Light Therapy and Alzheimer's Disease and Related Dementia: Past, Present, and Future

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Abstract

Sleep disturbances are common in persons with Alzheimer's disease or related dementia (ADRD), resulting in a negative impact on the daytime function of the affected person and on the wellbeing of caregivers. The sleep/wake pattern is directly driven by the timing signals generated by a circadian pacemaker, which may or may not be perfectly functioning in those with ADRD. A 24-hour light/dark pattern incident on the retina is the most efficacious stimulus for entraining the circadian system to the solar day. In fact, a carefully orchestrated light/dark pattern has been shown in several controlled studies of older populations, with and without ADRD, to be a powerful non-pharmacological tool to improve sleep efficiency and consolidation. Discussed here are research results from studies looking at the effectiveness of light therapy in improving sleep, depression, and agitation in older adults with ADRD. A 24-hour lighting scheme to increase circadian entrainment, improve visibility, and reduce the risk of falls in those with ADRD is proposed, and future research needs are discussed.

Keywords

Alzheimer's Disease; Circadian Rhythm; Light Therapy; Wayfinding; Lighting Design; Sleep; Light; Alzheimer's; Circadian

Introduction

Alzheimer's Disease and Related Dementia (ADRD) is the most common mental disorder diagnosed in elderly Americans, with an estimated 5.1 million people afflicted in 2010 [1]. Behavioral symptoms such as disturbed sleep-wake patterns, nocturnal wandering, agitation, and physical or verbal abuse are among the most prevalent reasons why individuals with ADRD transition to more controlled environments. Abnormal sleep patterns tend to increase with the progression of ADRD and are associated with caregiver stress from disturbed sleep but also with aggressive behavior during the day. Because of this, research has aimed at treating symptoms, particularly with non-pharmacological options due to a low risk of side effects.

Circadian Rhythms

Most species on the planet endogenously generate circadian rhythms, which are constantly aligned with the environment by factors that are external to the body, mainly light/dark patterns reaching the back of the eye. In mammals, circadian rhythms are generated and

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regulated by an internal biological clock located in the suprachiasmatic nuclei (SCN) of the hypothalamus of the brain. The biological clock in humans has a natural period that is slightly greater than 24 hours, and environmental cues, such as light/dark cycles (strongest time giver), social activities, and meal times, can reset and synchronize the clock daily, ensuring that our behavioral and physiological rhythms are synchronized with the external environment [2]. As diurnal species, humans who are synchronized to the 24-hour solar day are typically awake during daytime hours and asleep during nighttime hours. Light can phase advance or phase delay human circadian rhythms, depending upon when it is applied [3]. For example, light that is applied before the minimum core body temperature, which is reached approximately 1.5 to 2.5 hours before we naturally awaken, will delay the timing of the biological clock (e.g., one will wake up later the following day), and light applied after minimum core body temperature is reached will advance the timing of the biological clock (e.g., one will wake up earlier the following day).

Lighting Characteristics Affecting Circadian Rhythms

The formal definition of light as described by the Illuminating Engineering Society of North America (IESNA) is "radiant energy that is capable of exciting the human retina and creating a visual sensation" [4]. The neural machinery in the mammalian retina provides light information to both the visual and circadian systems, but the two systems process optical radiation (light) differently [5]. Rods, cones and a newly discovered photoreceptor, the intrinsically photosensitive retinal ganglion cells (ipRGCs) [6] participate in circadian phototransduction (how the retina converts light signals into neural signals for the biological clock). The quantity of polychromatic "white" light necessary to activate the circadian system is at least two orders of magnitude greater than the amount that activates the visual system. The circadian system is maximally sensitive to short-wavelength ("blue") light, with a peak spectral sensitivity at around 460 nm, while the visual system is most sensitive to the middle-wavelength portion of the visible spectrum, peaking at around 555 nm. Operation of the visual system does not depend significantly on the timing of light exposure, and thus responds well to a light stimulus at any time of the day or night. On the other hand, the circadian system is dependent on the timing of light exposure, as discussed above. In addition, while the visual system responds to a light stimulus very quickly (in milliseconds), the duration of light exposure needed to affect the circadian system can take minutes. For the visual system, spatial light distribution is critical for good visibility. It is not yet well-established how light incident on different portions of the retina affects the circadian system. It is also important to note that the short-term history of light exposure affects the sensitivity of the circadian system to light; the higher the exposure to light during the day, the lower the sensitivity of the circadian system to light, as measured by nocturnal melatonin suppression and phase shifting.

