REVIEW

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Light, sleep and circadian rhythms in older adults with Alzheimer's disease and related dementias

Practice points

- Light-dark patterns reaching the back of the eye set the timing of our biological clock, and synchronize us with the local time on Earth. Lack of synchrony, or circadian disruption, can lead to sleep disturbances, depression and anxiety, among other maladies.
- Older adults, including those with Alzheimer's disease and related dementias (ADRD), may exhibit reduced neuronal activity in the biological clock that governs circadian rhythms, along with reduced light reaching the back of the eye due to physiological changes in the aging eye.
- Lighting characteristics that are required to affect the circadian system are different from those that affect vision. The circadian system is a 'blue sky' detector and needs higher amounts of light than those required for visibility.
- Circadian sleep disorder leads to fragmented rest–activity patterns, resulting in more frequent naps during the daytime and reduced consolidated sleep at night, increased irritability and increased depressive symptoms.
- Older adults typically receive dim, constant light during waking hours. Light therapy, delivering high circadian stimulation during the day (circadian stimulus >0.3 or >400 lux at the eye of a bluish-white light) and low circadian stimulation during the evening (circadian stimulus <0.1 or <50 lux at the eye of a yellowish-white light), can help to deliver a robust light–dark pattern to residents. At a minimum, provide high light levels (e.g., sit residents outdoors or by windows) for at least 2 h in the morning to increase circadian stimulation in the morning. Residents should sleep in darkness, but nightlights delivering low, warm color lights, should be used to assist in navigation to the bathroom.
- Add new lighting delivering high circadian stimulation to spaces where residents spend the day, usually common or dining areas.

Alzheimer's disease and related dementias (ADRD) can cause sleep and behavioral problems that are problematic for ADRD patients and their family caregivers. Light therapy has shown promise as a nonpharmacological treatment, and preliminary studies demonstrate that timed light exposure can consolidate and improve nighttime sleep efficiency, increase daytime wakefulness and reduce evening agitation without the adverse effects of pharmacological solutions. Compliance with light treatment and the accurate measurement of light exposures during treatment, however, have presented barriers for the adoption of light therapy for ADRD. Recent research showing that the circadian system is maximally sensitive to short-wavelength light opens the way for the potential application of lower, more-targeted light intensities to maximize compliance and individualize light dose/timing in therapeutic settings.

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Lighting Research Center, Rensselaer Polytechnic Institute, 21 Union Street, Troy, NY 12180, USA; figuem@rpi.edu

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• older adults • sleep

Light is not just for vision. Light reaching the retina contributes not only to visual perception but also to nonvisual responses, such as the resetting of the biological clock. Humans have a biological clock located in the suprachiasmatic nuclei (SCN) that generates and regulates circadian rhythms, which are biological rhythms that repeat themselves approximately every 24 h. These include cycles such as sleep–wake, body temperature, hormone production and alertness. The daily light–dark pattern reaching the retina is the main input to synchronize the biological clock to the solar day. If humans are not exposed to a sufficient amount of light of the right spectrum, for a sufficient amount of time, and with the right timing, the biological clock becomes desynchronized with the solar day and humans may experience decrements in physiological functions, neurobehavioral performance and sleep [1–4].

A person is more likely to experience a good night of sleep when the circadian and homeostatic systems, both of which influence the sleep– wake cycle, are aligned. Sleep pressure increases with time awake, contributing to high sleep need at night. The circadian system sends an alerting signal to the body during the day, counteracting the increase of sleep pressure with time awake and a sleeping signal during the night, promoting a consolidated night of sleep. The circadian clock consolidates sleep and wake periods in part by driving two 'gating' zones: the wake maintenance zone, which occurs approximately 2–3 h prior to habitual sleep onset, and the sleep maintenance zone, which occurs approximately 2–3 h prior to habitual wake onset, close to the minimum core body temperature [5,6].

Another very well-known circadian rhythm is the cycle of melatonin production. Melatonin is a hormone produced by the pineal gland at night and under conditions of darkness. For diurnal species, such as humans, melatonin signals that it is time to sleep [7]. The timing of melatonin onset in the evening, referred to as dim light melatonin onset (DLMO), occurs approximately 2 h prior to natural bedtimes, and is used as a marker of the circadian clock [8].

Lighting characteristics affecting the circadian system

Lighting characteristics affecting the circadian system, as measured by acute melatonin suppression and phase shifting of DLMO, are different than those affecting visibility. Rods, cones and

the intrinsically photosensitive retinal ganglion cells participate in circadian phototransduction, which is how the retina converts light signals into neural signals for the biological clock [9]. It is now known that lower levels of light, less than those originally demonstrated in the 1980s, can acutely suppress nighttime melatonin production and affect the timing of melatonin onset and offset; however, light levels needed to affect melatonin are still higher than those needed to affect vision [10,11]. For example, a warm color (correlated color temperature of 2700 K or lower) nightlight delivering 1 lux at the cornea will allow one to safely navigate in a space at night, but it will not suppress the hormone melatonin [11,12]. Humans are 'blue sky detectors'; the peak sensitivity for acute melatonin suppression and phase shifting of DLMO is close to 460 nm [13–15].

The effects of light on the circadian system vary over the course of the 24-h day. Morning light, given after the trough of core body temperature that typically occurs in the second half of the night, will advance the timing of sleep in the following cycle, while evening light, given prior to the trough of core body temperature, will delay the timing of sleep [8].

Photic history, or the amount of light received during the previous day, determines the effectiveness of light on acute melatonin suppression and on the phase shifting of the timing of DLMO [16–18]. For maximum results of light therapy, it is also important to accurately measure light exposures over the 24-h day, as opposed to taking just a 'snapshot' measurement of light exposure at one certain place and time [19,20]. The circadian system seems to keep track of light exposure, and therefore, knowing an individual's light exposure history over the past 24 h can help determine the best light prescription for the next 24 h [20].

