for different age groups. Circadian rhythms were demonstrated in all series investigated and the overall 3-year mean and standard deviation of the average mesor, amplitude and acrophase for 4 sensors located on each quadrant of the left breast were calculated using group cosinor analyses and found to be 35.10 (0.32) degrees Centigrade, 0.43 (0.10) degrees Centigrade, and 16 hours and 27 minutes. Comparable values for similarly located sensors obtained from 4 subjects exhibiting normal ovulatory cycles and studied for 1 complete menstrual cycle were 34.13 (0.17) degrees Centigrade, 0.64 (0.05) degrees Centigrade and 21 hours and 6 minutes. Those for 2 subjects on OCs, studied for 1 cycle, were 33.78 (0.24) degrees Centigrade and 22 hours and 9 minutes. Computer simulation and practical experiments, based on changes in the residual sums of squares from target values obtained for days in the cycle prior to ovulation, indicated that this periovulatory increase in temperature is possibly detectable within 24 hours. The use of the chronobra and associated statistics may be of value in signalling the onset of the infertile phase of the menstrual cycle.

Keywords

Winget CM, Soliman MRI, Holley DC, Meylor JS **Year** 1992

Authors Winget CM, Soliman MRI, Holley DC, Meylor JS

Report Name Chronobiology of physical performance and sports medicine

Publication In: Touitou Y & Haus E, Ed. Biologic Rhythms in Clinical and Laboratory Medicine

Issue-page numbers Berlin, Heidelberg, Paris: Springer. pp. 230–242

URL N/A

Abstract N/A

Keywords

Winter SL, Bosnoyan-Collins L, Pinnaduwage D, Andrulis IL **Year** 2007

Authors Sherry L Winter, Lucine Bosnoyan-Collins, Dushanthi Pinnaduwage, and Irene L Andrulis

Report Name Expression of the Circadian Clock Genes Per1 and Per2 in Sporadic and Familial Breast Tumors

Publication Neoplasia.

Issue-page numbers 2007 October; 9(10): 797–800.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2040206/

Abstract There is a growing body of evidence implicating aberrant circadian clock expression in the development of cancer. Based on our initial experiments identifying a putative interaction between BRCA1 and the clock proteins Per1 and Per2, as well as the reported involvement of the circadian clock in the development of cancer, we have performed an expression analysis of the circadian clock genes Per1 and Per2 in both sporadic and familial primary breast tumors and normal breast tissues using real-time polymerase chain reaction. Significantly decreased levels of Per1 were observed between sporadic tumors and normal samples ($P < .00001$), as well as a further significant decrease between familial and sporadic breast tumors for both Per1 ($P < .00001$) and Per2 ($P < .00001$). Decreased Per1 was also associated with estrogen receptor negativity (53% vs 15%, $P = .04$). These results suggest a role for both Per1 and Per2 in normal breast function and show for the first time that deregulation of the circadian clock may be an important factor in the development of familial breast cancer. Aberrant expression of circadian clock genes could have important consequences on the transactivation of downstream targets that control the cell cycle and on the ability of cells to undergo apoptosis, potentially promoting carcinogenesis.

Keywords Circadian clock, gene expression, Per1, Per2, BRCA1

Wirz-Justice A, Benedetti F, Berger M, et al. **Year** 2005

Authors Wirz-Justice A, Benedetti F, Berger M, Lam RW, Martiny K, Terman M, Wu JC.

Report Name Chronotherapeutics (light and wake therapy) in affective disorders

Publication Psychol Med

Issue-page numbers 2005 Jul;35(7):939-44.

URL http://www.ncbi.nlm.nih.gov/pubmed/16045060

Abstract The Committee on Chronotherapeutics, delegated by the International Society for Affective Disorders (ISAD), makes the following recommendations after reviewing the evidence as of November 2004. (1) Wake therapy is the most rapid antidepressant available today: approximately 60% of patients, independent of diagnostic subtype, respond with marked improvement within hours. Treatment can be a single or repeated sleep deprivation, total (all night) or partial (second half of the night). Relapse can be prevented by daily light therapy, concomitant administration of SSRIs, lithium (for bipolar patients), or a short phase advance of sleep over 3 days following a single night of wake therapy. Combinations of these interventions show great promise. (2) Light therapy is effective for major depression--not only for the seasonal subtype. As an adjuvant to conventional antidepressants in unipolar patients, or lithium in bipolar patients, morning light hastens and potentiates the antidepressant response. Light therapy shows benefit even for patients with chronic depression of 2 years or more, outperforming their weak response to drugs. This method provides a viable alternative for patients who refuse, resist or cannot tolerate medication, or for whom drugs may be contraindicated, as in antepartum depression. (3) Given the urgent need for new strategies to treat patients with residual depressive symptoms, clinical trials of wake therapy and/or adjuvant light therapy, coupled with follow-up studies of long-term recurrence, are a high priority.

Keywords

Wirz-Justice A, Graw P, Kräuchi K, et al. **Year** 1996

Authors Anna Wirz-Justice, Peter Graw, Kurt Kräuchi, Asita Sarrafzadeh, Judie English, Josephine Arendt, Lothar Sand

Report Name 'Natural' light treatment of seasonal affective disorder

Publication Journal of Affective Disorders

Issue-page numbers Volume 37, Issues 2-3, 12 April 1996, Pages 109-120

URL http://www.sciencedirect.com/science/article/pii/016503279500081X

Abstract Patients with seasonal affective disorder (SAD) were treated for 1 week either with a daily 1-h morning walk outdoors (natural light) or low-dose artificial light (0.5 h @ 2800 lux). The latter treatment (given under double-blind conditions) can be considered mainly placebo and did not improve any of the depression self-ratings, whereas natural light exposure improved all self-ratings. According to the Hamilton depression score, 25% remitted after low-dose artificial light and 50% after the walk. Sleep duration or timing were not crucial for the therapeutic response. The morning walk phase-advanced the onset and/or offset of salivary melatonin secretion, but individual clinical improvement could not be correlated with specific phase-shifts. Morning cortisol was decreased. Low-dose artificial light did not modify melatonin or cortisol patterns. This is the first study to provide evidence for the use of outdoor light exposure as a potential alternative or adjuvant to conventional artificial light therapy in SAD.

Keywords Seasonal affective disorder, Placebo light therapy; Natural light exposure; Salivary melatonin; Cortisol

Wollina U, Hipler C, Schaarschmidt H

Year 1988

Authors Wollina U, Hipler C, Schaarschmidt H.

Report Name UV-A exposure of the human epidermis enhances the binding of antibodies to SSA/Ro in vitro

Publication Hautarzt [Article in German]

Issue-page numbers 1988 Mar;39(3):136-8.

URL http://www.ncbi.nlm.nih.gov/pubmed/3288598

Abstract Normal and psoriatic skin specimens (n = 15) were processed to give 4-micron-thick frozen sections and exposed to a single UV irradiation in vitro. We used monochromatic UV-B (313 nm) and UV-A (365 nm). The doses were as follows: 10(3)/10(4) J/m2 (UV-B) or 4.10(3)/8.10(4) J/m2 (UV-A). We investigated the effect on epidermal binding of antibodies to SSA/Ro using the indirect immunofluorescence technique. Untreated and UV-B-treated human skin failed to bind anti-SSA/Ro. UV-A exposure disclosed reticular or granular staining of epidermal nuclei and a perinuclear halo. The effect was nearly the same throughout the dosage range. The combination of UV-A and methoxsalen increased the intensity of staining. Normal and psoriatic skin behaved in the same way.

Keywords

Woo MM, Tai CJ, Kang SK et al.

Year 2001

Authors Woo MM, Tai CJ, Kang SK et al.

Report Name Direct action of melatonin in human granulosa-luteal cells

Publication J Clin Endocrinol Metab

Issue-page numbers 86:4789–4797 doi:10.1210/jc.86.10.4789. PMID:11600542

URL http://jcem.endojournals.org/content/86/10/4789

Abstract The direct involvement of melatonin in modulation of ovarian steroidogenesis, the high levels of melatonin found in human follicular fluid, and the presence of melatonin binding sites in the ovary led us to hypothesize that melatonin acts as a modulator of ovarian function. In contrast to the hypothalamus and pituitary, the mechanism of melatonin action at the level of the ovary is still poorly understood. In the present study, we investigated the gene expression of the two different forms of melatonin receptors in human granulosa-luteal cells, using RT-PCR. PCR products corresponding to the expected sizes of the melatonin receptor subtypes, mt1-R and MT2-R, were obtained from granulosa-luteal cells, and the authenticity of the PCR products was confirmed by Southern blot hybridization with cDNA probes. Subsequent cloning and sequence analysis revealed that the ovarian mt1-R and MT2-R cDNAs are identical to their brain counterparts. Because gonadotropins and GnRH acting through specific receptors in the human ovary regulate cellular functions, we investigated the role of melatonin in the regulation of FSH receptor, LH receptor, GnRH, and GnRH receptor levels. Treatment with melatonin (10 pm–100 nm) significantly increased LH receptor mRNA levels without altering the expression of the FSH receptor gene. Both GnRH and GnRH receptor mRNA levels were significantly decreased, to 61% and 45% of control levels, respectively, after melatonin treatment. Melatonin treatment alone had no effect on basal progesterone production but enhanced the effects of human CG-stimulated progesterone production. Because MAPKs are activated in response to a diverse array of extracellular stimuli leading to the regulation of cell growth, division, and differentiation, and because melatonin has been shown to modulate cellular proliferation and differentiation, in this study, we demonstrated that melatonin activated MAPK in a dose- and time-dependent manner. In summary, our studies demonstrate, for the first time, that melatonin can regulate progesterone production, LH receptor, GnRH, and GnRH receptor gene expression through melatonin receptors in human granulosa-luteal cells, which may be mediated via the MAPK pathway and activation of Elk-1. Our results support the notion that melatonin plays a direct role in regulating ovarian function.

Keywords

Authors Brittany Wood, Mark S. Rea, Barbara Plitnick, Mariana G. Figueiro

Report Name Light level and duration of exposure determine the impact of self-luminous tablets on melatonin suppression

Publication Applied Ergonomics

Issue-page numbers Available online 31 July 2012

URL http://www.sciencedirect.com/science/article/pii/S0003687012001159

Abstract

Exposure to light from self-luminous displays may be linked to increased risk for sleep disorders because these devices emit optical radiation at short wavelengths, close to the peak sensitivity of melatonin suppression. Thirteen participants experienced three experimental conditions in a within-subjects design to investigate the impact of self-luminous tablet displays on nocturnal melatonin suppression: 1) tablets-only set to the highest brightness, 2) tablets viewed through clear-lens goggles equipped with blue light-emitting diodes that provided 40 lux of 470-nm light at the cornea, and 3) tablets viewed through orange-tinted glasses (dark control; optical radiation <525 nm ≈ 0). Melatonin suppressions after 1-h and 2-h exposures to tablets viewed with the blue light were significantly greater than zero. Suppression levels after 1-h exposure to the tablets-only were not statistically different than zero; however, this difference reached significance after 2 h. Based on these results, display manufacturers can determine how their products will affect melatonin levels and use model predictions to tune the spectral power distribution of self-luminous devices to increase or to decrease stimulation to the circadian system.

Keywords Melatonin; Electronic displays; Tablets

Authors Wood JP, Lascaratos G, Bron AJ, Osborne NN.

Report Name The influence of visible light exposure on cultured RGC-5 cells.

Publication Mol Vis

Issue-page numbers 2007 Feb 11;14:334-44.

URL http://www.ncbi.nlm.nih.gov/pubmed/18344945?dopt=abstract

Abstract

PURPOSE:

To determine the effects of visible light on normal or metabolically compromised cultured rat RGC-5 cells.
METHODS:

Cultured RGC-5 cells were exposed to different durations as well as intensities of optical radiation, filtered to exclude wavelengths below 400 nm. Some cells were also subjected to metabolic compromise by depriving them of serum (serum deprivation; SD). Treated cells were assayed for cell viability using the 3,(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) reduction assay, for DNA breakdown by terminal deoxynucleotidyl transferase (TdT)-mediated d-UTP-linked nick end labeling (TUNEL), apoptotic protein activation by immunoblotting, and the production of reactive oxygen species (ROS) with dihydroethidium. A subset of cells was treated with 100 pM rotenone as an alternative means to induce metabolic stress; this was to determine that the influence of light on compromised cells was not specific to serum-deprivation alone.
RESULTS:

Exposure to the light for 48 h activated both caspase-3 and Bcl-associated X-protein (Bax) in cultured RGC-5 cells. Furthermore, light (1000 or 4000 lux), SD, and rotenone caused minor but significant decreases in cellular MTT reduction. SD and light also led to cellular DNA breakdown, although only light caused ROS production. Light (48 h) significantly exacerbated the effect of SD on MTT reduction and DNA cleavage. Furthermore, the antioxidant, trolox, significantly blunted the detrimental influence of light on cell viability, increase in TUNEL-positive cells, and the generation of ROS.
CONCLUSIONS:

Exposure to light was slightly, but significantly, harmful to healthy RGC-5 cells alone, but was much more toxic to those cells that were energetically compromised. Continuous light exposure can therefore detrimentally affect metabolically stressed RGC-5 cells. This may have implications for some ocular retinopathies such as glaucoma.

Keywords

Wood PA, Yang X, Hrushesky WJ

Year 2009

Authors Wood PA, Yang X, Hrushesky WJ.

Report Name Clock genes and cancer

Publication Integr Cancer Ther

Issue-page numbers December 2009 vol. 8 no. 4 303-308

URL http://ict.sagepub.com/content/8/4/303.abstract

Abstract Period genes (Per2, Per1) are essential circadian clock genes. They also function as negative growth regulators. Per2 mutant mice show de novo and radiation-induced epithelial hyperplasia, tumors, and an abnormal DNA damage response. Human tumors show Period gene mutations or decreased expression. Other murine clock gene mutations are not associated with a tumor prone phenotype. Shift work and nocturnal light exposure are associated with circadian clock disruption and with increased cancer risk. The mechanisms responsible for the connection between the circadian clock and cancer are not well defined. We propose that circadian disruption per se is not uniformly tumor promoting and the mechanisms for tumor promotion by specific circadian clock disturbances will differ dependent upon the genes and pathways involved. We propose that Period clock gene mutations promote tumorigenesis by unique molecular pathways. Per2 and Per1 modulate β-catenin and cell proliferation in colon and non-colon cancer cells. Per2 mutation increases intestinal β-catenin levels and colon polyp formation. Per2 mutation also increases ApcMin/+ -mediated intestinal and colonic polyp formation. Intestinal tumorigenesis per se may also alter clock function as a result of increased β-catenin destabilizing PER2 protein. Levels and circadian rhythm of PER2 in ApcMin/+ mouse intestine are markedly decreased, and selective abnormalities in intestinal clock gene and clock-controlled gene expression are seen. We propose that tumor promotion by loss of PERIOD clock proteins is unique to these clock genes as a result of altered β-catenin signaling and DNA damage response. PERIOD proteins may offer new targets for cancer prevention and control.