Light and the Aging Circadian System

Studies of the biological clock have shown a reduced neuronal activity in the SCN of the elderly, especially after the age of 80 [7], and reduced circadian rhythm amplitude after the age of 50 [8]. This suggests that, at a molecular level, the SCN becomes less responsive to entrainment stimuli such as light-induced neural signals from the retina. Further, it is suggested that some of the neural processes involved in the entrainment process might be dysfunctional or less effective as we age [9]. Light information travels from the retina to the SCN through the retinohypothalamic tract (RHT). Disturbances in circadian rhythms leading to poor sleep in older adults can be the result of dysfunctional circadian pathways or a pathway that cannot process light information with as much fidelity. Also, the first stage of phototransduction (when light signals are converted into neural signals) is negatively affected: older adults not only have reduced optical transmission at short wavelengths, which is maximally effective for the circadian system, they also lead a more sedentary

indoor lifestyle, with less access to bright light during the day [10–13], potentially increasing the risk for circadian disruption. In fact, Figueiro et al. measured, using a calibrated light-measuring device, circadian light exposures in healthy older adults and in persons with ADRD during two seasons (fall/winter and spring/summer). Using the metrics calculated from light/dark and activity/rest patterns collected over 5 consecutive days, they demonstrated that persons with ADRD are more disrupted than healthy older adults and that this circadian disruption is more pronounced during winter months, when there is less daylight availability [14].

Finally, changes in the amplitude and timing of melatonin and core body temperature, both output rhythms of the biological clock, may occur in older adults. Melatonin is a hormone produced at night and in darkness and is believed to be a timing messenger to the body, indicating to all cells that it is circadian night. Lower amplitudes of melatonin rhythms may be associated with reduced sleep efficiency and deterioration of internal circadian rhythms, affecting hormone production, alertness, and performance [15]. Furthermore, earlier timing of melatonin rhythms' peaks may induce earlier drops in core body temperature, resulting in early wake times (reviewed in [16]). These changes in biological markers, closely associated with the biological clock, may be a result of deterioration of the functioning of the biological clock.

Behavior, Mood, and Sleep Disturbances in Persons with ADRD

Sleep Disturbances

Sleep disturbances are among the more common neurobehavioral symptoms of ADRD. An increased tendency to fall asleep during the daytime, together with increased wakefulness during the night has been demonstrated in patients with advanced but also mild to moderate ADRD [17]. Research estimates that ADRD patients will spend approximately 40% of their night awake and a large portion of the solar day asleep [18–20]. Sleep disturbances eventually become too burdensome for familial caregivers and are the leading cause of persons with ADRD institutionalization [21–24].

An indirect, negative impact of sleep disturbances is the risk of falling, which is exacerbated by disrupted circadian rhythms because persons with ADRD are more likely to wake in the middle of the night under little or no light. Often these patients get out of bed, either to use the restroom or just wander around their room. Persons with ADRD are about 3 times more likely to fall [25–27] and their recovery is generally longer than that of healthy older adults [28].

Agitated Behavior

Once institutionalized, patients who suffer from the most sleep disturbances at night are likely to become aggressive during the day [29]. Sundowning—increased agitation in the late afternoon and early evening—may also contribute to aggressive behavior, and the aggression eventually leads to negative outcomes for both persons with ADRD and nursing staff; approximately 93% of nursing home residents and 42% of assisted living residents display dementia-related aggression [30–32].

