

Abstracts on Sleep

Campbell SS; Eastman CI; Terman M; Lewy AJ; Boulos Z; Dijk DJ.

Light treatment for sleep disorders: consensus report. I. Chronology of seminal studies in humans. *J. Biol Rhythms*, 1995 Jun, 10:2, 105-9

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Examination of the influence of the light-dark cycle on circadian rhythmicity has been a fundamental aspect of chronobiology since its inception as a scientific discipline. Beginning with Bünning's hypothetical phase response curve in 1936, the impact of timed light exposure on circadian rhythms of literally hundreds of species had been described. The view that the light-dark cycle was an important zeitgeber for the human circadian system, as well, seemed to be supported by early studies of blind and sighted subjects. Yet, by the early 1970s, based primarily on a series of studies conducted at Erling-Andechs, Germany, the notion became widely accepted that the light-dark cycle had only a weak influence on the human circadian system and that social cues played a more important role in entrainment. In 1980, investigators at the National Institute of Mental Health reported that bright light could suppress melatonin production in humans, thereby demonstrating unequivocally the powerful effects of light on the human central nervous system. This finding led directly to the use of timed bright light exposure as a tool for the study and treatment of human circadian rhythms disorders.

Dijk DJ; Boulos Z; Eastman CI; Lewy AJ; Campbell SS; Terman M.

Light treatment for sleep disorders; consensus report. II. Basic properties of circadian physiology and sleep regulation. *Biol Rhythms*, 1995 Jun, 10:2, 113-125.

Institute of Pharmacology, University of Zurich, Switzerland. J

The rationale for the treatment of sleep disorders by scheduled exposure to bright light in seasonal affective disorder, jet lag, shift work, delayed sleep phase syndrome, and in the elderly is, in part, based on a conceptual framework developed by nonclinical circadian rhythm researchers working with humans and other species. Some of the behavioural and physiological data that contributed to these concepts are reviewed, and some pitfalls related to their application to bright light treatment of sleep disorders are discussed. In humans and other mammals the daily light-dark (LD) cycle is a major synchroniser responsible for entrainment of circadian rhythms to the 24-h day, and phase response curve (PRCs) to light have been obtained. In humans, phase delays can be induced by light exposure scheduled before the minimum of the endogenous circadian rhythms of core body temperature (CBT), whereas phase advances are induced when light exposure is scheduled after the minimum of CBT. Since in healthy young subjects the minimum of CBT is located approximately 1 to 2 h before the habitual time of awakening, the most sensitive phase of the PRC to light coincides with sleep, and the timing of the monophasic sleep-wake cycle itself is a major determinant of light input to the pacemaker. The effects of light are mediated by the retinohypothalamic tract, and excitatory amino acids play a key role in the transduction of light information to the suprachiasmatic nuclei. LD cycles have direct 'masking' effects on many variables, including sleep, which complicates the assessment of endogenous circadian phase and the interpretation of the effects of light treatment on sleep disorders. In some rodents motor activity has been shown to affect circadian phase, but in humans the evidence for such a feedback of activity on the pacemaker is still preliminary. The endogenous circadian pacemaker is a major determinant of sleep propensity and sleep structure; these, however, are strongly influenced by the prior history of sleep and wakefulness. In healthy young subjects, light exposure schedules that do not curtail sleep but induce moderate shifts of endogenous circadian phase have been shown to influence the timing of sleep and wakefulness without markedly affecting sleep structure.

Shibui K; Uchiyama M; Iwama H; Ozaki S; Takahashi K; Okawa M.

Periodic fatigue symptoms due to desynchronisation in a patient with non-24h sleep-wake syndrome. *Psychiatry Clin Neurosci*, 1998 Oct, 52:5, 477-81

Department of Psychophysiology, National Institute of Mental Health, National Centre of Neurology and Psychiatry, Ichikawa, Japan.