Keywords

Wooten BR, Hammond BR

Year 2002

Authors Wooten BR, Hammond BR.

Report Name Macular pigment: influences on visual acuity and visibility

Publication Progress in Retinal and Eye Research

Issue-page numbers Volume: 21, Issue: 2, Publisher: Elsevier, Pages: 225-240

URL http://www.mendeley.com/research/macular-pigment-influences-on-visual-acuity-and-visibility/

Abstract There is increasing evidence that the macular pigment (MP) carotenoids lutein (L) and zeaxanthin (Z) protect the retina and lens from age-related loss. As a result, the use of L and Z supplements has increased dramatically in recent years. An increasing number of reports have suggested that L and Z supplementation (and increased MP density) are related to improved visual performance in normal subjects and patients with retinal and lenticular disease. These improvements in vision could be due either to changes in the underlying biology and/or optical changes. The optical mechanisms, i.e., preferential absorption of short-wave light, underlying these putative improvements in vision, however, have not been properly evaluated. Two major hypotheses are discussed. The acuity hypothesis posits that MP could improve visual function by reducing the effects of chromatic aberration. The visibility hypothesis is based on the idea that MP may improve vision through the atmosphere by preferentially absorbing blue haze (short-wave dominant air light that produces a veiling luminance when viewing objects at a distance).

Keywords

Wrba H, Lapin V, Dostal V **Year** 1975

Authors Wrba H, Lapin V, Dostal V

Report Name The influence of pinealectomy and of pinealectomy combined with thymectomy oncogenesis caused by polyoma virus in rats

Publication Osterr Z Onkol

Issue-page numbers 2:37–39. PMID:174046

URL http://www.ncbi.nlm.nih.gov/pubmed/174046

Abstract The inoculation of Polyoma virus suspension to neonatal pinealectomized rats did not provoke a growth of neoplasia. However, if the pinealectomy was combined with neonatal thymectomy, renal tumors occured in a rate of 50 of animals. An incidence of renal tumors was observed also in 57.6% of thymectomized rats, but not in non operated control group. The stimulating effect of pinealectomy on the growth of transplantable tumors has already been described several times (2, 3, 6, 8). The question of a possible change in the viral oncogenesis after pinealectomy was raised. For this reason Polyoma virus was used and its oncogenic effect was studied on the neonatally pinealectomized rats, on rats neonatally thymectomized and on neonatally pinealectomized rats which were simultaneously thymectomized.

Keywords

Wright J, Aldhous M, Franey C et al. **Year** 1986

Authors Wright J, Aldhous M, Franey C et al.

Report Name The effects of exogenous melatonin on endocrine function in man

Publication Clin Endocrinol (Oxf)

Issue-page numbers 24:375–382 doi:10.1111/j.1365-2265.1986.tb01641.x. PMID:3742833

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1986.tb01641.x/abstract?

Abstract At two different times of year (spring and autumn) an oral preparation of the pineal neurohormone melatonin, or placebo, was administered to 12 healthy volunteers (10 men and two women in spring: the same group minus one man in autumn) daily at 1700 h for 1 month (spring), or 3 weeks (autumn) using a double-blind cross-over protocol. The daily dose was 2 mg melatonin in 5 ml corn-oil, and placebo consisted of the vehicle only. In spring the anterior pituitary hormones LH, PRL, GH together with T4, cortisol, testosterone and melatonin were measured at 1– to 6–h intervals for 24 h in plasma on the day following the last dose. In autumn PRL, cortisol and melatonin levels were measured on the last day of treatment. Subjective fatigue, mood and sleep records were kept throughout the studies. Melatonin increased early evening fatigue and actual sleep, but had no effect on mood: these results are reported in full elsewhere. Melatonin administration had no effect on the levels or 24-h rhythm of LH, GH, T4, testosterone or cortisol. An earlier fall in the nocturnal PRL was observed on both occasions. Overall PRL levels were higher in spring than in autumn. In five of the subjects, the secretion of endogenous melatonin was advanced by 1–3 h in the presence of exogenous melatonin. These observations suggest that the potential therapeutic use of melatonin as a hypnotic or in the treatment of jet lag is unlikely to be complicated by undesirable endocrine effects.

Keywords

Wright KP Jr, Czeisler CA **Year** 2002

Authors Wright KP Jr, Czeisler CA

Report Name Absence of circadian phase resetting in response to bright light behind the knees

Publication Science

Issue-page numbers 297:571 doi:10.1126/science.1071697. PMID:12142528

URL http://www.sciencemag.org/content/297/5581/571.full

Abstract N/A

Keywords

Wright KP Jr, Gronfier C, Duffy JF, Czeisler CA **Year** 2005

Authors Wright KP Jr, Gronfier C, Duffy JF, Czeisler CA

Report Name Intrinsic period and light intensity determine the phase relationship between melatonin and sleep in humans

Publication J Biol Rhythms

Issue-page numbers 20:168–177 doi:10.1177/0748730404274265. PMID:15834113

URL http://jbr.sagepub.com/content/20/2/168.abstract

Abstract The internal circadian clock and sleep-wake homeostasis regulate the timing of human brain function, physiology, and behavior so that wakefulness and its associated functions are optimal during the solar day and that sleep and its related functions are optimal at night. The maintenance of a normal phase relationship between the internal circadian clock, sleep-wake homeostasis, and the light-dark cycle is crucial for optimal neurobehavioral and physiological function. Here, the authors show that the phase relationship between these factors—the phase angle of entrainment (ψ)—is strongly determined by the intrinsic period (τ) of the master circadian clock and the strength of the circadian synchronizer. Melatonin was used as a marker of internal biological time, and circadian period was estimated during a forced desynchrony protocol. The authors observed relationships between the phase angle of entrainment and intrinsic period after exposure to scheduled habitual wakefulness-sleep light-dark cycle conditions inside and outside of the laboratory. Individuals with shorter circadian periods initiated sleep and awakened at a later biological time than did individuals with longer circadian periods. The authors also observed that light exposure history influenced the phase angle of entrainment such that phase angle was shorter following exposure to a moderate bright light (~450 lux)–dark/wakefulness-sleep schedule for 5 days than exposure to the equivalent of an indoor daytime light (~150 lux)–dark/wakefulness-sleep schedule for 2 days. These findings demonstrate that neurobiological and environmental factors interact to regulate the phase angle of entrainment in humans. This finding has important implications for understanding physiological organization by the brain's master circadian clock and may have implications for understanding mechanisms underlying circadian sleep disorders.

Keywords phase angle of entrainment, circadian timing, circadian rhythms, light exposure, tau, psi

Wright KP Jr, Hughes RJ, Kronauer RE et al. **Year** 2001

Authors Kenneth P. Wright, Jr., Rod J Hughes, Richard E. Kronauer, Derk-Jan Dijk†, and Charles A. Czeisler

Report Name Intrinsic near-24-h pacemaker period determines limits of circadian entrainment to a weak synchronizer in humans

Publication Proc Natl Acad Sci USA

Issue-page numbers 98:14027–14032 doi:10.1073/pnas.201530198. PMID:11717461

URL http://www.pnas.org/content/98/24/14027.full

Abstract Endogenous circadian clocks are robust regulators of physiology and behavior. Synchronization or entrainment of biological clocks to environmental time is adaptive and important for physiological homeostasis and for the proper timing of species-specific behaviors. We studied subjects in the laboratory for up to 55 days each to determine the ability to entrain the human clock to a weak circadian synchronizing stimulus [scheduled activity–rest cycle in very dim (≈1.5 lux in the angle of gaze) light–dark cycle] at three ≈2
-h periods: 23.5, 24.0, and 24.6 h. These studies allowed us to test two competing hypotheses as to whether the period of the human circadian pacemaker is near to or much longer than 24 h. We report here that imposition of a sleep–wake schedule with exposure to the equivalent of candlelight during wakefulness and darkness during sleep is usually sufficient to maintain circadian entrainment to the 24-h day but not to a 23.5- or 24.6-h day. Our results demonstrate functionally that, in normally entrained sighted adults the average intrinsic circadian period of the human biological clock is very close to 24 h. Either exposure to very dim light and/or the scheduled sleep–wake cycle itself can entrain this near-24-h intrinsic period of the human circadian pacemaker to the 24-h day.

Keywords

Wright KP Jr., Bogan RK, Wyatt JK **Year** 2012

Authors Kenneth P. Wright Jr., Richard K. Bogan, James K. Wyatt

Report Name Shift work and the assessment and management of shift work disorder (SWD)

Publication Sleep Medicine Reviews

Issue-page numbers Available online 2 May 2012

URL http://www.sciencedirect.com/science/article/pii/S1087079212000251

Abstract Nearly 20% of the labor force worldwide, work shifts that include work hours outside 07:00 h to 18:00 h. Shift work is common in many occupations that directly affect the health and safety of others (e.g., protective services, transportation, healthcare), whereas quality of life, health, and safety during shift work and the commute home can affect workers in any field.

Increasing evidence indicates that shift-work schedules negatively influence worker physiology, health, and safety. Shift work disrupts circadian sleep and alerting cycles, resulting in disturbed daytime sleep and excessive sleepiness during the work shift. Moreover, shift workers are at risk for shift work disorder (SWD). This review focuses on shift work and the assessment and management of sleepiness and sleep disruption associated with shift work schedules and SWD. Management strategies include approaches to promote sleep, wakefulness, and adaptation of the circadian clock to the imposed work schedule. Additional studies are needed to further our understanding of the mechanisms underlying the health risks of shift work, understanding which shift workers are at most risk of SWD, to investigate treatment options that address the health and safety burdens associated with shift work and SWD, and to further develop and assess the comparative effectiveness of countermeasures and treatment options.

Keywords Shift work; Shift work disorder; Circadian rhythm; Circadian adaptation; Circadian misalignment;

Wu AH, Stanczyk FZ, Wang R, et al. ***Year*** 2012

Authors Anna H. Wu, Frank Z. Stanczyk, Renwei Wang, Woon-Puay Koh, Jian-Min Yuan, Mimi C. Yu

Report Name Sleep duration, spot urinary 6-sulfatoxymelatonin levels and risk of breast cancer among Chinese women in Singapore

Publication International Journal of Cancer

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1002/ijc.27653/abstract

Abstract We previously reported an inverse association between sleep duration and breast cancer risk in the prospective, population-based Singapore Chinese Health Study (SCHS) cohort (Wu et al., Carcinogenesis 2008;29:1244–8). Sleep duration was significantly positively associated with 6-sulfatoxymelatonin (aMT6s) levels determined in a spot urine, but aMT6s levels in breast cancer cases were lacking (Wu et al., Carcinogenesis 2008;29:1244–8). We updated the sleep duration–breast cancer association with 14 years of follow-up of 34,028 women in the SCHS. In a nested case–control study conducted within the SCHS, randomly timed, prediagnostic urinary aMT6s concentrations were compared between 248 incident breast cancer and 743 individually matched cohort controls. Three female controls were individually matched to each case on age at baseline interview (within 3 years), dialect group, menopausal status, date of baseline interview (within 2 years), date of urine sample collection (within 6 months) and timing of urine collection during the day (within 1 hr). Cox proportional hazards and conditional regression models with appropriate adjustment for confounders were used to examine the sleep– and aMT6s–breast cancer relationships. Breast cancer risk was not significantly associated with sleep duration; adjusted odds ratio (OR) for 9+ vs. ≤6 hr is 0.89 [95% confidence interval (95% CI) = 0.64–1.22]. Prediagnostic aMT6s levels did not differ between breast cancer cases and matched controls; adjusted OR for highest versus lowest quartiles is 1.00 (95% CI = 0.64–1.54). We conclude that sleep duration is not significantly associated with breast cancer risk reduction. Melatonin levels derived from randomly timed spot urine are unrelated to breast cancer. Randomly timed, spot urine-derived melatonin levels are noninformative as surrogates of nocturnal melatonin production.

Keywords sleep duration;

Wu H, Boackle SA, Hanvivadhanakul P, et al. ***Year*** 2007

Authors Wu H, Boackle SA, Hanvivadhanakul P, Ulgiati D, Grossman JM, Lee Y, et al.

Report Name Association of a common complement receptor 2 haplotype with increased risk of systemic lupus erythematosus

Publication PNAS

Issue-page numbers March 6, 2007 vol. 104 no. 10 3961-3966

URL http://www.pnas.org/content/104/10/3961

Abstract A genomic region on distal mouse chromosome 1 and its syntenic human counterpart 1q23–42 show strong evidence of harboring lupus susceptibility genes. We found evidence of linkage at 1q32.2 in a targeted genome scan of 1q21–43 in 126 lupus multiplex families containing 151 affected sibpairs (nonparametric linkage score 2.52, P = 0.006). A positional candidate gene at 1q32.2, complement receptor 2 (CR2), is also a candidate in the murine Sle1c lupus susceptibility locus. To explore its role in human disease, we analyzed 1,416 individuals from 258 Caucasian and 142 Chinese lupus simplex families and demonstrated that a common three-single-nucleotide polymorphism CR2 haplotype (rs3813946, rs1048971, rs17615) was associated with lupus susceptibility (P = 0.00001) with a 1.54-fold increased risk for the development of disease. Single-nucleotide polymorphism 1 (rs3813946), located in the 5′ untranslated region of the CR2 gene, altered transcriptional activity, suggesting a potential mechanism by which CR2 could contribute to the development of lupus. Our findings reveal that CR2 is a likely susceptibility gene for human lupus at 1q32.2, extending previous studies suggesting that CR2 participates in the pathogenesis of systemic lupus erythematosus.