Depression

A common symptom that manifests within older adults with ADRD is depression, likely because they experience greater social isolation. The American Geriatrics Society states that depression occurring simultaneously with dementia is the most common affliction for older adults in nursing homes [33]. Depression can lead to poorer health outcomes, psychological

distress, and functional impairment. In addition, these depressive symptoms can place added stress on caregivers in both institutions and homes [1].

Lighting for Persons with ADRD

Sleep Disturbances

Clinical research has shown that light therapy can consolidate rest and activity patterns in people with ADRD [34–51]. It is important to emphasize that almost none of the published studies utilized photometric terms or instrumentation appropriate to quantify the impact of light on the retina for circadian effectiveness. Table 1 summarizes several studies [34–51] that have investigated the effects of light therapy on sleep disturbances in persons with ADRD. Light levels reported in Table 1 are in photopic lux. Consequently, generalizations from these studies must remain qualitative (e.g., bright vs. dim) rather than quantitative. Nevertheless, bright light exposure during the morning (typically >1000 lux at the cornea) has been shown to improve nighttime sleep, increase daytime wakefulness, reduce evening agitation behavior, and consolidate rest/activity patterns of people with ADRD [34, 35, 38, 39–42, 47–51, 57]. All-day, uncontrolled exposure to >1000 lux at the cornea of a white light (4100K) improved sleep efficiency and cognition in persons with ADRD as well as reduced symptoms of depression [36, 43]. Dawn-dusk simulation—a lighting system that appropriately moderates light levels according to time of day—has had some success in a 3-week trial study [46]. Evening light exposure has also been shown to be effective in consolidating rest/activity rhythms of those with ADRD and helping them to sleep better at night [37, 39, 51]. Lower levels (30 lux at the cornea) of light sources that are more tuned to the spectral sensitivity of the circadian system, such as narrowband short-wavelength (blue) light administered for 2 hours in the early evening were also shown to be effective in increasing sleep efficiency in persons with ADRD [44,45].

Agitation

Bright light does appear to be a treatment possibility for aggressive behavior in ADRD patients. Burns et al. [52] showed improvements in Cohen-Mansfield Agitation Inventory (CMAI) and Crichton Royal Behavior Rating Scale (CRBRS) scores after 2 weeks of late morning (10:00–12:00) light therapy at 10,000 lux. Skjerve and colleagues [53] administered a bright light regimen of 5000–8000 lux for 45 minutes per day, which resulted in significant improvements in CMAI and Behavior Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) scores. Thorpe et al. [54] also showed that 30 minutes exposure to morning light (10,000 lux at the cornea) improved CMAI scores. It is suggested that the impact of light on reducing CMAI scores may be greater in those who have higher CMAI scores [55]. The effects of light therapy on agitation were also shown in those with vascular dementia, the second most common type of dementia [56].

Dowling and colleagues [57] found that exposing persons with ADRD to bright light at 2500 lux at varying times of day had diverse effects on aggressive behaviors. While both morning and afternoon exposures were successful in significantly altering the levels of aggressive behaviors, specifically agitation, depression, aberrant motor behavior, and appetite, the timing of treatment was of great importance in the outcome of treatment. Morning light exposure was shown to be more effective than afternoon light exposure in this case. Haffmans et al. [58], with a regimen of morning light therapy (30 minutes, between 08:00 and 11:00, from a 10,000 lux light box), improved motor restlessness in ADRD patients.

Depression

While positive effects of light therapy have been shown in some cases of depression [59, 60] mixed results have come with the attempt to treat depression symptoms in ADRD patients with light therapy.

In their long-term study, Riemersma-van der Lek and colleagues [43] showed a significant improvement in Cornell Scale for Depression in Dementia (CSDD) scores over an average length of 15 months of light therapy. Likewise, Hickman and colleagues [61] showed a positive effect for female ADRD patients when treated with morning bright light (2000–2500 lux), but researchers also believed that patients with higher CSDD scores were necessary for a better understanding of the influences of light therapy on depression.

