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Improved cognitive morning performance in healthy older adults following blue-enriched light exposure on the previous evening

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Abstract

Objectives—Exposure to light can have acute alerting and circadian phase-shifting effects. This study investigated the effects of evening exposure to blue-enriched polychromatic white (BEL) vs. polychromatic white light (WL) on sleep inertia dissipation the following morning in older adults.

Methods—Ten healthy older adults (average age = 63.3 yrs; 6F) participated in a 13-day study comprising three baseline days, an initial circadian phase assessment, four days with 2-h evening light exposures, a post light exposure circadian phase assessment and three recovery days. Participants were randomized to either BEL or WL of the same irradiance for the four evening light exposures. On the next mornings at 2, 12, 22 and 32 minutes after each wake time, the participants completed a 90-s digit-symbol substitution test (DSST) to assess working memory, and objective alertness was assessed using a wake EEG recording. DSST and power density from the wake EEG recordings were compared between the two groups.

Results—DSST performance improved with time awake ($p < 0.0001$) and across study days in both light exposure groups ($p < 0.0001$). There was no main effect of group, although we observed a significant day $\times$ group interaction ($p = 0.0004$), whereby participants exposed to BEL performed significantly better on the first two mornings after light exposures than participants in WL (post-hoc, $p < 0.05$). On those days, the BEL group showed higher EEG activity in some of the frequency bins in the sigma and beta range ($p < 0.05$) on the wake EEG.

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Conclusion—Exposure to blue-enriched white light in the evening significantly improved DSST performance the following morning when compared to polychromatic white light. This was associated with a higher level of objective alertness on the wake EEG, but not with changes in sleep or circadian timing.

Keywords

light; cognition; alertness; aging; circadian; sleep

1. Introduction

1.1 Sleep inertia

Sleep inertia is defined as the alertness and cognitive impairment evidenced upon awakening from sleep and which progressively improves over the initial ~two hours of wakefulness [1–3]. This performance impairment has been shown to worsen when the pre-sleep wake episode is prolonged, when waking up from deeper stages vs. lighter stages of Non Rapid Eye Movement Sleep (NREM) [4, 5], from NREM compared to REM sleep [6–8], and when waking up during the biological night vs. the biological day [8–10].

1.2 Age-related changes in sleep and circadian rhythms

Normal aging is associated with changes in sleep, including earlier bedtimes and wake times, reduced sleep consolidation with an increased number of night awakenings, and a decline in the amount and the amplitude of electroencephalogram (EEG) slow waves during the night [11, 12]. The cognitive and alertness impairments associated with sleep inertia have been hypothesized to lead to an increased risk of falls and other injuries upon awakening in older adults [8].

In addition to the age-related changes in sleep, there are also changes in the other major sleep regulatory process, the circadian timing system. Older adults are reported to have earlier timing of their endogenous circadian rhythms and to wake at an earlier biological time (a shorter phase angle of entrainment) [11, 13, 14]. This ‘misalignment’ has been hypothesized to contribute to age-related sleep disturbances.

1.3 Circadian phase shifting effects and cognitive effects of light exposure

Exposure to light has been shown to have intensity-, wavelength- and circadian phase-dependent effects on the circadian pacemaker [15–19]. These effects have been shown to be mediated through specialized intrinsically photosensitive retinal ganglion cells, containing the photopigment, melanopsin, with a peak sensitivity in the shorter-wavelength range of light (480nm) [18, 20, 21]. These effects of light are also enhanced in participants when they are in dim light compared to ordinary indoor light prior to the light exposure, suggesting a sensitizing effect of prior dim light exposure [22]. In addition to its well-described circadian phase shifting effect, light also has been shown to have acute alerting and cognitive effects [23–30], which are also enhanced when light exposure follows exposure to dim light [26, 31, 32]. Finally, effects of light exposure on EEG power density have been shown to persist even when the light exposure had ended [31, 33]. These acute effects of light on cognition were

shown in studies using polychromatic white light. In addition, wavelength-dependent effects of light on cognition have been shown: exposure to blue-enriched light 1.5 h after having performed a verbal word learning task has been recently shown to improve recall when compared to amber light [34]. Exposure to blue light, compared to violet light has been shown to increase activity in the hippocampus, amygdala and the locus coeruleus, which are associated with memory formation for the former and wakefulness/alertness for the latter [35].

1.4 Effects of evening light exposure on the sleep of healthy older adults with disrupted sleep

Previous studies have suggested beneficial effects of evening light exposures on the sleep and/or cognition of older adults [36–38].

