Abstracts

**Subjective Well-being is Modulated by circadian phase, Sleep Pressure, Age, and Gender.**


Subjective well-being largely depends on mood, which shows circadian rhythmicity and can be linked to rhythms in many physiological circadian markers, such as melatonin and cortisol. In healthy young volunteers mood is influenced by an interaction of circadian phase and the duration of time awake. The authors analyzed this interaction under differential sleep pressure conditions to investigate age and gender effects on subjective well-being. Sixteen healthy young (8 women, 8 men; 20-35 years) and 16 older volunteers (8 women, 8 men; 55-75 years) underwent a 40-h sleep deprivation (high sleep pressure) and a 40-h nap protocol (low sleep pressure) in a balanced crossover design under constant routine conditions. Mood, tension, and physical comfort were assessed by visual analogue scales during scheduled wakefulness, and their average formed a composite score of well-being. Significant variations in well-being were determined by the factors "age," "sleep pressure," and "circadian phase." Well-being was generally worse under high than low sleep pressure. Older volunteers felt significantly worse than the young under both experimental conditions. Significant interactions were found between "sleep pressure" and "age," and between "sleep pressure" and "gender." This indicated that older volunteers and women responded with a greater impairment in well-being under high compared with low sleep pressure. The time course of well-being displayed a significant circadian modulation, particularly in women under high sleep pressure conditions. The results demonstrate age- and/or gender-related modifications of well-being related to sleep deprivation and circadian phase and thus point to specific biological components of mood vulnerability.

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**Effect of Bright Light and Melatonin on Cognitive and Noncognitive Function in Elderly Residents of Group Care Facilities: a Randomized Controlled Trial.**


Riemersma-van der Lek RF, Swaab DF, Twisk J, Hol EM, Hoogendijk WJ, Van Someren EJ.

**CONTEXT:** Cognitive decline, mood, behavioral and sleep disturbances, and limitations of activities of daily living commonly burden elderly patients with dementia and their caregivers. Circadian rhythm disturbances have been associated with these symptoms. **OBJECTIVE:** To determine whether the progression of cognitive and noncognitive symptoms may be ameliorated by individual or combined long-term application of the 2 major synchronizers of the circadian timing system: bright light and melatonin. **DESIGN, SETTING, AND PARTICIPANTS:** A long-term, double-blind, placebo-controlled, 2 x 2 factorial randomized trial performed from 1999 to 2004 with 189 residents of 12 group care facilities in the Netherlands; mean (SD) age, 85.8 (5.5) years; 90% were female and 87% had dementia. **INTERVENTIONS:** Random assignment by facility to long-term daily treatment with whole-day bright (+/- 1000 lux) or dim (+-300 lux) light and by participant to evening melatonin (2.5 mg) or placebo for a mean (SD) of 15 (12) months (maximum period of 3.5 years). **MAIN OUTCOME MEASURES:** Standardized scales for cognitive and noncognitive symptoms, limitations of activities of daily living, and adverse effects assessed every 6 months. **RESULTS:** Light attenuated cognitive deterioration by a mean of 0.9 points (95% confidence interval [CI], 0.04-1.71) on the Mini-Mental State Examination or a relative 5%. Light also ameliorated depressive symptoms by 1.5 points (95% CI, 0.24-2.70) on the Cornell Scale for Depression in Dementia or a relative 19%, and attenuated the increase in functional
limitations over time by 1.8 points per year (95% CI, 0.61-2.92) on the nurse-informant activities of daily living scale or a relative 53% difference. Melatonin shortened sleep onset latency by 8.2 minutes (95% CI, 1.08-15.38) or 19% and increased sleep duration by 27 minutes (95% CI, 9-46) or 6%. However, melatonin adversely affected scores on the Philadelphia Geriatric Centre Affect Rating Scale, both for positive affect (-0.5 points; 95% CI, -0.10 to -1.00) and negative affect (0.8 points; 95% CI, 0.20-1.44). Melatonin also increased withdrawn behavior by 1.02 points (95% CI, 0.18-1.86) on the Multi Observational Scale for Elderly Subjects scale, although this effect was not seen if given in combination with light. Combined treatment also attenuated aggressive behavior by 3.9 points (95% CI, 0.88-6.92) on the Cohen-Mansfield Agitation Index or 9%, increased sleep efficiency by 3.5% (95% CI, 0.8%-6.1%), and improved nocturnal restlessness by 1.00 minute per hour each year (95% CI, 0.26-1.78) or 9% (treatment x time effect). CONCLUSIONS: Light has a modest benefit in improving some cognitive and noncognitive symptoms of dementia. To counteract the adverse effect of melatonin on mood, it is recommended only in combination with light. TRIAL REGISTRATION: controlled-trials.com/isrctn Identifier: ISRCTN93133646.

