Practice Parameters for the Use of Light Therapy in the Treatment of Sleep Disorders

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Summary: These clinical guidelines were developed by the Standards of Practice Committee and reviewed and approved by the Board of Directors of the American Academy of Sleep Medicine. The guidelines provide recommendations for the practice of sleep medicine in North America regarding the use of light therapy for treatment of various sleep disorders. This paper is based on a series of articles in the Journal of Biological Rhythms and also includes evidence tables from an updated Medline review covering the period January 1994 to December 1997. Evidence is presented by grade and level. Recommendations are identified as standards, guidelines, or options. Recommendations are provided for delayed sleep phase syndrome (DSPS), advanced sleep phase syndrome (ASPS), non-24-hour sleep-wake syndrome, jet lag, shift work, dementia, and sleep complaints in the healthy elderly. Light therapy appears generally safe if used within recommended intensity and time limits. Light therapy can be useful in treatment of DSPS and ASPS. Benefits of light therapy are less clear and treatment is an option in jet lag, shift work, and non-24-hour sleep-wake syndrome in some blind patients.

Key words: practice guidelines, practice parameters, light therapy, sleep disorders, delayed sleep phase syndrome, advanced sleep phase syndrome, jet lag, shift work, circadian rhythm disorders

INTRODUCTION

ENDOGENOUS CIRCADIAN RHYTHMS are in large part regulated by the hypothalamic suprachiasmatic nuclei (SCN) located near the bifurcation of the optic nerves. By regulating rhythms that promote sleep and wakening, the SCN are key regulators of sleep. It is now recognized that a number of sleep disorders are linked to abnormal circadian rhythms or a lack of coordination of the sleep-wake cycle with the individual's circadian rhythms.

The SCN are thought to be the primary circadian clock in man. The natural period of the circadian clock is normally slightly longer than 24 hours. External factors such as shift work can misalign sleep-wake cycles and circadian rhythms driven by the SCN. One of the most potent external factors that can alter the period of the SCN is light.

Recently, commercial devices have become available to provide artificial external light of varying intensities to treat patients with a variety of sleep disorders. This report provides clinical recommendations for the use of light therapy in sleep disorders.

METHODS

Based on the referenced review[1-7] and accompanying evidence tables, the Standards of Practice Committee of the American Academy of Sleep Medicine, in conjunction with specialists and other interested parties, developed this article and recommendations. In most cases, the conclusions are based on evidence from controlled studies that were published in peer-reviewed journals. When scientific data are insufficient or inconclusive, this is pointed out and the recommendations are based upon consensus opinion. Recommendation grades and evidence levels are identified.

The companion review paper series[1-7] was published prior to more recent emphasis on evidence based methodology for practice parameters. For this reason, evidence tables and supplemental text, which were not a part of the review papers, are provided in this paper on topics critical to the issues addressed by the practice parameters. The updated search for this paper was based on the following key words: light therapy, sleep disorders, delayed sleep phase syndrome, advanced sleep phase syndrome, non-24

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hour-sleep phase syndrome, jet lag, shift work, healthy elderly, dementia, demented, aging, elderly, circadian rhythm disorders, practice guidelines, and practice parameters in the Medline database from January 1994 to December 1997.

The Board of Directors of the American Academy of Sleep Medicine approved these recommendations. All members of the American Academy of Sleep Medicine's Standards of Practice Committee and Board of Directors completed detailed conflict-of-interest statements and were found to have no conflicts of interest with regard to this subject.

These practice parameters define principles of practice that should meet the needs of most patients in most situations. These guidelines should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed towards treating these disorders. The ultimate judgment regarding propriety of any specific care must be made by the physician in light of the individual circumstances presented by the patient and the available diagnostic and treatment options and resources.

The American Academy of Sleep Medicine expects these guidelines to have an impact on professional behavior, patient outcomes and, possibly, health care costs. These practice parameters reflect the state of knowledge at publication and will be reviewed, updated, and revised as new information becomes available.

Parentheses are used in this article to reference pertinent data in the accompanying evidence tables or the reference list from this position paper.

BACKGROUND

Over the past two decades, laboratory studies have demonstrated that scheduled light exposure can produce a dose-dependent phase shift in the endogenous circadian rhythms of a variety of variables. These variables include plasma or saliva melatonin, core body temperature, cortisol and a propensity to sleep. Light reaches the SCN through the retinohypothalamic tract and the geniculo-hypothalamic tract. Light pulses induce changes in the firing rates of specialized neurons in the SCN which in turn affect circadian rhythms.[5] A recent study suggests that extraocular light (such as behind the knees) may also affect circadian rhythms.[8]

The sleep-wake cycle is synchronized to the activity of the SCN. However, the output of the SCN cannot be easily and directly measured in humans. Two indirect measures of the phase of SCN activity are dim light melatonin secretion onset and timing of the core body temperature minimum. In clinical practice, diaries and other historical information, although imperfect, have been used to document the sleep-wake cycle as a reflection of the activity of the SCN.

The rationale for the use of light therapy evolves from the observation that circadian rhythms in humans can be phase shifted by scheduled exposure to light. Because of an endogenous pattern of light sensitivity, the direction of the phase shift can vary with the timing of the light exposure. The responses of circadian rhythms to light exposure have been summarized in Phase Response Curves (PRC). The PRC appears phase locked to the core body temperature and plasma melatonin concentration rhythm. In healthy young subjects, with a normal sleep pattern and temperature curve, the core body temperature minimum typically occurs approximately two hours before habitual wake time (around 4 to 5 a.m.). Light exposure prior to the endogenous minimum of the core body temperature will shift rhythms to a later clock time (i.e., will delay rhythms). For example, if sleep onset is normally at 10 p.m. and there is a two-hour phase delay, sleep onset will begin at midnight. Light exposure just after the endogenous circadian body temperature minimum will shift rhythms to an earlier clock time (i.e., will advance rhythms).

A number of sleep disorders may respond to light therapy. These include the circadian rhythm disorders of advanced sleep phase syndrome, delayed sleep phase syndrome, non-24 hour sleep-wake cycle, jet lag, and shift work. There is also age-related fragmented sleep in healthy and demented individuals which may include, in demented individuals, nocturnal delirium and sundowning. The age-related effects on sleep may be the result of age-related changes in circadian rhythms.

