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Impact of an Individually Tailored Light Mask on Sleep Parameters in Older Adults with Advanced Phase Sleep Disorder

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Abstract

Objective: This study investigated whether light delivered through the eyelids of sleeping persons might create phase delay in older adults who are adversely affected by advanced sleep phase disorder.

Participants: Thirty-two cognitively intact, community-dwelling participants aged 50 years (20 females, 12 males) with Pittsburgh Sleep Quality Index scores 5 (poor sleep) completed the study.

Methods: This within-subjects, randomized, two-treatment crossover design study exposed participants to an active “blue” ($\lambda_{\max} = 480$ nm) lighting intervention or a placebo “red” ($\lambda_{\max} =$

640 nm) control through closed eyelids during sleep for 8 weeks. Conditions were administered 1 hr after bedtime using custom-built light masks delivering a train of 2-s duration light pulses presented every 30 s for 2 hr (approximately 240 pulses/night). Dependent variables were subjective measures of sleep and depression (questionnaires) and objective measures of sleep (wrist actigraphy), analyzed using linear mixed models with treatment, period, and carryover as fixed effects.

Results: The actigraphy analysis found no effect of the intervention or the control condition on sleep start time, total sleep time, number of sleep bouts, or sleep efficiency, either compared to baseline or to one another. Subjective responses of study participants, however, indicated statistically significant ($p < 0.05$) improvement in seven of eight reported measures of sleep quality with both the intervention and the control condition, but no difference between the two conditions.

Conclusions: The participants reported improvement in sleep quality, but the intervention did not confer additional advantages after adjusting for period and carryover effects.

Keywords

advanced sleep phase disorder; blue light; circadian stimulus; light through closed eyelids during sleep; older adults

Older adults commonly experience impaired sleep (Blackwell et al., 2006; Dean, Weiss, Morris, & Chasens, 2017; Leger, Scheuermaier, Philip, Paillard, & Guilleminault, 2001; Sateia and Nowell, 2004; Scullin and Bliwise, 2015), with an estimated 48% of people aged 60 years and older having difficulty falling asleep and/or maintaining sleep, and over 20% reporting severe insomnia (Lichstein, Durrence, Riedel, Taylor, & Bush, 2004). Although disturbed sleep in older adults is frequently associated with chronic medical conditions, use of prescription medications, and mood disorders, circadian rhythm disturbances are a component of many sleep disturbances. Indeed, circadian rhythm abnormalities parallel the increased prevalence of sleep disorders associated with increasing age and cognitive impairment (Cedernaes et al., 2017; Lim, Gerstner, & Holtzman, 2014; Sharma et al., 1989).

Among the many physiological changes in sleep that accompany the aging process is a tendency for older adults to go to sleep and wake up earlier than younger adults. This process, which is termed phase advancement, is responsible for the average healthy older adult's sleep-wake cycle being approximately 60 min earlier than that of healthy younger adults (Kramer, Kerkhof, & Hofman, 1999; Kripke et al., 2005; Yoon et al., 2003). In some older persons, this physiological shift is especially large, and early evening sleep onset and early morning wakening adversely affect the individual's quality of life, a condition that is referred to as advanced sleep phase disorder (Palmer et al., 2003).

Laboratory studies have indicated that phase advancement in older adults can be ameliorated by exposure to light levels higher than those experienced at home (Cagnacci, Soldani, Romagnolo, & Yen, 1994; Lack, Wright, Kemp, & Gibbon, 2005). However, the optimal timing of such light exposure is approximately 4 hr before the time of the core body temperature minimum (CBT_{min}) (Cagnacci, et al., 1994), which in research settings has typically required participants either to be kept awake beyond their typical bedtime or

wakened after falling asleep to sit facing a full-spectrum light box for 2 hr or more (Kim et al., 2014; Kolodyazhniy et al., 2011; Lack, et al., 2005). Since such a method would be unacceptable outside the laboratory setting, we hypothesized that light exposure during sleep, if feasible, might be a potent method for creating phase delay in older adults whose lives are adversely affected by advanced sleep phase disorder.

Light delivered through closed eyelids while a person is sleeping, therefore, could potentially result in much greater phase shifts than exposure to light at any other time of the circadian day. Quantifying the stimulus and any resulting phase shift, however, requires measuring the amount of light transmitted through the eyelids. A study by Robinson et al. suggested that the human eyelid functions as a red-pass filter, transmitting 14.5% of 700-nm light but 3% of light at wavelengths 580 nm (Robinson, Bayliss, & Fielder, 1991). Similarly, Ando and Kripke showed that eyelid transmittance of red light (615–630 nm) was attenuated to 1/20 (5%), while blue (400–510 nm) and green (540–565 nm) light were attenuated to 1/100 (1%) of the dose on the eyelid surface (Ando and Kripke, 1996). In a more recent study, Bierman et al. showed that mean eyelid transmittance at 490 nm is approximately 0.4% and at 550 nm is approximately 0.5% (Bierman, Figueiro, & Rea, 2011).

In an experiment attempting to phase shift the timing of the circadian clock with light transmitted through closed eyelids, Cole et al. used a light mask that exposed participants to 2700 lux of white light, resulting in an exposure of about 57 lux at the cornea (Cole, Smith, Alcala, Elliott, & Kripke, 2002). In comparison to a placebo stimulus (0.1 lux of red light at the cornea), the white light stimulus produced significant melatonin phase shifts among selected participants with delayed sleep phase disorder. The researchers noted that the light mask was well tolerated by the study's participants and caused minimal sleep disturbance (Cole, et al., 2002).