In order to optimize the relative timing between the sleep episode and endogenous circadian rhythms, we exposed healthy older adults to bright evening light on four consecutive evenings. We randomized them to either blue-enriched or ordinary polychromatic white light of the same photon density [25]. In both groups, we significantly delayed the timing of their endogenous melatonin rhythm and found that after light exposure, the participants had prolonged REM sleep latency but otherwise no significant change in sleep efficiency, duration or overall sleep structure; as expected, the participants showed greater alertness during the evening light exposure sessions [25]. We also found no significant differences between the two groups in the phase delay shift magnitude, or the post light exposure timing of dim light melatonin onset relative to bedtime [25].

1.5 Study aim

Following up on earlier studies reporting that light exposure has long lasting effects on brain activity [31, 32], we hypothesized that on the mornings following evening light exposures in the study mentioned in 1.4, the participants would show improved cognitive performance and objective alertness compared to the days when they had not been exposed to bright evening light. Due to previous findings that monochromatic blue light exposure improved cognition but also elicited higher activity in alertness and memory formation-related regions [34, 35], we also hypothesized that participants exposed to the polychromatic blue-enriched white light would have enhanced cognitive performance compared to those who had been exposed to white polychromatic light of the same power density.

2. Methods

2.1 Population

We recruited healthy older adults (≥ 55 years old) with a sleep complaint (waking up too early and/or frequent nighttime awakenings) through newspaper advertisements, flyers, and by giving community talks on sleep and aging.

All participants were screened for medical, psychological and ophthalmological disorders through questionnaires, a medical history and physical examination, an ophthalmological examination, and a structured interview with a clinical psychologist. In addition, all study

participants underwent an overnight clinical polysomnography to screen for sleep apnea and periodic limb movement disorder. In total, 10 older adults (6 females; mean age 63.3 ± 3 yrs; $\pm$ SD) participated in this study.

2.2 Study design

Prior to entering the laboratory portion of the study, each participant spent two weeks at home following a self-selected, consistent ($\pm$ 30 minutes) 8-hour nightly sleep opportunity. Adherence was checked through a sleep diary, a wrist-worn activity monitor (Actiwatch-L, Respironics, Bend, OR, USA), as well as voicemail time-stamped call-ins from the participants when they went to bed and got out of bed each night. Following this pre-study segment, participants began the 13-day laboratory portion of the study. The study protocol was divided into 5 parts: 1) three baseline days (Days 1 to 3), 2) an initial circadian phase assessment (Days 4 and 5); 3), four intervention days during which they were exposed to either blue enriched or polychromatic white light for two hours each evening (Days 5 to 8); 4) a final circadian phase assessment (Days 9 and 10) and 5); three follow-up days similar to the baseline days (Days 11 to 13). On all days except Days 4 and 9, the participants were allowed to leave the laboratory from 4 h after their habitual wake time until 6 h before their habitual bedtime. During those same hours, the light blocking shades and the shutters of their laboratory room window were opened to let natural light into the room. During the 8-hour scheduled sleep episodes, all room lights were switched off. On the circadian phase assessment days (see below) as well as the 4 hours before bedtime on light exposure days (Days 5–8), the room lighting was dimmed (<3 lux). At all other times, the room lighting was typical indoor lighting delivered from a ceiling fixture (see Figure 1 for a schematic overview of the full study protocol).

2.3 Circadian phase assessments

The two circadian phase assessments (Days 4–5 and 9–10) were carried out to determine whether the lighting intervention produced any change in the timing of the dim light melatonin onset (DLMO). Each assessment consisted of controlled posture (“CP”, with the participant restricted to bed for the entire phase assessment), controlled dim lighting (see above), and collection of blood and/or saliva samples for melatonin assay. The first assessment (CP1) started at wake time on Day 4 and ended 4h after wake time on Day 5. The second assessment (CP2) started at wake time on Day 9 and ended 4h after wake time on Day 10.

2.4 Experimental light exposures

The 2-hour experimental light exposures (LE) took place on the evenings of Days 5 to 8 and began 3 hours before bedtime (see Figure 1). During the LE, the participant was required to remain seated approximately 30–50 cm directly facing the front of a 62 cm $\times$ 30 cm light box, and to keep his/her eyes open and directed towards the light box. Compliance was verified by a trained study team member who remained in the room throughout the LE. Irradiance and illuminance levels throughout the LE were regularly assessed using a research radiometer/power meter (Model IL 1400, International Light, Peabody, MA, USA). Each participant was randomly assigned to one of two different LE sources: polychromatic white fluorescent light (4100 K) or blue-enriched polychromatic white fluorescent light