Risk of Falls

Figueiro et al. [62, 63] proposed a novel night lighting approach to the living environment that could improve postural control and stability. They showed in a series of studies that the use of strips of LEDs placed around a doorframe, providing vertical and horizontal cues, decreased sway and reduced weight transfer time compared to having a typical nightlight providing dim lighting in the environment. In another study, Figueiro et al. [64] found that the addition of pathway lights to an environment lit with dim light from an incandescent nightlight increased velocity and decreased step length variability during walking.

Proposed 24-Hour Lighting Scheme

Figueiro [65] proposed, based on theoretical knowledge about how light impacts aging vision, circadian and perceptual systems, a 24-hour lighting scheme that is designed to provide: a) high circadian stimulation during the day and low circadian stimulation at night, b) good visual conditions during waking hours, and c) nightlights that are safe and minimize sleep disruption. It was proposed that high circadian stimulation be provided by 1000 lux or higher at the cornea from a circadian-effective white light source for at least 2 hours during the day. If longer exposures of light are planned, light levels may be reduced to no less than 600 lux at the cornea from the same circadian-effective white light source. No more than 60 lux at the cornea of a circadian-ineffective white light source (e.g., 2700K compact fluorescent lamp or LEDs) is recommended for general lighting in the evening hours.

Although the exact amount of light needed to impact the circadian systems of those with ADRD is not known, it is possible to theoretically compare a variety of practical light sources in terms of their ability to provide a criterion response by the circadian system (50% nocturnal melatonin suppression) for a fixed, small pupil size (2.3 mm diameter), as shown in Table 2 [66]. It should also be noted that the relationship between melatonin suppression and consolidation of rest/activity rhythms remains unclear. Since commercially available light meters are always calibrated in terms of the photopic luminous efficiency function, the levels of photopic illuminance needed at the eye are used as the measure of the amount of light needed to reach the criterion response. It is worth noting that under natural viewing conditions, pupil size can be larger than 2.3 mm in diameter, so a lower level of illuminance would be needed to reach this criterion level of melatonin suppression. Generally then, for light sources providing the same photopic light level, the greater the proportion of short-wavelength (visible) radiation from the source, the more effective it will be for stimulating the human circadian system. More importantly, although there is no compelling reason to assume that acute melatonin suppression and phase shifting of the timing of the biological clock respond differently to a light stimulus, it is important to keep in mind that the calculations presented in Table 2 are based on studies where only acute melatonin suppression was measured.

Further research should be conducted to determine minimum light levels needed to impact the circadian systems of those with ADRD and to verify how the estimations presented in Table 2 affect rest/activity patterns in those with ADRD. More importantly, it is not known how light levels can be reduced with increased duration of exposure. It has been shown in a 2-week light treatment study that delivering 30 minutes of a bright white light (4200 lux) in the morning to memory-impaired older adults and their caregivers improved sleep and mood in caregivers, but diminished sleep in those with memory impairment [67]. It has been suggested that light therapy's effect on sleep in those with ADRD is only measurable after 6 months of treatment possibly because these patients are slower to respond to the stimulus [43].

Daylight from windows and clerestories is a circadian-effective light source, but, it should not be assumed that there will always be enough circadian stimulation from daylight in architectural spaces [68]. Daylight levels in the room drop quickly as the distance from the window increases; 3–4 meters away from a window, daylight levels are quite low, even on a sunny day. It should be noted too that if sunlight from the window penetrates the room, discomfort glare will cause occupants to draw blinds or shades, eliminating daylight entirely from the space.

If energy consumption is a constraint, the architect can either select specific spaces to implement the proposed lighting scheme or follow a scheme similar to the one used in the experiments by Figueiro et al. [44, 45] by providing another layer of blue light in the morning. Portable luminaires providing diffuse blue light from LEDs (λ_{max} = 470 nm) can be placed on dining tables, around television screens, or attached to wheelchairs. It is not known, however, how successful compliance with these light delivery methods will be and how acceptable this kind of light source will be to users.