Extending this line of research in the first of a series of studies using narrowband spectrum light, Figueiro and Rea demonstrated that green light (wavelength of peak intensity [$\lambda_{\max}$] = 527 nm) delivered through the eyelids of sleeping participants using a light-emitting diode (LED) light mask acutely suppressed melatonin and phase shifted dim light melatonin onset (DLMO) when presented prior to the CBT_{min} (Figueiro and Rea, 2012). The light levels required to affect DLMO when delivered at the eyelids were extremely high, however, ranging from 17,000 to 50,000 lux, and the high heat generated by continuous operation of the LEDs was viewed as a barrier to developing the device for therapeutic use at home.

Employing the Rea et al. model of human circadian phototransduction (Rea, Figueiro, Bierman, & Hamner, 2012; Rea, Figueiro, Bullough, & Bierman, 2005), a subsequent laboratory study by Figueiro et al. demonstrated that flashing (2-s pulses, every 30 s) blue light ($\lambda_{\max}$ = 480 nm) from an LED light mask delayed DLMO if applied before the CBT_{min} (Figueiro, Plitnick, & Rea, 2014). In a related, placebo-controlled field study of participants reporting a history of early awakening insomnia (compared to an age-matched control group of normal sleepers), Figueiro showed that a 1-week exposure to the same flashing blue light stimulus (experienced for no longer than 3 hr, starting at least 1 hr after bedtime) delayed DLMO by an average of approximately 30 min (Figueiro, 2015). Exposure

to a flashing red light ($\lambda_{\max} = 640$ nm) stimulus of the same timing and duration, however, resulted in only a minimal delay of DLMO. Although this study successfully delayed DLMO among that study's participants, it remained unknown whether using the light mask for longer durations would delay circadian phase and sleep timing in persons with early sleep onset.

To that end, the present study tested the hypothesis that an 8-week exposure to a flashing blue light stimulus delivered through closed eyelids starting 1 hr after bedtime would significantly delay sleep in older adults with early sleep onset, compared to a flashing red light stimulus placebo control. This within-subjects, randomized, two-treatment crossover design study also investigated whether the duration of intervention would have an effect on sleep timing and sleep quality.

Methods and Materials

Participant Selection

Participants were recruited from community-dwelling residences through notices posted in local primary care physicians' offices, on local bulletin boards, in newspapers, and on the employee listserv of the University of North Carolina at Chapel Hill (UNC-CH). All participants were required to be aged ≥ 50 years and cognitively intact, anticipate remaining in their homes for at least 6 months, be capable of verbal responses in English, and register a Pittsburgh Sleep Quality Index (PSQI) questionnaire score of ≥ 5 , which indicates poor sleep (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).

Participants were enrolled between August 2014 and July 2016. Of the 402 participants who contacted the study office, 87% were deemed ineligible because they did not meet the study's criteria for being phase advanced: falling asleep before 9:00 p.m. (52% ineligible) and waking up before 5:00 a.m. (23%). Other reasons for ineligibility included obstructive sleep apnea (8%); age < 50 (1%); unwillingness to change sleep phase (2%); undergoing treatment for a sleep disorder (1%); taking melatonin ($< 1\%$); restless leg syndrome ($< 1\%$); and severe photosensitivity dermatitis, permanently dilated pupil, moderate/severe retinal disease, or other eye condition as judged by the study ophthalmologist ($< 1\%$). An additional 11% were excluded because they did not complete their eligibility evaluation due to scheduling problems or missing the study's enrollment period.

Of the 53 eligible participants, 46 enrolled in the study, 4 withdrew prior to the initiation of the lighting condition, and 5 were excluded because the study's recruitment goal had been met. Of the 46 participants who enrolled the study, 14 (30%) did not complete both intervention/control periods, 10 (71%) cited an inability to accustom to the light mask, and 4 (9%) found the study too burdensome.

The study was conducted in accordance with the Declaration of Helsinki, (World Medical Association, 2000) and was approved by the Institutional Review Boards (IRBs) of Rensselaer Polytechnic Institute and UNC-CH.

Intervention and Control Conditions

The active light was delivered to both retinæ through closed eyelids using the flashing blue light mask previously described in detail by Figueiro et al. (Figueiro, Bierman, & Rea, 2013) and shown in Figure 1. Briefly, the active light mask housed two blue LED arrays (maximum wavelength [$\lambda_{\max}$] = 480 nm, full width at half maximum [FWHM] = 24 nm), each one directly placed in front of each eyelid. A similarly designed light mask housing two red LED arrays ($\lambda_{\max}$ = 640 nm, FWHM = 25 nm) was used as the control condition (see Figure 1). The masks delivered a train of blue or red light pulses of 2-s duration that were presented every 30 s for no longer than 2 hr, resulting in a maximum total of approximately 240 pulses per night. The masks were held in place with an elastic strap that wrapped around the back of the participant's head.

The prescribed corneal irradiance levels for the active, blue light mask intervention were based upon circadian stimulus (CS) calculations (Rea, Figueiro, Bierman, & Bullough, 2010). The CS metric reflects the spectral and absolute sensitivities of the human circadian system and is defined in terms of equivalence to the estimated percentage, from 10% (threshold) to 70% (saturation), of light-induced nocturnal melatonin suppression following a 1-hr retinal exposure to a non-pulsing light through open eyelids and a fixed pupil diameter of 2.3 mm. Because individual eyelid transmittance measurements were not calculated for the participants in the present study, and to ensure that all participants received a significant corneal light stimulus, the irradiance for the blue light stimulus was set to provide a CS of 0.3 for the thickest eyelids measured in a previous eyelid transmittance study (Figueiro and Rea, 2012).