(Philips Lighting B.V, The Netherlands). The photon density of the two sources was designed to be equal, at a target level of $1.E+15$ photons/cm²/s, corresponding to 370 $\mu\text{W}/\text{cm}^2$ (white polychromatic light source) and 320 $\mu\text{W}/\text{cm}^2$ (blue enriched polychromatic white light source). The blue-enriched lamps were prototypes that were provided by Philips Lighting (Eindhoven, The Netherlands) for use in this study. Our aim had been to achieve light exposure levels that were powerful enough to have a phase delaying effect even though the participants were ambulatory during the day and therefore potentially exposed to bright (>1000 lux) light, which may have de-sensitized them to the effect of bright light exposure in the evening. However, we also attempted to minimize the potential negative side effects (such as glare) which would make the light exposure less likely to be adhered to in a complete ambulatory setting. As described in our previous publication [25], the irradiance and photon fluxes achieved in a vertical direction at the eye level, were not statistically different between the blue-enriched (370 $\mu\text{W}/\text{cm}^2$) and the white polychromatic light source (352 $\mu\text{W}/\text{cm}^2$).

2.5 Sleep inertia testing (SIT)

On the morning of every study day, participants were given a series of short cognitive test batteries (less than 6 minutes each) upon awakening to assess their performance and alertness and the dissipation of sleep inertia. The four test batteries occurred at 2, 12, 22 and 32 minutes after scheduled awakening. Each test battery included a 90-second digit-symbol substitution task (DSST; [39]) administered on a computer, followed by a 3-minute Karolinska Drowsiness Test (KDT; [40]). The participants remained in a semi-recumbent position in bed from the time they were awakened by a study staff member, until the last sleep inertia test battery was completed, approximately 40 minutes after scheduled wake time.

2.5.1 DSST—The DSST [39] consisted of the numbers 1–9 presented across the top of the computer screen, with a symbol below each number. A target box in the middle of the screen displayed a symbol, and the participant was instructed to press the number corresponding to the symbol as quickly and accurately as possible. The task continued for 1.5 minutes. Each time the DSST was administered, the symbols corresponding to each number were re-ordered so that the participant could not memorize the correct associations between tests. The number of correct trials per DSST session was used as the DSST raw score [8, 10, 41, 42].

2.5.2 Wake EEG Recordings—Prior to each scheduled sleep opportunity, electrodes were placed on the participant's face and scalp for EEG recordings. The montage included six scalp recording sites (C3, C4, Fz, Cz, Pz, Oz) in addition to two electrooculograms (LOC, ROC). The signals were recorded using an ambulatory recording system (Vitaport 3, Temec, The Netherlands). The EEG signals were high-pass filtered at a time constant of 1 s and low-pass filtered at 70 Hz (Bessel fourth-order antialiasing; > 80 dB). The signals were digitized with a resolution of 12 bit (range 500 μV ; sampling rate 256 Hz, storage rate 128 Hz), stored on a Flash RAM card, and downloaded offline at the end of the sleep inertia testing sessions.

Immediately following each DSST, a 3-min Karolinska Drowsiness Tests (KDT) was administered in order to better obtain artifact-free wake EEG data [43, 44]. During KDT testing, participants were asked to fix their gaze at a target and remain still without moving, least blinking, or talking.

After each study, the wake EEG recordings were visually scored in 30-s epochs according to standard criteria using a central derivation (Cz) referenced against mastoids to exclude microsleeps [45]. Next, all artifacts (due to blinking or movements) were manually marked and removed, and the remaining artifact-free EEG recordings were then subjected to spectral analysis by using a Fast Fourier Transform (Vitascore, Temec, The Netherlands). Because of blinks, movement artifacts and technical problems, 46 KDT recordings (out of 480 in total, i.e. 9.6%) were excluded prior to analysis. Artifact free 30-s epochs of waking EEG were averaged using 2-s windows, which resulted in a 0.5 Hz resolution.

2.6 Sleep scoring

In order to evaluate whether the sleep stages of the last hour of scheduled sleep had an impact on the following cognitive test battery, we scored the last hour of scheduled sleep on the two mornings where we found significant differences in performance between the two light exposure groups on the DSST (the sleep episode occurring between Day 5 and Day 6 and the sleep episode occurring between Day 6 and Day 7). The visual scoring was done in accordance with International Guidelines by a trained scorer (38, 39) Rechtschaffen & Kales guidelines [45], and updated with the new scoring rules of the American Association of Sleep Medicine [46]. Data from sleep scorings for other sleep episodes from this study were previously reported [25].