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The Human Circadian Clock’s Seasonal Adjustment Is Disrupted by Daylight Saving Time


Kantermann T, Juda M, Merrow M, Roenneberg T.

A quarter of the world’s population is subjected to a 1 hr time change twice a year (daylight saving time, DST). This reflects a change in social clocks, not environmental ones (e.g., dawn). The impact of DST is poorly understood. Circadian clocks use daylight to synchronize (entrain) to the organism's environment. Entrainment is so exact that humans adjust to the east-west progression of dawn within a given time zone. In a large survey (n = 55,000), we show that the timing of sleep on free days follows the seasonal progression of dawn under standard time, but not under DST. In a second study, we analyzed the timing of sleep and activity for 8 weeks around each DST transition in 50 subjects who were chronotyped (analyzed for their individual phase of entrainment). Both parameters readily adjust to the release from DST in autumn but the timing of activity does not adjust to the DST imposition in spring, especially in late chronotypes. Our data indicate that the human circadian system does not adjust to DST and that its seasonal adaptation to the changing photoperiods is disrupted by the introduction of summer time. This disruption may extend to other aspects of seasonal biology in humans.

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Circadian Phase Response Curves to Light in Older and Young Women and Men.


Kripke DF, Elliott JA, Youngstedt SD, Rex KM.

BACKGROUND: The phase of a circadian rhythm reflects where the peak and the trough occur, for example, the peak and trough of performance within the 24 h. Light exposure can shift this phase. More extensive knowledge of the human circadian phase response to light is needed to guide light treatment for shiftworkers, air travelers, and people with circadian rhythm phase disorders. This study tested the hypotheses that older adults have absent or weaker phase-shift responses to light (3000 lux), and that women’s responses might differ from those of men. METHODS: After preliminary health screening and home actigraphic recording baselines, 50 young adults (ages 18-31 years) and 56 older adults (ages 59-75 years) remained in light-controlled laboratory surroundings for 4.7 to 5.6 days, while experiencing a 90-min ultra-short sleep-wake cycle. Following at least 30 h in-lab baseline, over the next 51 h, participants were given 3 treatments with 3000 lux white light, each treatment for 3 h, centered at one of 8 clock times. The circadian rhythms of urinary aMT6s (a melatonin metabolite), free cortisol, oral temperature, and wrist activity were assessed at baseline and after treatment. RESULTS: Light (3000 lux for 3 h on 3 days) induced maximal phase shifts of about 3 h. Phase shifts did not differ significantly
in amplitude among older and young groups or among women and men. At home and at baseline, compared to the young, the older adults were significantly phase-advanced in sleep, cortisol, and aMT6s onset, but not advanced in aMT6s acrophase or the temperature rhythm. The inflection from delays to advances was approximately 1.8 h earlier among older compared to young participants in reference to their aMT6s rhythm peaks, and it was earlier in clock time. **CONCLUSION:** In these experimental conditions, 3000 lux light could shift the phase of circadian rhythms to about the same extent among older and young adults, but the optimal light timing for phase shifting differed. For an interval near 4 PM, bright light produced only negligible phase shifts for either age group.

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**The Treatment of Sleep Onset Insomnia with Bright Morning Light**

Sleep and Biological Rhythms 2007;5:173–179

**Lack L, Wright H, Paynter D.**

**BACKGROUND:** Sleep onset insomnia may be associated with a delayed circadian rhythm. The present study investigated the effectiveness of 1-week of bright morning light exposure in advancing the urinary melatonin rhythm and improving the sleep and daytime functioning of individuals with sleep onset insomnia. **METHOD:** The participants were assigned to either a bright-light condition (2500 lux) or a control, dim red light condition (100 lux). Sleep, insomnia severity and daytime functioning were monitored using sleep diaries, activity monitors and questionnaires during the pre-treatment and 3-week post treatment period. While there were no significant changes in the dim light control group, the bright light group had a significant 1 h 21 min phase advance of melatonin onset. **RESULTS:** Compared to pretreatment measures, over the 3-week follow-up period, the brightlight group had a greater decrease of sleep onset latency, a significant advance of sleep onset time and a significant increase of total sleep time of 51-min. The participants in the bright light group also reported a decrease in insomnia severity, less presleep (cognitive) anxiety and improved overall daytime functioning as well as less daytime fatigue and sleepiness than the control group. **CONCLUSION:** The study demonstrated that 1 week of bright morning light exposure can advance the melatonin onset and improve the sleep and daytime feelings of individuals with sleep onset insomnia whose circadian rhythm is relatively delayed.