A 43 year old man complaining of recurrent fatigue symptoms and sleep disorders occurring periodically every 4 weeks was studied. Using a wrist worn actigraphy and an ambulatory rectal temperature monitoring apparatus, his sleep-wake cycle and rectal temperature were measured continuously for 4 months, while diagnostic evaluation and therapeutic interventions were conducted. It was found that after he gave up an attempt to keep to a 24 h day, a free running sleep wake pattern appeared but his fatigue symptoms disappeared. An analysis of the relationship between his sleep-wake cycle and the rectal temperature rhythm found that his fatigue symptoms did not appear when both rhythms were synchronised with each other. Artificial bright light therapy entrained him to a 24 h day without relapsing of fatigue symptoms. Desynchronisation between a 24h sleep-wake schedule and his circadian pacemaker may have caused his periodically appearing fatigue symptoms.

Murphy PJ; Campbell SS;

Enhanced performance in elderly subjects following bright light treatment of sleep maintenance insomnia. *J Sleep Res*, 1996 Sep, 5:3, 165-72

Department of Psychiatry, Cornell Medical College, New York, USA.

Sixteen older individuals with sleep maintenance insomnia were treated with night-time bright-light exposure (BL) while living at home. Twelve consecutive days of acute light treatment were followed by a 3-mo maintenance light-treatment period. Subjects completed laboratory evaluation sessions on five separate occasions (prior to and following the acute light-treatment period, and once per month during the maintenance period). During each laboratory session, performance levels, sleep and core body temperature were measured. The performance battery consisted of four computerised tasks (Logical Reasoning, Stroop Congruency, Two Letter Visual Search, and Wilkinson Four-Choice Reaction Time) and was administered every 2h between 10:00 and 18:00 hours. Subjects improved significantly on three of the four tasks from pre-BL to post-BL. During the maintenance period, subjects who received active BL treatment maintained significantly higher performance levels than a control BL group. Light treatment improved sleep efficiently and delayed the phase of the body temperature rhythm. Performance improvements were significantly related only to sleep and not to circadian phase. The implications for non-circadian treatments of sleep maintenance insomnia and cognitive functioning in the elderly are discussed.

Kosaka M; Fukuda N; Kobayashi R; Honma H; Sakakibara S; Koyama E; Nakano O; Matsubara H.

Effects of short duration morning bright light in healthy elderly. II: Sleep and motor activity. *Psychiatry Clin Neurosci*, 1998 Apr, 52:2 252-3

Sapporo Hanazono Hospital, Japan.

Subjective sleep feelings and motor activity were measured in seven healthy elderly subjects for 6 days. The subjects were exposed to bright light (6000 lux) for 30 min in the morning or instructed to sit in front of a desktop lighting device without light. The average level of motor activity during the night was significantly decreased in the bright light condition, compared with the controlled condition. However, daytime motor activity did not show significant differences between the two conditions. From these findings, even a short duration of morning bright light is effective in maintaining sleep without changing daytime activity.

Terman M, Lewy AJ, Dijk DJ, Boulos Z, Eastman CI, Campbell SS.

Light treatment for sleep disorders: consensus report. IV. Sleep phase and duration disturbances. *J Biol Rhythms*. 1995 Jun;10(2):135-47.

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Advanced and delayed sleep phase disorders, and the hypersomnia that can accompany winter depression, have been treated successfully by appropriately timed artificial bright light exposure. Under entrainment to the 24-h day-night cycle, the sleep-wake pattern may assume various phase relationships to the circadian pacemaker, as indexed, for example, by abnormally long or short intervals between the onset of melatonin production or the core body temperature minimum and wake-up time. Advanced and delayed sleep phase syndromes and non-24-h sleep-wake syndrome have been variously ascribed to abnormal intrinsic circadian periodicity, deficiency of the entrainment mechanism, or--most simply--patterns of daily light exposure insufficient for adequate phase resetting. The timing of sleep is influenced by underlying circadian phase, but psychosocial constraints also play a major role. Exposure to light early or late in the subjective night has been used therapeutically to produce corrective phase delays or advances, respectively, in both the sleep pattern and circadian rhythms. Supplemental light exposure in fall and winter can reduce the hypersomnia of winter depression, although the therapeutic effect may be less dependent on timing.