2.7 Statistical analyses

2.7.1 DSST

2.7.1.1 Comparison of baseline days: We first tested whether there were any significant differences between the two groups on baseline days using a mixed model analysis (PROC MIXED) using the factors LIGHT (BEL or WL), TIME AWAKE (with 1 = DSSTs taken between 0 and 10 min after wake time, 2 = between 10 and 20 min after wake time, 3 = between 20 and 30 min after wake time and 4 = between 30 and 40 min after wake time), and DAY (Day 2, Day 3).

2.7.1.2 Normalization of DSST data relative to baseline: There was no significant difference between the two light groups at baseline (main effect of LIGHT $F_{1,8} = 1.76$; $p = 0.22$). Because we had inter-individual differences unrelated to the light group, we normalized the DSST data of each participant to their baseline. We therefore calculated for each individual the average correct DSST trials from the two baseline days (i.e. the 4 DSST trials on Day 2 and the 4 DSST trials on Day 3). We then subtracted each individual's baseline DSST average from each subsequent DSST raw score. This will be referred to as the DSST normalized score.

2.7.1.3 Testing effects of time awake, day of protocol and type of evening light exposure on DSST performance: Normalized DSST scores were then used as the outcome variable

in a mixed model analysis testing the following main effects: 1) 'DAY' (as a class variable); 2) time since awakening, 'TIME AWAKE'; and 3) LIGHT (BEL vs. WL).

2.7.1.4 Effect of awakening from REM vs. NREM on DSST performance: For the two days where we found a significant difference in DSST performance between the two light exposure groups, we also tested whether waking up from REM vs. NREM affected DSST performance. To do this, we first excluded data from participants who woke up more than 10 minutes before the scheduled awakening. This happened in 6 of the 20 sleep episodes. In the remaining 14 sleep episodes, we examined which sleep stage was predominant in the final 10 minutes of sleep, and further classified the sleep into NREM (N1, N2, N3) or REM sleep. We then examined in both univariate then adjusted (for light group, LIGHT) mixed model analyses the effect of waking up from REM vs. NREM on DSST performance on the two days where we had found a significant difference between the groups.

2.7.2 Wake EEG power density—We used the average EEG power density during the KDTs for each participant on the first morning of CP1 as the reference to which their EEG power density on other days of the protocol was compared.

We compared EEG power density from five different segments of the study as outlined in Table 1. The different segments of the study were described as a main effect of 'CONDITION' with each segment corresponding to a different condition (see Table 1).

We first averaged relative EEG power density for each 3 minute SIT session on each day. We then examined whether there was an effect of time awake across each of the mornings by comparing each 0.5 Hz frequency bin between 1 and 25 Hz across the four SITs taken each morning. We did not find a statistically significant effect of time awake (see section 3.2 below), and therefore EEG power density across all four sleep inertia test (SIT) sessions each day was collapsed.

2.7.3 Correlation between relative EEG power density and DSST performance —To determine whether the differences in DSST performance we found between the two groups on days 6 and 7 could be attributed to light exposure-dependent changes in relative EEG power density, we averaged the four normalized DSST scores for each participant (on each day) by performing Pearson's correlations between the relative EEG power density for each frequency bin and average DSST performance on that respective day. We first ran the correlations on combined WL and BEL group data, and second on the WL and BEL groups separately.

Analyses of the wake EEG spectra were done on log-transformed raw data to approximate the normal distribution. Statistical analyses were performed with the software SAS (SAS Institute Inc, Cary, NC, USA, version 9.1.3). For each frequency bin, we used a mixed regression model with the factor 'LIGHT' and the factor 'CONDITION' (as described above) and the interaction between the two main effects. For significant main effects or interactions, post hoc analysis was performed by using a Tukey-Kramer test with p-value adjustment for multiple comparisons.

3. Results

3.1 DSST

3.1.1 Comparison of the two groups on baseline days—We found no statistically significant difference in the average number of correct DSST trials between the blue-enriched light group (BEL) and the white light group (WL) on the Baseline Days (39.92 ± 7.19 and 34.29 ± 6.27 , respectively, $F_{1,8}=1.75$, $p=0.22$). We did not find a significant effect of day (Day 2 vs. Day 3; $F_{1,9}=0.00$, $p=0.9$, Figure 2).