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**Insomnia in Patients With Neurodegenerative Conditions.**

Sleep Med. 2007 Dec;8 Suppl 4:S27–34.

**Dauvilliers Y.**

Comorbid insomnia and other sleep disturbances are common in patients with neurodegenerative disorders, such as Parkinson's or Alzheimer's disease. Insomnia in patients with neurological conditions may occur as a direct consequence of the disease itself or may be secondary to factors associated with the condition, such as pain, depression or the effects of medications. Disturbed sleep can have a significant impact on the patient's cognitive and physical function and may be associated with distress and depression. Insomnia also impacts patients' and caregivers' quality of life and is often cited as one of the primary reasons for patient institutionalization. Management of insomnia in patients with neurological disorders should be individualized to each patient's needs. The type of insomnia and any underlying causes of disturbed sleep must first be determined. Non-pharmacological interventions, such as behavioral modification, should be considered for all patients. Bright light therapy may be an effective treatment option for patients with disturbed sleep-wake patterns. Medications causing sleep problems should be withdrawn or doses and/or timing adjusted, whenever possible. Several pharmacological options are available to relieve the symptoms of insomnia as short-term treatment.
Treating Chronobiological Components of Chronic Insomnia

Sleep Med. 2007 Sep;8(6):637-44.

Lack LC, Wright HR.

Circadian rhythms have a strong effect on the ability to sleep across the 24-h period. Maximum sleepiness occurs at the phase of lower endogenous core body temperature. This period is bracketed by two periods of alertness: a "wake-maintenance zone" occurring 6-10h before the time of core temperature minimum, and a "wake-up zone" occurring 4-7h after the minimum. Therefore, if the circadian rhythm drifts earlier with respect to the attempted sleep period, the wake-up zone can impinge on the end of the normal sleep period resulting in premature awakening and the development of early morning awakening insomnia. Similarly, a delay of the circadian rhythm can impose the wake-maintenance zone on the attempted bedtime and lead to sleep onset insomnia. Therefore, these two types of insomnia should be treatable with chronobiologic effects such as bright light and, possibly, melatonin administration. Bright light stimulation at normal wake-up time and melatonin administration 4-8h before normal bedtime can phase advance circadian rhythms to an earlier time. While morning bright light has been efficacious for sleep onset insomnia, evening melatonin administration has yet to be tested. Early morning awakening insomnia has been treated with phase delays imposed by evening bright light but not yet with morning melatonin administration. There is now sufficient evidence to warrant the consideration of chronobiologic manipulations such as bright light therapy for the treatment of chronic sleep onset and early morning awakening insomnia that show evidence of circadian delay or advance, respectively.

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The Treatment of Early-Morning Awakening Insomnia with 2 Evenings of Bright Light.


Lack L, Wright H, Kemp K, Gibbon S.

STUDY OBJECTIVE: To assess the effectiveness of brief bright-light therapy for the treatment of early-morning awakening insomnia. PARTICIPANTS: Twenty-four healthy adults with early-morning awakening insomnia were assigned to either the bright-light condition (2,500-lux white light) or the control (dim red light) condition. MEASUREMENTS AND RESULTS: The circadian phase of rectal temperature and urinary melatonin rhythms were assessed with 26-hour constant routines before and after 2 evenings of light therapy. Sleep and daytime functioning were monitored using sleep diaries, activity monitors, and mood scales before light therapy and for 4 weeks during the follow-up period. While there were no significant circadian phase changes in the dim-light control group, the bright-light group had significant 2-hour phase delays of circadian temperature and melatonin rhythm. Compared to pretreatment measures, over the 4-week follow-up period, the bright-light group had a greater reduction of time awake after sleep onset, showed a trend toward waking later, and had a greater increase of total sleep time. Participants in the bright-light condition also tended to report greater reductions of negative daytime symptoms, including significantly fewer days of feeling depressed at the 4-week follow-up, as compared with the control group. CONCLUSION: Two evenings of bright-light exposure phase delayed the circadian rhythms of early-morning awakening insomniacs. It also improved diary and actigraphy sleep measures and improved some indexes of daytime functioning for up to 1 month after light exposure. The study suggests that a brief course of evening bright-light therapy can be an effective treatment for early-morning awakening insomniacs who have relatively phase advanced circadian rhythms.
Association of Morning Illumination and Window Covering with Mood and Sleep Among Post menopausal Women.