Keywords

Wu J, Algvere PV, Seregard S

Year 2006

Authors Jiangmei Wu; Peep V. Algvere; Stefan Seregard

Report Name The impact of optical radiation to the retina

Publication RetinaToday

Issue-page numbers 2006; 3(1)

URL http://www.retinatoday.org/rt/rt.nsf/docCat?OpenForm&Section=teleretina&Action=Papers&ActionSec=Articles&Language=EN&Cat=&Start=1&Count=100&uniiddoc=BF32A0D5(

Abstract

Optical radiation being defined as a spectral range of 100-10,000 nm comprises ultraviolet radiation, visible light (400-760 nm) and infrared radiation. The way in which light penetrates tissue and the optical properties of the ocular media plays an important role in determining the exposure of the retina and thus the type of photobiological effects produced. The transmittance of the cornea and that of the lens changes, however, considerably with age. Light is a necessary prerequisite for vision but it may damage the sight organ itself. At least three types of radiation insult arise from the spectral range 400 1400 nm, the so-called retina hazard region. Photochemical damage has been the most extensively explored form of light damage on account of its potential role in causing retinal damage under ambient conditions. At least some light damage may be initiated by the visual pigments in the photoreceptors. Generally speaking, rods are more apt to photochemical damage than cones. The characteristics of photochemical damage is the formation of free radicals that can attack many molecule types and render them inactive. The biochemical and physiological features determine the particular susceptibility of the retina to oxidative damage. Two classes of photochemical damage of the retina have been proposed. "Class I" damage has an action spectrum identical to the absorption spectrum of the visual pigment, whilst "Class II" damage has an action spectrum that peaks at short wavelength, providing the basis for the concept of “blue light hazard”. The susceptibility of the retina to light damage can be influenced by spectral components of light sources, light intensity, light-dark cycle, adaptive status, age as well as genetic background. The impact of photochemical damage on age-related maculopathy has been discussed in the current review. The lipofuscin flurophores seem to play an important role in the blue light hazard phenomenon by enhancing the oxidative damage induced by free radicals in response to blue light irradiation. It thus supports the hypothesis that light irradiation, aging changes in the retina and retinal degeneration are all related.

Keywords Optical radiation, photochemical damage, blue light, retina, age-related maculopathy.

Wu J, Dauchy RT, Tirrell PC, et al. **Year** 20100

Authors Jinghai Wu, Robert T. Dauchy, Paul C. Tirrell, Steven S. Wu, Erin M. Dauchy, David E. Blask, and Michael W. Greene

Report Name Abstract 1047: Circadian disruption induced by light at night upregulates PCNA expression in tissue-isolated human breast cancer xenografts in nude rats

Publication Cancer Res

Issue-page numbers April 15, 2010; 70(8 Supplement): 1047

URL http://cancerres.aacrjournals.org/cgi/content/meeting_abstract/70/8_MeetingAbstracts/1047?sid=afd3ffa3-eedd-417f-a794-6f9508554a74

Abstract

The circadian system and the cell cycle are two global regulatory systems in animals and humans. Previous studies have shown that disruption of either the circadian system or the cell cycle increases the risk of cancer in humans. However, the molecular mechanisms of circadian-mediated cell cycle dysregulation are not completely understood. Because proliferating cell nuclear antigen (PCNA) plays an essential role in DNA replication and cell cycle regulation, we studied the circadian regulation and disruption of PCNA in an in vivo animal model of human breast cancer. In tissue-isolated ER- MCF-7 human breast cancer xenografts grown in female nude rats exposed to a normal 12L:12D circadian condition, PCNA protein levels were maximal in the morning (2 h after lights on) but remained at very low levels throughout the rest of the 24 h period. To determine whether circadian disruption alters PCNA protein expression, xenograft-bearing nude rats were exposed to low intensity of light at night (LAN) (0.08 μW/cm2). PCNA protein was continuously expressed at a high level throughout the 24 h period in breast cancer xenografts growing in nude rats exposed to the LAN. Exposure of tumor-bearing rats to LAN also resulted in significantly accelerated growth of these xenografts. Moreover, several signaling cascades related to cell growth were examined. Daily rhythms of Akt and MAPK activation in the human breast cancer tumors were disrupted by LAN but did not track the changes in PCNA expression; however, PDK1 activation directly correlated with PCNA expression. Expression of PKC{delta} and PKC{alpha}, downstream targets of PDK1, was differentially elevated by LAN in xenografts in a manner consistent with their reported roles in cell proliferation. In contrast, LAN did not disrupt the rhythmic expression of either PCNA, PKC{delta}, or PKC{alpha} in the liver of the tumor-bearing rats. Expression of insulin-like growth factor 1 receptor (IGF-1R) protein, an upstream signaling molecule for PDK1, also correlated with the expression pattern of PDK1/PKC/PCNA in tumor-bearing rats exposed to LAN. Exposure of tumor-bearing rats to LAN disrupted the circadian rhythm of IGF-1R protein levels in the liver. Finally, circulating IGF-1 concentrations showed circadian disruption in LAN-exposed tumor-bearing nude rats. Thus, interruption of the IGF-1 signaling pathway may constitute a novel molecular mechanism of circadian regulated tumor growth. Taken together, our results suggest that LAN-induced disruption of circadian rhythms in cell signaling cascades accelerates tumor growth in vivo through continuous up-regulation of PCNA.
In: Proceedings of the 101st Annual Meeting of the American Association for Cancer Research

Keywords

Authors Jinghai Wu, Robert T. Dauchy, Paul C. Tirrell, Steven S. Wu, Darin T. Lynch, Potjana Jitawatanarat, Christine M. Burrington, Erin M. Dauchy, David E. Blask, and Michael W. Gr

Report Name Light at Night Activates IGF-1R/PDK1 Signaling and Accelerates Tumor Growth in Human Breast Cancer Xenografts

Publication Cancer Research

Issue-page numbers April 1, 2011 71; 2622-31

URL http://cancerres.aacrjournals.org/content/71/7/2622.abstract

Abstract

Regulation of diurnal and circadian rhythms and cell proliferation are coupled in all mammals, including humans. However, the molecular mechanisms by which diurnal and circadian rhythms regulate cell proliferation are relatively poorly understood. In this study, we report that tumor growth in nude rats bearing human steroid receptor-negative MCF-7 breast tumors can be significantly accelerated by exposing the rats to light at night (LAN). Under normal conditions of an alternating light/dark cycle, proliferating cell nuclear antigen (PCNA) levels in tumors were maximal in the early light phase but remained at very low levels throughout the daily 24-hour cycle period monitored. Surprisingly, PCNA was expressed in tumors continually at a high level throughout the entire 24-hour period in LAN-exposed nude rats. Daily fluctuations of Akt and mitogen activated protein kinase activation in tumors were also disrupted by LAN. These fluctuations did not track with PCNA changes, but we found that activation of the Akt stimulatory kinase phosphoinositide-dependent protein kinase 1 (PDK1) directly correlated with PCNA levels. Expression of insulin-like growth factor 1 receptor (IGF-1R), an upstream signaling molecule for PDK1, also correlated with fluctuations of PDK1/PCNA in the LAN group. In addition, circulating IGF-1 concentrations were elevated in LAN-exposed tumor-bearing nude rats. Finally, RNAi-mediated knockdown of PDK1 led to a reduction in PCNA expression and cell proliferation in vitro and tumor growth in vivo, indicating that PDK1 regulates breast cancer growth in a manner correlated with PCNA expression. Taken together, our findings demonstrate that LAN exposure can accelerate tumor growth in vivo, in part through continuous activation of IGF-1R/PDK1 signaling.

Keywords

Wu J, Seregard S, Algvere PV

Year 2006

Authors Wu J, Seregard S, Algvere PV.

Report Name Photochemical damage of the retina

Publication Surv Ophthalmol

Issue-page numbers Sep-Oct;51(5):461-81.

URL http://www.ncbi.nlm.nih.gov/pubmed/16950247

Abstract Visual perception occurs when radiation with a wavelength between 400 and 760 nm reaches the retina. The retina has evolved to capture photons efficiently and initiate visual transduction. The retina, however, is vulnerable to damage by light, a vulnerability that has long been recognized. Photochemical damage has been widely studied, because it can cause retinal damage within the intensity range of natural light. Photochemical lesions are primarily located in the outer layers at the central region of the retina. Two classes of photochemical damage have been recognized: Class I damage, which is characterized by the rhodopsin action spectrum, is believed to be mediated by visual pigments, with the primary lesions located in the photoreceptors; whereas Class II damage is generally confined to the retinal pigment epithelium. The action spectrum peaks in the short wavelength region, providing the basis for the concept of blue light hazard. Several factors can modify the susceptibility of the retina to photochemical damage. Photochemical mechanisms, in particular mechanisms that arise from illumination with blue light, are responsible for solar retinitis and for iatrogenic retinal insult from ophthalmological instruments. Further, blue light may play a role in the pathogenesis of age-related macular degeneration. Laboratory studies have suggested that photochemical damage includes oxidative events. Retinal cells die by apoptosis in response to photic injury, and the process of cell death is operated by diverse damaging mechanisms. Modern molecular biology techniques help to study in-depth the basic mechanism of photochemical damage of the retina and to develop strategies of neuroprotection.

Keywords

Wu T, Dong Y, Yang Z, et al.

Year 2009

Authors Tao Wu, Yue Dong, Zhiqiu Yang, Hisanori Kato, Yinhua Ni and Zhengwei Fu

Report Name Differential Resetting Process of Circadian Gene Expression in Rat Pineal Glands after the Reversal of the Light/Dark Cycle via a 24 h Light or Dark Period Transition

Publication Chronobiology International

Issue-page numbers 26:5, 793-807

URL http://informahealthcare.com/doi/abs/10.1080/07420520903044208

Abstract Although studies involving the circadian response to time-zone transitions indicate that the circadian clock usually takes much longer to phase advance than delay, the discrepancy between the circadian resetting induced by photoperiod alteration via a dark or light period transition has yet to be investigated. In mammals, the pineal gland is an important component in the photoneuroendocrine axis, regulating biological rhythms. However, few studies have systematically examined the resetting process of pineal clock-gene expression to date. We investigated the resetting processes of four clock genes (Bmal1, Cry1, Per1, Dec1) and AANAT in the rat pineal gland after the light-dark (LD) reversal via a 24 h light or dark period transition. The resynchronization of the SCN-driven gene AANAT was nearly complete in three days in both situations, displaying similar resetting rates and processes after the differential LD reversals. The resetting processes of the clock genes were characterized by gene-specific, phase-shift modes and differential phase-shift rates between the two different LD reversal modes. The resetting processes of these clock genes were noticeably lengthened after the LD reversal via the light period transition in comparison to via the dark period transition. In addition, among the four examined clock genes, Per1 adjusted most rapidly after the differential LD reversals, while the rhythmic Cry1 expression adjusted most slowly.

Keywords Light/dark reversal, AANAT, Per1, Pineal gland, Rat

Wu WT, Chen YC, Reiter RJ

Year 1988

Authors Wu WT, Chen YC, Reiter RJ

Report Name Day-night differences in the response of the pineal gland to swimming stress

Publication Proc Soc Exp Biol Med

Issue-page numbers 187:315–319. PMID:3347608

URL http://www.ncbi.nlm.nih.gov/pubmed/3347608

Abstract The effect of swimming stress on pineal N-acetyltransferase activity, hydroxyindole-O-methyltransferase (HIOMT) activity, and melatonin content was studied during the day and night in adult male rats. At night, elevated pineal activity was suppressed by light exposure before the animals swam. During the day, swimming for 2 hr did not stimulate NAT activity unless the animals were pretreated with desmethylimipramine (DMI), a norepinephrine uptake blocker. Pineal melatonin content after daytime swimming exhibited a weak rise, unless DMI was injected, in which case melatonin levels showed a highly significant increase. Swimming at night caused a greater (compared to daytime levels) increase in NAT activity in both noninjected and DMI-injected rats. Melatonin levels at night were highly significantly stimulated (compared to daytime values) even without pretreatment of the rats with DMI. The greater response of the rat pineal to swimming stress at night may relate either to an increase in the number of beta-adrenergic receptors in the pinealocyte membrane at night or to a reduced capacity of the sympathetic neurons in the pineal to take up excess circulating catecholamines. Pineal HIOMT activity was not influenced by swimming (with or without DMI) either during the day or at night.

Keywords

Wu Y, Yanase E, Feng X, et al.

Year 2010

Authors Wu Y, Yanase E, Feng X, Siegel MM, Sparrow JR.

Report Name Structural characterization of bisretinoid A2E photocleavage products and implications for age-related macular degeneration

Publication PNAS

Issue-page numbers April 5, 2010, doi: 10.1073/pnas.0913112107

URL http://www.pnas.org/content/early/2010/03/29/0913112107

Abstract Fluorescent bisretinoids, such as A2E and all-trans-retinal dimer, form as a by-product of vitamin A cycling in retina and accumulate in retinal pigment epithelial (RPE) cells as lipofuscin pigments. These pigments are implicated in pathological mechanisms involved in several vision-threatening diseases including age-related macular degeneration. Efforts to understand damaging events initiated by these bisretinoids have revealed that photoexcitation of A2E by wavelengths in the visible spectrum leads to singlet oxygen production and photooxidation of A2E. Here we have employed liquid chromatography coupled to electrospray ionization mass spectrometry together with tandem mass spectrometry (MS/MS), to demonstrate that A2E also undergoes photooxidation-induced degradation and we have elucidated the structures of some of the aldehyde-bearing cleavage products. Studies in which A2E was incubated with a singlet oxygen generator yielded results consistent with a mechanism involving bisretinoid photocleavage at sites of singlet molecular oxygen addition. We provide evidence that one of the products released by A2E photodegradation is methylglyoxal, a low molecular weight reactive dicarbonyl with the capacity to form advanced glycation end products. Methylglyoxal is already known to be generated by carbohydrate and lipid oxidation; this is the first report of its production via bisretinoid photocleavage. It is significant that AGE-modified proteins are detected in deposits (drusen) that accumulate below RPE cells in vivo; drusen have been linked to age-related macular degeneration pathogenesis. Whereas various processes play a role in drusen formation, these findings are indicative of a contribution from lipofuscin photooxidation in RPE.

Keywords

Wu Y-H, Zhou J-N, Balesar R et al. **Year** 2006

Authors Wu Y-H, Zhou J-N, Balesar R et al.

Report Name Distribution of MT1 melatonin receptor immunoreactivity in the human hypothalamus and pituitary gland: colocalization of MT1 with vasopressin, oxytocin, and corticotropin-relea

Publication J Comp Neurol

Issue-page numbers 499:897–910 doi:10.1002/cne.21152. PMID:17072839

URL http://onlinelibrary.wiley.com/doi/10.1002/cne.21152/abstract?