The criterion CS of 0.3 is equivalent to a 30% melatonin suppression after a 1-hr exposure to a given light stimulus. The mean $\pm$ standard deviation (SD) eyelid irradiance from the blue light mask that was required to achieve this CS value was calculated to be 225 watts per square meter (W/m^2) $\pm$ 7.6 W/m^2 (27,493 lux $\pm$ 966 lux), which would have delivered a corresponding CS of 0.43 to a participant having the mean eyelid transmittance calculated by Bierman et al.¹⁷ The red light mask eyelid irradiance was matched to that for the blue light mask and, after taking eyelid transmissions at these two wavelengths into account, the mean $\pm$ SD red light mask eyelid irradiance was set to 7 W/m^2 $\pm$ 0.3 W/m^2 (1507 lux $\pm$ 4.6 lux). A corresponding CS < 0.001 would have been delivered by the red light mask to a participant having the mean eyelid transmittance calculated by Bierman et al. (Bierman, et al., 2011).

Study Measures

Study outcomes included objective measures of sleep quality and subjective measures of sleep quality and depression. The subjective measures were recorded during both baseline observation periods and during the final week of the intervention and control periods (see Protocol) using the following instruments: the Pennsylvania Sleep Quality Index (PSQI) (Buysse, et al., 1989), specifically addressing the PSQI overall quality and the PSQI sleep efficiency subscale; the Medical Outcomes Study Sleep Adequacy and Sleep Problems (MOS Sleep) scales (Hays and Stewart, 1992); the Epworth Sleepiness Scale (ESS) (Johns, 1991); the Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep

Disturbance (PROMIS-SD) and Sleep-Related Impairment (PROMIS-SRI) scales (Buysse et al., 2010); and the Patient Health Questionnaire-9 (PHQ-9), a measure associated with DSM-IV diagnostic criteria for depression (Kroenke, Spitzer, & Williams, 2001).

Sleep quality was quantitated based on wrist actigraphy using the Actiwatch device (Philips Respironics, Murrysville, PA, USA). The Actiwatch, a small digital accelerometer worn on a participant's nondominant wrist, was used to collect physical activity data, recording it in 1-min epochs continuously over a rest interval (i.e., when the participant was in bed), allowing for objective measurement of sleep and wake intervals. The resulting actigraphy data were analyzed using the manufacturer-designed and -recommended Actiware software, version 3.4 (Philips Respironics). The epoch length was set to 1, the wake threshold selection was set to "high", and the immobile minutes for sleep onset and sleep end was set to 10 min.

These data were augmented by participant-recorded sleep logs noting evening in-bed times and morning out-of-bed times.

For this study, the following objective actigraphy-based measures were examined:

1. Sleep start time, measured as the exact point on a 24-hr clock that begins a participant's sleep interval as automatically calculated by the Actiware software based on participants' actigraphy data.
2. Time in bed, measured in minutes, as the time elapsed between the start and end times of participants' rest intervals.
3. Number of sleep bouts, defined as consecutive 60-s data recording periods (epochs) that were classified as "sleep" by the Actiware software.
4. Total sleep time, measured in minutes, as the total number of epochs classified by the Actiware software as "sleep" during the rest interval (time in bed).
5. Sleep efficiency, reported as a percentage and measured as total sleep time (determined by the Actiware software) divided by the time in bed (determined by the participant-reported sleep logs) multiplied by 100.

To estimate daytime light exposure, participants wore a Daysimeter, a calibrated light-measuring device, as a pendant (Bierman, Klein, & Rea, 2005), (Figueiro, Hamner, Bierman, & Rea, 2013). The Daysimeter is calibrated in terms of orthodox photopic illuminance (measured in lux) and circadian illuminance (CL_A), the latter of which is then converted to a CS value following the procedure described in Rea et al. (Rea, et al., 2010). Baseline physical activity data were collected from participants using the Actiwatch.

To monitor for adverse ophthalmic effects, the participants received an eye examination prior to initiating the intervention and at the end of the study. This exam consisted of an ophthalmologic evaluation, functional testing (dilated eye examination, visual acuity, Amsler Grid evaluation, and pressure measurement), and ultrahigh-resolution optical coherence tomography (OCT), a non-invasive test that evaluates the anatomy of the retina in the region of the macula via high-resolution anatomical mapping of the retinal cell layers (Jorge et al., 2004; Kaushik, Gupta, & Gupta, 2004; Schatz, Eriksson, Ponjavic, & Andréasson, 2004).

The occurrence of potential adverse events was solicited once per week via telephone assessment during the intervention/control periods. If a serious adverse event was reported (e.g., hospitalization, fall), the participant was asked to determine whether, in his or her opinion, the event definitely was, possibly was, or was not related to the lighting. Any adverse event that was determined to be related to the lighting conditions was reported to the safety officer and the IRB. To evaluate for side effects of the lighting conditions, participants were also interviewed about the frequency and severity of the following symptoms on a weekly basis: seeing spots, problems with glare, eye burning or irritation, eye redness, jitteriness, severe agitation, skin rash on the face or arms, headache, dizziness, nausea, and any other reaction attributable to the light. The study's safety officer (a physician not otherwise involved in the study) reviewed adverse events and side effects three times during the study.

Protocol

The study protocol consisted of two 8-week intervention/control periods in which each participant wore either the intervention (blue light) or control (red light) mask every night, with the order of presentation of the two conditions randomized by the study's biostatistician. Each study period was preceded by a 2-week observation period, when baseline data were collected (Figure 2). Participants were free to go to bed and rise whenever they wished. Participants who took prescribed sedative medications or drank caffeinated beverages were asked to adhere to their regular daily regimen during the study period, if possible. Any deviations were reported to and noted by the research team.

