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Blue light spectrum and its effects on selected aspects of human
sleep and cognition

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Summary

Background: Since the discovery of ipRGCs (intrinsic photosensitive retinal ganglion cells) in the retina, new research possibilities for studying the effects of light on the regulation of various behavioral and physiological functions that are independent of image formation arose. As ipRGCs are most sensitive to light of short wavelengths (460-480nm), this dissertation focuses on current topics related to the use of blue light, emphasizing its influence on circadian rhythms, sleep and cognitive performance and possible applications in clinical and non-clinical settings.

Aims: The first study aimed to explore the effects of 20 minutes of narrow-bandwidth light exposure of different wavelengths on various neuropsychological and neurophysiological parameters of vigilance in healthy volunteers. The objective of the second study was to assess the effect of combining CBT-I (cognitive-behavioral therapy for insomnia) with wearing blue-light blocking glasses 90 minutes before bedtime on subjective and objective sleep parameters and daily symptoms (anxiety, depression, hyperarousal). The third study aimed to examine subjective sleep quality in a population of healthy volunteers and its association with evening and night light exposure to screens of media devices.

Methods: In the first study, twelve healthy volunteers went through 3 sessions of 20 minutes of light exposure of different wavelengths (455, 508, and 629 nm, with an irradiance of 14 µW/cm2), while EEG was recorded (including ERP (event-related potential) P300 and spectral characteristics) and behavioral data (subjective sleepiness, reaction time) gathered. In the second study, 30 patients completed a CBT-I group therapy program, with groups randomly assigned to either active (blue-light filtering glasses) condition, or placebo (glasses without filtering properties) condition. Patients were continually monitored by wristwatch actigraphy, kept their sleep diaries, and completed a standard questionnaire battery at admission and after the end of the program. Lastly, 693 participants in total completed an online questionnaire battery consisting of several sleep-related questionnaires: PSQI, FSS, MCTQ, MEQ and added questions assessing the timing and character of the evening and night exposure to electronic devices (TV, PC, tablets and phones) and the use of various filters blocking short-wavelength light.

Results: Our analyses showed that the short-wavelength light condition (455nm) in the first study, was found to be the most effective in terms of its alerting effect for the following variables: subjective sleepiness, the latency of P300 response and absolute EEG power in higher beta (24-34 Hz) and gamma (35-50 Hz) range. The second study showed a greater reduction of anxiety symptoms in the active vs. placebo group of patients and significant prolongation of subjective total sleep time in the active group. When pre- and post-treatment results were compared in both groups separately, significant differences were observed for the scores in the

depression and hyperarousal scales in the active group only. In the active group, there was also a significant reduction of subjective sleep latency and an increase of subjective total sleep time without a change in objective sleep duration, which was significantly shortened in the placebo group. In the third study, our analyses showed that longer cumulative exposure to screen light in the evening was associated with greater sleep inertia in the morning and longer sleep latency on workdays. Furthermore, exposure to screen light 1.5h before sleep or during night awakenings was also associated with a decreased chance to wake up before the alarm time, larger social jet-lag, more pronounce daytime dysfunction, decreased subjective sleep quality, and more fatigue. A statistical trend for an increase in the duration of sleep on weekdays was also found in participants using blue-light filters in the evening hours.

Conclusion: Our results provide valuable insight into the alerting effects of short-wavelength (blue) light. We also show that avoiding blue light in the evening may help reduce the phase-delaying effect of light and facilitate an improvement in sleep parameters and psychiatric symptoms. Altogether, these results may contribute to the development of new lighting or light-filtering systems and may also be applicable for healthy sleep promotion in both the general and clinical populations.

Souhrn

Úvod: Od objevu ipRGC buněk sítnice se rozšířily možnosti vědeckého zkoumání vlivu světla na regulaci širokého spektra behaviorálních a fyziologických funkcí nezávislých na tvorbě obrazu. Vzhledem k tomu, že jsou ipRGC nejvíce citlivé na světlo krátkých vlnových délek (460-480nm) se tato dizertace zaměří primárně na vliv modrého světla na cirkadiánní systém, spánek, kognitivní funkce, a možné využití v klinické i neklinické oblasti.

Cíle: Cílem první studie bylo prozkoumat vliv 20-minutové expozice monochromatickému světlu různých vlnových délek na vybrané neuropsychologické a neurofyziologické parametry vigility u zdravých dobrovolníků. Druhá studie zkoumala efekt kombinace KBT-I a večerního nošení brýlí blokujících modré světlo na subjektivní a objektivní parametry spánku a denní symptomy (úzkost, deprese, hyperarousal). Cílem třetí studie bylo prozkoumat subjektivní kvalitu spánku u zdravé populace a její spojitost s večerním a nočním vystavováním se umělému světlu z obrazovek elektronických zařízení.