Experimental designs have only in a limited way addressed the issue of comparing efficacy of bright light, delivered by natural sunlight, versus that delivered by artificial light sources. This issue could be pertinent throughout the review but perhaps has the greatest implications for the jet lag and shift work sections. Unintended natural bright light exposure can be common in these situations and may have unplanned (and even adverse) effects both as a confounder of experimental design and of clinical intervention. In addition, the relative ease and inexpensive nature of obtaining exposure by sunlight, compared to requiring special equipment, makes this a practical consideration for potential therapeutic use. It may be possible for the reader to speculate about the effects of natural light from the artificial light data, but direct evidence is lacking.

Unless otherwise specified, the designation of sleep disorders in this paper will follow the International Classification of Sleep Disorders (ICSD).[9] Specific guidelines for diagnosis for each disorder are included in the ICSD.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis is often similar for the following group of circadian sleep disorders but an established diagnosis should be identified in order to utilize light therapy

appropriately. The differential diagnoses typically included are: delayed sleep phase syndrome (DSPS), advanced sleep phase syndrome (ASPS), other forms of primary and secondary insomnia including depression, non-24-hour sleep-wake syndrome, irregular sleep-wake disorder, shift work, jet lag, and voluntary shifts of sleep-wake schedules.

I. General Recommendations

Following the safety and general recommendations sections, each of the conditions for which practice parameter recommendations were considered will be addressed by topic. The classification for evidence was adapted from the suggestions of Sackett[10] (Table 1). Recommendations are given as standards, guidelines and options, as defined in Table 2. Unless otherwise specified, the recommendations in this paper are supported by Level II to Level V evidence.

TABLE 1. Classification of Evidence

Recommendation Grades	Evidence Levels	Study Design
A	I	Randomized well-designed trials with low-alpha & low-beta errors*
B	II	Randomized trials with high-beta errors*
C	III	Nonrandomized controlled or concurrent cohort studies
C	IV	Nonrandomized historical cohort studies
C	V	Case series

*Alpha error refers to the probability (generally set at 95% or greater) that a significant result (e.g., $p<0.05$) is the correct conclusion of the study or studies. Beta error refers to the probability (generally set at 80% or 90% or greater) that a nonsignificant result (e.g., $p>0.05$) is the correct conclusion of the study or studies. The estimation of beta error is generally the result of a power analysis. The power analysis includes a sample size analysis which projects the size of the study population necessary to ensure that significant differences will be observed if actually present.

TABLE 2. Definitions

Term	Definition
Standard	This is a generally accepted patient-care strategy which reflects a high degree of clinical certainty. The term standard generally implies the use of Level I Evidence, which directly addresses the clinical issue, or overwhelming Level II Evidence.
Guideline	This is a patient-care strategy which reflects a moderate degree of clinical certainty. The term guideline implies the use of Level II Evidence or a consensus of Level III Evidence
Option	This is a patient-care strategy which reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.

Safety and Side Effects

a) A prescribing physician should be aware of dosage recommendations, potential side effects and recommended light intensity limits if light therapy is to be used.[5] (Standard)

b) Light therapy appears to be a generally safe treatment option for some circadian rhythm disorders when used within reported guidelines for light intensity and time limits.[1,6,7] (Guideline) Based on one study, light intensity of 10,000 lux for 1250 hours over 5 years produced no major side effects.[12] The authors note minor side effects such as eye irritation were controlled by dose reduction. Other side effects reported include irritability, headache, nausea, increased sensation of glare, erythema reactions usually from UV light (which can be prevented with UV-shielding), dryness of eyes, and dryness of skin (which can be prevented with a humidifier). Rarely, light therapy may provoke a hypomanic state in patients with bipolar affective disorders.[13]

Treatment Objectives and Indications

Treatment is indicated only if there is a desire on the patient's part to resolve symptoms. The objective is to achieve a sleep onset at either a more socially acceptable time or at a time that provides sufficient sleep in keeping with the work schedule or lifestyle. Specific recommendations based on specific disorders will be given under each condition.

Alternative Strategies

Proper sleep hygiene is recommended as an adjunct to any light therapy. Some ASPS or DSPS patients may have an extrinsic type of the syndrome where external influences such as work hours or social obligations are driving the advanced or delayed sleep onset.[9] In such cases, modification of the external influence may treat the syndrome. New data on these alternatives as well as data on pharmacotherapy approaches are evolving in the literature but analysis of those data is not within the scope of this project.

Follow-Up

Many patients may have initial success but relapse due to failure to maintain the treatment progress. Use of counseling and other means of ensuring adherence to treatment has not been examined.[1-7] Objective documentation is generally limited to a shift in the core body temperature minimum, a shift in the onset of dim light melatonin secretion or in the peak of the melatonin rhythm, information the patient has recorded in diaries, or actigraphic measurement of rest/activity patterns. Subjective documentation is also used by asking patients if they have responded.

Light Therapy Dose Levels

Tables 3 through 6 present light therapy dose levels. This is a rapidly evolving area of investigation and these dosage recommendations may change. Recommendations in this paper will be based on the studies identified but the reader is encouraged to check the most current literature since this data is changing rapidly as more studies become available.

2.0 RECOMMENDATIONS FOR SPECIFIC DISORDERS

2.1 DELAYED SLEEP PHASE SYNDROME

Delayed sleep phase syndrome is a disorder in which the major sleep episode is delayed in relation to the desired clock time and results in symptoms of sleep-onset insomnia and/or difficulty in awakening at the desired time.[9] Core body temperature minimum and peak of the melatonin rhythm are shifted to later in the morning than normal (Table 3).

Treatment Objectives and Indications

Based on the human PRC, a phase advance will take place if the subject is exposed to light after the peak of melatonin rhythm or minimum of core body temperature, usually in the early morning.

Supported by Level II and Level III evidence, the following practice parameter with regard to light therapy in the treatment of DSPS is a Grade B-C recommendation.

a) Light therapy appears to have potential utility, based on current study data, in the treatment of DSPS.[7] (Guideline) For use of light therapy in the treatment of DSPS, 2000 to 2500 lux from 6 to 9 a.m. and optionally wearing dark goggles from 4 p.m. to dusk is an approach that has been studied with apparent effectiveness (Table 3). However, some patients will have a temperature minimum during or after this light exposure time period and may not respond or respond paradoxically with a phase delay rather than a phase advance. In those patients who do not respond as expected and in whom information such as sleep diary entries or, if available, melatonin rhythm or core body temperature suggests a peak rhythm or core body temperature minimum at a time after the exposure to light therapy, a later morning time period for light therapy (e.g., after 9 a.m.) may be tried.

b) The minimum or optimal duration of light therapy for DSPS is unknown. (Option) In one study, 12 days of bright light was successful in shifting core body temperature and improving sleep efficiency and was rated better than dim light (Table 3). In addition, the duration of therapy necessary to provide continuing effectiveness is unknown as is the possibility of tolerance (i.e., loss of benefit over time) to the therapy.