Abstract Melatonin is implicated in numerous physiological processes, including circadian rhythms, stress, and reproduction, many of which are mediated by the hypothalamus and pituitary. The physiological actions of melatonin are mainly mediated by melatonin receptors. We here describe the distribution of the melatonin receptor MT1 in the human hypothalamus and pituitary by immunocytochemistry. MT1 immunoreactivity showed a widespread pattern in the hypothalamus. In addition to the area of the suprachiasmatic nucleus (SCN), a number of novel sites, including the paraventricular nucleus (PVN), periventricular nucleus, supraoptic nucleus (SON), sexually dimorphic nucleus, the diagonal band of Broca, the nucleus basalis of Meynert, infundibular nucleus, ventromedial and dorsomedial nucleus, tuberomamillary nucleus, mamillary body, and paraventricular thalamic nucleus were observed to have neuronal MT1 receptor expression. No staining was observed in the nucleus tuberalis lateralis and bed nucleus of the stria terminalis. The MT1 receptor was colocalized with some vasopressin (AVP) neurons in the SCN, colocalized with some parvocellular and magnocellular AVP and oxytocine (OXT) neurons in the PVN and SON, and colocalized with some parvocellular corticotropin-releasing hormone (CRH) neurons in the PVN. In the pituitary, strong MT1 expression was observed in the pars tuberalis, while a weak staining was found in the posterior and anterior pituitary. These findings provide a neurobiological basis for the participation of melatonin in the regulation of various hypothalamic and pituitary functions. The colocalization of MT1 and CRH suggests that melatonin might directly modulate the hypothalamus–pituitary–adrenal axis in the PVN, which may have implications for stress conditions such as depression.

Keywords melatonin receptor; MT1; hypothalamus; human; immunocytochemistry; colocalization; vasopressin; corticotropin-releasing

Wurtman RJ, Axelrod J, Potter LT **Year** 1964

Authors Wurtman RJ, Axelrod J, Potter LT

Report Name The uptake of H3-melatonin in endocrine and nervous tissues and the effects of constant light exposure

Publication J Pharmacol Exp Ther

Issue-page numbers 143:314–318. PMID:14161142

URL http://jpet.aspetjournals.org/content/143/3/314

Abstract The uptake of circulating H3-melatonin was examined in endocrine and other tissues, in cats and rats. It was found that the pineal gland, iris-choroid, ovary, and other endocrine and peripheral nervous structures took up and retained this compound. The high uptake by ovary was unrelated to hemodynamic factors. Exposure of rats to constant light markedly inhibited the

concentration of melatonin by ovary, but not by heart. Bovine pineal slices were found to concentrate H3-melatonin. Subcellular distribution studies in pineal, ovary, and adrenal showed that most of the retained H3-melatonin was confined to the soluble supernatant fraction.

Keywords

Wyse CA

Year 2012

Authors Cathy A. Wyse

Report Name Does human evolution in different latitudes influence susceptibility to obesity via the circadian pacemaker?

Publication BioEssays

Issue-page numbers Early View (Online Version of Record published before inclusion in an issue)

URL http://onlinelibrary.wiley.com/doi/10.1002/bies.201200067/abstract;jsessionid=81C726667F16EC1FA73CD3260581914B.d02t04?systemMessage=Wiley+Online+Library+will+be

Abstract The variable photoperiods of Northern latitudes challenge the entrainment capacity of the circadian pacemaker, which evolved under constant photoperiods in Equatorial regions. Entrainment to the erratic photoperiods facilitated by artificial light presents an additional challenge. Metabolic dysfunction and obesity are potential consequences of such desynchronization of circadian and environmental rhythms.

Keywords circadian; latitude; migration; obesity

Wyse CA, Selman C, Page MM, et al.

Year 2011

Authors C.A. Wyse, C. Selman, M.M. Page, A.N. Coogan, D.G. Hazlerigg

Report Name Circadian desynchrony and metabolic dysfunction; did light pollution make us fat?

Publication Medical Hypotheses

Issue-page numbers In Press, Corrected Proof

URL http://www.sciencedirect.com/science/article/pii/S0306987711004762

Abstract Circadian rhythms are daily oscillations in physiology and behaviour that recur with a period of 24 h, and that are entrained by the daily photoperiod. The cycle of sunrise and sunset provided a reliable time cue for many thousands of years, until the advent of artificial lighting disrupted the entrainment of human circadian rhythms to the solar photoperiod. Circadian desynchrony (CD) occurs when endogenous rhythms become misaligned with daily photoperiodic cycles, and this condition is facilitated by artificial lighting.

This review examines the hypothesis that chronic CD that has accompanied the availability of electric lighting in the developed world induces a metabolic and behavioural phenotype that is predisposed to the development of obesity. The evidence to support this hypothesis is based on epidemiological data showing coincidence between the appearance of obesity and the availability of artificial light, both geographically, and historically. This association links CD to obesity in humans, and is corroborated by experimental studies that demonstrate that CD can induce obesity and metabolic dysfunction in humans and in rodents.

This association between CD and obesity has far reaching implications for human health, lifestyle and work practices. Attention to the rhythmicity of daily sleep, exercise, work and feeding schedules could be beneficial in targeting or reversing the modern human predisposition to obesity.

Keywords

Authors Wysenbeek AJ, Block DA, Fries JF.

Report Name Prevalence and expression of photosensitivity in systemic lupus erythematosus

Publication Ann Rheum Dis

Issue-page numbers 1989 June; 48(6): 461–463.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1003788/

Abstract

Photosensitivity was assessed in 125 patients with systemic lupus erythematosus (SLE) and in 281 patients with rheumatoid arthritis (RA) as controls. Photosensitivity was reported by 87/119 (73%) patients with SLE and in 62/269 (23%) patients with RA; involving the face in 72/122 (59%) patients with SLE, then arms, chest, and neck. Patients with SLE reported that sun exposure could exacerbate various systemic symptoms, 51/121 (42%) reported medical treatment for photosensitivity and 41/118 (35%) reported that photosensitivity had a significant impact on their lifestyle. There was no significant difference in disease severity, as judged by physician or laboratory results, between patients scoring high or low on the photosensitivity scale.

Keywords

XU W, van Bommel W

Year 2011

Authors Wei XU and Wout van Bommel

Report Name INFERIOR VERSO SUPERIOR: INFERIOR RETINAL LIGHT EXPOSURE

Publication LIGHT & ENGINEERING

Issue-page numbers Vol. 19 #2

URL http://www.sveto-tekhnika.ru/files/2011/LE22011.pdf

Abstract

The present study was designed to investigate the differential pupil response when the light stimulus was adjusted to full, inferior and superior retinal fi eld respectively. Twenty-fi ve subjects were tested by 10-second light stimulus (470 nm, 1012 photons/cm2/sec retinal irradiance). The pupil of the right eye of each subject was recorded by an infrared digital video camera before, during, and after the light stimulus. The results demonstrated that full retinal light exposure and inferior retinal light exposure were signifi cantly different from superior retinal light exposure ($p<0.005$). Findings support the conclusion that the retinal photoreceptors located in the inferior retinal area are more sensitive or denser photoreceptor distribution is found in the inferior retinal area.

Keywords light exposure, retinal photoreceptors, pupil contraction

Authors Yan L, Silver R

Report Name Differential induction and localization of mPer1 and mPer2 during advancing and delaying phase shifts

Publication Eur J Neurosci

Issue-page numbers 16:1531–1540 doi:10.1046/j.1460-9568.2002.02224.x. PMID:12405967

URL http://www.mendeley.com/research/differential-induction-and-localization-of-mper1-and-mper2-during-advancing-and-delaying-phase-shifts/

Abstract The mechanism whereby brief light exposure resets the mammalian circadian clock in a phase dependent manner is not known, but is thought to involve Per gene expression. At the behavioural level, a light pulse produces phase delays in early subjective night, phase advances in late subjective night, and no phase shifts in mid-subjective night or subjective day. To understand the relationship between Per gene activity and behavioural phase shifts, we examined light-induced mPer1 and mPer2 expression in the suprachiasmatic nucleus (SCN) of the mouse, in the subjective night, with a view to understanding SCN heterogeneity. In the VIP-containing region of the SCN (termed 'core'), light-induced mPer1 expression occurs at all times of the subjective night, while mPer2 induction is seen only in early subjective night. In the remaining regions of the SCN (termed 'shell'), a phase delaying light pulse produces no mPer1 but significant mPer2 expression, while a phase advancing light pulse produces no mPer2 but substantial mPer1 induction. Moreover, following a light pulse during mid-subjective night, neither mPer1 nor mPer2 are induced in the shell. The results reveal that behavioural phase shifts occur only when light-induced Per gene expression spreads from the core to the shell SCN, with mPer1 expression in shell corresponding to phase advances, and mPer2 corresponding to phase delays. The results indicate that the time course and the localization of light-induced Per gene expression in SCN reveals important aspects of intra-SCN communication.

Keywords

Authors Yang JH, Bassinger SF, Gross RL, Wu SM.

Report Name Blue light–induced generation of reactive oxygen species in photoreceptor ellipsoids requires mitochondrial electron transport

Publication Invest. Ophthalmol. Vis. Sci.

Issue-page numbers March 2003 vol. 44 no. 3 1312-1319

URL http://www.iovs.org/content/44/3/1312.full

Abstract

purpose. To investigate whether photoreceptor ellipsoids generate reactive oxygen species (rOx) after blue light illumination.

methods. Cultured salamander photoreceptors were exposed to blue light (480 ± 10 nm; 10 mW/cm2). The light-induced catalytic redox activity in the culture was monitored with the use of 3,3′-diaminobenzidine (DAB). Tetramethylrhodamine ethyl ester (TMRE) and 2′,7′-dichlorodihydro-fluorescein acetate (DHF-DA) were used as probes to measure the mitochondrial membrane potential and intracellular rOx, respectively.

results. A significant deposit of DAB polymers was found in the culture after exposure to blue light. Basal levels of rOx were observed in photoreceptor ellipsoids when cells were stained with DHF-DA. This staining colocalized with TMRE. After exposure to blue light, a sharp increase of rOx immediately occurred in the ellipsoids of most photoreceptors. When the light intensity was reduced, the response kinetics of rOx generation were slowed down; however, comparable amounts of rOx were generated after a standard time of exposure to light. The production of rOx in photoreceptors was markedly decreased when an antioxidant mixture was included in the medium during exposure to light. Rotenone or antimycin A, the respiratory electron transport blockers at complex I and III, respectively, significantly suppressed the light-evoked generation of rOx.

conclusions. A robust amount of rOx is produced in the ellipsoid when photoreceptors are exposed to blue light. This light-induced effect is antioxidant sensitive and strongly coupled to mitochondrial electron transport. The cumulative effect of light on rOx generation over time may implicate a role for mitochondria in light-induced oxidative damage of photoreceptors.

Keywords

Yang M-Y, Chang J-G, Lin P-M et al. **Year** 2006

Authors Ming-Yu Yang, Jan-Gowth Chang, Pai-Mei Lin, Kai-Ping Tang, Yen-Hsu Chen, Hugo You-Hsien Lin, Ta-Chih Liu, Hui-Hua Hsiao, Yi-Chang Liu and Sheng-Fung Lin

Report Name Downregulation of circadian clock genes in chronic myeloid leukemia: alternative methylation pattern of hPER3

Publication Cancer Sci

Issue-page numbers 97:1298–1307 doi:10.1111/j.1349-7006.2006.00331.x. PMID:16999817

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1349-7006.2006.00331.x/pdf

Abstract Disruption of circadian rhythm is believed to play a critical role in cancer development. To gain further insights into the roles of circadian genes in chronic myeloid leukemia (CML), we analyzed peripheral blood from 53 healthy individuals and 35 CML patients for the expression of the nine circadian genes. The expression levels of hPER1, hPER2, hPER3, hCRY1, hCRY2 and hBMAL1 were significantly impaired in both chronic phase and blastic crisis of CML cases compared with those in healthy individuals ($P < 0.001$). Methylation studies in the promoter areas of these six genes revealed that only the CpG sites of the hPER3 gene were methylated in all of the CML patients, and the methylated CpG frequencies differed significantly in patients at blastic crisis (8.24 ± 0.73) or at chronic phase (4.48 ± 0.48). The CpG sites of the hPER2 gene were also methylated in 40% of the CML patients. No mutation was found within the coding region of hPER3 in CML cases. Our results suggest that the downregulated hPER3 expression in CML is correlated with the inactivation of hPER3 by methylation.

Keywords

Yasuniwa Y, Izumi H, Wang K, et al. **Year** 0

Authors Yoshihiro Yasuniwa, Hiroto Izumi, Ke-Yong Wang, Shohei Shimajiri, Yasuyuki Sasaguri, Kazuaki Kawai, Hiroshi Kasai, Takashi Shimada, Koichi Miyake, Eiji Kashiwagi, Gen Hira

Report Name Circadian Disruption Accelerates Tumor Growth and Angio/Stromagenesis through a Wnt Signaling Pathway

Publication PLoS One

Issue-page numbers 2010; 5(12): e15330.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3009728/

Abstract Epidemiologic studies show a high incidence of cancer in shift workers, suggesting a possible relationship between circadian rhythms and tumorigenesis. However, the precise molecular mechanism played by circadian rhythms in tumor progression is not known. To identify the possible mechanisms underlying tumor progression related to circadian rhythms, we set up nude mouse xenograft models. HeLa cells were injected in nude mice and nude mice were moved to two different cases, one case is exposed to a 24-hour light cycle (L/L), the other is a more “normal” 12-hour light/dark cycle (L/D). We found a significant increase in tumor volume in the L/L group compared with the L/D group. In addition, tumor microvessels and stroma were strongly increased in L/L mice. Although there was a hypervascularization in L/L tumors, there was no associated increase in the production of vascular endothelial cell growth factor (VEGF). DNA microarray analysis showed enhanced expression of WNT10A, and our subsequent study revealed that WNT10A stimulates the growth of both microvascular endothelial cells and fibroblasts in tumors from light-stressed mice, along with marked increases in angio/stromagenesis. Only the tumor stroma stained positive for WNT10A and WNT10A is also highly expressed in keloid dermal fibroblasts but not in normal dermal fibroblasts indicated that WNT10A may be a novel angio/stromagenic growth factor. These findings suggest that circadian disruption induces the progression of malignant tumors via a Wnt signaling pathway.