Participants wore the Daysimeter device starting 2 weeks prior to the study and continued to do so for the study's duration (the device can continuously log data for up to 6 months). A research team member visited each participant on a weekly basis to deliver and retrieve one of two Daysimeters that were exclusively worn by the participant on alternating weeks over the course of the study. When a Daysimeter was delivered, the device worn by the participant during the preceding week was returned to the laboratory for data download. Participants wore an Actiwatch during each baseline observation period and during the final week of both intervention/control periods. A research team member visited the participants' homes at the conclusion of each period to retrieve the Actiwatch and administer the questionnaires.

The appropriate light mask (intervention or control) was delivered to each participant during the final week of the baseline observation period, concurrent with the administration of questionnaires. The light masks were worn while sleeping during each intervention/control period, and participants documented any safety/adverse effects data in diaries for the weekly assessments via telephone. The participants were informed that the efficacy of both light treatments was unknown and being evaluated by the study, and thus remained unaware of which one was the active intervention.

The light mask was programmed to turn on no earlier than 1 hr after bedtime and turn off after running for 2 hr. Participants were not exposed to light before bedtime. The train of light pulses was thus timed to occur during the expected delay range of the circadian phase response curve, thereby targeting the criterion 2-hr phase shift that was established at the

beginning of the study. Every evening, participants were asked to connect their light mask to the computer and enter their expected bedtime. An application designed for the study then registered that expected bedtime and programmed the light mask to turn on 1 hr later. The light mask maintained a digital log of its flashing period to verify participant compliance and permit the researchers to confirm that the light mask had turned on during the night. The digital log was automatically downloaded and saved to the computer when the mask was connected to the computer on the following night. A research team member downloaded the weekly light mask data to a portable USB drive during the weekly visits to exchange Daysimeters, and those data were downloaded to the project server upon the researcher's return to the laboratory.

Compliance with the study protocol was determined at two levels. First, the digital logs of the light masks were used to verify compliance of each participant's use of the mask. Second, the digital logs, participant-recorded sleep logs, and actigraphy data were also used to verify the compliance of participants who properly used the light mask and wore the Actiwatch for the entire protocol.

Data Analyses

Visual inspection of the actigraphy data was performed prior to analysis, and data that were recorded while the Actiwatch was not worn were excluded (e.g., periods identified as such in the participants' sleep logs and when actigraphy data indicated no activity for more than 30 consecutive minutes). Days with more than 10% missing data were excluded from the analyses, and 1-week data collection periods with fewer than 2 days of valid data were excluded entirely. Data were analyzed separately for all participants who enrolled in the study ($N = 46$, the 'intent-to-treat' analysis), and for two overlapping groups of 'compliant' participants: those who were in compliance with the light mask, and those who were in compliance with both the light mask and actigraph.

The analytic strategy employed linear mixed models with the sleep measures and actigraphy data as dependent variables and random intercepts for the study participants. The fixed effects were: (1) dichotomous variables for the intervention condition (i.e., blue light) and control condition (i.e., red light), respectively, with the 2 weeks of baseline measurement prior to use of the light mask (in each period) as the reference, and (2) period, coded as "1" for the second period and "-1" for the first period. The use of "cell mean" coding for period allowed the intercept term to be interpreted as the mean outcome averaged across the 4 weeks of baseline measurements. Due to the crossover design of the study, carryover effects were also estimated in the models: the carryover of first-period blue light and first-period red light, respectively, into the baseline of the second period. The treatment effect was assessed as the net effect of the intervention (i.e., exposure to blue light) on participants' subjective and objective sleep after accounting for the control effect (i.e., exposure to red light). Participant-level covariates (e.g., gender, age, functional status) were not adjusted, since participants served as their own controls. Statistical significance was defined as $p < 0.05$.

The primary outcome of interest was delay in sleep onset. The linear mixed models allowed for different numbers of observations per participant and gave robust inference for the primary intent-to-treat analyses ($N = 46$) with respect to possible mechanisms for missing

outcome data; in particular, they gave valid inference for participant dropout or missed visits that were “missing-at-random” (i.e., the probability of a missed visit was allowed to depend upon the participant’s treatment status as well as their outcome status at observed visits).

Results

Study Drop Out, Demographics, and Compliance with Protocol

Thirty-two (69.6%) of the 46 enrolled participants completed the study. Compared with those who withdrew from the study, participants who completed the study were significantly more likely to be older ($p = 0.013$) and African American ($p = 0.04$). Of the 32 participants who completed the study, the mean age was 62.6 years, 63% were female, 59% were white, and 50% had a 4-year college degree or higher (Table 1). The digital logs from the light masks verified the compliance of 23 participants who properly used the light mask for the entire study (see Table 1). Among these, the logs and actigraphy verified the compliance of 17 participants who used the light mask and wore the Actiwatch for the entire study.

Actigraphy and Subjective Sleep Questionnaires

When unadjusted actigraphic measures were analyzed (Table 2), the intervention demonstrated no statistically significant effects ($p > 0.05$) on time in bed, total sleep time, sleep efficiency, number of sleep bouts, or sleep start time (i.e. onset). Likewise, the model-adjusted analysis for the time of sleep onset did not find a significant overall treatment effect on sleep phase (Table 3). After adjusting for period and carryover effects, neither the intervention nor control treatment significantly differed from baseline for all study participants ($N = 46$), for patients compliant with the light mask ($n = 23$), or for the subset of participants compliant with the light mask and the actigraph ($n = 17$). Sleep onset time increased for all participants ($p = 0.029$) and light mask + Actiwatch compliant participants ($p = 0.052$) between the first and second periods by +16.5 and +19.3 min, respectively. Global tests for carryover effects found no statistically significant effects.