Sleep & circadian disruption in normal aging & ADRD patients

Between 40 and 70% of older adults suffer from sleep disturbances or disorders, which are especially prevalent among Alzheimer's disease and related dementias (ADRD) patients [21]. Older adults, in particular, those with ADRD, may exhibit reduced neuronal activity in the SCN, where the biological clock that governs circadian rhythms is located, along with reduced circadian rhythm amplitude due in part to the fact that at a molecular level, the SCN becomes

less responsive to light for entrainment [22]. It has been demonstrated that fractal activity patterns, which are robust in healthy physiological systems, are governed by the SCN and are significantly altered in those with dementia [23,24]. Additionally, when discussing the effects of light on the aging population, it is important to keep in mind that the first stage of phototransduction, when light signals are converted into neural signals, is negatively affected in this population: older adults have reduced optical transmission at short wavelengths [25,26]. Less light reaches the back of the eye due to lens thickening, and reduced light on the retina allows circadian rhythms to get out of sync [21,27]. In addition to less light reaching the back of the eye, efferent signals from the retina to the biological clock can also be reduced. For example, glaucoma has been associated with the degenerative loss of intrinsically photosensitive retinal ganglion cells, which is the main conduit of light signals from the retina to the SCN [28]. There are indications that those suffering from glaucoma with severe visual field defect, a condition whose incidence is associated with advancing age, suffer from higher rates of sleep disturbances, anxiety and depression [29]. Moreover, older adults, especially those with ADRD, typically lead a more sedentary indoor lifestyle, with less access to bright light during the day, potentially increasing the risk for circadian disruption [30–32]. Without exposure to a regular, daily pattern of light and dark, circadian rhythms can become irregular [33]. Circadian misalignment resulting from irregular light–dark patterns or from age-dependent changes in light sensitivity or in the circadian system response likely plays a role in poor sleep [27]. When the circadian system is disturbed, it can lead to poor sleep quality in older adults, even if they have no other significant health issues [34]. While sleep and circadian rhythms are closely related, disruption of sleep can occur independently of circadian rhythms disruptions. Light therapy may not be as effective, if effective at all, in treating these non-circadian sleep disturbances.

ADRD is the most common type of dementia diagnosed in older Americans. While individuals with ADRD can have similar sleep problems as healthy older adults, they tend to exhibit more random patterns of rest and activity rather than the consolidated patterns of healthy, older adults [35]. This lack of rest–activity pattern consolidation, along with related nocturnal wandering, is one of the main reasons why individuals with ADRD are transitioned from the home to more controlled environments.

In 2012 Figueiro *et al.* quantified circadian light exposure and activity levels of healthy older adults compared with older adults with ADRD during summer and winter months [36]. Circadian light exposures were measured using the Daysimeter, a calibrated, personal meter. Details about the operation of the Daysimeter are described elsewhere [19], but this device was designed to specifically measure light as it affects the circadian system. Each of the 16 healthy older adults and 21 ADRD patients wore a wrist Daysimeter [19] to measure light and activity levels for 1 week. Results of the quantitative study show that individuals with ADRD experienced lower circadian light levels, exhibited lower activity levels and had greater disruption to their rest–activity patterns than healthy older adults. The findings also show that people with ADRD experience lower levels of circadian light exposure and greater levels of rest–activity disruption during the winter than in summer. These results are consistent with earlier studies demonstrating that middle-aged adults are exposed to approximately 58 min of bright white light per day [31] while older adults in assisted living facilities were exposed to bright light for only 35 min per day [37]. Older adults with ADRD living in nursing homes experience as little as 2 min per day [38,39]. Given that current lighting in nursing homes and assisted living facilities is generally dim and constantly on, it is not surprising that sleep disturbances are common in this population [40].

Moe *et al.* [41] determined whether disrupted sleep–wake cycles could predict impaired cognition by observing 78 ADRD patients and 38 healthy control participants in an overnight lab study. Participants did not have any reported sleep problems. A stronger relationship was found between cognition and sleep with the ADRD patients; in other words, they found a negative correlation between nighttime waking and cognitive performance. Cognitive function decreased with more time awake and longer rapid eye movement (REM) sleep latency, while more REM and slow-wave sleep were associated with better cognition.

These studies suggest that while circadian and sleep disturbances may be common in older adults, including those with ADRD, light, which is the strongest time giver for the circadian system, has a potential to promote entrainment and improve sleep in this population. Therefore, light has the potential to become a powerful treatment for mitigating poor sleep quality frequently found in the older population, including those with dementia. Medications, often prescribed for sleep problems, have low effectiveness [42,43] and are associated with adverse effects, such as worsening confusion, falls and hip fractures [44–49]. A meta-analysis of sedative/hypnotic medications for older people with insomnia concluded that the benefits of sleep medication may not justify the increased risk [50]. Adverse side effects of light therapy may include eye strain and headaches [51] although other studies did not show any significant differences in side effects between light treatment and control experimental conditions [52]. The goal of this literature review is to identify studies that had used light as an intervention to improve sleep and behavior in patients diagnosed with ADRD.

Light therapy for ADRD patients: a review of the literature

A search in Medline was performed in April– October 2016 and once again in December 2016 using the terms: Alzheimer's disease, dementia, light therapy, phototherapy, sleep and circadian rhythms. Studies from 1980 to 2016 that had used light as an intervention to improve sleep and/or behavior in ADRD patients were identified. The search yielded 305 results. After reading the abstracts, only those studies that discussed light as an intervention to reduce sleep disturbances and improve behavior (mood, depression and agitation) were selected, yielding a total of 25 articles. **Table 1** details these studies and a summary of their findings is discussed below.

Fetveit *et al.* [61] demonstrated that exposure to 2 h of bright light (6000–8000 lux at the cornea) in the morning for at least 2 weeks substantially improved the sleep efficiency of 11 older adults with dementia. Alessi *et al.* [67] showed that five consecutive days of 30-min exposure to sunlight, increased physical activity, structured bedtime and control of light and noise at night resulted in a significant decrease in daytime sleeping in intervention participants compared with controls. Further, they showed that intervention participants had increased participation in social and physical activities as well as social conversation.

Analyzing actigraph data, Van Someren *et al.* [55] found that increased illumination in the living environment of 22 ADRD patients increased the stability of their rest–activity rhythm following 4 weeks of treatment. A ceilingmounted light fixture containing polychromatic light was installed in the common areas where the patients spent most of their waking time. Patients received an average of 1136 ± 89 lux at the cornea from the new lighting, although the amount of light received ranged from 790–2190 lux at the cornea depending on their position relative to a window. Bright light treatment was most effective in residents with relatively unimpaired vision, as opposed to those with severe visual deficits. Interdaily stability, which is a measure of the consistency in rest–activity patterns over the course of many days, increased (i.e., coupling of the rhythm to environmental time givers, such as mealtimes), indicating a more steadfast organization of the circadian rest–activity rhythm. This was the first field study demonstrating that unattended light during the daytime could improve rest–activity rhythms in ADRD patients.