2.2 ADVANCED SLEEP PHASE SYNDROME

Advanced sleep phase syndrome is a disorder in which the major sleep episode is advanced in relation to the desired clock time and results in symptoms of compelling evening sleepiness, an early sleep onset, and an awakening that is earlier than desired.[9] Core body temperature minimum and peak melatonin rhythm occur earlier in the morning than usual.

Treatment Objectives and Indications

Based on the human PRC, a phase delay will take place if the subject is exposed to light soon after the dim light melatonin secretion onset or core body temperature maximum, usually in the evening.

Supported by Level II and Level III evidence, the following practice parameter with regard to light therapy in the treatment of ASPS is a Grade B-C recommendation.

a) Light therapy appears to have potential utility, based on current study data, in the treatment of ASPS.[7] (Guideline) For the use of light therapy in the treatment of ASPS, 2500 lux for four hours from 8 p.m. to midnight, or 4000 lux for two or three hours from 8 or 9 p.m. to 11 p.m. are approaches that have been studied with apparent effectiveness (Table 3). However, some patients may have a temperature maximum substantially before this time period and may not respond with a phase delay. In those patients exposure to light at an earlier time period may be attempted.

b) The minimum or optimal duration of light therapy for ASPS is unknown. (Option) In one study 25 days of bright light was successful in shifting core body temperature and improving sleep efficiency and performance (Table 3). In addition, the duration of therapy necessary to provide continuing benefit is unknown as is the possibility of tolerance (i.e., loss of effectiveness over time) to the therapy.

2.3 NON-24-HOUR SLEEP-WAKE SYNDROME

Non-24-hour sleep-wake syndrome is a syndrome in which patients fall asleep at a different time each day because the circadian period differs from 24 hours.[9] For example, on day one the patient may fall asleep at 10 p.m., day two at 12 midnight, day three at 2 a.m. etc. Patients may have either insomnia or hypersomnia depending on which phase of the circadian cycle they are in when trying to sleep. Core body temperature cycles may be greater in length than normal. Blind individuals are a special case since the normal sleep-wake cycle may be longer than 24 hours and if no light reaches the SCN, there may not be natural resetting of the circadian clock to 24 hours. Totally blind individuals, such as those whose eyes have been enucleated, comprise a minority of the legally blind. These individuals will have no retinal response to light and may have free-running circadian rhythms. Light therapy is of no confirmed benefit in these patients. However, some blind individuals who have this syndrome may be responsive to light therapy despite no apparent perception of visible light.

Treatment Objectives and Indications

Currently there are very few studies on which to base a strategy but some reports suggest that morning light may work (Table 3). Other studies are negative (Table 3). Based on the phases of the light PRC, a phase advance will take place if the subject is exposed to light at a time soon after the peak melatonin rhythm or core body temperature minimum in the morning, which would regularize the circadian cycle to a more typical sleep/wake cycle. However, care needs to be taken to ensure that the patient is not in a portion of the PRC such that the morning light exposure occurs after the dim light melatonin secretion onset or core body temperature maximum and before the temperature minimum or peak melatonin rhythm. In such a case, there could be no response or a phase delay.

Supported by Level III evidence, the following practice parameter with regard to light therapy in the treatment of non-24-hour sleep-wake syndrome is a Grade C recommendation.

a) Light therapy may be of benefit in treating some blind patients with non-24-hour sleep-wake syndrome.[7] (Option) For the use of light therapy in the treatment of non-24-hour sleep-wake syndrome, 3300 lux for one hour between 6 and 8 a.m. is an approach that has been studied with apparent effectiveness for blind persons. No recommendation for sighted individuals is made since insufficient data is available (Table 3). If the expected response does not occur, an adjustment of the timing of the light exposure may be attempted to produce the phase advance or delay depending on information such as sleep diary entries or, if available, core body temperature maximum or minimum or dim light melatonin secretion onset or peak of the melatonin rhythm.

b) The minimum duration of light therapy for non-24 hour sleep-wake syndrome is unknown. (Option) In one study 14 days of bright light was successful in improving symptoms and increasing melatonin secretion (Table 3). In addition, the duration of therapy necessary to provide continuing effectiveness is unknown as is the possibility of tolerance (i.e., loss of effectiveness over time) to the therapy.

2.4 JET LAG

Jet lag is produced by transmeridian travel across multiple time zones. This leads to difficulty in initiating or maintaining sleep, daytime sleepiness, decrements in daytime alertness and performance, gastrointestinal distress, and other psychosomatic manifestations.[1,9] Although only symptoms produced by altered temporal relations between the circadian timing system and the new local day-night cycle are attributable to jet lag, similar symptoms may be caused by flight-related stress, fatigue, and sleep loss. These latter symptoms are likely to resolve in a few days.

Treatment Objectives and Indications

Supported by conflicting Level II to Level V evidence, the following practice parameter with regard to light therapy in jet lag is a Grade C recommendation.

While the evidence is minimal and sometimes conflicting, bright light exposure at destination in order to enhance circadian re-entrainment would appear safe and potentially beneficial for travelers across multiple time zones.[1] (Option)

Bright light exposure in the morning at destination after eastward travel could potentially enhance phase-advance re-entrainment (Table 4). Some evidence supports using bright light therapy in the range of 2000-5000 lux for about three hours in the morning for about three days at destination. However, conflicting evidence also exists. One problematic issue is that after crossing a large number of time zones, morning bright light exposure at destination may be associated with undesirable phase shifts if administered prior to the circadian body temperature minimum [see earlier discussion in background section]. Studies using less direct experimental designs suggest that similar levels of bright light in the evening at destination might enhance phase-delay re-entrainment after westward travel (Table 4).