When the participant-reported subjective measures of sleep quality were analyzed, however, seven of eight measures significantly improved relative to baseline ($p < 0.05$; Table 4). However, the estimated treatment effect (calculated as intervention minus control) was not statistically significant for any of the measures. Global tests for carryover effects on the total sample found a significant carryover effect for the PSQI overall sleep quality measure ($F_{2,98} = 4.36$, $p = 0.015$) and an approaching significant carryover effect for the MOS Sleep measure ($F_{2,97.8} = 2.94$, $p = 0.058$). All other measures demonstrated no significant ($p > 0.111$) carryover effects in the total sample. We also examined the results for participants who complied with the light mask ($n = 23$) and the light mask and Actiwatch ($n = 17$) and found no treatment effect results that qualitatively varied from the above conclusions. Significant global tests for carryover effects were found for both sub-samples for both the PSQI overall sleep ($p = 0.002$, $p = 0.011$) and PSQI sleep efficiency ($p = 0.007$, $p = 0.032$) measures.

Acceptance of the Light Mask

As part of the study protocol, participants were interviewed weekly for reports of any symptoms that they thought might have been attributable to the light mask. Table 5 displays the percentages of weekly reports indicating adverse events for those subjects who completed the intervention (blue light mask) and control (red light mask) periods, respectively.

Two hospitalizations and one fall occurred among the study participants, but neither the participants nor the reviewing physicians attributed those events to the experiment. One adverse event was a non-emergency wrist surgery, one was a non-emergency heart surgery and one was due to a trip and fall that occurred in a garage during the day. For both the control and intervention combined, the most commonly reported side effects were irritability (16.4%), difficulty concentrating (15.9%), headache (14.9%), eye burning or irritation (13.1%), and eye redness (8.9%). Three of these side effects (i.e., eye redness, headache, and irritability) were reported differentially at $p < 0.05$ between the intervention and control condition (see Table 5), and the majority of participants' reports did not attribute any of those side effects to the light or mask use.

Discussion

This study evaluated the impact of a light mask built to deliver bursts of short-wavelength (blue) ($\lambda_{\max} = 480$ nm) or a placebo, long-wavelength (red) ($\lambda_{\max} = 640$ nm) light through the eyelids of sleeping persons in the phase delay portion of the sleep phase of individuals aged 50 years with symptomatic advanced sleep phase disorder. To our knowledge, this is the first study to investigate the long-term (i.e., 8 weeks) impact of a lighting intervention designed to deliver flashing light on participants' retinæ while asleep. Results from wrist actigraphy (see Tables 2 and 3) found no effect of the intervention or the control condition on sleep start time, total sleep time, number of sleep bouts, or sleep efficiency, either compared to baseline or to one another. Participants' subjective responses, however, indicated statistically significant improvement in all reported measures of sleep quality with both the intervention and the control condition, but no difference between the two conditions (see Table 4). Overall, the results indicate that although wearing the sleep mask improved subjective sleep quality, the lighting intervention did not confer additional advantages beyond the control condition after adjusting for period and carryover effects.

The lack of response to the intervention that we observed in the participants was similar to that observed by Palmer et al., who also studied community-dwelling older persons with advanced sleep phase syndrome (Palmer, et al., 2003). In that study, the experimental condition was exposure to 2–3 hr of approximately 250 lux of white light before bedtime, and the investigators were similarly disappointed that a light exposure that had appeared promising in the laboratory setting was not duplicated when applied in the field.

These results are also consistent with those of Sharkey et al., who tested a morning blue light intervention to advance DLMO in college students who exhibited delayed sleep (Sharkey, Carskadon, Figueiro, Zhu, & Rea, 2011). Specifically, they showed that those in the intervention group had the same phase advance as those in the control group. The total light

exposures over the course of the day, which were also measured with the Daysimeter, were not significantly different between the two groups. Their conclusion was that both morning and evening light should be monitored in order to obtain the desired phase shift. In the present study, to avoid burden on the participants, there was no control of morning light exposure, which could have counteracted the delaying effect of the light mask intervention. The Daysimeter data also showed no significant differences in hourly CS exposures between the two experimental conditions, with all participants receiving, on average, CS > 0.2 from 9:00 a.m. until 6:00 p.m. For comparison, Figueiro et al. showed that exposure to a CS = 0.3 during the day leads to better sleep, mood, and improved behavior in patients with Alzheimer's disease and related dementias (Figueiro et al., 2014). Moreover, it is well known that greater amounts of light during the day reduce the impact of evening light on the circadian system (Hébert, Martin, Lee, & Eastman, 2002). Therefore, the impact of the light treatment employed in our study could have been reduced due to participants' photic history.