Satlin *et al.* [53] examined whether evening light exposure (1500–2000 lux at the cornea) would improve sleep–wake patterns and reduce agitation in ADRD patients, and found an increase in circadian amplitude and improvement in intradaily variability (i.e., consolidated rest–activity patterns during the day) but not in interdaily stability (i.e., more consolidated rest–activity rhythms over the course of successive days). They also found that evening light exposure decreased nighttime activity and sundowning symptoms. Lyketsos *et al.* [58] administered 1 h of light (10,000 lux at the cornea) each morning for 2 weeks to ADRD patients with agitated behaviors and found that these individuals with agitated behaviors slept more hours at night, when exposed to bright light in the morning.

Mishima *et al.* [54] exposed 14 patients with dementia to 2 h of light (3000–5000 lux at the cornea measured at a distance of 1 meter) each morning for 4 consecutive weeks and observed a significant increase in nighttime sleep duration and a significant reduction in agitated behavior. In a later study, Mishima *et al.* [57] examined the therapeutic effects of 2 weeks of morning bright light (5000–8000 lux at the cornea) on rest–activity rhythm disorders in 12 patients with vascular dementia and ten ADRD patients. The 2 weeks of morning bright light induced a significant reduction in both nighttime activity and percentages of nighttime activity to total

activity compared with the pretreatment period, and compared with the dim light condition in the vascular dementia group, but not in the ADRD group.

Ancoli-Israel *et al.* [62] administered light (2500 lux at the cornea) for 2 h in the morning or the evening for ten consecutive days and found both groups of ADRD patients (those who received morning and those who received evening light) exhibited more consolidated sleep at night, as measured by average length of maximum nocturnal sleep bouts. Using the same dataset, Ancoli-Israel *et al.* [63] evaluated the effect of the lighting intervention on agitated behavior in these patients. Morning light delayed the acrophase of agitation by 1.63 h but there was no significant effect on observational ratings of agitation. Yamadera *et al.* [59] found that 4 weeks of morning bright light (3000 lux at the cornea) administered to 27 ADRD patients resulted in improved mental status scores, decreased percentage of daytime naps/naptime, increased percentage of nighttime sleep time and decreased percentage of nighttime awakenings.

Skjerve *et al.* [64] investigated sleep–wake rhythm disturbances and behavioral symptoms in subjects with severe dementia. Bright light treatment was given daily for 45 min in the morning to ten patients with severe dementia, sleep–wake rhythm disturbances and significant behavioral symptoms. Light treatment consisted of 5000–8000 lux at the cornea measured at a distance of 0.3–0.5 m. The patients' behavioral symptoms improved with treatment. No changes in sleep–wake measures were found, although an advance of the activity rhythm acrophase was identified during treatment. The results suggested that short-term bright light improves behavioral symptoms and certain aspects of activity rhythm disturbances, even in severely demented patients.

Dowling *et al.* [66] tested the effects of morning versus evening light, hypothesizing that morning bright light (≥2500 lux at the cornea) should result in the most improvement with a phase advance in the rest–activity rhythm of ADRD patients. Conversely, afternoon light exposure would phase delay the rhythm. No significant differences in actigraphy-based measures of nighttime sleep or daytime wake were found. However, both groups evidenced a significantly more stable rest–activity rhythm acrophase over the 10-week treatment period compared with the controls. The study concluded that 1 h of bright

light exposure may provide sufficient additional input to the circadian pacemaker to facilitate entrainment to the 24-h day. When examining morning light therapy treatment, their results indicated that subjects with the most impaired rest–activity rhythm responded significantly and positively to the 1-h light intervention [65].

McCurry *et al.* [74] tested the effects of walking, light exposure and a combination intervention (walking, light and sleep education) on total wake time and subjective sleep quality in ADRD patients living in independent community settings. Participants in the walking, light and combination intervention showed significant improvements in total wake times and sleep efficiency, and the effect was larger in those who had greater adherence to the experimental protocol.

Sloane *et al.* [69] showed a statistically significant improvement in nighttime sleep with morning or all-day light (>2500 lux at the cornea), with greater improvement among persons with severe dementia. The authors claim that the effect size was greater than has been reported using prescription sleep medicines in long-term care populations. Using the same data set, Hickman *et al.* [68] showed that, compared with all day and evening light exposures, morning light had the greatest effect on both sexes. Depressive symptoms decreased in women and increased in men after morning light exposure.

To determine whether the progression of cognitive and noncognitive symptoms may be ameliorated by individual or combined longterm application of bright light and melatonin, Riemersma-van der Lek *et al.* [70] conducted a long-term, double-blind, placebo-controlled study with 189 elderly patients with dementia living in nursing homes. Light alone was found to attenuate both cognitive deterioration by as much as 5%, as determined by the Mini Mental Status Examination and the increase in functional limitations, as determined by the Activities of Daily Living Scale. Oral melatonin alone shortened sleep onset latency and increased sleep duration, but also increased withdrawn behavior. The light and melatonin treatment increased sleep efficiency and improved nocturnal restlessness, thus indicating that the adverse effect of melatonin on mood can be counteracted when administered as part of treatment with light for cognitive and noncognitive function.

However, not all studies to date have shown a positive effect of light on sleep disturbances or rest–activity rhythms of those with dementia.

ABRS: Agitated Behavior Rating Scale; AD: Alzheimer's disease; ADRD: Alzheimer's disease and related dementias (and Alzheimer's-type dementia); Behave-AD: Behavioral Pathology in Alzheimer's Disease scale; BIMS: Brief Interview for Mental Status; CCT: Correlated color temperature; CDR: Clinical Dementia Rating; CMAI: Cohen-Mansfield Agitation Index; CSDD: Cornell Scale for Depression in Dementia; DSM: Diagnostic and Statistical Manual of Mental Disorders; GDS: Geriatric Depression Scale; IS: Interdaily stability; IV: Intradaily variability; K: Kelvin; L5: Least active 5-h period; LBD: Lewy body dementia; M10: Most active 10-h period; MD: Mixed dementia (AD and VD); MDS-COGS: Minimum Data Set Cognition Scale; MMSE: Mini-Mental State Examination; MOSES: Multi-Observational Scale for Elderly Subjects; NI-ADL: Nurse-informant adaptation; NINCDS-ADRDA: National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association; NPI-Q: Neuropsychiatric Inventory; PGCARS: Philadelphia Geriatric Center Affect Rating Scale; PGCMS: Philadelphia Geriatric Center Morale Scale; PSQI: Pittsburgh Sleep Quality Index; RA: Relative amplitude; SD: Standard deviation; SDI: Sleep Disorders Inventory; SDQ: Sleep Disorders Questionnaire; SE: Sleep efficiency; SEM: Standard error of the mean; SOL: Sleep onset latency; TSD: Total sleep duration; VD: Vascular dementia.