Rosenthal NE, Joseph-Vanderpool JR, Levendosky AA, Johnston SH, Allen R, Kelly KA, Souetre E, Schulz PM, Starz BK

Phase-shifting effects of bright morning light treatment in patients with delayed sleep phase syndrome. *Sleep* 13(4): 354-361, 1990.

ABSTRACT: bright light has recently been shown to have phase-shifting effects on human circadian rhythms. In this study we applied this effect to 20 patients with delayed sleep phase syndrome (DSPS) who were unable to fall asleep at conventional clock times and had a problem staying alert in the morning. In a controlled treatment study, we found that 2 h of bright light exposure in the morning together with light restriction in the evening successfully phase advanced circadian rhythms of core body temperature and multiple sleep latencies in these patients. This finding corroborates the importance of light for entraining human circadian rhythms

McIntyre IM, Armstrong SM, Norman TR, Burrows GD.

Treatment of seasonal affective disorder with light: preliminary Australian experience. . Aust N Z J Psychiatry. 1989 Sep;23(3):369-72.

Department of Psychiatry, University of Melbourne, Austin Hospital, Heidelberg, Victoria

Six patients with a history of Seasonal Affective Disorder (SAD) were treated with bright artificial light. Patients presented with at least two consecutive years of loss of energy, difficulty in working, loss of interest in activities, difficulty in concentrating, increased somnolence, over-eating (carbohydrate craving) and depressed mood. All received seven consecutive days of full-spectrum bright light with an intensity greater than 2,500 lux at a distance of three feet. Evening exposure for two hours resulted in significant clinical improvement. The main improvements were a return to normal sleeping patterns, a reduction in eating habits, improved energy level, a desire to continue with interests and activities and an improvement in mood. Possible mechanisms for the clinical effects of bright light treatment are discussed.

Dijk DJ, Boulos Z, Eastman CI, Lewy AJ, Campbell SS, Terman M.

Light treatment for sleep disorders: consensus report. II. Basic properties of circadian physiology and sleep regulation. J Biol Rhythms. 1995 Jun;10(2):113-25.

Institute of Pharmacology, University of Zurich, Switzerland.

The rationale for the treatment of sleep disorders by scheduled exposure to bright light in seasonal affective disorder, jet lag, shift work, delayed sleep phase syndrome, and the elderly is, in part, based on a conceptual framework developed by nonclinical circadian rhythm researchers working with humans and other species. Some of the behavioral and physiological data that contributed to these concepts are reviewed, and some pitfalls related to their application to bright light treatment of sleep disorders are discussed. In humans and other mammals the daily light-dark (LD) cycle is a major synchronizer responsible for entrainment of circadian rhythms to the 24-h day, and phase response curves (PRCs) to light have been obtained. In humans, phase delays can be induced by light exposure scheduled before the minimum of the endogenous circadian rhythm of core body temperature (CBT), whereas phase advances are induced when light exposure is scheduled after the minimum of CBT. Since in healthy young subjects the minimum of CBT is located approximately 1 to 2 h before the habitual time of awakening, the most sensitive phase of the PRC to light coincides with sleep, and the timing of the monophasic sleep-wake cycle itself is a major determinant of light input to the pacemaker. The effects of light are mediated by the retinohypothalamic tract, and excitatory amino acids play a key role in the transduction of light information to the suprachiasmatic nuclei. LD cycles have direct "masking" effects on many variables, including sleep, which complicates the assessment of endogenous circadian phase and the interpretation of the effects of light treatment on sleep disorders. In some rodents motor activity has been shown to affect circadian phase, but in humans the evidence for such a feedback of activity on the pacemaker is still preliminary. The endogenous circadian pacemaker is a major determinant of sleep propensity and sleep structure; these, however, are also strongly influenced by the prior history of sleep and wakefulness. In healthy young subjects, light exposure schedules that do not curtail sleep but induce moderate shifts of endogenous circadian phase have been shown to influence the timing of sleep and wakefulness without markedly affecting sleep structure.