Metodika: V první studii bylo 12 zdravých dobrovolníků vystaveno celkem třem 20-minutovým expozicím světlu různých vlnových délek (455, 508, and 629 nm, zářivost 14 µW/cm2), při nichž podstoupili měření EEG (vč. EP P300 a

spektrálních charakteristik) a behaviorálních proměnných (subjektivní ospalost a reakční čas). Ve druhé studii celkem 30 jedinců s nespavostí absolvovalo standardní psychoterapeutický program pro léčbu nespavosti. Současně byli nahodile přiřazeni do aktivní (nosili brýle blokující modré světlo) nebo placebo skupiny (brýle bez filtračních charakteristik), a instruováni k nošení brýlí 90 minut před spánkem. Po celou dobu studie jim byla aktigrafy monitorována pohybová aktivita, denně vyplňovali spánkové deníky a baterii standardních dotazníků administrovaných při přijetí a po ukončení docházky do skupiny. V třetí studii celkem 693 pacientů vyplnilo online baterii dotazníků vztahujících se k spánku (PSQI, FSS, MCTQ, MEQ) a zodpovědělo otázky mapující délku a charakter večerního/nočního vystavení se displejům elektronických zařízení a použití filtrů blokujících modré světlo.

Výsledky: Analýzy v první studii ukázaly, že modré světlo (455nm) mělo nejvýraznější nabuzující účinek, který se projevil v následujících proměnných: subjektivní ospalost, latence P300 odpovědi a absolutní EEG výkon v pásmech vyšší bety (24-34 Hz) a gamy (35-50 Hz). Druhá studie ukázala vyšší pokles symptomů úzkosti v aktivní skupině ve srovnání s placebo skupinou. Současně došlo k signifikantnímu prodloužení subjektivní délky spánku u skupiny s brýlemi filtrujícími modré světlo. Při dalším srovnání efektu intervencí se prokázalo, že v skupině pacientů s brýlemi blokujícími modré světlo došlo k signifikantnímu poklesu skóru v škálách deprese a hyperarousalu, a to pouze u aktivní skupiny. V aktivní skupině se také prokázala signifikantně kratší spánková latence a prodloužení subjektivní délky spánku beze změn v objektivní délce spánku, která se naopak u placebo skupiny zkrátila. V třetí studii bylo zjištěno, že delší kumulativní expozice světlu obrazovek ve večerních hodinách je spojena se silnější spánkovou opilostí následující den ráno a delší spánkovou latencí v pracovních dnech. Dále jsme zjistili, že expozice světlu min. 90 minut před usnutím je spojena s nižší šancí se probudit před budíkem, větším sociálním jet-lagem, výraznějšími denními dysfunkcemi, sníženou subjektivní kvalitou spánku a vyšší únavou. Také se prokázala tendence k delšímu spánku v pracovní dny při používání filtrů blokujících modrou složku barevného spektra.

Závěr: Naše výsledky přinášejí cenný vhled do problematiky modrého světla a jeho prokognitivního účinku. Rovněž přinášejí důkazy o tom, že blokování modrého světla ve večerních hodinách může zmírnit fázový posun, zlepšit kvalitu spánku a přinést úlevu od psychiatrických symptomů. Celkově můžou být tyto výsledky přínosem při vývoji nových systémů osvětlení nebo filtrování světla a mohou mít také preventivní a terapeutický potenciál v obecné i klinické populaci.