2.5 SHIFT WORK

Individuals who work night, rotating, or early morning shifts often describe sleep disruption. Also noted may be complaints of fatigue, sleepiness, gastrointestinal disturbances, and impaired job performance, which could impact personal and public safety.[9]

Treatment Objectives and Indications

Evidence supports that it is possible to shift circadian rhythms into alignment with a night-work/day-sleep schedule by controlling the subject's exposure to light and darkness in a controlled experimental environment.[6] Field studies with shift workers are not as supportive of this concept. Work schedules are not always structured properly to permit a shift in circadian rhythms and social and environmental zeitgebers that conflict with daytime sleep. In addition, study design may be affected by confounding variables as described in the background section.

Supported by Level II to Level IV evidence, the following practice parameters with regard to bright light in shift work therapy are Grade C recommendations.

a) Bright light prior to the core body temperature minimum may be helpful in shifting workers from a day to evening to night rotating work schedule.[6] (Option) The period of time and length of exposure in which to appropriately apply bright light have not been adequately deter-

mined. However, light intensities between 5,000 and 10,000 lux applied for three to six hours prior to the core body temperature minimum may be effective (Table 5). Less intense light for shorter periods may be effective in maintaining an effect over subsequent nights. The use of welder's goggles (No. 5 lens) upon leaving work (to prevent natural light exposure when work termination occurs during daylight hours) may be useful adjunct although this has not been vigorously tested (Table 5).

b) Bright light after the core body temperature minimum may be helpful in shifting workers from a night to evening to day schedule.[6] (Option) The timing and duration of exposure for bright light administration have not been adequately determined.

Practical application studies, actually using shift workers pursuing their jobs and lives, are extremely limited. However, the principals of using bright light after the core body temperature minimum to phase advance (and after the core body temperature maximum and before the temperature minimum to phase delay) could reasonably apply in the above situations. Sufficient studies are not available to evaluate long term effectiveness of the procedures as most workers will be intermittently shifting schedules frequently.

2.6 SEASONAL AFFECTIVE DISORDER (SAD)

Seasonal Affective Disorder (SAD) is a subtype of a mood disorder characterized by recurring episodes of major depression whose onset and remission seem to relate to particular seasons, most often beginning in autumn/winter and fully remitting in spring.

The fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[14] recommends the "seasonal pattern specifier" be reserved for patients whose major depressive episodes are related to particular seasons of the year. Crucial to the diagnosis, the depressive episodes in SAD must have occurred during the last two years without any nonseasonal episodes during this period; seasonally linked psychosocial stressors (e.g., seasonal unemployment, school schedule) as causative should be excluded.[14]

The prevalence of SAD appears to vary with age and sex. Younger persons are at higher risk for winter depressive episodes. Women comprise 60-90% of persons with seasonal pattern (hence the majority of women and a mean age in the late thirties in the studies).

Patients with SAD often have symptoms commonly seen in "atypical depression" (i.e., difficulty waking, hypersomnia, fatigue, loss of energy, carbohydrate craving, increased appetite, and weight gain).[15] However, not all patients have these symptoms, and they are not required for the diagnosis of SAD.[14]

Hypersomnia is frequently associated with SAD and for that reason it is mentioned here. The diagnosis of hypersomnia is subjective and based on historical information. Bright light therapy for depression in SAD may improve the hypersomnia. Conversely, the presence of hypersomnia may predict a response of the depression of SAD to light therapy.[7] However, as the disorder is primarily a mood disorder and not commonly primarily managed by the sleep disorder specialist, it will not be further analyzed. Newer references[16-18] provide additional information about SAD not found in the JBR series and these and other recent studies should be consulted to help guide the interested reader regarding the use of light therapy as a treatment adjunct in this disorder.

3.0 AGE-RELATED DISTURBANCES

3.1 HEALTHY ELDERLY

Elderly individuals have changes in sleep architecture that may produce symptoms of insomnia and hypersomnia.[4] There is a decrease in sleep efficiency, a decrease in SWS, and increase in arousals, and a decrease in latency to REM sleep onset. The amount of time awake after sleep onset frequently increases. In addition, there is frequently a phase advance in sleep onset and termination.

Treatment Objectives and Indications

See recommendations and evidence for ASPS.

A major complaint in healthy elderly is insomnia with early awakening, related in part to an advanced phase of the core body temperature rhythm or dim light onset melatonin secretion.[4] Two of the three studies in Table 3 address ASPS in elderly populations. **Adequate studies are not available to provide specific recommendations on light therapy to treat other causes of insomnia in this group.**

3.2 DEMENTIA

Dementia can lead to profound changes in sleep patterns with sundowning (nocturnal delirium) being one of the most disturbing.[9] The sleep-wake cycle becomes disrupted with frequent arousals during the nocturnal sleep period and frequent bouts of sleep during the day.[4] Frequently, these patients are institutionalized with inadequate exposure to sufficient light to affect the SCN. Sleep architecture in this population is often markedly disrupted with decreased sleep efficiency, decreased REM sleep, increased latency to REM sleep onset, increase latency to sleep onset, increased stage one, little or no SWS, marked increase in arousals, and many daytime naps.[4] It may be hypothesized that bright light therapy might improve the sleep-wake patterns and reduce agitation in patients with dementia who have severe sundowning.

Treatment Objectives and Indications

The application of light therapy for sleep-wake and behavioral disturbances in dementia is quite recent. Only two articles are available for evidence (Table 6). While it may be useful, more study is needed with larger patient samples, blinded evaluators, and parallel designs to determine if improvements are due to behavioral structuring, increased daytime activity, or increased total duration of daytime light exposure. **No specific recommendation is made about the clinical use of light therapy in dementia patients.**

IMPLICATIONS FOR FUTURE CLINICAL INVESTIGATION OF LIGHT THERAPY

Light therapy appears to have a good safety record. For syndromes associated with phase advances and delays, light therapy appears to have clinical utility. More work needs to be done to establish the place of light therapy to induce phase shifts in the context of clinical situations such as shift work, where social factors may considerably exceed and confound the results that light therapy can achieve. Even more work is needed in conditions such as aging and dementia, in which phase shifts may not be crucial elements in the clinical disorder.

ADDENDUM

Although not available in the published literature at the time of completion of these parameters, three articles by Eastman et al, Lewy et al and Terman et al are in press in the Archives of General Psychiatry. They provide further positive evidence on benefits of light therapy in SAD. The reader is urged to seek these and any new additional articles in this active area of research at the time of therapy consideration especially for additional information on light exposure intensities and experimental protocols.