3.1.2 Effect of time awake, day of protocol and type of evening light exposure on DSST performance—There was a significant effect of TIME AWAKE ($F_{3,27}=18.28$, $p<0.0001$, Figure 2), such that during the first test (i.e. in first 10 min after awakening) the participants completed significantly fewer trials than during tests done between the three later tests (the average score increased by $+3.48$, $p=0.0006$; $+4.75$ $p<0.0001$ and $+5.02$, $p<0.0001$ per test, respectively). We also found a significant main effect of DAY, such that participants in each light group performed better on Days 7, 8, 11, 12 and 13 than on the other days of the protocol ($F_{11,88}=12.16$; $p<0.0001$, all post hoc tests between these days and all other days in the protocol were significant ($p<0.05$), except for the post-hoc comparison between Day 8 and Day 9 ($p>0.05$), see Fig. 2). We found no significant main effect of LIGHT ($F_{1,8}=0.79$; $p=0.39$), but there was a significant ‘LIGHT $\times$ DAY’ interaction ($F_{11,88}=3.5$; $p=0.0004$), such that participants who had been exposed to the BEL on the evening before performed significantly better on Days 6 and 7 than those who had been exposed to WL ($p=0.02$ and $p=0.04$, respectively, see Fig. 2). This corresponded to an effect size of 1.2, calculated for an F-test with repeated measures (4 per participant) with an $\alpha = 0.02$, power of 0.95 and the sample size of 10 divided into 2 groups.

3.1.3 Effect of awakening from REM vs. NREM on DSST performance on days 6 and 7—As mentioned in the methods, we were able to analyze the information for 14 sleep episodes out of 20 in total as we excluded those who had more than 10 minutes of wake prior to scheduled awakening. Overall, there was no significant difference in cognitive performance between waking from REM or NREM sleep: when waking from REM, the normalized DSST score was 5 ± 6 and when waking from NREM, it was 3.5 ± 8.7 ($p = 0.96$).

When adjusting for LIGHT, in the blue light group the average normalized DSST score in those waking from NREM was 9.45 ± 6.7 and in those waking from REM 7.8 ± 4.4 , while in the white light group it was -1.66 ± 7.18 and 2.65 ± 5.1 , respectively (effect of LIGHT, $p=0.001$; no significant effect of waking up from REM vs. NREM). Overall, there was therefore no effect of REM vs. NREM on DSST performance in this group.

3.2 Wake EEG power density

We found no significant differences between the five study conditions in the lower EEG frequency bins (from 0 to 8 Hz), or differences between the light groups, or any interaction between these two factors in that EEG frequency range (all p-values for main effects of CONDITION, LIGHT, and CONDITION $\times$ LIGHT interaction: > 0.05). In some of the EEG

frequency bins of the sigma range (i.e. between 13.5–14 Hz and 15–15.5 Hz) the BEL group showed significantly higher EEG power density than the WL group (main effect of LIGHT; $F_{1,7}=6.97$, $p=0.03$ and $F_{1,7}=9.16$, $p=0.02$, respectively).

We also found a $\text{CONDITION} \times \text{LIGHT}$ interaction ($F_{4,27} = 2.76$; $p<0.05$), such that during the LE days condition (as defined in Table 1: i.e., sleep inertia testing performed between day 6 to day 8 included), the BEL group had higher EEG power density in the sigma range than the WL group (between 13.5–15.5 Hz; $p<0.05$; Fig. 3). Moreover, in the last days of the protocol (days 11, 12, 13), following the second CP (PostCP2, see Table 1), the BEL group displayed significantly higher EEG power density than the WL group in some frequency bins of the alpha/sigma range (specifically from 12.5 to 15 Hz and from 15.5 to 16 Hz) and beta ranges (17.5–18 Hz, 18–18.5 Hz, 19–19.5 Hz, 20–20.5, 20.5–21 Hz, 22.5–23 Hz, 23.5–24 Hz and 24–24.5 Hz; $p<0.05$, Figure 3).

We also found a significant effect of CONDITION , such that EEG power density in some frequency bins of the beta range was higher in both groups during BL conditions (specifically, 22.5–25 Hz), on LE days (specifically, 23–24.5 Hz and 25–25.5 Hz) and PostCP2 (specifically 22.5–23.5 Hz and 24–25 Hz) when compared to CP2 (all $p<0.05$ for effect of condition and post hoc analysis $p<0.05$, see Figure 4 Panels A, B, and C, respectively). In addition, on LE days, EEG alpha activity between 8.5 and 9 Hz was higher than during BL ($F_{4,27}=3.73$, $p=0.015$, post hoc, $p=0.03$, data not shown) and between 12.5 and 13 Hz was higher than during CP2 ($F_{4,27}=2.89$, $p=0.04$, post hoc $p=0.03$, see Figure 4).