Keywords

Authors Kun-Tu Yeh, Ming-Yu Yang, Ta-Chih Liu, Jui-Chang Chen, Wen-Ling Chan, Sheng-Fung Lin, Jan-Gowth Chang MD

Report Name Abnormal expression of period 1 (PER1) in endometrial carcinoma

Publication J Pathol

Issue-page numbers 206:111–120 doi:10.1002/path.1756. PMID:15809976

URL http://onlinelibrary.wiley.com/doi/10.1002/path.1756/abstract?systemMessage=Wiley+Online+Library+will+be+disrupted+8+Oct+from+10-14+BST+for+monthly+maintenance

Abstract The development of endometrial carcinoma (EC) is a multiple-step process, which includes inactivation of tumour suppressor genes, activation of oncogenes, and disturbance of cancer-related genes. Recent studies have shown that the circadian cycle may influence cancer development and prognosis. In this study, the expression of a circadian gene, PER1, was examined in 35 ECs and paired non-tumour tissues by real-time quantitative reverse transcription-polymerase chain reaction (RT-PCR) and immunohistochemistry. Expression levels of PER1 were significantly decreased in EC, and mutational analysis of the coding regions, together with methylation analysis of cytosine-phosphate guanosine (CpG) sites in the promoter area, was performed to investigate the possible mechanisms. The analyses detected four single nucleotide polymorphisms in both tumour and non-tumour tissues, which had no relationship with the expression of PER1. In the promoter area of the PER1 gene, the CpG sites were methylated in 31.4% of ECs, but in 11.4% of paired non-tumour tissues ($p < 0.05$). These results suggest that the down-regulation of PER1 expression in EC was partly due to inactivation of the PER1 gene by DNA methylation of the promoter and partly due to other factors. Analysis of the relationships between the expression of PER1, P53, c-MYC, cyclin A, cyclin B, and cyclin D1 showed no definite relationship. These results suggest that down-regulation of the PER1 gene disrupts the circadian rhythm, which may favour the survival of endometrial cancer cells.

Keywords circadian cycle; PER1; endometrial carcinoma; expression; cell cycle; RT-PCR

Yie SM, Brown GM, Liu GY et al. **Year** 1995

Authors Yie SM, Brown GM, Liu GY et al.

Report Name Melatonin and steroids in human pre-ovulatory follicular fluid: seasonal variations and granulosa cell steroid production

Publication Hum Reprod

Issue-page numbers 10:50–55 doi:10.1093/humrep/10.1.50. PMID:7745070

URL http://humrep.oxfordjournals.org/content/10/1/50.abstract

Abstract Follicular fluid samples were obtained from the largest pre-ovulatory follicle of 120 women undergoing in-vitro fertilization and were examined for melatonin by enzyme-linked immunosorbent assay and the steroids oestradiol and progesterone by radioimmunoassay. The concentrations (mean ± SE) of melatonin (213.4 ± 18.9 pmol/1) and progesterone (20.1 ± 1.1 μmol/l) in follicular fluid during the autumn and winter (dark) months were significantly higher than during the spring and summer (light) months, melatonin (138.4 ± 12.5 pmol/1) and progesterone (11.6 ± 0.8 μmol/l). By contrast, oestradiol concentrations were significantly lower during the dark months than during the light months (264.7 ± 44.1 and 661.8 ± 55.1 nmol/l respectively). There was a positive correlation between follicular fluid melatonin and progesterone concentrations ($r = 0.271$, $P < 0.05$, $n = 120$) and a negative relationship between melatonin and oestradiol ($r = -0.254$, $P < 0.05$, $n = 120$). The effects of melatonin alone and in combination with human chorionic gonadotrophin (HCG) or follicle stimulating hormone (FSH) on steroidogenesis by human granulosa cell culture were also investigated. Melatonin had minimal effects on oestradiol or progesterone production by granulosa cells. Interestingly, the oestradiol response in culture appeared to be different according to the time of the year when harvested. During the light period oestradiol production was enhanced. Melatonin also synergized with HCG in increasing progesterone production on days 6 and 7 after treatment during both light and dark periods. FSH stimulated oestradiol production by the cells on day 2 of culture. Melatonin had no effect on FSH stimulation of oestradiol production. The results of this study suggest that melatonin may be involved in the regulation of steroidogenesis by the human ovaries.

Keywords follicular fluid, granulosa cells, melatonin, seasonal variation, steroids

Yie SM, Niles LP, Younglai EV **Year** 1995

Authors S M Yie, L P Niles and E V Younglai

Report Name Melatonin receptors on human granulosa cell membranes

Publication J Clin Endocrinol Metab

Issue-page numbers 80:1747–1749 doi:10.1210/jc.80.5.1747. PMID:7745030

URL http://jcem.endojournals.org/content/80/5/1747.short?cited-by=yes&legid=jcem;80/5/1747

Abstract Putative melatonin binding sites were detected in the membrane fraction of gonadotropin-stimulated human granulosa cells using the melatonin analogue 2-[125I]-iodomelatonin (125I-IML). Saturation studies and Scatchard analysis revealed the presence of a major binding site with a Kd of 99 pM. Guanosine triphosphate shifted the receptor affinity to 380 pM. In competition studies, the rank order of potency of indoles for inhibition of 125I-IML binding at these sites was typical of melatonin receptors: 2-iodomelatonin > melatonin > N-acetylserotonin > 5-methoxytryptamine > serotonin. Culture of cells for 7 days in vitro increased receptor density but not the affinity. These findings strongly suggest that melatonin found in follicular fluid may have a physiological role.

Keywords

Yokoya M, Shimizu H

Year 2011

Authors Masana Yokoya and Hideyasu Shimizu

Report Name Estimation of Effective Day Length at Any Light Intensity Using Solar Radiation Data

Publication Int J Environ Res Public Health

Issue-page numbers 2011 November; 8(11): 4272–4283.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3228570/

Abstract

The influence of day length on living creatures differs with the photosensitivity of the creature; however, the possible sunshine duration (N0) might be an inadequate index of the photoperiod for creatures with low light sensitivity. To address this issue, the authors tried to estimate the effective day length, i.e., the duration of the photoperiod that exceeds a certain threshold of light intensity. Continual global solar radiation observation data were gathered from the baseline surface radiation network (BSRN) of 18 sites from 2004 to 2007 and were converted to illuminance data using a luminous efficiency model. The monthly average of daily photoperiods exceeding each defined intensity (1 lx, 300 lx, … 20,000 lx) were calculated [defined as Ne(lux)]. The relationships between the monthly average of global solar radiation (Rs), N0, and Ne(lux) were investigated. At low light intensity (<500 lx), Ne(lux) were almost the same as N0. At high light intensity (>10,000 lx), Ne(lux) and Rs showed a logarithmic relationship. Using these relationships, empirical models were derived to estimate the effective day length at different light intensities. According to the validation of the model, the effective day length for any light intensity could be estimated with an accuracy of less than 11% of the mean absolute percentage error (MAPE) in the estimation of the monthly base photoperiod. Recently, a number of studies have provided support for a link between day length and some diseases. Our results will be useful in further assessing the relationships between day length and these diseases.

Keywords solar radiation, effective day length, luminous efficiency, light intensity, circadian rhythm

Yoo S-H, Yamazaki S, Lowrey PL et al. **Year** 2004

Authors Seung-Hee Yoo, Shin Yamazaki,Phillip L. Lowrey, Kazuhiro Shimomura, Caroline H. Ko, Ethan D. Buhr, Sandra M. Siepka, Hee-Kyung Hong, Won Jun Oh, Ook Joon Yoo, Mich

Report Name PERIOD2:LUCIFERASE real-time reporting of circadian dynamics reveals persistent circadian oscillations in mouse peripheral tissues

Publication Proc Natl Acad Sci USA

Issue-page numbers 101:5339–5346 doi:10.1073/pnas.0308709101. PMID:14963227

URL http://www.pnas.org/content/101/15/5339.full

Abstract

Mammalian circadian rhythms are regulated by the suprachiasmatic nucleus (SCN), and current dogma holds that the SCN is required for the expression of circadian rhythms in peripheral tissues. Using a PERIOD2::LUCIFERASE fusion protein as a real-time reporter of circadian dynamics in mice, we report that, contrary to previous work, peripheral tissues are capable of self-sustained circadian oscillations for >20 cycles in isolation. In addition, peripheral organs expressed tissue-specific differences in circadian period and phase. Surprisingly, lesions of the SCN in mPer2Luciferase knockin mice did not abolish circadian rhythms in peripheral tissues, but instead caused phase desynchrony among the tissues of individual animals and from animal to animal. These results demonstrate that peripheral tissues express self-sustained, rather than damped, circadian oscillations and suggest the existence of organ-specific synchronizers of circadian rhythms at the cell and tissue level.

In mammals, a circadian pacemaker located in the suprachiasmatic nucleus (SCN) of the anterior hypothalamus rests at the top of a circadian hierarchy to drive circadian rhythms of behavior and activity at the organismal level (1–4). In multicellular organisms, it has become clear that, in addition to circadian pacemakers located in the CNS, there are oscillators in peripheral tissues (5–8). Perhaps the most compelling example is the discovery that Rat-1 fibroblasts are capable of circadian gene expression after serum stimulation (9). Currently, a wide range of peripheral tissues has been shown to have some capacity for circadian oscillations; however, in all such cases, there appears to be a dichotomy between the SCN and peripheral oscillators. The SCN can express persistent, self-sustained oscillations (>30 cycles in isolation), whereas peripheral rhythms damp out after two to seven cycles (7). This finding has led to a widely accepted hierarchical model of the mammalian circadian system in which the SCN acts as a pacemaker, independently able to both generate and sustain its own circadian oscillations, and necessary to drive circadian oscillations in peripheral cells of neural and non-neural origin (4, 7, 8, 10). Consistent with this model is the observation that peak expression of core circadian genes in peripheral tissues is phase-delayed by 3–9 h relative to their maximal expression in the SCN, suggesting that the SCN phase leads and drives the peripheral circadian rhythms (11–13). Furthermore, in the absence of the SCN, whether by lesioning this structure in the living animal or ex vivo culturing of peripheral tissues, rhythms in circadian gene expression damp after two to seven cycles (7, 14, 15).

To address whether the persistence of circadian rhythms differs in peripheral tissues as compared to the SCN, we have used the mouse Period2 (mPer2) locus to create a real-time gene expression reporter of circadian dynamics. Here, we report the generation of mPer2Luciferase (mPer2Luc) knockin mice in which a Luc gene is fused in-frame to the 3′ end of the endogenous mPer2 gene. Previous work from a number of laboratories using the mPer1 (rather than the mPer2) locus has shown that the SCN expresses persistent circadian rhythms in reporter gene activity, whereas peripheral organs fail to do so (7, 16–18). In contrast, in mPer2Luc mice, we find that both SCN and peripheral tissues in explant cultures show robust and self-sustained circadian rhythms for at least 20 days. Furthermore, in SCN-lesioned mPer2Luc mice, we observe a persistent circadian oscillation in bioluminescence in peripheral tissues, yet from tissue to tissue within each animal and among animals, a gradual loss of phase coordination develops. These results demonstrate that peripheral tissues contain self-sustained circadian oscillators that are as robust as those found in the SCN. Furthermore, the long-term persistence of the oscillations suggests the existence of previously unrecognized synchronizing mechanisms in peripheral organs.

Keywords

Authors In-Young Yoon, Do-Un Jeong, Ki-Bum Kwon, Sang-Bum Kang, and Byoung-Gun Song

Report Name Bright Light Exposure at Night and Light Adaptation of Night Shift Workers

Publication SLEEP

Issue-page numbers Vol. 25, No. 3, 2002

URL http://www.journalsleep.org/Articles/250312.pdf

Abstract

Summary: With practical applicability in mind, we wanted to observe whether nocturnal alertness, performance, and daytime sleep could be improved by light exposure of tolerable intensity and duration in a real work place. We also evaluated whether attenuating morning light was important in adaptation of real night shift workers. Twelve night shift nurses participated in this study. The study consisted of three different treatment procedures: Room Light (RL), Bright Light (BL), and Bright Light with Sunglasses (BL/S). In RL, room light exposure was given during the night shift and followed by 1 hr exposure to sunlight or 10,000 lux light the next morning (from 08:30 to 09:30). In BL, a 4-hour nocturnal light exposure of 4,000-6,000 lux (from 01:00 to 05:00) was applied and followed by the same morning light exposure as in RL. In BL/S, the same nocturnal light exposure as in BL was done with light attenuation in the morning. Each treatment procedure was continued for 4 days in a repeated measures, cross-over design. Nocturnal alertness was measured by a visual analog scale. Computerized performance tests were done. Daytime sleep was recorded with actigraphy. The most significant overall improvement of sleep was noted in BL/S. BL showed less improvement than BL/S but more than RL. Comparison of nocturnal alertness among the 3 treatments produced similar results: during BL/S, the subjects were most alert, followed by BL and then by RL.

Real night shift workers can improve nocturnal alertness and daytime sleep by bright light exposure in their work place. These improvements can be maximized by attenuating morning light on the way home.

Keywords night shift worker; alertness; sleep; bright light; sunglasses

Yoon I-Y, Kripke DF, Elliott JA et al. **Year** 2003

Authors In-Young Yoon, Daniel F Kripke, Jeffrey A Elliott, Shawn D Youngstedt, Katharine M Rex, Richard L Hauger

Report Name Age-related changes of circadian rhythms and sleepwake cycles

Publication J Am Geriatr Soc

Issue-page numbers 51:1085–1091 doi:10.1046/j.1532-5415.2003.51356.x. PMID:12890070

URL http://www.mendeley.com/research/agerelated-changes-circadian-rhythms-sleepwake-cycles/

Abstract

OBJECTIVES: To compare relationships between the sleep-wake cycle and endogenous circadian rhythms in young and older adults and to examine correlates between evening naps and circadian rhythms in older adults. DESIGN: For 1 week of home recording, subjects wore wrist-activity monitors and kept daily sleep logs. After the home monitoring, subjects entered the laboratory on a 90-minute sleep-wake schedule and were monitored on this schedule for at least 30 hours. SETTING: Community living and laboratory. PARTICIPANTS: Sixty-seven young adults, aged 18 to 32, and 56 older adults, aged 60 to 75, who were healthy and had few sleep complaints. MEASUREMENTS: Times of nocturnal sleep, out-of-bed napping, and illumination were obtained at home. Sleep propensity and oral body temperature (OBT) were measured in the laboratory, along with circadian rhythms of cortisol and 6-sulfatoxymelatonin (aMT6s, assayed from urine samples collected every 90 minutes). RESULTS: Home sleep times and illumination acrophases (fitted peak times) were advanced in older adults. The phase angles (time intervals) between onset of aMT6s and sleep onset were not changed in older adults, but sleep offset was more advanced than acrophase and offset of aMT6s with aging. Acrophases of cortisol and sleep propensity were advanced in older adults to the same extent as sleep times, but OBT was less advanced than sleep times. Older adults who took evening naps showed more advanced sleep offset and circadian rhythms of aMT6s, but there were no differences in the phase angles of sleep onset and circadian rhythms of aMT6s and cortisol compared with older adults who did not take evening naps. CONCLUSION: Measuring different circadian markers suggested different phase relationships between the sleep-wake cycle and endogenous circadian rhythms in aging. Early awakening in older adults cannot be explained simply by a relative phase advance of the circadian system. Evening naps and advanced illumination may play a role in the advance of the circadian system in aging.