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Table 3. *Evidence for Delayed, Advanced, and Non-24 Hour Sleep Phase Syndromes*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
					Phase Delay			
Dijk (19)/ II B	RCT crossover	Time course of REM & NREM sleep and spectral EEG composition analyzed after BL or DL exposure.	n=8 / 23.1±2.5	SSS, Groningen sleep complaint scale, PSG, plasma melatonin levels	DL: 1 lux, 0600-0900h, 3 consecutive days. BL: 2000 lux, 0600-0900h, 3 consecutive days	May not be generalizable to patients with DSPS; no data on outcome of long-term use	Phase advance of melatonin 1 hr early (sleep onset held constant in both conditions); NREM and REM unaffected; Groningen not affected; SSS not reported	Data suggests that shifting the human circadian pacemaker by 1h does not affect non-REM sleep homeostasis.
Rosenthal (20)/ II B	RCT crossover	Effects of BL examined for phase-shifting human circadian rhythms in DSPS	n=20 / not reported	Pre- and post- treatment questionnaire, 24h CBT, MSLTs	DL: 300 lux, 2h in a.m. for 2 weeks; clear goggles worn 4pm to dusk. BL: 2500 lux, 2h in a.m. for 2 weeks; clear goggles worn 4pm to dusk	Data may not be readily generalizable since age and gender not reported. No data on long-term use.	CBT advanced by 1h, 25m with BL; MSLT (9 & 11 a.m. latencies) phase advanced with BL; BL rated better than dim light	Light therapy may entrain human circadian rhythms
Cauter (21)/ III C	NCT	Magnitude and direction of immediate phase shifts of human rhythms examined following a single exposure-sure to BL pulse or physical activity	n=17 / 20 - 30	Serum melatonin, CBT, TSH, cortisol	DL: < 300 lux. BL: single dose 5000 lux, 3h based on minimum body temperature	May not be generalizable to patients with DSPS; no data on outcome of long-term use	On day after LT, MT & CBT shifted 1 h; cross-over to phase advance about 1 h after temperature minimum; TSH dampened on day 2; no change in amplitude of MT or temperature	Exposure to light at approximately the time of the minimum body temperature resulted in phase advances averaging less than 1h in magnitude

Table 3. *Evidence for Delayed, Advanced, and Non-24 Hour Sleep Phase Syndromes*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Morris (22)/ III C	Nonran-domized CCS	Endogenous circadian rhythms in sleep-onset insomniacs compared to good sleepers in DSPS	n=22 / 20 - 45	Rectal temperature, PSG	None	May not be generalizable	Rectal temperature delayed 2.5 h in DSPS patients compared to good sleeping controls	Early morning insomnia may result from phase advanced circadian rhythms & sleep maintenance insomnia may result from an abnormal phase relationship
					Phase Advance			
Campbell (23)/ II B	Control-led trial.	Efficacy of BL exposure in the treat-ment of sleep main-tenance insomnia examined in ASPS	n=16 / mean=70.4	CBT, PSG for sleep architecture by telemetry for 4 nights at baseline. RTSW during the day	DL: 50 lux, 2h between 2000-2300h, 12 days BL: 4000 lux, 2h between 2000-2300h, 12 days	No data on long term use; may not be generalizable to younger persons with ASPS. Subjects not randomized.	Sleep efficiency improved with NREM stage 2 and less wakening and NREM stage 1. CBT delayed 2.21h ($p<0.01$) by BL. Bedtime delayed 29m ($p<0.01$). Time in bed not dif-ferent and RTSW not affected	Results indicate that timed exposure to BL may be effective in the treatment of age-related sleep maintenance insomnia
Drennan (24)/ II B	RCT cross-over		n=9 / 18 - 34	PSG, CBT, mood	DL: 300 lux, 1800-2300h, 3 consecutive nights. BL: 3800-6500 lux, 1800-2100h first night, 2300h second & third nights	May not be generalizable to patients with ASPS; no data on outcome of long-term use	CBT phase delayed 3h; sleep latency delayed only 9m; no effect on mood; no delay in REM onset	
Murphy (25)/ II B	Controlled Trial. Subjects assigned to treat-ment on alterna-ting basis	Effectiveness of nighttime BL exposure examined in subjects with sleep maintenance insomnia in ASPS	n=13 / mean=73.1	PSG for sleep architecture for 3-4 nights on 5 different occasions over 15 weeks, CBT, performance battery	Control: 4000 lux, 2100-2300h, 10 days followed by 4000 lux, 1500-1700h, 15 days Treatment: 4000 lux, 2100-2300h, 10 days followed by 4000 lux, 1500-1700h, 15 days	No data on long term use; may not be generalizable to younger persons with ASPS	BL at 2100-2300h delayed CBT, improved performance and improved sleep efficiency compared to BL at 1500-1700h	BL therapy for sleep maintenance insomnia may be efficacious in improving sleep disturbances.

Table 3. *Evidence for Delayed, Advanced, and Non-24 Hour Sleep Phase Syndromes*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Non-24 Hour Sleep Wake Disorder								
Czeisler (26)/ III C	NCT	Input of light to the circadian pacemaker evaluated by testing the ability of BL to decrease plasma MT concentrations in blind persons with non-24 hour sleep wake syndrome	n=11 / 18 - 73 (controls aged 20-25)	Plasma melatonin, ophthalmologic evaluation, sleep history	DL: eyes covered BL: 6000-13700 lux, 90-100m, single dose; 2 patients twice exposed additional 3h	No data on long-term use	Some blind persons do not entrain to a 24h day, others can entrain for non-photic reasons; others have light response seen in serum melatonin suppression and may entrain to a 24h day	The visual subsystem that mediates the light-induced suppression of MT secretion remains functionally intact in some sightless patients.
Partonen (27) III C	NCT	Effects of BL on MT secretion examined in blind subjects and sighted controls with non-24 hour sleep wake disorder	n=18 (7 blind subjects, 11 sighted controls) / mean=51.7 (blind subjects); mean=44.3 (sighted subjects)	Melatonin in saliva; serum 25 hydroxy vitamin D, pretreatment questionnaire, armpit temperature, SSS, mood	DL: none BL: 3300 lux, 1h in 4 blind, 5 sighted subjects; 3300 lux, 15m in 3 blind, 6 sighted subjects. Both exposed 0600-0800h, 14 consecutive days	No data on long-term use; no blind control group	In blind, MT secretion significantly increased at 2300h compared to 2100h in sighted controls. Both sighted and blind had improvement in SSS.	BL administered in the morning may decrease subjective sleepiness and improve mood in blind subjects.