3.3 Correlation between EEG power density and DSST performance on days 6 and 7

When analyzing both BEL and WL groups together, on day 6 of the protocol, there was a significant negative relationship between EEG power density and DSST performance in the theta range at 5.5 – 6 Hz: Pearson's R value = -0.72 , $p = 0.017$; and between 6.5 – 7 Hz: Pearson's R value = -0.64 , $p = 0.049$. On day 7 of the protocol, there was a significant negative relationship between EEG power density and DSST performance in one frequency bin in the theta range (5.5 – 6 Hz, $R = -0.78$, $p=0.01$). When looking at each group separately, we found no association between relative EEG power density in the WL group and DSST performance on either day. In the BEL group, on day 7, we found a negative relationship in one frequency bin in the EEG theta range (between 5.5 – 6 Hz, $R = -0.88$, $p = 0.04$).

4. Discussion

In this randomized study with a between-within design, we compared the effects of two different evening light conditions on subsequent cognitive performance and objective alertness the following morning in healthy older adults. We found that participants who had been exposed on the previous evening to blue-enriched light performed significantly better on a working memory task (DSST) on the next morning than those in the white light group, following the first two evening light exposures. We also found that EEG power density was higher in some frequency ranges of the sigma and beta ranges during the BEL than the WL condition.

Sleep inertia has been shown to worsen with an extended duration of wakefulness before sleep [4, 5, 47]. Some studies also have shown larger sleep inertia when waking up during the biological night vs. the biological day [8–10] (i.e., a circadian effects), or (3) waking up from NREM vs. REM sleep [6–8].

We first address the question whether a change in prior duration of wakefulness, (i.e. caused by a homeostatic effect) might have had an effect on sleep inertia in our study. Since we carefully controlled for prior sleep history and as shown in our previous paper [25], the two groups did not show any significant difference in their sleep efficiency, EEG sleep stages or sleep architecture before or after light exposure, making a reduced duration of wakefulness before sleep an unlikely mechanism through which the BEL would have had improved cognition compared to the WL. A study by Murphy and Campbell [38], showed improved daytime cognitive performance (sleep inertia was not assessed in that study) in older adults with sleep maintenance insomnia following evenings of light exposure over 15 weeks, however, this improvement in performance was associated with an improvement in sleep efficiency, in contrast to what we found in our study.

Another influence on cognitive performance upon awakening is the relative circadian phase relationship with sleep-wake timing [8]. It was shown that waking up and testing closer to the trough of core body temperature leads to worse performance with cognitive testing occurring about 8 hours after core body temperature trough leading to improved performance [8, 48].

In our study, we aimed to have two light exposure conditions with the same photon density albeit with different spectral power distribution. As a result, both groups experienced circadian phase delays of similar magnitudes, resulting in a comparable phase angle of entrainment between the circadian cycle and the sleep wake cycle in both groups on the constant postures preceding and following the four light exposure evenings as we previously reported [25]. Although we did not measure circadian phase on the two specific days where we found the DSST performance differences between groups, it is unlikely that the mechanism for the better performance in the BEL group was due to the BEL group testing at a more favorable circadian phase (for example, further away from the dim light melatonin onset) compared to the WL group on these days. We could only speculate that circadian amplitude was more enhanced in the BEL than the WL group which might have improved cognitive performance the next morning.

Another potential modifier of performance upon awakening is whether the participant awoke from REM vs. NREM sleep with awakening from REM sleep being associated with better performance [8]. We found however no significant difference in DSST performance when comparing the effect of waking from REM vs. NREM sleep, even when comparing DSST scores within each light group: the BEL group participants had significantly higher DSST scores than the participants in the WL group, both when waking from REM and from NREM sleep.

Another intriguing hypothesis was that evening light exposure with the BEL may have either a longer lasting effect on sleep-wake regulation, such that it provided a ‘stabilizing’ effect on

the circadian clock which then led to the enhanced performance the next morning, or that light may have a direct effect on the brain. Indeed, as mentioned in the introduction, older healthy adults undergo age-related changes in the function of their circadian pacemaker, leading to increased sleep fragmentation but also to the decrease in amplitude of known endogenous rhythms (for example melatonin [49] or urine output, [50]). Light exposure and melatonin intake have been shown to improve the sleep fragmentation observed in older adults with insomnia [36, 51], maybe by giving a stronger daily resetting signal to the circadian clock, which would ‘stabilize’ the clock, leading to higher amplitude of rhythms, for example of sleep and wakefulness signals. To explore whether our evening light exposures may have had either a prolonged and/or potentiating effect on the sleep wake signals (i.e. by either suppressing a drowsy or sleep drive and/or increasing a wake drive), we analyzed the EEG wake spectra obtained at the same time as the DSST. Since the BEL group had higher EEG activity throughout all sleep inertia testing of the study in the higher sigma range (i.e. between 13.5–14 Hz and 15–15.5 Hz) it might be, that this could have caused also better performance. However, cognitive performance on the DSST on baseline days, during the first and second constant posture, and in the three final days of the protocol was not significantly different between the two groups and we did not find any correlation between those frequency bins and DSST performance. Therefore it is unlikely that this overall differences in EEG activity between the two groups could explain that the BEL group performed significantly better than the WL group on the DSST following evening light exposure.