Good visual conditions for waking hours can be provided by lighting that is high, on the task, glare-free with no direct or reflected view of the light source, with softer shadows throughout the space, with balanced illuminance levels, and with good color rendering characteristics [69].

Just as important, the proposed 24-hour lighting scheme should provide nightlights that reduce the risk of falls and help maintain sleep. Figueiro [65] proposed the use of nightlights that provide visual information about the local environment (5 to 10 lux at the cornea) as well as perceptual information that enables the residents to orient [62–64]. The proposed nightlights accent the rectilinear architectural features in the room as well as accentuate horizontal pathways to the bathroom. The use of motion sensors with dim nightlights eliminates the need to find switches in the dark and helps residents to remain asleep when caregivers enter the room. The use of low light levels allows older people to navigate through the space safely without disrupting their sleep. This proposed novel nightlighting system needs to be tested in persons with ADRD and installed in the field, but it has promising features to help reduce the risk of falls in those with ADRD.

Conclusions

Past: Persons with ADRD exhibit random patterns of rest and activity rather than the consolidated sleep/wake cycle found in healthy, older adults. This lack of sleep consolidation is one of the main reasons why they are institutionalized. Light therapy has been shown to improve rest/activity rhythms and sleep efficiency in persons with ADRD in some, but not all, studies, presumably through consolidation of their circadian rhythms. *Present:* While additional research is still needed to test the effectiveness of a 24-hour lighting scheme on vision, circadian regulation, and the risk of falls in older adults with

ADRD, it must be true that the proposed lighting scheme discussed here will provide a better light/dark pattern for the circadian system than the dim unvarying ones commonly found in senior care facilities. *Future*: Positive results can be obtained, however, if thoughtful, quantitative lighting solutions based upon basic principles of circadian regulation are designed while still paying attention to maintaining good vision and safety while awake and minimizing sleep disruption at night.

Acknowledgments

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Table 1

Bright light therapy studies, lighting characteristics given by researchers and effects seen.

Author	Protocol	Participants	Light Level (lux)	Exposure Duration	Results
Satlin et al. 1992[37]	open clinical trial-evening bright light	10 hospital patients	1500–2000	2 hours 19:00–21:00	sleep wake patterns (ID variability) improved, nighttime activity decreased, improved ratings of sleep-wakefulness
Colenda et al. 1997[47]	single subject, 28 days total	5 community dwelling	2000	2 hours 07:00–09:30	no significant changes from baseline in acrophase, mesor or amplitude in 4 of 5 subjects
Van Someren et al. 1997[36]	open trial	22 inpatients	varied mean = 1130	all day	increased interdaily stability
Okumoto et al. 1998[50]	open trial	1 nursing home resident	4000	2 hours 09:30–11:30	consolidated sleep episodes at night
Koyama et al. 1999[49]	open trial	6 nursing home residents	4000	late morning	percent sleep increased and percent wakefulness in daytime increased in 3 of the 6 subjects; in the other 3, sleep onset was advanced
Lyketosos et al. 1999[38]	randomized controlled crossover trial	15 inpatients in a chronic care facility	10,000	1 hour morning	significant improvement in nocturnal sleep amount after 4 weeks
Yamadera et al. 2000[40]	1-week adaptation, 1-week pre-treatment, 4-week treatment	27 hospital patients	3000	09:00–11:00	significant improvement in circadian rhythms disturbances and in cognition
Ancoli-Israel et al. 2002[51]	randomized controlled trial; evening bright light, morning bright light, evening dim red light or daytime sleep restriction	77 nursing home residents	2500	17:30–19:30 or 09:30–11:30	no improvements in nighttime sleep or daytime alertness in any group; morning bright light delayed the peak of the activity, increased mean activity and improved activity rhythmicity
Fetveit et al. 2003[34]	open non-randomized	11 nursing home residents	6000–8000	2 hours within 08:00–11:00	sleep efficiency increased, total wake time reduced, sleep onset latency reduced
Ancoli-Israel et al. 2003[39]	randomized controlled trial; morning bright light, morning dim red light or evening bright light	92 nursing home residents	2500	2 hours 09:30–11:30 or 2 hours 17:30–19:30	more consolidated sleep at night and improve rhythm stability
Fontana Gasio et al. 2003[46]	randomized controlled trial	13 nursing home residents	mean = 200	all day dawn-to-dusk simulator	earlier onset sleep time and longer sleep duration
Figueiro et al. 2003[45]	placebo controlled crossover design; 2 weeks of 640-nm (red) light and 2 weeks of 470-nm (blue) light	4 nursing home residents	30	2 hours 18:00–20:00	470-nm light delayed decline in tympanic temperature and increased observations of nighttime sleep efficiency
Fetveit and Bjortvan 2005[48]	pre-treatment, treatment and post treatment	11 nursing home residents	6000–8000	2 hours within 08:00–11:00	average and total daytime nap duration were reduced
Dowling et al. 2005[41]	randomized bright light to usual light and randomized morning bright light to afternoon bright light	46 nursing home residents	>2500 mean = 7500	1 hour between 09:30–10:30	no significant changes in sleep efficiency, sleep time, wake time, or number of awakenings between experimental group and control group;