Table 3. *Evidence for Delayed, Advanced, and Non-24 Hour Sleep Phase Syndromes*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Sack (28)/ III C	NCT	Free-running temperature, cortisol, and MT rhythms examined in totally blind people with non-24 hour sleep wake disorder	n=28 (20 blind subjects, 8 sighted subjects) / 29 - 57	Plasma melatonin (n=20), cortisol (n=4), sleep propensity (n=1)	None	May not be applicable to blind persons of an older or younger age	3 subjects with entrained, normal phase melatonin rhythm; 3 subjects with entrained atypical phase melatonin rhythm; 11 subjects with free running melatonin (10>24h); 3 subjects with unstable melatonin rhythm	

DSPS, delayed sleep phase syndrome; ASPS, advanced sleep phase syndrome; N24HSW, non-24 Hour sleep-wake syndrome; MSLT, multiple sleep latency test; PSG, polysomnography; RCT, randomized controlled trial; NCT, nonrandomized controlled trial; CCS, case control study; RTSW, repeated test of sustained wakefulness; SSS, Stanford sleepiness scale; BL, bright light; DL, dim light; MT, melatonin

*Refer to Table 1 for Classification of Evidence

Table 4. *Evidence for Jet Lag*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Deacon (29)/ II B	Random-ized, placebo-controlled double-blind crossover study	Study examined the effects of melatonin and placebo on adaptation to a rapid 9h advance phase shift in the presence and absence of inappropriate BL exposue	7 / 22 - 26	Urine melatonin, CBT, VAS, sleep logs, perform-ance tasks	Following 5 days of a gradual 9h delay phase shift, readaption to rapid 9h advance phase shift studied using four treat-ment conditions: 1) placebo; 2) MT only; 3) BL therapy: 2000 lux, 0800-1200h for 2 days; 4) MT and BL therapy	Randomization process not clearly defined; small sample size; no PSG data examined; morn-ing BL exposure may not have been given long enough.	5/7 delayed MT with morning BL. No effect found on CBT rhythm. Per-formance, mood, and alertness im-proved transiently with BL over place-bo. No change in sleep patterns found.	Morning BL may not enhance phase advancement w with eastward travel in this experimental model with delays persisting. However, morning BL does not appear to be harmful in terms of performance, mood, and alertness.
Hirsch-field (30)/ II B	RCT	Study examined effects of DL, BL, and zolpidem on TSH and thyroid hormones after an 8 hour phase advance shift.	8 / 21 - 33	PSG, TSH	BL: >2000 lux from 2300h (day 2) - 1500h (day 3); 2300 (day 3) to end. DL: approximately 200 lux while alternated with 0 lux while asleep	Only order of interventions, not subjects, were randomized. Results may not be generalizable as all subjects were young healthy adults. Small sample size.	In subjects exposed to BL therapy, TSH levels declined by 25±8% vs control subjects ($p<0.001$). BL subjects experi-enced greater sleep efficiency, less wake time, and greater REM sleep than DL subjects ($p<0.05$)	BL can blunt the expected rebound TSH peak after a phase-advance and normalize sleep-wake schedules after such phase advance shifts.
Moline (31)/ III C	NCT	Study assessed ability of diet or BL to prevent jet lag simulated by a 6 hour easterly time zone shift. Subjects (male marines) lived in individual, time-isolation apartments for 15 consecutive days.	23 / 18 - 30	CBT, VAS, MAST, MC, VST, peg-board, PSG	BL: 2500 lux prior to mid-sleep point, then on awakening for 3 days for 4h. DL: 300-500 lux while awake, 0 lux while asleep	Randomization of subjects not explicitly defined; diet modification occurred with BL exposure. Results may not be gen-eralizable as all subjects were young males.	BL hindered the temperature amplitude and phase readjust-ment. BL did not affect cognition but did improve mood and alertness more than in controls.	PSG data did not indicate an effect from BL on entrainment but BL did affect mood and alertness.

Table 4. *Evidence for Jet Lag*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Deacon (32)/ V C	Case series	Study assessed the ability of controlled exposure to moderately BL at night to delay and darkness/sleep to delay circadian rhythms in subjects without environmental isolation.	6 / 22 - 26	Blood, saliva, and urine MT, VAS	1200 lux for 3 consecutive days at 2000-0200h, 2200-0400h and 2400-0600h respectively	Small sample size. No PSG data examined.	MT measurements showed that 5/6 subjects phase delayed by 1.97±0.32h to 2.67±0.3h one day post treatment. All subjects phase delayed in alertness rhythm after the first exposure of BL therapy with adaptation by the second day.	Moderately BL in the evening appears to be able to phase-delay MT and alertness rhythms.
Honma (33)/ V C	Nonran-domized crossover	Use of artificial BL examined for accelerating re-entrainment after an 8 hour advance.	5 / 20 - 24	CBT, MT	BL: 5000 lux, 3h for 3 days at 0700-1000h, 0400-0700h, 0100-0400h. DL: not specified	Small sample size; lux level of DL not specified.	4/5 subjects phase advanced faster with BL therapy than with DL therapy. One subject re-entrained by phase delay.	BL appears to enhance phase-advance re-entrain-ment with exposure in the subjective morning.
Wever (34)/ V C	Crossover	Compared re-entrainment behavior after two simulated 6 hour westward shifts in two week intervals.	2 / 19 & 21	CBT	BL: >3000 lux for 9 days. DL: approximately 300 lux for 14 days	Small sample size. No PSG data examined.	BL subjects entrained a mean 1.4h/day. DL subjects entrained a mean 1.0h/day.	BL is more effective than DL in inducing a phase delay.

BL, bright light; DL, dim light; MT, melatonin; CBT, core body temperature; TSH, thyroid stimulating hormone; VAS, visual analogue scale; MAST, memory and search task; MC, verbal reasoning task; VST, visual search task.