We found higher EEG activity in the sigma and beta range in the BEL during light exposure days compared to the WL. It is possible that this higher EEG activity in those frequency ranges reflected higher levels of cortical arousal, translating into increased alertness and cognitive performance. Beta activity has indeed been associated higher cortical activity [52]. In our earlier report, we found that in the post light exposure evenings, participants in both the WL and BEL group rated themselves as more alert and had higher EEG power density in some frequency bins in the alpha and beta ranges compared to the pre-light exposure evening [25]. In addition, others [33, 53] showed that evening light exposures had longer lasting effects on EEG power density into the subsequent sleep episode.

We ran a correlation analysis in order to determine whether better cognitive performance was associated with waking EEG activity on days 6 and 7 of the protocol (where we had found the differences in DSST performance). We found that some EEG frequency bins in the theta range were negatively correlated with better DSST performance but did not find any significant association between any frequency bin in the beta or sigma ranges and DSST performance. This could mean either that we did not have enough power to find an association between the relative increase in EEG power density in those frequency bins in the BEL group compared to the WL group and DSST performance, or that there was in fact no relationship. Therefore, if not mediated through improvement in objective alertness, the differences between the two groups may have been mediated by direct effects of light on certain brain structures. As described in an earlier study using functional Magnetic Resonance Imaging [35], exposure to monochromatic blue light was shown to increase activity in the hippocampus and the locus coeruleus compared to exposure to violet light.

The blue-enriched light used in our study may have had a similar effect on those subcortical and limbic structures, leading to improvements in the DSST performance.

After those two evening light exposures, subsequent DSST scores were no longer significantly different between the two groups. This was due to the WL group increasing their scores and therefore ‘catching up’ with the BL group. The fact that the BEL group did not improve further may reflect a threshold effect whereby the participants had reached their best performance and could not improve further. Subsequently in both groups, DSST scores returned back to baseline levels during the second constant posture, on both days, and then rose again on the last three days, which we attribute to the dim light conditions of the constant posture. Since we found no significant difference in sleep architecture and sleep duration before and after light exposure (except for REM sleep latency) a difference in sleep could not explain the significant drop in performance in both groups on the second constant posture days.

The only difference compared to previous days (light exposure days) and following days (post second constant posture days) were the acute testing conditions: during the light exposure days, the participants tested in normal indoors light setting (about 90 lx) while during the constant postures, they tested in dim light. Similarly, on the following last days of the protocol, DSST performance improved again compared to the two days of the second constant posture, corresponding to testing under the normal indoors light setting. A similar pattern was found for objective alertness, whereby EEG power density on the mornings following an evening light exposure when testing was done under 90 lx showed significant higher activity in some frequency bins in the sigma and beta ranges across all participants. This increased activity completely faded on the two days of the second constant posture when the participants tested under dim light conditions. And it reappeared when they tested again in the 90 lx conditions. These acute effects of light on cognition and alertness are in accordance with other studies which also found acute alerting effects of light [23, 24, 26, 27].

Our main limitation was the small sample size (ten participants in total, five in each group) which definitely limits the generalizability of our findings. This may also have led to type II errors (lack of effects because of the limited sample size). A second limitation was the absence of a control group exposed only to dim light during the light exposure days. Such a group could have helped us better understand the mechanism leading to improvement in performance throughout the study, in particular distinguishing for the WL group whether the improvement was a result of the evening light exposures or whether it was only due to a learning effect. A last limitation is that we did not control for light exposures during daytime, when participants were free to leave the laboratory. They might have got different light exposures and followed different activities, which additionally modulated the results in our small study group.

It will be important to see if there is everyday applicability of such a protocol as older adults may not be willing to adhere with a 2-hour evening light exposure. Whether similar results could be achieved with a more user-friendly source of light, or intermittent exposure to light, remains to be tested.