High-level, low-glare ambient lighting system. Bright conditions delivered mean ± SD light levels ranging from 2495 \pm 179 lux to 2641 ± 259 lux between two facilities. Standard condition delivered mean ± SD light level of Outcomes: nighttime sleep 606 ± 179 lux

Devices: digital handheld light meter (positioned away from subject, ≅4 ft above floor, pointed toward ceiling; manufacturer not specified). Actiwatch-L (Mini Mitter Inc., OR, USA) measures, daytime sleepiness measures, circadian rhythm measures (mesor, amplitude, IV, IS)

Nighttime sleep significantly increased for subjects in morning bright light and all day bright light. Morning bright light advanced phase by 29 min, and evening bright light delayed phase by 15 min. No other significant effects were observed, and strength of activity–rest patterns was not influenced by any treatment condition [69]

Lighting devices/levels **Measurement devices/outcome**

Ceiling-mounted Philips TLD 840 and 940 fluorescent tubes (Philips Lighting, Eindhoven, The Netherlands) fitted with Plexiglas diffusers.

Bright light exposure targeted at ≅1000 lux, control lighting targeted at ≅300 lux

measures Devices: Actiwatch (Cambridge Neurotechnology, Cambridge, England). Mixed-effect regression analysis performed with MLwiN 2.0 software (Centre for Multilevel Modelling, University of Bristol, Bristol, UK), and SPSS 14.0 (IBM Corp., Armonk, NY, USA) employed for T-tests, chi-squared tests, and logistic regressions Outcomes: actigraphy data analyzed for SE, SOL and TSD sleep measures. Standardized scales for cognitive (MMSE, CSDD, PGCMS) and noncognitive (PGCARS, MOSES, NPI-Q, CMAI), symptoms, limitations of activities of daily living (NI-ADL), and adverse effects assessed every 6 months

Bright light exposure reduced subjects' cognitive deterioration (as measured via MMSE) by relative measure of 5% while also improving CSDD scores for depressive symptoms by 19%. Bright light also slowed increase in functional limitations over time by 53%. Melatonin reduced SOL by 19% and increased TSD by 6%. Melatonin had an adverse effects, however, on PGCARS scores (both positive and negative affects). The melatoninonly condition increased withdrawn behavior (as measured via MOSES). Bright light combined with melatonin treatment (as measured via CMAI) reduced aggressive behavior by 9%, increased SE by 3.5% and improved nocturnal restlessness by 9%. Authors concluded that light provides modest benefit for some cognitive and noncognitive dementia symptoms, and recommended that melatonin be used only in combination with light to reduce its adverse effects on mood [70]

Findings Ref.

Bright light administered via APOLLO Brite Lite IV boxes (Orem, UT, USA) to supplement daylight, as needed. Light boxes delivered 10,000 lux at 26 in and 2500 lux at 48 in. Control group exposed to indoor lighting only (range = 150–200 lux)

Devices: rest–activity data activity monitor (AW-64; Mini Mitter Co., Inc., OR, USA). The actigraphy data were analyzed using Actiware Sleep Version 3.2 Statistical analyses performed using SPSS V.14.0 0 (IBM Corp., Armonk, NY, USA). Cal LIGHT 400 light (Cooke Corp., MI, USA) meters used to monitor exposures in gaze direction of each subject at least once per treatment Outcomes: sleep–wake measures and rest–activity measures, both parametric (amplitude, acrophase, goodness of fit to R^2) and nonparametric (IS, IV, L5, M10, amplitude, relative amplitude)

collected via wrist-worn Actiwatch received by LM and LP groups. Daytime sleep decreased for Authors found no significant difference in intervention doses the LM group (66 min) and increased for both LP and control groups by 25 and 50 min, respectively. The groups showed significant differences between baseline and post intervention in respect to several rest–activity variables. The LM group, specifically, showed significantly better results for parametric and nonparametric amplitude, goodness of fit to $R²$ and M10. Both LM and LP groups phase advanced (63 min and 34 min, respectively) and control group phase delayed (21 min), but these results were not statistically significant. In general, LM group had improvements in daytime somnolence, nighttime sleep, daytime activity and sleep ratio. Authors concluded that light treatment plus melatonin, and not light treatment alone, improved subject performance in sleep–wake and rest–activity measures

[71]

In the study by Ancoli-Israel *et al.* [60], bright light exposure (2500 lux at the cornea) did not produce significant improvement in nighttime sleep and daytime alertness. The authors suggested that these negative results were due to the subjects' level of dementia. They did, however, find that increasing the exposure to morning light made the circadian rhythm of rest–activity significantly more robust in this population. Dowling *et al.* [71] found no effect of light treatment alone on nighttime sleep, daytime wake or rest–activity rhythms, but were able to demonstrate an increase in daytime wakefulness and activity levels with concurrent administration of oral melatonin. Sloane*et al.* [76] showed a positive effect of a tailored light treatment (bluish white light, correlated color temperature = 13,000 K) designed to deliver 400 lux at the cornea, in selfreported sleep in caregivers of ADRD patients living at home, but not in sleep and behavior of the patients themselves. Van Hoof *et al.* [73] did not find a significant effect on behavior and tympanic temperature rhythms in dementia patients after they were exposed to 500 lux at the cornea of a 17,000 K light source. Burns *et al.* [72] exposed dementia patients to either 10,000 lux at the cornea (treatment condition) or 100 lux at the cornea (control) of light for four consecutive weeks and measured agitation and depression scores as well as actigraphy. Results showed very little effect of light treatment on agitation and depression and only a slight indication that sleep was improved, especially in the winter months.

Colenda *et al.* [56] used light visors to deliver 2000 lux of light at the cornea each morning for 10 days to community-dwelling AD patients and found no consistent biological effect of the light treatment on sleep, noting that perhaps light visors may be an inadequate means of providing light treatment.