*Refer to Table 1 for Classification of Evidence

Table 5: *Evidence for Shift Work*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Costa (35)/III	NCT	Effects of BL expo-sure in female nurses examined in relation to night work tolerance	14 / 21 - 29	Work load; psychophysical, mood, physical fitness, and fatigue mea-sures. Auditory reaction time; search and memory test. Plasma cortisol MT, adrenaline, nonadrenaline, oral temperature	BL: 2350 lux for four 20m periods before and during shift, two consecutive nights Normal light: 100 lux, two consecu-tive nights	No randomization (self-controls). No data on long term effects. Results may not be generalizable to permanent or slow rotating shift night work. Intensity bias.	Positive effects of BL seen in psychophysical conditions, physical fitness, sleep patterns, sleepiness, performance efficiency. BL did not affect hormonal measurements.	Results suggest that positive effects of BL observed cannot be attributed to shifts in the internal clock.
Czeisler (36)/II	RCT	Functioning of the circadian pacemaker assessed in control vs treatment subjects to determine the extent of adaptation to a week of night work.	8 / 22 - 29	Body tempera-ture, plasma cortisol concen-tration, urinary excretion rate, mood, alertness, cogni-tive performance, physical activity, HR	BL: 7000-12000, 0015-0745h, 4 nights and dark conditions during the day. DL: 150 lux, 0015-0745h, 4 nights and no restrictions during the day	Small sample size. Results may not be generalizable to older subjects or females. Alertness and cognitive per-formance measured subjectively.	For controls, the mean times of the initial and final nadirs of the endogenous circadian temperature cycle were similar; in treatment group, the mean final temperature occurred 9.6h later than the initial temperature. Performance and alertness scores were significantly higher in the treatment group following LT than in the control group.	Maladaptation of the human circadian system to night work might be treated effectively with scheduled exposure to BL at night and darkness during the day.
Iwata (37)/III	NCT	Effects of BL on subjective mental state assessed under two series of 5 consecutive workshift rotations comprising one normal, two night, and two evening shifts.	10 / 24 - 40	VAS. Fatigue rated subjectively	First series: 250 lux at eye level. Second series: 3000 lux for 30m around 0200-0300h during night shifts, 2000-2100 during evening shifts	Study not randomized or controlled. Small sample size. Measurements based on subjective ratings. Chronic effect of light not examined. Results may not be generalizable.	BL improves eagerness and reduces tension. Vigor, eagerness, appetite, and impairment improved nearly significantly or significantly due to BL during the night but not evening shifts.	Results suggest that bright artificial light improves the mental state of nurses during night, but not evening, shift work.

Table 5: *Evidence for Shift Work*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Budnick (38)/III	NCT, crossover	Program of scheduled BL and dark to alter circadian pacemakers of shift workers evaluated. Baseline period of 1.5 months, study period of 3 months, post-light period of 1 month	13 / 24 - 52	SSS, MT	30-1500 lux of ambient light throughout shift; 5000-8000 lux standing, 4000-6000 lux sitting on at least half of the 12h night shift	Classification bias, decreased participation and compliance over course of study. Response bias, recall bias, time differences in duration of base-line, study, and post-study periods not accounted for.	Some significant changes were noted in the subjective results concerning reported sleep and alertness measures, but most findings perceived alertness at work, sleep patterns, and work performance were mixed & inconsistent.	BL appears to significantly suppress secretion of MT. BL adversely affected the workers perceived ability to adapt to being off work.
Koller (39)/III	Observational study	Effect of timing and intensity of light on psychophysiological adaptation processes evaluated using salvia measurements of MI and cortisol obtained every 2h for 24h	14 / 25 - 50	Continuous recording of light exposure; MT and cortisol; daily activities log; continuous ambulatory monitoring	10-6000 lux. Light intensity measured using photocell affixed at eye level; measured every 30s for 48h.	Intensity bias.	Avoidance of morning light was associated with better adaptation of circadian rhythms to night shift. Hormonal phase positions showed significant inverse relationship with light exposure. Light avoidance correlated with earlier sleep onset and longer sleep hours.	Interaction of a phase shifted activity cycle and the light/dark exposure may lead to different degrees of adaptation to the prevailing activity/rest requirements, depending on dose and phase position of BL exposure.

Table 5: *Evidence for Shift Work*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Koller (40)/III	Observa-tional study	Light exposure measured during 48h on work days and 48h on days off using photocell	6 / mean=32.8 for night watch subjects mean=37.3 for day watch subjects	Continuous recording of light exposure; daily activities log; continuous ambulatory monitoring; subjective state questionnaire; MT and cortisol	10-3000 lux. Light intensity measured using photocell affixed to a spectacle frame; measured every 15s for 48h	Subjects not randomly selected. Small sample size. Intensity bias was noted as well as subject measures of mood and alertness.	Night watches and day watches spent 13 m and 52m respectively above 1500 lux on work days and 3m and 89m respectively on days off. Night watches had no higher exposure during days off, possibly due to a light avoidance tendency in permanent night workers. BL would probably increase desynchronization between subjective state, sleep, and activity.	BL exposure may increase desynchronization between subjective state, sleep, and activity.
Stewart (41)/III	NCT	Effects of LT in NASA personnel working on shifted schedules examined. LT consisted of sche-dules for exposure to intense light, avoid-ance of light, and sleep and was admin-istered at times of day that phase-delay circadian rhythms. Control group received no therapy.	18 / mean=36.6 for treatment group mean=32.9 for control group	Post-study survey to rate daytime sleep, job perform-ance, readjust-ment to normal sleep and work schedules; sleep logs; daily symptom ratings; SSS; Owl-Lark questionnaire; Circadian Type Inventory.	8800-10670 lux. Time of day of LT varied so that exposure occurred during the most sensitive phase of phase-response curve. 80-250 lux for all subjects during night shifts	Subjective response measures. No randomization. Small sample size. Results may not be generalizable. Intensity bias; bias from laboratory performance of study rather than on a work site. Subjects had a schedule preference during this study.	Treatment group rated their speed or work, concentration, and alertness while on duty significantly higher than controls. In controls, sleep was more frequently disturbed by arousal, the duration of the main sleep episode was shorter, and considerably more time was spent napping than in the treatment group. Physical and emotional symptoms were worse in controls than in treatment subjects.	LT is both feasible and beneficial for personnel who must work on shifted schedules.