Keywords

Youn HY, Chou BR, Cullen AP, Sivak JG. **Year** 2009

Authors Hyun-Yi Youn, B Ralph Chou, Anthony P Cullen, Jacob G Sivak

Report Name Effects of 400 nm, 420 nm, and 435.8 nm radiations on cultured human retinal pigment epithelial cells

Publication Journal of photochemistry and photobiology B Biology

Issue-page numbers Volume: 95, Issue: 1, Pages: 64-70

URL http://www.mendeley.com/research/effects-of-400-nm-420-nm-and-4358-nm-radiations-on-cultured-human-retinal-pigment-epithelial-cells/

Abstract The present study demonstrates narrowband short-wavelengths radiation- (400, 420, and 435.8 nm) induced cellular damage of cultured human retinal pigment epithelial cells using in vitro biological assays to determine wavelengths that are responsible for photochemical lesions of the retina. This work involved the exposure of retinal pigment epithelial (RPE) cells (ARPE-19) to narrowband light of three different wavelengths (400, 420, and 435.8 nm) using a xenon arc lamp and interference filters. Cellular viability, mitochondrial distribution, and nucleic acid (both DNA and RNA) damage were quantified after various energy levels of exposure, using the Alamar blue assay, and confocal laser scanning microscopy with two fluorescent stains (Rhodamine 123 and Acridine Orange). The results clearly show that 400 nm light radiation can cause significant dose-dependent decreases in RPE cell viability as well as degradations of DNA/RNA and mitochondria in RPE cells, while 420 and 435.8 nm light radiation cause no cellular damage. While further evaluations may be needed to assess specificity and confounding factors of these assessment tools, the results may be a matter for consideration in future IOL design efforts.

Keywords

Young MW, Kay SA **Year** 2001

Authors Young MW, Kay SA

Report Name Time zones: a comparative genetics of circadian clocks

Publication Nat Rev Genet

Issue-page numbers 2:702–715 doi:10.1038/35088576. PMID:11533719

URL http://www.math.osu.edu/vigre/mathbio/young.pdf

Abstract The circadian clock is a widespread cellular mechanism that underlies diverse rhythmic functions in organisms from bacteria and fungi, to plants and animals. Intense genetic analysis during recent years has uncovered many of the components and molecular mechanisms comprising these clocks. Although autoregulatory genetic networks are a consistent feature in the design of all clocks, the weight of evidence favours their independent evolutionary origins in different kingdoms.

Keywords

Young RW

Year 1988

Authors Young RW.

Report Name Solar radiation and age-related macular degeneration

Publication Surv Ophthalmol

Issue-page numbers 1988 Jan-Feb;32(4):252-69.

URL http://www.ncbi.nlm.nih.gov/pubmed/3279560

Abstract Age-related macular degeneration (AMD) involves a progressive impairment of the outer layers in the center of the retina. Experimental studies have demonstrated that bright light preferentially damages precisely the region that degenerates in AMD. The evidence that solar radiation is responsible for some of the deteriorative changes that lead to AMD is examined in this review. In the primate eye, the high-energy portion of the solar spectrum is most hazardous to retinal molecules, with damaging effects increasing as photon energy rises. This action spectrum is explicable by the quantum laws which describe the interaction of radiation with matter. High-energy visible and ultraviolet photons can produce molecular damage by a photochemical mechanism. The lesion is exacerbated by oxygen, which initiates free-radical chain reactions (photodynamic effects). Melanin exerts a protective effect against damage from sunlight. In the human retina, documented lesions from solar radiation range from the acute effects of sun-gazing to injuries resulting from prolonged periods of exposure in brightly illuminated environments. The damage occurs in the same region that degenerates in AMD. A cataractous lens and ocular melanin both protect the retina against AMD, as predicted by the radiation hypothesis. Identification of an environmental factor that evidently plays a role in the etiology of AMD provides the basis for a program of preventive medicine.

Keywords

Youngstedt SD, Kripke DF, Elliott JA, Klauber MR

Year 2001

Authors Youngstedt SD, Kripke DF, Elliott JA, Klauber MR

Report Name Circadian abnormalities in older adults

Publication J Pineal Res

Issue-page numbers 31:264–272 doi:10.1034/j.1600-079X.2001.310311.x. PMID:11589762

URL http://onlinelibrary.wiley.com/doi/10.1034/j.1600-079X.2001.310311.x/abstract?systemMessage=Wiley+Online+Library+will+be+disrupted+8+Oct+from+10-14+BST+for+monthly

Abstract This study examined the circadian phase adjustment of symptomatic elders ages 60–79 years in comparison with that of young, healthy adults ages 20–40 years. Seventy-two elders with complaints of insomnia or depression, and 30 young, healthy adults were assessed for 5–7 days at home. Sleep and illumination were recorded with Actillume wrist monitors and sleep diaries. Urine was collected over two 24-hr periods and assayed for 6-sulphatoxymelatonin (6-smt). The volunteers were then observed continuously for 5 nights and 4 days in the laboratory. In the laboratory, sleep periods were fixed at 8 hr with polysomnographic assessment of sleep, apnea-hypopnea, and nocturnal myoclonus. Circadian dispersion, defined as the mean variation of 6-smt acrophase from the median age-specific acrophase, was significantly greater in the older vs. young adults. Likewise, circadian malsynchronization, defined as the absolute number of hours (advance or delay) between the 6-smt acrophase and the middle of the sleep period, was significantly greater in the older vs. young volunteers. For the older volunteers, multiple regressions were calculated associating sleep with potential correlates of sleep disturbance. Nocturnal myoclonus and circadian malsynchronization were more strongly associated with sleep impairment than other factors (e.g., sleep apnea, depression). These observations suggest that circadian malsynchronization might be a common and significant cause of disturbed sleep among adults over age 60.

Keywords malsynchronization; phase dispersion; 6-sulphatoxymelatonin

Youssef PN, Sheibani N, Albert DM — ***Year*** 2011

Authors P N Youssef, N Sheibani and D M Albert

Report Name Retinal light toxicity

Publication Eye

Issue-page numbers 25, 1–14; doi:10.1038/eye.2010.149; published online 29 October 2010

URL http://www.nature.com/eye/journal/v25/n1/full/eye2010149a.html

Abstract The ability of light to enact damage on the neurosensory retina and underlying structures has been well understood for hundreds of years. While the eye has adapted several mechanisms to protect itself from such damage, certain exposures to light can still result in temporal or permanent damage. Both clinical observations and laboratory studies have enabled us to understand the various ways by which the eye can protect itself from such damage. Light or electromagnetic radiation can result in damage through photothermal, photomechanical, and photochemical mechanisms. The following review seeks to describe these various processes of injury and many of the variables, which can mitigate these modes of injury.

Keywords light-induced retinopathy; light-induced retinal degeneration; phototoxic retinopathy; photochemical; photomechanical; photothermal

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Yu EA, Weaver DR — ***Year*** 2011

Authors Elizabeth A. Yu and David R. Weaver

Report Name Disrupting the circadian clock: Gene-specific effects on aging, cancer, and other phenotypes

Publication Aging (Albany NY)

Issue-page numbers 2011 May; 3(5): 479–493.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3156599/

Abstract The circadian clock imparts 24-hour rhythmicity on gene expression and cellular physiology in virtually all cells. Disruption of the genes necessary for the circadian clock to function has diverse effects, including aging-related phenotypes. Some circadian clock genes have been described as tumor suppressors, while other genes have less clear functions in aging and cancer. In this Review, we highlight a recent study [Dubrovsky et al., Aging 2: 936-944, 2010] and discuss the much larger field examining the relationship between circadian clock genes, circadian rhythmicity, aging-related phenotypes, and cancer.

Keywords circadian rhythms, clock, Bmal1, period, cryptochrome, cancer, aging

Zaidi FH, Hull JT, Peirson SN, et al. **Year** 2007

Authors Farhan H. Zaidi, Joseph T. Hull, Stuart N. Peirson, Katharina Wulff, Daniel Aeschbach, Joshua J. Gooley, George C. Brainard, Kevin Gregory-Evans, Joseph F. Rizzo, Charles A

Report Name Short-Wavelength Light Sensitivity of Circadian, Pupillary, and Visual Awareness in Humans Lacking an Outer Retina

Publication Current Biology

Issue-page numbers Volume 17, Issue 24, 2122-2128, 18 December 2007

URL http://www.cell.com/current-biology/abstract/S0960-9822%2807%2902273-7

Abstract As the ear has dual functions for audition and balance, the eye has a dual role in detecting light for a wide range of behavioral and physiological functions separate from sight [1,2,3,4,5,6,7,8,9,10,11]. These responses are driven primarily by stimulation of photosensitive retinal ganglion cells (pRGCs) that are most sensitive to short-wavelength (~480 nm) blue light and remain functional in the absence of rods and cones [8,9,10]. We examined the spectral sensitivity of non-image-forming responses in two profoundly blind subjects lacking functional rods and cones (one male, 56 yr old; one female, 87 yr old). In the male subject, we found that short-wavelength light preferentially suppressed melatonin, reset the circadian pacemaker, and directly enhanced alertness compared to 555 nm exposure, which is the peak sensitivity of the photopic visual system. In an action spectrum for pupillary constriction, the female subject exhibited a peak spectral sensitivity (λmax) of 480 nm, matching that of the pRGCs but not that of the rods and cones. This subject was also able to correctly report a threshold short-wavelength stimulus (~480 nm) but not other wavelengths. Collectively these data show that pRGCs contribute to both circadian physiology and rudimentary visual awareness in humans and challenge the assumption that rod- and cone-based photoreception mediate all “visual” responses to light.

Keywords circadian

Zamanian Z, Kakooei H, Ayattollahi SMT, Dehghani M **Year** 2010

Authors Z. Zamanian, H. Kakooei, S.M.T. Ayattollahi and M. Dehghani

Report Name Effect of Bright Light on Shift Work Nurses in Hospitals

Publication Pakistan Journal of Biological Sciences

Issue-page numbers 13: 431-436

URL http://scialert.net/fulltext/?doi=pjbs.2010.431.436&org=11

Abstract The aim of this study are to assess, in a hospital setting, the effects of Bright Light (BL) on the rhythms in body temperature, plasma melatonin, plasma cortisol and subjective alertness during shift work. In our experimental design, 34 healthy shift work nurses from a university hospital were exposed to bright light (4500 lux) during two break times (21:15 to 22; 00 and 3:15 to 4:00) for four consecutive weeks. In this survey, the subjects were studied under 24 h of realistic conditions during which their plasma cortisol and plasma melatonin was measured at 3 h intervals. In addition, their body temperatures were measured during and after night shift work. Subjective alertness and fatigue were evaluated with the Karolinska Sleepiness Scale (KSS) and Visual Analog Scale (VOI). It was found that bright light administration significantly suppressed nighttime melatonin levels during night shift, most strongly at 2:00 a.m. A one-way ANOVA, with repeated measurement design, revealed that Bright Light (BL) tended to increase cortisol levels and body temperature and improved alertness significantly during night shift. These results demonstrate that photic stimulation in a hospital setting can have a powerful influence on the adjustment of the circadian system.

Keywords

Zapka M, Heyers D, Liedvogel M, et al. **Year** 2010

Authors Manuela Zapka, Dominik Heyers, Miriam Liedvogel, Erich D. Jarvis, and Henrik Mouritsen

Report Name Night-time neuronal activation of Cluster N in a day- and night-migrating songbird

Publication Eur J Neurosci

Issue-page numbers 2010 August; 32(4): 619–624.

URL http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2924469/

Abstract

Magnetic compass orientation in a night-migratory songbird requires that Cluster N, a cluster of forebrain regions, is functional. Cluster N, which receives input from the eyes via the thalamofugal pathway, shows high neuronal activity in night-migrants performing magnetic compass guided behaviour at night, whereas no activation is observed during the day, and covering up the birds' eyes strongly reduces neuronal activation. These findings suggest that Cluster N processes light-dependent magnetic compass information in night-migrating songbirds. The aim of this study is to test if Cluster N is active during day-time migration. To answer this question, we used behavioural molecular mapping based on ZENK activation to investigate if Cluster N is active in the meadow pipit (Anthus pratensis), a day- and night-migratory species. We found that Cluster N of meadow pipits shows high neuronal activity under dim-light at night, but not under full room-light conditions during the day. These data raise the possibility that, in day- and night-migratory meadow pipits, the light-dependent magnetic compass, which requires an active Cluster N, may only be used during night-time, whereas another magnetosensory mechanism and/or other reference system(s), like the sun or polarized light may be used as primary orientation cues during the day.

Keywords meadow pipit, magnetoperception, magnetic sense, bird migration, navigation

Authors Zeeb H, Blettner M, Hammer GP, Langner I

Report Name Cohort mortality study of German cockpit crew, 1960–1997

Publication Epidemiology

Issue-page numbers 13:693–699.doi:10.1097/00001648-200211000-00014 PMID:12410011

URL http://journals.lww.com/epidem/Abstract/2002/11000/Cohort_Mortality_Study_of_German_Cockpit_Crew,.14.aspx

Abstract

Background. Cockpit crew in civil aviation are exposed to several potential health hazards, among them cosmic ionizing radiation. To assess the influence of occupational and other factors on mortality we conducted a cohort study among cockpit crew.

Methods. All pilots and other cockpit personnel of two German airlines were traced through registries and other sources for the period 1960-1997. Standardized mortality ratios, with German population rates as the reference, were calculated. We estimated the individual radiation dose based on individual job histories and assessed dose-response trends in stratified and regression analyses.

Results. We compiled a cohort of 6061 male cockpit personnel, yielding 105,037 person-years of observation. The maximum estimated individual radiation dose was 80.5 mSv. Among 255 deaths overall (standardized mortality ratio [SMR] = 0.48; 95% confidence interval [CI] = 0.42-0.54) there were 76 cancer deaths (SMR = 0.56; CI = 0.43 - 0.74). Most cancer and cardiovascular SMRs were reduced. A slight increase was seen for brain cancer (SMR = 1.68; CI = 0.66-3.62). Employment duration was associated with the all-cancer mortality in Poisson regression analyses. No other dose-response relation was found.

Conclusions. German cockpit crew have a low overall and cancer mortality. The role of occupational causes, and particularly cosmic radiation, appears limited.

Keywords

Authors Zeeb H, Blettner M, Langner I et al.