It is also possible that the lack of a treatment effect was due to inadequate or ineffective delivery of the intervention. Continuous light would have been the preferred method of delivery, but bursts of light were used instead because continuous delivery resulted in overheating of the light mask. This strategy may well have led to the participants' reduced tolerance of, and thereby reduced exposure to, the intervention. Indeed, all of the CS calculations used in the present study were based on a continuous light exposure, whereas the present study's retinal light exposures (irradiance × time) were only 7% of what would have resulted from a continuous 1-hr exposure. The uncertainties associated with quantifying retinal light exposures are outlined in Figueiro et al. (Figueiro, Bierman, et al., 2013). It should be noted, however, that Figueiro et al. demonstrated in a laboratory setting that 2-s pulses of a 480 m light administered every 30 s during a 60-min exposure significantly suppressed melatonin and phase shifted DLMO (Figueiro, Plitnick, & Rea, 2014). Consistently, Zeitzer et al. showed, in a laboratory setting, that flashing light (a 2-ms flash every 30 sec) delivered for 1 hr during sleep significantly delayed the timing of participants' circadian salivary melatonin rhythms compared to a dim light condition (Zeitzer, Fiscaro, Ruby, & Heller, 2014).

In a follow-up field study employing the same protocol used in the present study, Figueiro et al. showed that wearing the blue light mask for 1 week delayed participants' DLMO by 34 min (Figueiro et al., 2015). More importantly, in that same field study, participants' sleep was significantly delayed with the intervention. Given that data were not collected until the last week of the present study, it is impossible to know whether there was a phase delay in participants' sleep after the first week of the intervention that had not been sustained for 8 weeks.

A significant minority of participants (22% of those enrolled in the study) were unable to accustom to the light mask because they were wakened by the bursts of light. In our previous laboratory and field studies, we observed a much higher acceptance rate, with only one participant withdrawing from a single study due to an inability to accustom to the light mask (Figueiro, 2015). This difference may have been due to the age of the participants in the current study, which was older than in previous studies, and the length of the study, which was of much longer duration than our previous published studies. Nevertheless, the

acceptance and compliance to the long-term use of such a light treatment may not be as high as other light treatments that deliver light while the patient is awake. Moreover, those who were able to tolerate the intervention often preferred one color light over the other, but these preferences were not consistent and neither condition was associated with significant alterations in objective sleep measures. It should be noted that the participants reported improvements in all subjective sleep measures after both the intervention and the control condition, suggesting that perhaps the act of wearing the light mask may have improved sleep hygiene. This self-reported improvement in sleep quality, however, cannot be directly attributed to the light mask use and may have been due to other reasons, such as a research participation effect.

A few limitations of our study should be discussed. First, despite the fact that our inclusion criteria clearly required bedtimes before 9 p.m., the actigraph data suggest that some participants were falling asleep after 10 p.m., indicating that they may not have had early sleep onset insomnia, as indicated by self reports. Second, we did not collect circadian marker data (e.g., DLMO) in this field study, so it is not known whether any circadian phase shifting resulted from the intervention. Given that we did not collect circadian marker data, it is not possible to know whether other factors, such as social obligations, dictated participants' bedtimes. Finally, while we measured participants' light exposures, we did not control light during the day, especially during the morning hours, which could have counteracted the intervention because morning light advances the circadian clock. Future studies should test the efficacy of the light mask in combination with orange-tinted goggles to eliminate any light exposure at the wrong circadian times.

In conclusion, while laboratory and field studies have demonstrated that both continuous and flashing light delivered through closed eyelids during sleep can acutely suppress melatonin and phase delay DLMO over short periods of time (e.g., 1 day or 1 week), our long-term study failed to observe a significant impact on sleep times in those suffering from early sleep onset.

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Figure 1.

Mask used to deliver pulses of light through closed eyelids during sleep. The light mask contained 2 blue LED arrays (Intervention; $\lambda_{\text{max}} = 480 \text{ nm}$, FWHM = 24 nm) or 2 red LED arrays (Control; $\lambda_{\text{max}} = 640 \text{ nm}$, FWHM = 25 nm) for each eyelid.

Figure 2.

The within-subjects, randomized, two-treatment crossover protocol used for the study. Participants responded to the questionnaires assessing self-reported sleep (PSQI, MOS Sleep, ESS, PROMIS-SD, and PROMIS-SRI) and depression (PHQ-9) during the second weeks (2 and 16) of each baseline observation period (BL1 and BL2) and during the final weeks (10 and 24) of each intervention/control period. The Actiwatch was worn during the two baseline observation periods (weeks 1, 2, 15, and 16) and during the final weeks (10 and 24) of each intervention/control period. Participants wore a Daysimeter beginning 2 weeks prior to and through the duration of the study. The intervention/control periods were separated by a 4-week washout (W/O) period.

Table 1.

Number and percentage (unless otherwise noted) of study participants' characteristics.

Characteristic		Total (N = 46)	Completed study and were light mask compliant (n = 23)	Completed the study and were light mask + Actiwatch compliant (n = 17)
Age at intake (mean [SD])		60.8 (7.4)	62.8 (1.8)	64.2 (2.1)
Female		30 (65)	14 (61)	11 (65)
Race:	African American	14 (30)	11 (48)	8 (47)
	White	32 (70)	12 (52)	9 (53)
Education:	High school/GED	8 (17)	4 (17)	3 (18)
	< 4 years college	15 (33)	7 (30)	6 (35)
	4 years college	23 (50)	12 (52)	8 (47)
Marital status:	Never married	6 (13)	4 (17)	3 (18)
	Married	27 (59)	12 (52)	8 (47)
	Divorced	13 (28)	7 (30)	6 (35)
Sleep with another person in the room		26 (57)	11 (48)	7 (41)
Alcoholic drinks/day:	0	26 (57)	16 (70)	12 (71)
	1	15 (33)	6 (26)	4 (24)
	2–4	5 (11)	1 (4)	1 (6)
Caffeinated drinks/day:	0	9 (20)	5 (22)	4 (24)
	1	9 (20)	5 (22)	3 (18)
	2–4	28 (61)	13 (57)	10 (59)
Health problems	Heart disease	1 (2)	0 (0)	0 (0)
	Arthritis	16 (35)	12 (52)	9 (53)
	Osteoporosis	6 (13)	1 (4)	1 (6)
	Depression	9 (20)	2 (9)	1 (6)
	Anxiety	6 (13)	3 (13)	3 (18)
	Alcoholism	2 (4)	1 (4)	0 (0)

Table 2.