Table 5: *Evidence for Shift Work*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Whitson (42)/III	NCT	Three different 7-day protocols combining BL exposure with sleep shifting exam-ined to determine the effectiveness in elicit-ing a 12h phase-shift delay in astronauts. Goggles in daytime for sleep was the control.	8 / not reported	Saliva and urine MT; cortisol	7000-12000 lux, 2-6h daily prior to scheduled sleep periods. Subjects slept either in the daytime, or went to bed progressively later and slept later over a 6 day period.	Compliance with treatment protocols neither monitored nor recorded. Small sample size. Results may not be generalizable. Intensity and laboratory environment bias.	Combination of BL and sleep shifting was reasonably effective (within 2h of the anticipated phase delay) in shifting the circadian cycle by nearly 12h over a 7 day period in 7 astronauts. MT rhythm was suppressed during the first days of treat-ment, but cortisol was not.	BL and sleep shifting appears reasonably effective in shifting the circadian cycle by nearly 12h over a 7-day period.
Eastman (43)/III	NCT 2x2 design: light (BL, DL), goggles (yes, no)	Effects of BL during night shift and dark goggles worn during the day shift examined for phase shifting the circadian rhythm of temperature to realign with a 12h shift of sleep.	50 / 19 - 38	CBT; daily sleep logs; profile of mood states	BL: 5000 lux, 6h on first 2 night shifts. DL: 500 lux. Ten baseline days followed by eight night-work/day-sleep days.	No discussion of work or school routines. Other social and environ-mental zeitgebers were not evaluated or discussed. Volunteerism bias--subject recruitment not discussed. Combination of both laboratory and at home study with addition of actual work environment.	BL subjects with gog-gles experienced a 7.9h phase shift. DL sub-jects without goggles experienced a 3.2h phase shift. Phase de-lay never occurred with-out goggles. Large phase shifts were associated with more sleep & less fatigue	BL may help circadian rhythms shift, despite the fact that subjects are exposed to the competing 24-hour zeitgebers.
Eastman (44)/IV	NCT with historical controls	BL durations of 0, 3, and 6h during simu-lated night shifts examined for phase shifting the circadian rectal temperature rhythm to align with a 12h shift of the sleep schedule.	46 / 18 - 44	CBT, daily sleep log, profile of mood states	BL: 5000 lux for 0, 3, or 6h DL: 500 lux. Ten base-line days with nighttime sleep were followed by 8 night-shift, day-sleep periods.	Study used historical controls. Subject selection bias (volunteers used).	No differences found in 3h vs 6h BL exposure. Large phase shifts associated with more sleep, less fatigue, more vigor and less mood disturbance.	BL was better than DL during the night shift for phase shifting the circadian temperature rhythm to align with a 12h shift of the sleep schedule.

Table 5: *Evidence for Shift Work*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Campbell (45)/III	NCT	Effects of BL therapy assessed in middle-aged individuals undergoing a simu-lated shift-work regimen for three consecutive nights.	26 / mean=49.1	CBT, performance tests, alertness tests	BL: >4000 lux, 2400-044h on day 1. 1000 lux, 2400-0800h on days 2 and 3. DL: <100 lux for all 3 night shifts.	Intensity, subject selection bias (volunteers), and bias from simulated night shift.	BL was effective in resetting the circadian clocks by more than six hours; however, there was little effect on measures of on-duty alertness and perform-ance or on off-duty sleep.	Middle aged subjects may be less phase-tolerant than young subjects.
Mitchell (46)/III	2x2 factorial BL (con-flicting or facilitat-ing) and direction of shifted sleep/dark (delayed vs advanced)	Simulated night shift field study comparing BL exposure to either facilitate or conflict with adaptation of the sleep/dark schedule.	32 / mean=27.7	CBT, morningness-eveningness questionnaire, daily sleep logs	5000 lux, first 3h of night shift followed by 500 lux for 5h. BL timed according to the light PRC to delay or advance rhythms.	Simulated night shift environment and intensity bias.	Largest shifts produced by delayed sleep/dark cycle and facilitating BL. Smallest shift produced by advancing sleep/dark cycle and conflicting BL.	Appropriate timing of BL is important in achieving a circadian adaptation to the night shift. Individual differences play an important role in the ability of the circadian system to phase shift.
Eastman (47)/III	NCT clinical series, two interventi onal groups without a control.	Sleep schedules shifted 12h in subjects to accommodate eight or more consecutive simulated night shifts. A stationery light exposure period was compared to a sequentially delayed 1 hour light exposure.	24 / 20 - 39	CBT, sleep logs, VAS, profile of mood states, light log	5000 lux, 3-6h durations. Dark goggles worn outside during daylight hours.	Intensity bias from variable light schedules, simulated work environment bias and lack of control group.	Circadian temperature rhythm phase shifted approximately 2h/day in 21/24 subjects. The direction of the shift depended on the timing of light exposure relative to the baseline temperature phase. Sleep was disturbed and fatigue was increased during the first few days after the shift of the sleep-wake schedule.	

RCT, randomized controlled trial; NCT, nonrandomized controlled trial; LT, light therapy; BL, bright light; DL, dim light; VAS, visual analogue scale; SSS, Stanford Sleepiness Scale; CBT, core body temperature; MT, melatonin;

*Refer to Table 1 for Classification of Evidence

Table 6. *Evidence for Dementia*

Reference/ Grade of Evidence*	Study design	Study Conditions	# / age of subjects	Study parameters	Light therapy	Bias	Results	Conclusions
Mishima (48)/ III C	Observa-tional study	Effects of morning BL therapy on sleep and behavior disorders examined in fourteen elderly dementia patients and ten controls	n=24 / mean=75	Abnormal behavior scores; averages for total, nocturnal, and daytime sleep; melatonin levels	3000-5000 lux, 0900-1100h for four weeks	Patient selection bias; population bias; some outcome results not provided.	Amplitude of melatonin secretion significantly reduced. LT did not cause any significant change in serum mela-tonin levels. Demented subjects exposed to LT showed significant lengthening of nocturnal sleep and diminished daytime sleep. Fre-quency of abnormal behavior disorders was significantly decreased during LT compared to prior to LT.	Results suggest that morning BL is a an effective synchronizer that can normalize disturbed sleep and substantially reduce the frequency of behavior disorders in elderly people with dementia.
Satlin (49)/ V C	Uncon-trolled open clinical trial	Effects of evening BL pulses to improve sleep-wake patterns and reduce agitation examined in Alzheimer's patients with severe sundowning	10 / mean=70.1	Baseline, treatment, post-treatment ratings for agitation, sleep-wake patterns, use of restraints, and use of prn medication	1500-2000 lux, 1900-2100h for one week	Small sample size; subjective response; raters not blinded to treatment; no control group.	8/10 subjects experienced improved sleep/wake patterns. Ratings of agitation, use of restraints, and use of prn medication did not change on any shift.	Evening BL may ameliorate sleep wake cycle disturbances in some patients with Alzheimer's disease.

LT, Light therapy; BL, Bright light

*Refer to Table 1 for Classification of Evidence