Given that not all of the published studies yielded positive outcomes, it is not surprising that a Cochrane review conducted in 2002, which included only five studies that met their inclusion criteria (relevant, randomized controlled trials in which bright light treatment was compared with a control group for the effect on managing sleep, behavioral, mood or cognitive disturbances), concluded that there was not enough evidence to assess the value of light treatment for people with dementia [78]. A recent Cochrane review conducted in 2014 included eight studies that met their inclusion criteria and that had available data for their analyses. Authors, again, concluded that there is not enough evidence to justify the use of light therapy to improve sleep and behavior in ADRD patients [79].

One explanation for the mixed results may be that current light therapy approaches for sleep disturbances in older adults are not formalized in terms of amount, spectrum, timing, distribution and duration, leading, in some cases, to a weakening of the therapeutic effects of light. In fact, Forbes *et al.* in their latest Cochrane review [79] analyzed studies that used a variety of light therapy approaches. None of the studies

included in their analyses controlled or measured the actual light dose received by participants. Pooling data from these studies where the various light delivery methods were used without any control of how much light subjects were actually being exposed to during the intervention may have affected the outcomes of their analyses. This is an important point to consider, because in studies where carefully controlled light stimulus was delivered, a positive impact of light on sleep quality of those with ADRD was in fact found [75,80]. Another possibility for these mixed results is the variation in care between the various facilities. While light–dark patterns are important for circadian entrainment, which in turn is important for good sleep quality, many other factors (e.g., activity and feeding times) may affect behavior in this population.

In general, the only formalized recommendations for light treatment (amount, spectrum, timing and duration) are those used to treat symptoms of seasonal affective disorder (SAD). Sufferers of SAD are expected to be exposed to 10,000 lux at the cornea of white light for 30 min or 2500 lux at the cornea of the same white light for 2 h. Those recommendations were developed based on studies conducted by Lewy *et al.* [10] nearly 30 years ago, when the knowledge of nonvisual effects of light on circadian regulation was very limited. While this recommendation has been successful in treating symptoms of SAD, clinicians often find that patients have a difficult time complying with the recommendations because the high light levels of white light can be very uncomfortable, resulting in squinting and gaze aversion. Since much more is now known about the retinal phototransduction mechanisms that drive the circadian system, there is a much higher likelihood that more modest and more comfortable light doses can be used as a reliable, nonpharmacological treatment for circadian sleep disturbances so commonly found in those with ADRD. In fact, Figueiro *et al.* [75] recently showed a positive effect of a more comfortable lighting intervention designed to maximally affect the circadian system in ADRD patients living in long-term care facilities, and even more recently demonstrated that innovative delivery methods can be employed to ensure patients' compliance with such interventions [77]. The same principle can be used in any population suffering from circadian sleep disorders. It is important to note, however, that light therapy may not be as effective – or may not be effective at all – at treating noncircadian sleep disorders, such as insomnia, also commonly experienced by older adults.

Future perspective

Although there is not a complete understanding of the effects of light on the aging circadian system outside laboratory conditions, it is clear that a distinct, repeated pattern of light and dark is needed to help maintain the synchrony between the aging circadian system and the solar day. [81] With that in mind, it is important to design

separate lighting systems for daytime and nighttime activities. Lighting in the built environment should provide high circadian light stimulation during the day and low circadian stimulation at night, good visual performance (e.g., reading) during waking hours and low-level nightlights that enable safe navigation through the space and that minimize sleep disruption.

During daytime hours, light levels in indoor environments should be high enough to activate the circadian system. This can be accomplished with the use of daylight or electric lighting systems. Care should be taken to avoid introducing glare in the space. The combination of high levels of 'cool' light sources (a minimum of 400– 600 lux at the cornea and CCT >5000 K) during the day and 'warm' light sources (no more than 80–100 lux at the cornea; CCT <2800 K) in the evening promotes circadian entrainment better than current lighting system designs (i.e., constant dim light). As detailed in Figueiro [81], the cool light source at that light level for a 1-h duration will provide good circadian stimulation. A similar lighting specification was shown to improve restless behavior in patients with dementia [82].

In addition to impacting the aging circadian system, light can also impact the aging perceptual system. Sight and visibility are important for good perception; therefore, it is important to provide light that will support the perceptual system. At night, light levels should be dim and allow for safe navigation, especially in bedrooms and bathrooms [81,83–85]. It is also important to encourage older people to increase their exposure to light–dark patterns as part of their wellness program. Daylight can be added into the home environment, especially in long-term care settings, by adding skylights, clerestory windows and sunrooms.

Future clinical research should focus on testing these new lighting schemes that are designed to specifically deliver a strong daytime circadian stimulation to ADRD patients. But, it is imperative that the light doses that subjects are receiving be measured. It is also important to point out that light therapy that promotes better sleep may not only improve the quality of life for those with ADRD and their caregivers, but it may also have an important clinical relevance. Recent research suggests that sleep quantity and quality may be directly linked to ADRD [86,87]; other more recent studies suggest that cortical responses are reduced with accrued sleep debt [88], which is common in those who suffer from circadian misalignment. Therefore, studies should be designed to remove barriers to the use of effective nonpharmacological therapies that increase sleep efficiency. Finally, when assessing the effect of light on sleep and behavior in ADRD patients, it is important to also consider other environmental factors and comorbidities (e.g., ophthalmological diseases [89]) and other therapies, such as cognitive behavior therapy and exercise [74]. Future studies should investigate whether light can be more effective at treating sleep and behavior disturbances if combined with some of these other therapies.

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References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

- Leproult R, Holmback U, Van Cauter E. Circadian misalignment augments markers of insulin resistance and inflammation, independently of sleep loss. *Diabetes Metab.* 63(6), 1860–1869 (2014).
- 2 Van Cauter E, Spiegel K, Tasali E, Leproult R. Metabolic consequences of sleep and sleep loss. *Sleep Med.* 9(Suppl. 1), S23–S28 (2008).
- 3 Sack RL, Auckley D, Auger RR *et al.* Circadian rhythm sleep disorders: part I, basic principles, shift work and jet lag disorders. An American Academy of Sleep Medicine review. *Sleep* 30(11), 1460–1483 (2007).
- 4 Sack RL, Auckley D, Auger RR *et al.* Circadian rhythm sleep disorders: part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm. An American Academy of Sleep Medicine review. *Sleep* 30(11), 1484–1501 (2007).
- 5 Borbély AA. A two process model of sleep regulation. *Hum. Neurobiol.* 1(3), 195–204 (1982).
- 6 Daan S, Beersma DG, Borbély AA. Timing of human sleep: recovery process gated by a circadian pacemaker. *Am. J. Physiol.* 246(2 Pt 2), R161–R183 (1984).
- 7 Arendt J. *Melatonin and the mammalian pineal gland (1st edition)*. Chapman & Hall, London, UK (1995).
- 8 Khalsa SB, Jewett ME, Cajochen C, Czeisler

CA. A phase response curve to single bright light pulses in human subjects. *J. Physiol.* 549(Pt 3), 945–952 (2003).