Youngstedt SD, Leung A, Kripke DF, Langer RD

BACKGROUND: The antidepressant and sleep-promoting effects of light exposure might be useful for treating agerelated mood and sleep disorders. METHOD: In view of recent evidence suggesting beneficial effects of morning light, this study examined the associations of mood and sleep with morning light exposure, 24 h environmental illumination, and the degree to which the volunteers’ bedroom windows were covered in the morning. We examined 459 postmenopausal women participating an ancillary study of the Women’s Health Initiative conducted at the University of California, San Diego Clinical Center, San Diego, CA, USA. At baseline, volunteers completed a 4-week sleep-recall questionnaire. Volunteers were then assessed for 5–7 days in their home environments with actigraphic wrist monitors. During home recording, self-reported mood was assessed. Morning illumination during the first 4 h after arising, 24-h illumination mesor (cosine-fitted mean), and illumination acrophase (cosine-fitted peak time) were calculated. Sleep was scored each night using validated wrist actigraphic methods. A sleep diary was completed each morning. During two 24-h periods, urine was collected approximately every 2 h during wakefulness and following any voidings during the sleep period. Cosinefitting established the acrophase of urinary 6-sulfatoxymelatonin (aMT6s) excretion. RESULTS: Morning illumination and 24-h illumination were modestly associated with better mood and sleep. Associations of light with mood and sleep were consistently greater for subjects whose body clocks were delayed relative to the group median. Less morning window covering in the subjects’ bedrooms was associated with more morning light and less depressed mood. CONCLUSION: The results suggest that both morning and 24-h light exposure may be beneficial for older adults.

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Daytime Exposure to Bright Light, as Compared to Dim Light, Decreases Sleepiness and Improves Psychomotor Vigilance Performance.

Sleep 2003;26(6):695-700

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

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.
Increased Light Exposure Consolidates Sleep and Strenghens Circadian Rhythms in Severe Alzheimer’s Disease Patients

Behav Sleep Med 2003;1(1):22-36


Sleep in the nursing home environment is extremely fragmented, possibly in part as a result of decreased light exposure. This study examined the effect of light on sleep and circadian activity rhythms in patients with probable or possible Alzheimer’s disease. Results showed that both morning and evening bright light resulted in more consolidated sleep at night, as measured with wrist actigraphy. Evening light also increased the quality of the circadian activity rhythm, as measured by a 5-parameter extended cosine model (amplitude, acrophase, nadir, slope of the curve, and relative width of the peak and trough). Increasing light exposure throughout the day and evening is likely to have the most beneficial effect on sleep and on circadian rhythms in patients with dementia. It would behoove nursing homes to consider increasing ambient light in multipurpose rooms where patients often spend much of their days.

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Morning Bright Light Therapy for Sleep and Behavior Disorders in Elderly Patients with Dementia


Mishima K, Okawa M, Hishikawa Y, Hozumi S, Hori H, Takahashi K.

METHOD: Fourteen inpatients with dementia showing sleep and behavior disorders (average age = 75 years), and 10 control elderly people (average age = 75 years) were carefully observed for 2 months. RESULTS: Four weeks of morning light therapy markedly improved sleep and behavior disorders in the dementia group. The measurement of sleep time and the serum melatonin values suggests that sleep and behavior disorders in the dementia group are related to decreases in the amplitude of the sleep-wake rhythm and decreases in the levels of melatonin secretions. CONCLUSION: Morning light therapy significantly increased total and nocturnal sleep time and significantly decreased daytime sleep time. These results indicate that morning bright light is a powerful synchronizer that can normalize disturbed sleep and substantially reduce the frequency of behavior disorders in elderly people with dementia.

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The Effect of Evening Bright Light in Delaying the Circadian Rhythms and Lengthening the Sleep of Early Morning Awakening Insomniacs

Sleep 1993 Aug;16(5):436-43

Lack L, Wright H.

Past studies have predicted that early morning awakening insomnia is associated with advanced or early circadian rhythms. Because bright light stimulation in the evening can delay the phase of circadian rhythms, we tested its effects on nine (4 females, 5 males) early morning awakening insomniacs. Their sleep was evaluated with wrist actigraphy and their temperature and melatonin circadian rhythms were measured in constant routine procedures. In the initial evaluation, the temperature rhythm phase positions of these insomniacs did appear to be earlier than normal. The subjects were then exposed to bright light stimulation (2,500 lux) from 2000 to 2400 hours on two consecutive evenings. Following the evening bright light treatment, temperature rhythm phase markers were delayed 2-4 hours and melatonin phase markers were delayed 1-2 hours. Sleep onset times were not changed but the mean final wake-up time was delayed from 0459 hours to 0611 hours, resulting in a mean increase of total sleep time of > 1 hour. This pilot study suggests that evening bright light stimulation may be an effective nondrug treatment for early morning awakening insomnia.