Report Name Mortality from cancer and other causes among airline cabin attendants in Europe: a collaborative cohort study in eight countries

Publication Am J Epidemiol

Issue-page numbers 158:35–46.doi:10.1093/aje/kwg107 PMID:12835285

URL http://aje.oxfordjournals.org/content/158/1/35.full

Abstract There is concern about the health effects of exposure to cosmic radiation during air travel. To study the potential health effects of this and occupational exposures, the authors investigated mortality patterns among more than 44,000 airline cabin crew members in Europe. A cohort study was performed in eight European countries, yielding approximately 655,000 person-years of follow-up. Observed numbers of deaths were compared with expected numbers based on national mortality rates. Among female cabin crew, overall mortality (standardized mortality ratio (SMR) = 0.80, 95% confidence interval (CI): 0.73, 0.88) and all-cancer mortality (SMR = 0.78, 95% CI: 0.66, 0.95) were slightly reduced, while breast cancer mortality was slightly but nonsignificantly increased (SMR = 1.11, 95% CI: 0.82, 1.48). In contrast, overall mortality (SMR = 1.09, 95% CI: 1.00, 1.18) and mortality from skin cancer (for malignant melanoma, SMR = 1.93, 95% CI: 0.70, 4.44) among male cabin crew were somewhat increased. The authors noted excess mortality from aircraft accidents and from acquired immunodeficiency syndrome in males. Among airline cabin crew in Europe, there was no increase in mortality that could be attributed to cosmic radiation or other occupational exposures to any substantial extent. The risk of skin cancer among male crew members requires further attention.

Keywords aviation; cohort studies; cosmic radiation; mortality; neoplasms; occupational exposure

Authors Zeitzer JM, Daniels JE, Duffy JF, Klerman EB, Shanahan TL, Dijk DJ, Czeisler CA.

Report Name Do plasma melatonin concentrations decline with age?

Publication Am J Med

Issue-page numbers 107:432–436 doi:10.1016/S0002-9343(99)00266-1. PMID:10569297

URL http://www.ncbi.nlm.nih.gov/pubmed/10569297

Abstract

PURPOSE:

Numerous reports that secretion of the putative sleep-promoting hormone melatonin declines with age have led to suggestions that melatonin replacement therapy be used to treat sleep problems in older patients. We sought to reassess whether the endogenous circadian rhythm of plasma melatonin concentration changes with age in healthy drug-free adults.
METHODS:

We analyzed the amplitude of plasma melatonin profiles during a constant routine in 34 healthy drug-free older subjects (20 women and 14 men, aged 65 to 81 years) and compared them with 98 healthy drug-free young men (aged 18 to 30 years).
RESULTS:

We could detect no significant difference between a healthy and drug-free group of older men and women as compared to one of young men in the endogenous circadian amplitude of the plasma melatonin rhythm, as described by mean 24-hour average melatonin concentration (70 pmol/liter vs 73 pmol/liter, P = 0.97), or the duration (9.3 hours vs 9.1 hours, P = 0.43), mean (162 pmol/liter vs 161 pmol/liter, P = 0.63), or integrated area (85,800 pmol x min/liter vs 86,700 pmol x min/liter, P = 0.66) of the nocturnal peak of plasma melatonin.
CONCLUSION:

These results do not support the hypothesis that reduction of plasma melatonin concentration is a general characteristic of healthy aging. Should melatonin replacement therapy or melatonin supplementation prove to be clinically useful, we recommend that an assessment of endogenous melatonin be carried out before such treatment is used in older patients.

Keywords

Zeitzer JM, Dijk D, Kronauer RE, et al. **Year** 2000

Authors Jamie M Zeitzer, Derk-Jan Dijk, Richard E Kronauer, Emery N Brown and Charles A Czeisler

Report Name Sensitivity of the human circadian pacemaker to nocturnal light: melatonin phase resetting and suppression

Publication The Journal of Physiology

Issue-page numbers 526, 695-702.

URL http://jp.physoc.org/content/526/3/695.abstract

Abstract

1. Ocular exposure to early morning room light can significantly advance the timing of the human circadian pacemaker. The resetting response to such light has a non-linear relationship to illuminance. The dose-response relationship of the human circadian pacemaker to late evening light of dim to moderate intensity has not been well established.

2. Twenty-three healthy young male and female volunteers took part in a 9 day protocol in which a single experimental light exposure6.5 h in duration was given in the early biological night. The effects of the light exposure on the endogenous circadian phase of the melatonin rhythm and the acute effects of the light exposure on plasma melatonin concentration were calculated.

3. We demonstrate that humans are highly responsive to the phase-delaying effects of light during the early biological night and that both the phase resetting response to light and the acute suppressive effects of light on plasma melatonin follow a logistic dose-response curve, as do many circadian responses to light in mammals.

4. Contrary to expectations, we found that half of the maximal phase-delaying response achieved in response to a single episode of evening bright light (~9000 lux (lx)) can be obtained with just over 1 % of this light (dim room light of ~100 lx). The same held true for the acute suppressive effects of light on plasma melatonin concentrations. This indicates that even small changes in ordinary light exposure during the late evening hours can significantly affect both plasma melatonin concentrations and the entrained phase of the human circadian pacemaker.

Keywords melatonin, circadian

Authors Lixia Zha, Lulu Fan, Guoping Sun, Hua Wang, Tai Ma, Fei Zhong, Wei Wei

Report Name Melatonin sensitizes human hepatoma cells to endoplasmic reticulum stress-induced apoptosis

Publication Journal of Pineal Research

Issue-page numbers Accepted Article (Accepted, unedited articles published online for future issues) DOI: 10.1111/j.1600-079X.2011.00946.x

URL http://onlinelibrary.wiley.com/doi/10.1111/j.1600-079X.2011.00946.x/abstract

Abstract Endoplasmic reticulum stress-mediated cell apoptosis is implicated in the development of cancer. Melatonin induces apoptosis in hepatocellular carcinoma in experimental studies but the effects of melatonin on endoplasmic reticulum (ER) stress-induced apoptosis in hepatocellular carcinoma has not been tested. Differences in ER-stress induced apoptosis in human hepatoma cells and normal human hepatocyte were investigated by exposure to tunicamycin (ER stress inducer). Significant differences were observed in the rate of apoptosis between HepG2 cells (hepatoma cells) and HL-7702 cells (normal human hepatocyte cells). The expression of cyclooxygenase-2 (COX-2) was increased in HepG2 cells but not in HL-7702 cells. Furthermore, down-regulation of COX-2 expression using the COX-2 inhibitor, celecoxib, increased tunicamycin induced apoptosis concomitant with the up-regulation of pro-apoptotic transcription factor CHOP (GADD153) and down-regulation of B-cell lymphoma 2/Bcl-2–associated X protein (Bcl-2/Bax) ratio, suggesting that inhibition of COX-2 sensitized human hepatoma cells to ER stress induced apoptosis. Interestingly, co-treatment with tunicamycin and melatonin also decreased the expression of COX-2 and significantly increased the rate of apoptosis by elevating the levels of CHOP and reducing the Bcl-2/Bax ratio. These results demonstrate that melatonin sensitizes human hepatoma cells to ER stress-induced apoptosis by down-regulating COX-2 expression, increasing the levels of CHOP and decreasing the ratio of Bcl-2/Bax .

Keywords melatonin; endoplasmic reticulum stress; HCC; COX-2; apoptosis

Year 2010

Authors Zhang R, Naughton DP.

Report Name Vitamin D in health and disease: current perspectives

Publication Nutrition Journal

Issue-page numbers 2010, 9:65 doi:10.1186/1475-2891-9-65

URL http://www.nutritionj.com/content/9/1/65

Abstract

Vitamin D is a group of fat-soluble prohormones which were identified after the discovery of the anti-rachitic effect of cod liver oil in the early part of the 20th century. The vitamin found in cod liver oil was designated "D" following Vitamin A, B and C, which had been discovered earlier [1]. The two major biologically inert precursors of vitamin D are vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) [2,3]. Vitamin D3 is formed when 7-dehydrocholesterol in the skin is exposed to solar ultraviolet B (UVB, 290-320 nm), and then converted to previtamin D3. In a heat-dependent process, previtamin D3 is immediately converted to vitamin D. Excess UVB rays transform previtamin D3 into biologically inactive metabolites, tachysterol and lumisterol. Vitamin D2 is plant derived, produced exogenously by irradiation of ergosterol, and enters the circulation through diet [1].

Both vitamin D precursors resulting from exposure to the sunshine and the diet are converted to 25-hydroxyvitamin D [25(OH)D] (calcidiol) when they enter the liver [4]. 25(OH)D is the major circulating form of vitamin D and is used to determine vitamin D status. In order to be biologically active, additional hydroxylation in the kidneys is needed to form active 1,25-dihydroxyvitamin D [1,25(OH)2D] (calcitriol) [5]. The process of vitamin D formation is summarized in Figure 1. Humans obtain vitamin D through dietary intake and exposure to sunlight. Very few foods naturally contain vitamin D. Oily fish such as salmon, mackerel, and sardines are rich in vitamin D3. Egg yolks are reported to contain vitamin D though the amounts are highly variable. Moreover, the cholesterol content of egg yolks makes it a poor source of vitamin D. Also, a small number of foods are fortified with vitamin D such as milk, orange juice and some bread and cereals [6,7]. A list of vitamin D content in different food sources is shown in Table 1.
Vitamin D plays an important role in maintaining an adequate level of serum calcium and phosphorus. Without vitamin D, only 10 to 15% of dietary calcium and about 60% of phosphorus is absorbed [8-10]. Therefore vitamin D has a great effect in forming and maintaining strong bones. It has also recently been found that vitamin D receptors exist in a variety of cells thus it has a biological effect on more than mineral metabolism. The aim of this report is to review key aspects relating to vitamin D deficiency, its causes, and studies on prevention of and treatment of major conditions/diseases. Thus, following a general literature review on deficiency and its causes, an overview of major meta-analyses of Vitamin D supplementation is given. This systematic approach covers meta-analyses listed in Pubmed during the past 2 decades.

Keywords

Zhao ZY, Touitou Y

Year 1993

Authors Zi-Yan Zhao and Yvan Touitou

Report Name Kinetic changes of melatonin release in rat pineal perifusions at different circadian stages. Effects of corticosteroids

Publication Acta Endocrinol (Copenh)

Issue-page numbers 129:81–88. PMID:8351960

URL http://www.eje.org/content/129/1/81.abstract

Abstract

The kinetic characteristics of melatonin release were documented in perifused pineal glands removed from rats sacrificed at six circadian stages (light/dark =12:12): three during the light phase, i.e. 3, 7 and 11 hours after light onset (HALO), and three during the dark phase, i.e. 15, 19 and 23 HALO. Whatever the circadian stage, the melatonin release decreased during the first 3–4 h and then remained fairly constant and roughly similar up to 8 h of perifusion. However, the kinetics of the release in the first 3 h differed in perifusions of pineal glands removed during the light (progressive decline during 3 h) as compared to perifusions of pineal glands removed during the dark (sharp decline during the first hour and then a progressive decline until reaching a constant level after 3 h).

As the effects of steroid administration on melatonin secretion are a matter of controversy, we also studied the direct effects and their circadian stage dependence, if any, of corticosterone, deoxycorticosterone and dexamethasone on melatonin secretion by pineal glands removed 7 HALO (about the middle of the light phase) and 19 HALO (about the middle of the dark phase). High concentrations of corticosterone (0.8 × 10−1 mol/l) and dexamethasone (0.4×10−3 mol/l) resulted in a significant ($p<0.001$) inhibitory effect on melatonin production (about a 50% and a 30% decrease, respectively) whatever the circadian stage, whereas lower concentrations (10−4–10−5 mol/l of both steroids did not affect melatonin production. In addition, neither pharmacological (1.06 × 10−5 mol/l) nor physiological (for the rat) concentrations (2.1 × 10−7 mol/l) of deoxycorticosterone had any significant effect on pineal melatonin production. These data clearly show the time dependence of the kinetics of melatonin release and an effect of adrenocortical steroids on pineal melatonin production that may be quite different according to the steroid and dosage.

Keywords

Zheng B, Larkin DW, Albrecht U et al. ***Year*** 1999

Authors Binhai Zheng, David W. Larkin, Urs Albrecht, Zhong Sheng Sun, Marijke Sage, Gregor Eichele, Cheng Chi Lee and Allan Bradley

Report Name The mPer2 gene encodes a functional component of the mammalian circadian clock

Publication Nature

Issue-page numbers 400:169–173 doi:10.1038/22659. PMID:10408444

URL http://www.nature.com/nature/journal/v400/n6740/abs/400169a0.html

Abstract Circadian rhythms are driven by endogenous biological clocks that regulate many biochemical, physiological and behavioural processes in a wide range of life forms1. In mammals, there is a master circadian clock in the suprachiasmatic nucleus of the anterior hypothalamus. Three putative mammalian homologues (mPer1, mPer2 and mPer3) of the Drosophila circadian clock gene period (per) have been identified2,3,4,5,6,7,8. The mPer genes share a conserved PAS domain (a dimerization domain found in Per, Arnt and Sim) and show a circadian expression pattern in the suprachiasmatic nucleus. To assess the in vivo function of mPer2, we generated and characterized a deletion mutation in the PAS domain of the mouse mPer2 gene. Here we show that mice homozygous for this mutation display a shorter circadian period followed by a loss of circadian rhythmicity in constant darkness. The mutation also diminishes the oscillating expression of both mPer1 and mPer2 in the suprachiasmatic nucleus, indicating that mPer2 may regulate mPer1in vivo. These data provide evidence that an mPer gene functions in the circadian clock, and define mPer2 as a component of the mammalian circadian oscillator.

Keywords

Zhu Y, Brown HN, Zhang Y et al. ***Year*** 2005

Authors # Yong Zhu1,

Report Name Period3 structural variation: a circadian biomarker associated with breast cancer in young women

Publication Cancer Epidemiol Biomarkers Prev

Issue-page numbers 14:268–270. PMID:15668506

URL http://cebp.aacrjournals.org/content/14/1/268.abstract

Abstract Circadian disruption has been indicated as a risk factor for breast cancer in recent epidemiologic studies. A novel finding in circadian biology is that genes responsible for circadian rhythm also regulate many other biological pathways, including cell proliferation, cell cycle regulation, and apoptosis. Therefore, mutations in circadian genes could conceivably result in deregulation of these processes and contribute to tumor development, and be markers for susceptibility to human cancer. In this study, we investigated the association between an exonic length variation in a circadian gene, Period3 (Per3), and breast cancer risk using blood samples collected from a recently completed breast cancer case-control study in Connecticut. There were 389 Caucasian cases and 432 Caucasian controls included in our analysis. We found that the variant Per3 genotype (heterozygous + homozygous 5-repeat alleles) was associated with an increased risk of breast cancer among premenopausal women (odds ratio, 1.7; 95% confidence interval, 1.0-3.0). Our finding suggests that the circadian genes might be a novel panel of potential biomarkers for breast cancer and worth further investigation.