Objective measures of sleep quality during the intervention (blue light mask) and control (red light mask) periods.

Total Sample (<i>N</i> = 46)	Mean (SD) Value			
	Intervention (blue light)		Control (red light)	
	Baseline (<i>n</i> = 37)	Final week ^a (<i>n</i> = 33)	Baseline (<i>n</i> = 42)	Final week ^a (<i>n</i> = 30)
Wrist actigraphy				
Time in bed (min) ^b	452 (71)	460 (70)	464 (75)	470 (93)
Sleep time (min)	354 (67)	360 (82)	375 (74)	375 (93)
Sleep efficiency (%) ^c	78.5 (12.0)	78.8 (14.9)	81.1 (9.8)	80.5 (14.7)
Sleep bouts (<i>n</i>)	17.0 (6.7)	15.8 (9.7)	16.1 (7.7)	15.7 (8.2)
Sleep start time	22:16 (1:13)	22:25 (1:34)	22:18 (1:12)	22:19 (1:15)
Sleep log				
Sleep start time	21:46 (1:07)	21:50 (1:05)	21:52 (1:06)	21:50 (1:05)
Light mask compliant (<i>n</i> = 23)	Baseline (<i>n</i> = 23)	Final week ^a (<i>n</i> = 21)	Baseline (<i>n</i> = 23)	Final week ^a (<i>n</i> = 22)
Wrist actigraphy				
Time in bed (min) ^b	460 (69)	458 (77)	462 (75)	480 (101)
Sleep time (min)	346 (62)	348 (86)	370 (76)	387 (82)
Sleep efficiency (%) ^c	75.3 (12.8)	76.7 (16.5)	80.1 (11.2)	81.5 (10.6)
Sleep bouts (<i>n</i>)	17.7 (7.3)	16.3 (10.8)	15.5 (8.2)	15.4 (8.5)
Sleep start time	22:22 (1:08)	22:26 (1:32)	22:14 (1:00)	22:21 (0:57)
Sleep log				
Sleep start time	21:43 (0:56)	21:53 (1:03)	21:51 (1:03)	21:56 (1:06)
Light mask + Actiwatch compliant (<i>n</i> = 17)	Baseline (<i>n</i> = 17)	Final week ^a (<i>n</i> = 16)	Baseline (<i>n</i> = 17)	Final week ^a (<i>n</i> = 14)
Wrist actigraphy				
Time in bed (min) ^b	473 (53)	467 (67)	465 (65)	479 (99)
Sleep time (min)	353 (65)	331 (73)	360 (53)	369 (52)
Sleep efficiency (%) ^c	74.5 (14.1)	71.8 (16.3)	77.6 (11.3)	78.2 (8.8)
Sleep bouts (<i>n</i>)	18.8 (7.4)	18.9 (10.0)	17.6 (7.4)	18.3 (6.4)
Sleep start time	22:27 (1:10)	22:29 (1:42)	22:15 (0:58)	22:23 (1:01)
Sleep log				
Sleep start time	21:44 (0:50)	21:47 (1:05)	21:51 (1:03)	21:52 (1:13)

Notes:

(a) The final week assessments occurred during weeks 10 and 24 of the study (see Figure 2). All unadjusted differences were not statistically significant between intervention and control ($p > 0.05$).

(b) Time in bed is determined by participant report.

(c) Sleep efficiency is sleep time determined by Actiwatch divided by the time in bed determined by participant report.

Table 3.

Estimated effect of the lighting intervention (blue light mask) in delaying sleep onset based on actigraphy measurements.

Effect of intervention ^a	Estimate (min)	SE	DF	<i>t</i> value	Pr > <i>t</i>
All participants (<i>N</i> = 46)					
Overall Treatment Effect	−0.4	7.5	1411	−0.05	0.96
Period ^b	16.5	7.5	1411	2.19	0.029
Intervention	1.9	6.7	1423	0.29	0.78
Control	2.3	7.6	1420	0.31	0.76
Carryover of intervention	−12.2	9.8	1423	−1.24	0.21
Carryover of control	−15.5	10.3	1423	−1.51	0.13
Participants compliant with light mask (<i>n</i> = 23)					
Overall Treatment Effect	−1.6	8.1	860	−0.20	0.84
Period ^b	6.5	4.1	860	1.59	0.11
Intervention	−5.9	7.6	859	−0.78	0.44
Control	−4.2	8.1	859	−0.53	0.60
Carryover of intervention	−8.9	10.9	866	−0.81	0.42
Carryover of control	−11.0	10.8	863	−1.02	0.31
Participants compliant with light mask + Actiwatch (<i>n</i> = 17)					
Overall Treatment Effect	−9.2	9.9	640	−0.93	0.35
Period ^b	19.3	9.9	640	1.95	0.052
Intervention	−13.5	9.7	639	−1.39	0.17
Control	−4.3	9.1	639	−0.47	0.64
Carryover of intervention	−9.9	14.0	645	−0.71	0.48
Carryover of control	−18.6	12.7	641	−1.47	0.14

Notes:

(a) Overall treatment effect = shift in bed time attributable to the blue light intervention relative to the control condition (red light), adjusting for period effects and crossover effects, as well as random effects in a linear mixed model; Intervention effect = blue light mask trial period compared with baseline; Control effect = red light mask trial period compared with baseline. Sleep parameters measured using accelerometers (Actiwatch) worn by study participants. All analyses controlled for period and carryover effects.