- 9 Hattar S, Lucas RJ, Mrosovsky N *et al.* Melanopsin and rod-cone photoreceptive systems account for all major accessory visual functions in mice. *Nature* 424 75–81 (2003).
- 10 Lewy A, Wehr T, Goodwin T, Newsome D, Markey S. Light suppresses melatonin secretion in humans. *Science* 210(4475), 1267–1269 (1980).
- 11 Zeitzer JM, Dijk DJ, Kronauer R, Brown E, Czeisler C. Sensitivity of the human circadian pacemaker to nocturnal light: melatonin phase resetting and suppression. *J. Physiol.* 526(3), 695–702 (2000).
- 12 Rea MS, Figueiro MG. A working threshold for acute nocturnal melatonin suppression from "white" light sources used in architectural applications. *J. Carcinog. Mutagen.* 4(3), 1000150 (2013).
- 13 Brainard GC, Hanifin JP, Greeson JM *et al.* Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. *J. Neurosci.* 21(16), 6405–6412 (2001).
- 14 Thapan K, Arendt J, Skene DJ. An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans. *J. Physiol.* 535(1), 261–267 (2001).
- 15 Rea MS, Figueiro MG, Bullough JD, Bierman A. A model of phototransduction by the human circadian system. *Brain Res. Rev.* 50(2), 213–228 (2005).
- 16 Chang AM, Scheer FA, Czeisler CA. The human circadian system adapts to prior photic history. *J. Physiol.* 589(Pt 5), 1095–1102 (2011).
- 17 Chang AM, Scheer FA, Czeisler CA, Aeschbach D. Direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans depend on prior light history. *Sleep* 36(8), 1239–1246 (2013).
- 18 Hebert M, Martin SK, Lee C, Eastman CI. The effects of prior light history on the suppression of melatonin by light in humans. *J. Pineal Res.* 33(4), 198–203 (2002).
- 19 Figueiro MG, Hamner R, Bierman A, Rea MS. Comparisons of three practical field devices used to measure personal light exposures and activity levels. *Light. Res. Technol.* 45(4), 421–434 (2013).
- 20 Rea MS, Bierman A, Ward G, Figueiro MG. Field tests of a model of the human circadian oscillator. Presented at: *SLEEP 2014, the 28th Annual Meeting of the American Academy of Sleep Medicine.* MN, USA 31st May–4th June 2014.
- 21 Van Someren EJ. Circadian and sleep disturbances in the elderly. *Exp. Gerontol.* 35(9–10), 1229–1237 (2000).
- 22 Swaab DF, Dubelaar EJ, Hofman MA, Scherder EJ, Van Someren EJ, Verwer RW. Brain aging and Alzheimer's disease; use it or lose it. *Prog. Brain Res.* 138, 343–373 (2002).
- 23 Hu K, Van Someren EJ, Shea SA, Scheer FA. Reduction of scale invariance of activity fluctuations with aging and Alzheimer's disease: involvement of the circadian pacemaker. *Proc. Natl Acad. Sci. USA* 106(8), 2490–2494 (2009).
- 24 Hu K, Harper DG, Shea SA, Stopa EG, Scheer FA. Noninvasive fractal biomarker of clock neurotransmitter disturbance in humans with dementia. *Sci. Rep.* 3, 2229 (2013).
- 25 Brondsted AE, Lundeman JH, Kessel L. Short wavelength light filtering by the natural human lens and IOLs – implications for entrainment of circadian rhythm. *Acta Ophthalmol.* 91(1), 52–57 (2013).
- 26 Turner PL, Mainster MA. Circadian photoreception: ageing and the eye's important role in systemic health. *Br. J. Ophthalmol.* 92(11), 1439–1444 (2008).
- 27 Van Someren EJ. Circadian rhythms and sleep in human aging. *Chronobiol. Int.* 17(3), 233–243 (2000).
- 28 Drouyer E, Dkhissi-Benyahya O, Chiquet C *et al.* Glaucoma alters the circadian timing system. *PLoS ONE* 3(12), e3931 (2008).
- 29 Agorastos A, Skevas C, Matthaei M *et al.* Depression, anxiety, and disturbed sleep in glaucoma. *J. Neuropsychiatry Clin. Neurosci.* 25(3), 205–213 (2013).
- 30 Shochat T, Martin J, Marler M, Ancoli-Israel S. Illumination levels in nursing home patients: effects on sleep and activity rhythms. *J. Sleep Res.* 9(4), 373–379 (2000).
- 31 Espiritu RC, Kripke DF, Ancoli-Israel S *et al.* Low illumination experienced by San Diego adults: association with atypical depressive symptoms. *Biol. Psychiatry* 35(6), 403–407 (1994).
- 32 Campbell SS, Kripke DF, Gillin JC, Hrubovcak JC. Exposure to light in healthy elderly subjects and Alzheimer's patients. *Physiol. Behav.* 42(2), 141–144 (1988).
- 33 Van Someren EJ, Riemersma-Van Der Lek RF. Live to the rhythm, slave to the rhythm. *Sleep. Med. Rev.* 11(6), 465–484 (2007).
- 34 Kim SJ, Benloucif S, Reid KJ *et al.* Phaseshifting response to light in older adults. *J. Physiol.* 592(1), 189–202 (2014).
- 35 Hatfield CF, Herbert J, Van Someren EJ, Hodges JR, Hastings MH. Disrupted daily activity/rest cycles in relation to daily cortisol rhythms of home-dwelling patients with early Alzheimer's dementia. *Brain* 127(Pt 5), 1061–1074 (2004).
- 36 Figueiro MG, Hamner R, Higgins P, Hornick T, Rea MS. Field measurements of light exposures and circadian disruption in two populations of older adults. *J. Alzheimers Dis.* 31(4), 711–715 (2012).
- 37 Sanchez R, Ge YR, Zee PC. A comparison of the strength of external zeitgeber in young and older adults. *Sleep Res.* 22, 416 (1993).
- 38 Ancoli-Israel S, Kripke DF. Now I lay me down to sleep: the problem of sleep fragmentation in elderly and demented residents of nursing homes. *Bull. Clin. Neurosci.* 54, 127–132 (1989).
- 39 Weldemichael DA, Grossberg GT. Circadian rhythm disturbances in patients with Alzheimer's disease: a review. *Int. J. Alzheimers Dis.* 2010, 716453 (2010).
- 40 Sinoo MM, Van Hoof J, Kort HSM. Light conditions for older adults in the nursing home: assessment of environmental illuminances and colour temperature. *Build. Environ.* 46(10), 1917–1927 (2011).
- 41 Moe KE, Vitiello MV, Larsen LH, Prinz PN. Symposium: cognitive processes and sleep disturbances: sleep/wake patterns in Alzheimer's disease: relationships with cognition and function. *J. Sleep Res.* 4(1), 15–20 (1995).
- 42 Morin CM, Colecchi C, Stone JA, Sood R, Brink D. Behavioral and pharmacological therapies for late-life insomnia. *JAMA* 281(11), 991–999 (1999).
- 43 Meuleman JR, Nelson RC, Clark RL. Evaluation of temazepam and diphenhydramine as hypnotics in a nursing-home population. *Drug Intell. Clin. Pharm.* 21(9), 716–720 (1987).
- 44 Chavez B. Pharmacotherapy in managing insomnia: assessing patient needs and outcomes. *US Pharm.* 30(2), HS23–HS26 (2005).
- 45 Tinetti ME. Preventing falls in elderly persons. *N. Engl. J. Med.* 348, 42–49 (2003).
- 46 Tinetti ME, Speechley M, Ginter SF. Risk factors of falls among elderly persons living in the community. *N. Engl. J. Med.* 319, 1701–1707 (1988).
- 47 Cumming RG, Klineberg J. Psychotropics, thiazide diuretics and hip fractures in the elderly. *Med. J. Aust.* 158(6), 414–417 (1993).
- 48 Ray WA, Griffin RM, Downey W. Benzodiazepines of long and short