Keywords breast cancer, circadian gene, period3

Authors Zhu Y, Leaderer D, Guss C, Brown HN, Zhang Y, Boyle P, Stevens RG, Hoffman A, Qin Q, Han X, Zheng T.

Report Name Ala394Thr polymorphism in the clock gene NPAS2: a circadian modifier for the risk of non-Hodgkin's lymphoma

Publication Int J Cancer

Issue-page numbers 120:432–435 doi:10.1002/ijc.22321. PMID:17096334

URL http://www.ncbi.nlm.nih.gov/pubmed/17096334

Abstract Circadian disruption is theorized to cause immune dysregulation, which is the only established risk factor for non-Hodgkin's lymphoma (NHL). Genes responsible for circadian rhythm are also involved in cancer-related biological pathways as potential tumor suppressors. However, no previous studies have examined associations between circadian genes and NHL risk. In this population-based case control study (n = 455 cases; 527 controls), we examined the only identified nonsynonymous polymorphism (Ala394Thr; rs2305160) in the largest circadian gene, neuronal PAS domain protein 2 (NPAS2), in order to examine its impact on NHL risk. Our results demonstrate a robust association of the variant Thr genotypes (Ala/Thr and Thr/Thr) with reduced risk of NHL (OR = 0.66, 95% CI: 0.51-0.85, p = 0.001), especially B-cell lymphoma (OR = 0.61, 95% CI: 0.47-0.80, p <or= 0.0001). These findings provide the first molecular epidemiologic evidence supporting a role of circadian genes in lymphomagenesis, which suggests that genetic variations in circadian genes might be a novel panel of promising biomarkers for NHL and warrants further investigation.

Keywords

Zhu Y, Stevens RG, Hoffman AE, et al. **Year** 2011

Authors Yong Zhu, Richard G. Stevens, Aaron E. Hoffman, Anne Tjonneland, Ulla B. Vogel, Tongzhang Zheng, and Johnni Hansen

Report Name Epigenetic Impact of Long-Term Shiftwork: Pilot Evidence From Circadian Genes and Whole-Genome Methylation Analysis

Publication Chronobiology International

Issue-page numbers Dec., 2011, Vol. 28, No. 10 , Pages 852-861 (doi:10.3109/07420528.2011.618896)

URL http://informahealthcare.com/doi/abs/10.3109/07420528.2011.618896?prevSearch=allfield%253A%2528light-at-night%2529&searchHistoryKey=

Abstract Epigenetic association studies have demonstrated differential promoter methylation in the core circadian genes in breast cancer cases relative to cancer-free controls. The current pilot study aims to investigate whether epigenetic changes affecting breast cancer risk could be caused by circadian disruption through exposure to light at night. Archived DNA samples extracted from whole blood of 117 female subjects from a prospective cohort conducted in Denmark were included in this study. A polymerase chain reaction (PCR)-based method was used for detection of gene-promoter methylation, whereas genome-wide methylation analysis was performed using the Illumina Infinium Methylation Chip. Long-term shiftwork resulted in the same promoter hypomethylation of CLOCK and hypermethylation of CRY2, as was previously observed in breast cancer case-control studies. Genome-wide methylation analysis further discovered widespread methylation alterations in shiftworkers, including changes in many methylation- and cancer-relevant genes. Pathway analysis of the genes with altered methylation patterns revealed several cancer-related pathways. One of the top three networks generated was designated as “DNA replication, recombination, and repair, gene expression, behavior” with ESR1 (estrogen receptor α) featured most prominently in the network, underscoring the potential breast cancer relevance of the genes differentially methylated in long-term shiftworkers. These results, although exploratory, demonstrate the first evidence of the cancer-relevant epigenetic effects of night shiftwork, which warrant further investigation. Considering there are millions of shiftworkers worldwide, understanding the effects of this exposure may lead to novel strategies for cancer prevention and new policies regulating shiftwork.

Read More: http://informahealthcare.com/doi/abs/10.3109/07420528.2011.618896?prevSearch=allfield%253A%2528light-at-night%2529&searchHistoryKey=

Keywords Cancer, Circadian genes, Genome-wide methylation, Shiftwork

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Zhu Y, Stevens RG, Leaderer D et al. **Year** 2008

Authors Zhu Y, Stevens RG, Leaderer D, Hoffman A, Holford T, Zhang Y, Brown HN, Zheng T.

Report Name Non-synonymous polymorphisms in the circadian gene NPAS2 and breast cancer risk

Publication Breast Cancer Res Treat

Issue-page numbers 107:421–425 doi:10.1007/s10549-007-9565-0. PMID:17453337

URL http://www.ncbi.nlm.nih.gov/pubmed/17453337

Abstract Three known non-synonymous polymorphisms (Ala394Thr, Ser471Leu and Pro690Ala) in the largest circadian gene, Neuronal PAS domain protein 2 (NPAS2), were genotyped in a breast cancer case-control study conducted in Connecticut, USA (431 cases and 476 controls). We found that women with the heterozygous Ala394Thr genotype were significantly associated with breast cancer risk compared to those with the common homozygous Ala394Ala (OR = 0.61, 0.46-0.81, P = 0.001). This is the first evidence demonstrating a role of the circadian gene NPAS2 in human breast cancer, suggesting that genetic variations in circadian genes might be a novel panel of biomarkers for breast cancer risk.

Keywords

Zlotos DP

Year 2005

Authors Zlotos DP

Report Name Recent advances in melatonin receptor ligands

Publication Arch Pharm Chem Life Sci (Weinheim)

Issue-page numbers 338:229–247 doi:10.1002/ardp.200400996. PMID:15952241

URL http://www.ncbi.nlm.nih.gov/pubmed/15952241

Abstract Melatonin is a hormone exerting its multiple actions mainly through two G-protein-coupled receptors MT(1) and MT(2). Exploring the physiological role of each of these subtypes requires subtype selective MT(1) and MT(2) ligands. While several MT(2)-selective ligands were developed in the 1990s, no selective agonists and antagonists for the MT(1) subtype were described. The present article reviews mela toninergic ligands developed in the current millennium focusing on subtype selective agents and on drug candidates. Notable compounds are the MT(1)-selective agonists 35 and 134, MT(1)-selective antagonists 117 and 131, MT(2)-selective agonists 58, 70, 79, 97 and 125, MT(2)-selective antagonists 27, 73 and 119, and the highly potent non-selective agonist 120. The non-selective agonists agomelatine 2, and ramelteon 87 are drug candidates as antidepressive agent and for the treatment of insomnia and circadian rhythm disfunction, respectively.

Keywords

Zmrzljak UP, Rozman D

Year 2012

Authors Ursula Prosenc Zmrzljak and Damjana Rozman

Report Name Circadian regulation of endobiotic and xenobitoic detoxification pathways: the time matters

Publication Chem. Res. Toxicol.

Issue-page numbers Just Accepted Manuscript DOI: 10.1021/tx200538r Publication Date (Web): February 3, 2012

URL http://pubs.acs.org/doi/abs/10.1021/tx200538r

Abstract Metabolic processes have to be regulated tightly to prevent waste of energy and to ensure sufficient detoxification. Most anabolic processes operate timely when energy intake is the highest while catabolism takes place in energy spending periods. Endobiotic and xenobiotic metabolism are therefore under circadian control. Circadian regulation is mediated through suprachiasmatic nucleus (SCN), a master autonomous oscillator of the brain. Although many peripheral organs have their own oscillators the SCN is important in orchestrating and entraining organs according to the environmental light cues. However, light is not the only signal for entrainment of internal clocks. For endobiotic and xenobitoic detoxification pathways the food composition and intake regime are equally important. The rhythm of the liver as organ where the major metabolic pathways intersect depends on SCN signals, signals from endocrine tissues and, importantly, the type and time of feeding or xenobiotics ingestion. Several enzymes are involved in detoxification processes. Phase I is composed mainly of cytochromes P450 which are regulated by nuclear receptors. Phase II enzymes modify the phase I metabolites while phase III includes membrane transporters responsible for elimination of modified xenobiotics. Phases I – III of drug metabolism are under strong circadian regulation, starting with the drug sensing nuclear receptors and ending with drug transporters. Disturbed circadian regualtion (jet-lag, shift work, dysfunction of core clock genes) leads to changed periods of activity, sleep disorders, disturbed glucose homeostasis, breast or colon cancer and metabolic syndrome. As many xenobiotics influence the circadian rhythm of the liver, bad drug administration timing can worsen the above listed effects. This review will cover the major hepatic circadian regulation of endogenous and xenobiotic metabolic pathways and will provide examples of how good timing of drug administration can change a drug failure to treatment success.

Keywords

Zubidat AE, Nelson RJ, Haim A **Year** 2010

Authors Abed E. Zubidat, Randy J. Nelson, Abraham Haim

Report Name DIFFERENTIAL EFFECTS OF PHOTOPHASE IRRADIANCE ON METABOLIC AND URINARY STRESS HORMONE CONCENTRATIONS IN BLIND AND SIGHTED RODENTS

Publication Chronobiology International

Issue-page numbers 27:3, 487-516

URL http://informahealthcare.com/doi/abs/10.3109/07420521003678577

Abstract

The effects of different photophase irradiance levels on the daily rhythms of energy expenditure (DEE, calculated from oxygen consumption, VO2) and urinary metabolites of stress hormones in sighted (Microtus socialis) and blind (Spalax ehrenbergi) rodents were compared. Five groups of each species were exposed to different irradiance levels (73, 147, 293, 366, and 498 μW/cm2) under short photoperiod (8L:16D) condition with constant ambient temperature 25 ± 2°C for 21 days before assessments. As light intensity increased from 73 μW/cm2, both species reduced DEE, especially among M. socialis. Cosinor analysis revealed significant ultradian rhythms in VO2 of M. socialis with period length being inversely related to irradiance level. Conversely, in S. ehrenbergi, robust 24 h VO2 rhythms were detected at all irradiances. In M. socialis, significant 24 h rhythms in urinary output of adrenaline were detected only at 293 μW/cm2, whereas for cortisol, unambiguous rhythms were detected at 73 and 147 μW/cm2. Distinct adrenaline daily rhythms of S. ehrenbergi were observed at 73 and 293 μW/cm2, whereas this species exhibited significant rhythms in cortisol at 147 and 293 μW/cm2. Changes in photophase irradiance levels affected stress hormone concentrations in a dose-dependent manner. There were significant negative and positive correlations of M. socialis and S. ehrenbergi stress hormones, respectively, with increasing irradiance. Our results indicate photophase light intensity is another environmental factor that can significantly affect entrainment of mammalian daily rhythms. Both low and high irradiance conditions can trigger stress responses, depending on the species' natural habitat.

Keywords Arginine vasopressin, HPA axis, Masking, Predation pressure, Retinal photoreceptors, Stress hormone metabolites, Subterranean

Zubidat AE, Ben-Shlomo R, Haim A

Year 2007

Authors Abed Elsalam Zubidat, Rachel Ben-Shlomo and Professor Abraham Haim

Report Name Thermoregulatory and Endocrine Responses to Light Pulses in Short-Day Acclimated Social Voles (Microtus socialis)

Publication Chronobiology International

Issue-page numbers 24:2, 269-288

URL http://informahealthcare.com/doi/abs/10.1080/07420520701284675

Abstract In mammals, nocturnal light pulses (NLP) have been demonstrated to affect physiology and behavior. However, the impact of NLP as a stressor has been less broadly examined. The purpose of this study was to examine the effect of NLP (three 15 min 450 lux light pulses) during each scotophase on both thermoregulation and endocrine stress responses under short-day (SD; 8L:16D) acclimation. Voles were acclimated to either SD (SD voles) or SD+NLP (NLP voles). Resistance to cold was estimated by measurements of body temperature (Tb) during cold exposure (5°C). Daily rhythms of energy expenditure (calculated from oxygen consumption), urine production, and urinary adrenaline and serum cortisol levels were measured. Tb values of SD voles were generally unaffected by the cold stimulus, whereas in NLP voles, resistance to cold was markedly lowered. While SD- and NLP voles showed similar ultradian characteristics in energy expenditure with a period of 3.5 h, mean energy expenditure levels were lowest for voles exposed to NLP-treatment. In SD voles, but not in NLP voles, urine production rates showed clear time variations and were consistently highest for SD voles, with significant differences during the scotophase. Both mean total urinary adrenaline and serum cortisol levels were significantly elevated in NLP-treated voles compared with the control group. Taken together, the results suggest that NLP negatively affects winter acclimatization of thermoregulatory mechanisms of M. socialis, probably by mimicking summer acclimatization, and consequently the thermoregulatory mechanisms respond inappropriately to ambient conditions. One important finding of this study is that NLP may act as a stressor and correspondingly impose a major threat to the physiological homeostasis of M. socialis, such that over-winter survival might be compromised.

Keywords Nocturnal light pulses, Thermoregulation, Stress response, Corticosteroids, Catecholamine

Zylka MJ, Shearman LP, Weaver DR, Reppert SM

Year 1998

Authors Zylka MJ, Shearman LP, Weaver DR, Reppert SM

Report Name Three period homologs in mammals: differential light responses in the suprachiasmatic circadian clock and oscillating transcripts outside of brain

Publication Neuron

Issue-page numbers 20:1103–1110 doi:10.1016/S0896-6273(00)80492-4. PMID:9655499

URL http://www.ncbi.nlm.nih.gov/pubmed/9655499

Abstract We have cloned and characterized the mouse cDNA of a third mammalian homolog of the Drosophila period gene and designated it mPer3. The mPER3 protein shows approximately 37% amino acid identity with mPER1 and mPER2 proteins. The three mammalian PER proteins share several regions of sequence homology, and each contains a protein dimerization PAS domain. mPer3 RNA levels oscillate in the suprachiasmatic nuclei (SCN) and eyes. In the SCN, mPer3 RNA levels are not acutely altered by light exposure at different times during subjective night. This contrasts with the acute induction by light of mPer1 and mPer2 RNA levels during early and late subjective night. mPer3 is widely expressed in tissues outside of brain. In liver, skeletal muscle, and testis, mPer RNAs exhibit prominent, synchronous circadian oscillations. The results highlight the differential light responses among the three mammalian Per genes in the SCN and raise the possibility of circadian oscillators in mammals outside of brain and retina.

Keywords