Author	Protocol	Participants	Light Level (lux)	Exposure Duration	Results
					improved rhythm stability in those with most impaired rest-activity rhythms
Alessi et al. 2005[35]	randomized controlled trial	118 nursing home residents	sunlight >10,000	at least 30 minutes	significant decrease daytime sleep and decrease in duration of nighttime awakenings; increased participation in social activities
Figueiro and Rea 2005[44]	placebo controlled crossover design; 10 days of 640-nm (red) light and 10 days of 470-nm (blue) light crossover	4 nursing home residents	30	2 hours 17:00–19:00	increased observations of nighttime sleep efficiency after 470-nm light exposure compared to 640-nm light
Sloane et al. 2007[42]	intervention trial; morning bright light, evening bright light and all day bright light	66 inpatient and residential care	2500	2 hours 07:00–11:00 or 2 hours 16:00–20:00 or 07:00–20:00	nighttime sleep increased in the morning and all day light groups, morning light phase advance and evening light phase delay
Riemersma-van der Lek et al. 2008[43]	long term (3.5 yrs) randomized double blind placebo-controlled whole-day bright or dim light and evening melatonin or placebo	189 care facility residents	Bright: 1000 Dim: 300	09:00–18:00	bright light alone attenuated cognitive deterioration by a relative 5%, ameliorated depressive symptoms by a relative 19%, and attenuated the increase in functional limitations over time by relative 53%

Table 2

Photopic illuminance to achieve 50% melatonin suppression. Several practical light sources with the required photopic illuminance (lux, or lm/m^2) levels at the eye, having a fixed pupil diameter of 2.3 mm, for 50% nocturnal melatonin suppression after one hour exposure (adapted from [66]). Although the absolute numbers will vary depending on pupil area, duration of exposure, exact spectral power distribution of the light source, distance from the source, the numbers in Table 2 can be used to determine the relative effectiveness of these different light sources as it may impact acute melatonin suppression, one marker of the biological clock. Whether or not these values are the same for estimating phase shifting of the timing of the biological clock by these light sources is still not established.

Light Source	Illuminance (lux)
2700 K compact fluorescent (Greenlite15WELS-M)	1220
2856 K incandescent A lamp	820
3350 K linear fluorescent (GE F32T8 SP35)	1180
4100 K linear fluorescent (GE F32T8 SP41)	1070
5200 K LED phosphor white (Luxeon Star)	430
6220 K linear fluorescent (Philips Colortone 75)	550
8000 K fluorescent (OSRAM Sylvania Lumilux Skywhite)	610
Blue LED (Luxeon Rebel, λ_{max} = 470 nm)	50
Daylight (CIE D65)	525