We have found an effect of evening light exposures on the following morning's cognition in healthy older adults whose phase angle of entrainment between core body temperature trough/melatonin peak and wake time has been shown to be shorter than that in young adults. This potential effect of light should be particularly interesting to test also in situations when the sleep episode of older adults is timed at adverse circadian times (such as in shift workers) as a countermeasure for shift workers' induced cognitive impairments.

To summarize, this study gives further evidence that light may have longer lasting effects. We showed that evening light exposure influenced the following morning's objective alertness and cognitive performance. The fact that the effects were more prominent in the blue enriched light group suggests that they may be mediated through the melanopsin-dependent intrinsically photosensitive retinal ganglion cells. A larger study would be needed to confirm whether light exposure can indeed have beneficial and longer lasting effects also on other physiological and behavioral functions.

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Highlights

- We exposed healthy older adults to evening blue-enriched vs. ordinary white light.
- Blue-enriched light exposure improved working memory performance the next morning.
- This effect was not due to changes in circadian timing or sleep quality.
- This effect was not due to waking from REM vs. NREM.
- Blue-enriched light exposure also increased objective alertness on the wake EEG the next morning.

Fig. 1. Representation of the full 13-day semi-ambulatory protocol

Days 1–3: baseline days; days 4–5: first constant posture (CP1); days 5–8: days with the evening light exposure intervention; days 9–10: second constant posture (CP2); days 11–13: post CP2 days. Filled bars represent the 8 hour sleep episodes, hashed bars represent procedures done in a dim light (< 3 lx) setting, open bars represent wake episodes in 90 lx setting and/or outdoors light, open bars with a sun symbol (☀) represent the 2-hour evening light exposure session. On all days, except for days 4 and 9, participants were allowed to leave the laboratory from 4 hours after wake time to 6 hours before bedtime. Sleep inertia

tests (DSST and KDT) occurred at all wake times, from day 2 to day 13, every 10 minutes, starting from 1 minute after wake time and ending 40 minutes after wake time.

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Fig. 2. Average (SEM) number of correct DSST trials normalized to individual baseline average score in the blue-enriched (BEL, full circles) and 4100 K polychromatic white light group (WL, open circles)

There was a significant main effect of TIME AWAKE within each session, no main effect of LIGHT, a significant main effect of DAY with both groups scoring significantly higher on days 7, 8, 11, 12, 13 compared to other days, and a significant 'LIGHT-by-DAY' interaction whereby the BEL group scored significantly higher than the WL group on days 6 and 7 of the protocol (post hoc testing $p < 0.05$, as indicated by *). The shaded gray areas represent testing done in dim light conditions (< 3 lx) during the two constant postures while on all other days, testing was done in standard room light levels (90 lx).

Fig. 3. Average (SEM) EEG power density for each 0.5 Hz frequency bin relative to that measured on the first day of the first constant posture (day 4 of protocol, shown by the dotted line (—)) in the group exposed to blue-enriched light (BEL, filled circles) and the 4100K polychromatic white light (WL, open circles) in each condition defined in table 1. Panel A: baseline days (BL), Panel B: second day of first constant posture (CP1). Panel C: Light exposure days (LEdays), Panel D: Second constant posture days (CP2). Panel E: three days following second constant posture (PostCP2). Filled triangles indicate significant differences between groups in post-hoc testing of the 'CONDITION-by- LIGHT' interaction.

Fig. 4. Average (SEM) EEG power density relative to the first morning of the first CP (shown by the dotted line (—)) illustrating in which frequency bins significant differences in overall relative power density (all participants) were found in the post hoc testing of a significant effect of CONDITION

In all panels, post hoc testing significance is shown with filled triangles: Panel A shows the comparison between baseline days (BL; open circles) and the two days of the second constant posture (CP2; filled circles). Panel B shows the comparison between the three post light exposure days (LE days) (open circles) compared to the two days of the second constant posture (CP2; filled circles). Panel C shows the comparison between the three days

following the second constant posture (final days of the protocol, PostCP2; open circles) and that on the two days of the second constant posture (CP2; filled circles).

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Table 1

Coding of conditions in relation with the day(s) within the protocol and background light conditions at the time of testing for the EEG power spectra analysis. Day 4 of the protocol (1st day of CP1) was used as baseline.

Condition	Abbreviation	Day(s) of protocol	Background light levels at the time of testing (in lux)
Baseline days	BL	2, 3	90
Constant posture 1	CP1	5	3<
Light exposure days	LEdays	6, 7, 8	90
Constant posture 2	CP2	9, 10	3<
Post constant posture	PostCP2	11, 12, 13	90