elimination half-life and the risk of hip fracture. *JAMA* 262(23), 3303–3307 (1989).

- 49 Allain H, Bentue-Ferrer D, Polard E, Akwa Y, Patat A. Postural instability and consequent falls and hip fractures associated with use of hypnotics in the elderly. *Drugs Aging* 22(9), 749–765 (2005).
- 50 Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ* 331(7526), 1169 (2005).
- **• This meta-analysis of sedative/hypnotic medications for older people with insomnia concluded that the benefits of sleep medication may not justify the increased risk.**
- 51 Levitt AJ, Joffe RT, Moul DE *et al.* Side effects of light therapy in seasonal affective disorder. *Am. J. Psychiatry* 150(4), 650–652 (1993).
- 52 Volz HP, Mackert A, Stieglitz RD. Sideeffects of phototherapy in nonseasonal depressive disorder. *Pharmacopsychiatry* 24(4), 141–143 (1991).
- 53 Satlin A, Volicer L, Ross V, Herz L, Campbell S. Bright light treatment for behavioral and sleep disturbances in patients with Alzheimer's disease. *Am. J. Psychiatry* 149, 1028–1032 (1992).
- 54 Mishima K, Okawa M, Hishikawa Y, Hozumi S, Hori H, Takahashi K. Morning bright light therapy for sleep and behavior disorders in elderly patients with dementia. *Acta Psychiatr. Scand.* 89(1), 1–7 (1994).
- 55 Van Someren EJ, Kessler A, Mirmiran M, Swaab DF. Indirect bright light improves circadian rest–activity rhythm disturbances in demented patients. *Biol. Psychiatry* 41(9), 955–963 (1997).
- **•• This was the first field study demonstrating that unattended light during the daytime could improve rest–activity rhythms in Alzheimer's disease and related dementias (ADRD) patients.**
- 56 Colenda CC, Cohen W, McCall WV, Rosenquist PB. Phototherapy for patients with Alzheimer disease with disturbed sleep patterns: results of a community-based pilot study. *Alzheimer Dis. Assoc. Disord.* 11(3), 175–178 (1997).
- 57 Mishima K, Hishikawa Y, Okawa M. Randomized, dim light controlled, crossover test of morning bright light therapy for rest–activity rhythm disorders in patients with vascular dementia and dementia of Alzheimer's type. *Chronobiol. Int.* 15(6), 647–654 (1998).
- 58 Lyketosos CG, Lindell Veiel L, Baker A, Steele C. A randomized, controlled trial of bright light therapy for agitated behaviors in dementia patients residing in long-term care. *Int. J. Geriatr. Psychiatry* 14(7), 520–525 (1999).
- 59 Yamadera H, Ito T, Suzuki H, Asayama K, Ito R, Endo S. Effects of bright light on cognitive and sleep–wake (circadian) rhythm disturbances in Alzheimer-type dementia. *Psychiatry Clin. Neurosci.* 54(3), 352–353 (2000)
- 60 Ancoli-Israel S, Martin JL, Kripke DF, Marler M, Klauber MR. Effect of light treatment on sleep and circadian rhythms in demented nursing home patients. *J. Am. Geriatr. Soc.* 50(2), 282–289 (2002).
- 61 Fetveit A, Skjerve A, Bjorvatn B. Bright light treatment improves sleep in institutionalised elderly – an open trial. *Int. J. Geriatr. Psychiatry* 18(6), 520–526 (2003).
- 62 Ancoli-Israel S, Gehrman P, Martin JL *et al.* Increased light exposure consolidates sleep and strengthens circadian rhythms in severe Alzheimer's disease patients. *Behav. Sleep Med.* 1(1), 22–36 (2003).
- 63 Ancoli-Israel S, Martin JL, Gehrman P *et al.* Effect of light on agitation in institutionalized patients with severe Alzheimer disease. *Am. J. Geriatr. Psychiatry* 11(2), 194–203 (2003).
- 64 Skjerve A, Holsten F, Aarsland D, Bjorvatn B, Nygaard HA, Johansen IM. Improvement in behavioral symptoms and advance of activity acrophase after short-term bright light treatment in severe dementia. *Psychiatry Clin. Neurosci.* 58(4), 343–347 (2004).
- 65 Dowling GA, Hubbard EM, Mastick J, Luxenberg JS, Burr RL, Van Someren EJ. Effect of morning bright light treatment for rest–activity disruption in institutionalized patients with severe Alzheimer's disease. *Int. Psychogeriatr.* 17(2), 221–236 (2005).
- 66 Dowling GA, Mastick J, Hubbard EM, Luxenberg JS, Burr RL. Effect of timed bright light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease. *Int. J. Geriatr. Psychiatry* 20(8), 738–743 (2005).
- 67 Alessi CA, Martin JL, Webber AP, Cynthia Kim E, Harker JO, Josephson KR. Randomized, controlled trial of a nonpharmacological intervention to improve abnormal sleep/wake patterns in nursing home residents. *J. Am. Geriatr. Soc.* 53(5), 803–810 (2005).
- 68 Hickman SE, Barrick AL, Williams CS *et al.* The effect of ambient bright light therapy on depressive symptoms in persons with dementia. *J. Am. Geriatr. Soc.* 55(11), 1817–1824 (2007).
- 69 Sloane PD, Williams CS, Mitchell CM *et al.* High-intensity environmental light in dementia: effect on sleep and activity. *J. Am. Geriatr. Soc.* 55(10), 1524–1533 (2007).