Lowden A, Akerstedt T, Wibom R.

Suppression of sleepiness and melatonin by bright light exposure during breaks in night work. J Sleep Res. 2004 Mar;13(1):37-43.

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Night work is non-optimal for performance and recuperation because of a lack of circadian influence that fully promote a night orientation. Our study assessed, in an industrial setting, the effects of bright light exposure (BL) on sleepiness, sleep and melatonin, during night work and during the following readaptation to day work. In a crossover design, 18 workers at a truck production plant were exposed to either BL (2500 lx) during breaks or normal light during four consecutive weeks. Twenty minute breaks were initiated by 67% of the workers between 03:00 and 04:00 hours. Sleep/wake patterns were assessed through actigraphs and ratings were given in a sleep/wake diary. Saliva melatonin was measured at 2-h intervals before, during and after night shift weeks. A significant interaction demonstrated a reduction of sleepiness in the BL condition particularly on the first two nights at 04:00 and 06:00 hours. Day sleep in the BL condition was significantly lengthened. Bright light administration significantly suppressed melatonin levels during night work and most strongly at 02:00 hours. Daytime melatonin during the readaptation after night work remained unaffected. The present findings demonstrate the feasibility and benefits of photic stimulation in industrial settings to increase adaptation to night work.

Crowley SJ, Lee C, Tseng CY, Fogg LF, Eastman CI.

Combinations of bright light, scheduled dark, sunglasses, and melatonin to facilitate circadian entrainment to night shift work. *J Biol Rhythms.* 2003 Dec;18(6):513-23

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Various combinations of interventions were used to phase-delay circadian rhythms to correct their misalignment with night work and day sleep. Young participants (median age = 22, n = 67) participated in 5 consecutive simulated night shifts (2300 to 0700) and then slept at home (0830 to 1530) in darkened bedrooms. Participants wore sunglasses with normal or dark lenses (transmission 15% or 2%) when outside during the day. Participants took placebo or melatonin (1.8 mg sustained release) before daytime sleep. During the night shifts, participants were exposed to a moving (delaying) pattern of intermittent bright light (approximately 5000 lux, 20 min on, 40 min off, 4-5 light pulses/night) or remained in dim light (approximately 150 lux). There were 6 intervention groups ranging from the least complex (normal sunglasses) to the most complex (dark sunglasses + bright light + melatonin). The dim light melatonin onset (DLMO) was assessed before and after the night shifts (baseline and final), and 7 h was added to estimate the temperature minimum (Tmin). Participants were categorized by their amount of reentrainment based on their final Tmin: not re-entrained (Tmin before the daytime dark/sleep period), partially re-entrained (Tmin during the first half of dark/sleep), or completely re-entrained (Tmin during the second half of dark/ sleep). The sample was split into earlier participants (baseline Tmin < or = 0700, sunlight during the commute home fell after the Tmin) and later participants (baseline Tmin > 0700). The later participants were completely re-entrained regardless of intervention group, whereas the degree of re-entrainment for the earlier participants depended on the interventions. With bright light during the night shift, almost all of the earlier participants achieved complete re-entrainment, and the phase delay shift was so large that darker sunglasses and melatonin could not increase its magnitude. With only room light during the night shift, darker sunglasses helped earlier participants phase-delay more than normal sunglasses, but melatonin did not increase the phase delay. The authors recommend the combination of intermittent bright light during the night shift, sunglasses (as dark as possible) during the commute home, and a regular, early daytime dark/sleep period if the goal is complete circadian adaptation to night-shift work.