(b) Estimate shown is twice estimated regression coefficient due to cell mean coding for period.

Analyses were performed using SAS, version 9 (SAS Institute, Cary, NC).

Table 4.

Model-adjusted effects (SE) of the lighting intervention (blue light mask) and the control condition (red light mask) relative to baseline, and to one another, on subjective measures of sleep quality and depression.

Instrument	Intervention	<i>p</i> value	Control	<i>p</i> value	Treatment	<i>p</i> value
All participants (<i>N</i> = 46)						
PSQI overall score	−1.9 (0.5)	< 0.001	−1.3 (0.5)	0.018	−0.6 (0.5)	0.21
PSQI sleep efficiency	6.9 (2.9)	0.020	7.7 (3.2)	0.017	−0.7 (2.8)	0.79
MOS sleep adequacy	16.1 (4.4)	< 0.001	14.0 (4.8)	0.004	2.1 (4.2)	0.63
MOS sleep problems	−11.3 (2.4)	< 0.001	−10.1 (2.6)	< 0.001	−1.21 (2.3)	0.61
ESS	−1.9 (0.6)	0.003	−1.8 (0.7)	0.010	−0.1 (0.6)	0.85
PROMIS-SD	−3.2 (0.9)	< 0.001	−2.3 (1.0)	0.019	−0.9 (0.9)	0.27
PROMIS-SRI	−2.5 (0.8)	0.004	−1.9 (0.9)	0.037	−0.6 (0.8)	0.48
PHQ-9	−1.2 (0.4)	0.005	−1.3 (0.5)	0.006	0.1 (0.4)	0.90
Participants compliant with light mask (<i>n</i> = 23)						
PSQI overall score	−2.8 (0.6)	< 0.001	−1.8 (0.6)	0.006	−1.0 (0.6)	0.085
PSQI sleep efficiency	10.9 (3.3)	0.002	8.9 (3.4)	0.010	2.0 (3.0)	0.51
MOS sleep adequacy	21.9 (5.6)	< 0.001	17.9 (5.7)	0.003	4.0 (5.1)	0.44
MOS sleep problems	−13.3 (3.4)	< 0.001	−12.4 (3.4)	< 0.001	−0.9 (3.1)	0.76
ESS	−2.4 (0.8)	0.006	−2.1 (0.9)	0.016	−0.3 (0.8)	0.73
PROMIS-SD	−3.5 (1.2)	0.005	−3.0 (1.2)	0.016	−0.5 (1.1)	0.66
PROMIS-SRI	−2.8 (1.2)	0.020	−2.8 (1.2)	0.022	0.004 (1.1)	1.00
PHQ-9	−1.4 (0.5)	0.013	−1.6 (0.5)	0.004	0.3 (0.5)	0.59
Participants compliant with light mask + Actiwatch (<i>n</i> = 17)						
PSQI overall score	−2.3 (0.8)	0.005	−1.5 (0.7)	0.049	−0.8 (0.7)	0.22
PSQI sleep efficiency	8.2 (3.8)	0.038	7.8 (3.6)	0.034	0.4 (3.3)	0.91
MOS sleep adequacy	13.4 (6.8)	0.054	11.6 (6.3)	0.071	1.8 (5.9)	0.76
MOS sleep problems	−10.0 (4.3)	0.026	−8.9 (4.0)	0.032	−1.0 (3.8)	0.78
ESS	−1.2 (0.9)	0.22	−1.3 (0.9)	0.14	0.1 (0.8)	0.88
PROMIS-SD	−3.1 (1.5)	0.050	−2.4 (1.4)	0.11	−0.7 (1.3)	0.59
PROMIS-SRI	−2.6 (1.3)	0.059	−2.1 (1.2)	0.10	−0.5 (1.2)	0.67
PHQ-9	−0.8 (0.7)	0.25	−1.1 (0.6)	0.087	0.3 (0.6)	0.59

Note: Treatment effect = intervention effect minus control effect. Analyses controlled for period and carryover effects via linear mixed models. Note: Analyses were performed using Proc MIXED, SAS, version 9 (SAS Institute, Cary, NC). *P* values are reported as final cell entries.

Table 5.

Prevalence of adverse effects attributed to the lighting conditions reported during weekly telephone assessments by participants who completed one or both study periods.

Adverse effect	Reports/treatment week (percent)		<i>p</i> value ^c
	Intervention ^a (blue light)	Control ^b (red light)	
Anxiety	6.7	3.4	0.079
Blurred vision	4.8	4.9	0.99
Difficulty concentrating	17.8	13.9	0.25
Difficulty focusing	7.8	6.0	0.40
Eye burning or irritation	13.8	12.4	0.62
Eye redness	11.5	6.4	0.035*
Eyestrain	9.3	7.1	0.35
Headache	19.3	10.5	0.004*
Irritability	20.4	12.4	0.016*
Jitteriness	3.7	3.4	0.82
Nausea	2.6	0.8	0.095
Seeing spots	2.2	4.9	0.10
Skin rash on face	1.5	1.5	0.99

Notes:

- (a) reports are based on the 35 participants who completed the intervention condition;
- (b) reports are based on the 38 participants who completed the control condition;
- (c) based on chi-squared statistic, significant values ($p < 0.05$) are indicated with an asterisk (*).