	- **• This research showed a statistically significant improvement in nighttime sleep with morning or all-day light, showing greater improvement among persons with severe dementia.**
- 70 Riemersma-Van Der Lek RF, Swaab DF, Twisk J, Hol EM, Hoogendijk WJ, Van Someren EJ. Effect of bright light and melatonin on cognitive and noncognitive function in elderly residents of group care facilities: a randomized controlled trial. *JAMA* 299(22), 2642–2655 (2008).
- 71 Dowling GA, Burr RL, Van Someren EJ *et al.* Melatonin and bright-light treatment for rest–activity disruption in institutionalized patients with Alzheimer's disease. *J. Am. Geriatr. Soc.* 56(2), 239–246 (2008).
- 72 Burns A, Allen H, Tomenson B, Duignan D, Byrne J. Bright light therapy for agitation in dementia: a randomized controlled trial. *Int. Psychogeriatr.* 21(4), 711–721 (2009).
- 73 Van Hoof J, Schoutens AMC, Aarts MPJ. High colour temperature lighting for institutionalised older people with dementia. *Build. Environ.* 44(9), 1959–1969 (2009).
- 74 Mccurry SM, Pike KC, Vitiello MV, Logsdon RG, Larson EB, Teri L. Increasing walking and bright light exposure to improve sleep in community-dwelling persons with Alzheimer's disease: results of a randomized, controlled trial. *J. Am. Geriatr. Soc.* 59(8), 1393–1402 (2011).
- 75 Figueiro MG, Plitnick B, Lok A *et al.* Tailored lighting intervention improves measures of sleep, depression and agitation in persons with Alzheimer's disease and related dementia living in long-term care facilities. *Clin. Interv. Aging* 9, 1527–1537 (2014).
- **• Shows a positive effect of a comfortable lighting intervention designed to maximally affect the circadian system in ADRD patients living in long-term care facilities.**
- 76 Sloane P, Figueiro M, Garg S *et al.* Effect of home-based light treatment on persons with dementia and their caregivers. *Light. Res. Technol.* 47(2), 161–176 (2015).
- Figueiro M, Plitnick B, Rea M. Research note: a self-luminous light table for persons with Alzheimer's disease. *Light Res. Technol.* 48(2), 253–259 (2016).
- 78 Montgomery P, Dennis J. Bright light therapy for sleep problems in adults aged 60+. *Cochrane Database Syst. Rev.* (2), CD003403 (2002).
- 79 Forbes D, Blake CM, Thiessen EJ, Peacock S, Hawranik P. Light therapy for improving cognition, activities of daily living, sleep, challenging behaviour, and psychiatric disturbances in dementia. *Cochrane Database Syst. Rev.* 2, CD003946 (2014).
- **• This review concluded there is insufficient evidence for light therapy improving sleep and behavior in ADRD patients, but none of the studies employed carefully controlled light sources.**
- 80 Hanford N, Figueiro MG. Light therapy and Alzheimer's disease and related dementia: past, present, and future. *J. Alzheimers Dis.* 33(4), 913–922 (2013).
- 81 Figueiro MG. A proposed 24 h lighting scheme for older adults. *Light. Res. Technol.* 40(2), 153–160 (2008).
- **• This publication summarizes studies demonstrating that a distinct, repeated**

pattern of light and dark is needed to help maintain the synchrony between the aging circadian system and the solar day.

- 82 Van Hoof J, Aarts MPJ, Rense CG, Schoutens AMC. Ambient bright light in dementia: effects on behaviour and circadian rhythmicity. *Build. Environ.* 44(1), 146–155 (2009).
- 83 Figueiro MG, Gras L, Rea M, Plitnick B, Rea MS. Lighting for improving balance in older adults with and without risk for falls. *Age Ageing* 41(3), 392–395 (2012).
- 84 Figueiro MG, Plitnick B, Rea MS, Gras LZ, Rea MS. Lighting and perceptual cues: effects on gait measures of older adults at high and low risk for falls. *BMC Geriatrics* 11, 49 (2011).
- 85 Figueiro MG, Rea MS. LEDs: improving the sleep quality of older adults. Presented at: *CIE Midterm Meeting and International Lighting Congress.* León, Spain, 12–21 May 2005.
- 86 Benedict C, Byberg L, Cedernaes J *et al.* Self-reported sleep disturbance is associated with Alzheimer's disease risk in men. *Alzheimer Dement.* 11(9), 1090–1097 (2015).
- 87 Lucey BP, Bateman RJ. Amyloid-beta diurnal pattern: possible role of sleep in Alzheimer's disease pathogenesis. *Neurobiol. Aging* 35(Suppl. 2), S29–S34 (2014).
- 88 Muto V, Jaspar M, Meyer C *et al.* Local modulation of human brain responses by circadian rhythmicity and sleep debt. *Science* 353(6300), 687–690 (2016).
- 89 Jean-Louis G, Kripke D, Cohen C, Zizi F, Wolintz A. Associations of ambient illumination with mood: contribution of ophthalmic dysfunctions. *Physiol. Behav.* 84(3), 479–487 (2005).