Ruger M, Gordijn MC, Beersma DG, de Vries B, Daan S.

Acute and phase-shifting effects of ocular and extraocular light in human circadian physiology. *J Biol Rhythms.* 2003 Oct;18(5):409-19.

Department of Animal Behavior, University of Groningen, The Netherlands.

Light can influence physiology and performance of humans in two distinct ways. It can acutely change the level of physiological and behavioral parameters, and it can induce a phase shift in the circadian oscillators underlying variations in these levels. Until recently, both effects were thought to require retinal light perception. This view was challenged by Campbell and Murphy, who showed significant phase shifts in core body temperature and melatonin using an extraocular stimulus. Their study employed popliteal skin illumination and exclusively considered phase-shifting effects. In this paper, the authors explore both acute effects and phase-shifting effects of ocular as well as extraocular light. Twelve healthy males participated in a within-subject design and received all of three light conditions--(1) dim ocular light/no light to the knee, (2) dim ocular light/bright extraocular light to the knee, and (3) bright ocular light/no light to the knee--on separate nights in random order. The protocol consisted of an adaptation night followed by a 26-h period of sustained wakefulness, during which a 4-h light pulse was presented at a time when maximal phase delays were expected. The authors found neither immediate nor phase-shifting effects of extraocular light exposure on melatonin, core body temperature (CBT), or sleepiness. Ocular bright-light exposure reduced the nocturnal circadian drop in CBT, suppressed melatonin, and reduced sleepiness significantly. In addition, the 4-h ocular light pulse delayed the CBT rhythm by -55 min compared to the drift of the CBT rhythm in dim light. The melatonin rhythm shifted by -113 min, which differed significantly from the drift in the melatonin rhythm in the dim-light condition (-26 min). The failure to find immediate or phase-shifting effects in response to extraocular light in a within-subjects design in which effects of ocular bright light are confirmed strengthens the doubts raised by other labs of the impact of extraocular light on the human circadian system.

Phipps-Nelson J, Redman JR, Dijk DJ, Rajaratnam SM.

Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. *Sleep*. 2003 Sep15;26(6):695-700.

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STUDY OBJECTIVES: This study examined the effects of bright light exposure, as compared to dim light, on daytime subjective sleepiness, incidences of slow eye movements (SEMs), and psychomotor vigilance task (PVT) performance following 2 nights of sleep restriction. **DESIGN:** The study had a mixed factorial design with 2 independent variables: light condition (bright light, 1,000 lux; dim light, < 5 lux) and time of day. The dependent variables were subjective sleepiness, PVT performance, incidences of SEMs, and salivary melatonin levels. **SETTING:** Sleep research laboratory at Monash University. **PARTICIPANTS:** Sixteen healthy adults (10 women and 6 men) aged 18 to 35 years (mean age 25 years, 3 months). **INTERVENTIONS:** Following 2 nights of sleep restriction (5 hours each night), participants were exposed to modified constant routine conditions. Eight participants were exposed to bright light from noon until 5:00 pm. Outside the bright light exposure period (9:00 am to noon, 5:00 pm to 9:00 pm) light levels were maintained at less than 5 lux. A second group of 8 participants served as controls for the bright light exposure and were exposed to dim light throughout the entire protocol. **MEASUREMENTS AND RESULTS:** Bright light exposure reduced subjective sleepiness, decreased SEMs, and improved PVT performance compared to dim light. Bright lights had no effect on salivary melatonin. A significant positive correlation between PVT reaction times and subjective sleepiness was observed for both groups. Changes in SEMs did not correlate significantly with either subjective sleepiness or PVT performance. **CONCLUSIONS:** Daytime bright light exposure can reduce the impact of sleep loss on sleepiness levels and performance, as compared to dim light. These effects appear to be mediated by mechanisms that are separate from melatonin suppression. The results may assist in the development of treatments for daytime sleepiness.