1 Introduction

The mechanism by which the circadian system perceives light is one of the most exciting discoveries in modern biology. In addition to rods and cones, a third type of photoreceptive cells in the retina, the ipRGC (intrinsically photosensitive retinal ganglion cells), was discovered (Brainard, Hanifin, Rollag, et al., 2001; Hattar, Liao, Takao, Berson, & Yau, 2002; Thapan, Arendt, & Skene, 2001) and opened new research possibilities for studying the effects of light on the regulation of various behavioral and physiological functions that are independent of image formation (termed non-image-forming – NIF visual functions) (LeGates, Fernandez, & Hattar, 2014). The ipRGCs express the photopigment melanopsin and are predominantly sensitive to short-wavelength (blue) light (between 460-480nm). Initially, the ipRGCs were thought only to influence circadian rhythms, as they integrate and transmit photic information directly to the suprachiasmatic nucleus (SCN), the central circadian pacemaker/oscillator. SCN entrains the circadian timing system to the daily 24-h light/dark cycle and regulates the neural network of melatonin suppression (Blume, Garbazza, & Spitschan, 2019). However, many brain areas other than the SCN also receive direct projections from the ipRGCs and therefore represent vital targets of the NIF system by potentiating effects of light on pupillary constriction, sleep-wake cycle, alertness, and mood (Fernandez et al., 2018; Prayag, Münch, Aeschbach, Chellappa, & Gronfier, 2019). All these functions are not only regulated by natural daylight but are influenced by artificial lighting systems as well. In particular, this is the case in the evening and night hours, as the increasing use of light-emitting devices that contain a considerable proportion of shorter wavelengths of light has been associated with a high prevalence of insufficient sleep, affecting a majority of children (Falbe et al., 2015), adolescents (Hale et al., 2018) and adults (Exelmans & Van den Bulck, 2016; Yang, Yang, Mai, Zhou, & Ma, 2018). Aside from adverse effects of night exposure on our sleep and circadian rhythms (problems with sleep initiation and propensity, melatonin suppression, circadian phase delay, less slow-wave sleep) (Cajochen et al., 2011; Chang, Aeschbach, Duffy, & Czeisler, 2015; J. R. Cho, Joo, Koo, & Hong, 2013; van der Lely et al., 2015; Zeitzer, Fisicaro, Ruby, & Heller, 2014), short-wavelength (blue) light has also been associated with improvements in cognitive functioning (enhancing attention, working and declarative memory as well as executive functions (Cajochen et al., 2011; Gaggioni, Maquet, Schmidt, Dijk, & Vandewalle, 2014; Rahman et al., 2014; Rodriguez-Morilla, Madrid, Molina, & Correa, 2017; Slama, Deliens, Schmitz, Peigneux, & Leproult, 2015; Vandewalle, Maquet, & Dijk, 2009) or decision-making processes (Alkozei, Smith, & Killgore, 2016)). Thus, applying light or light-filtering interventions and recommendations may lead to new ways of fighting circadian desynchronization and enhancing one's cognitive functioning. Several approaches incorporating blue-light and its filtration will be the main focus of this doctoral thesis.

The first chapter of the theoretical summary covers the fundamentals of image- and non-image forming functions of light and light's role in regulating

circadian rhythms. It further deals with different aspects and parameters of light and their effect on physiological functions, emphasizing the role of blue (short-wavelength) light that will be the focus of the following chapters. The second chapter aims at exploring the influence of daylight and artificial light on sleep with a focus on melatonin suppression, phase-shift, and changes in sleep micro- and macrostructure. The third chapter explains the possible role of short-wavelength light in cognitive enhancement and underlying physiological mechanisms. The fourth chapter moves on to the chronotherapeutic potential of light and light-blocking interventions. Its main focus is on blocking short-wavelength light, artificial dawn simulation, and possible risks associated with evening and night exposure to artificial light. Finally, the fifth chapter offers some perspectives on future research in this area, emphasizing the use of spectral-tuning or bio-dynamic lighting in creating a circadian-friendly environment for clinical and non-clinical applications and the potential use of metameric light sources.

The experimental part covers three separate studies that are related to the topic of this dissertation. The first study compares light of three different wavelengths (455nm, 508nm, 629nm) and their effect on subjective and objectives parameters of vigilance. Using several electrophysiological and cognitive measures, we aim to provide further evidence regarding the alerting effects of short-wavelength light and thus contributing to future studies and potential applications in lighting or light-filtering technology.

The second study explores the potential of blue-light blocking glasses as an adjunct to a cognitive-behavioral therapy group program in patients with insomnia. This randomized controlled trial aimed to assess the effect of CBT-I (cognitive-behavioral therapy for insomnia) in combination with blue-light blocking glasses intervention that required the patients to wear glasses 90 minutes before scheduled bedtime. Subjective and objective (actigraphy-based) sleep parameters and other related measures (sleepiness, hyperarousal, symptoms of depression, and anxiety) were compared in active and placebo groups, opening new possibilities of using this cheap and easy-to-use chronotherapeutic tool in clinical and non-clinical populations.

The third study, being a large online questionnaire survey, aimed at screening a healthy adult population for the use of screen-based devices during the evening and night hours and its association with subjectively perceived sleep quality and other sleep-related parameters. The main focus of this study was to assess sleep in relation to "light-hygiene" recommendations (avoiding LED screen exposure in the evening and at night). Although the presence of light-hygiene parameters in current literature is very sparse, they are especially crucial for developing future interventions and strategies directly aimed at adhering to sleep (and light) hygiene recommendations with the potential to improve one's sleep.

The final discussion offers insight and concludes the three separate discussions of each of the presented studies, their limitations, and potential perspectives on future research.

2 Aims and Hypotheses

Research aims, and hypotheses

The primary objective of this thesis was to further clarify the contribution of the short-wavelengths to the cognition-enhancing properties of light and their potential role in disturbing our sleep. We aimed to explore the effects of narrow-bandwidth (monochromatic) light on the vigilance. We further aimed to test the potential of blue-light filtration when used as an adjunct to a standard psychotherapeutic intervention in insomnia patients. And lastly, our aim was to explore the characteristics of light exposure in the evening and during the night and their role in influencing our sleep and next-day functioning.

Study 1 - Alerting effects of short-wavelength (blue) light during the day

This study aimed to compare LED light of three different wavelengths (455nm, 508nm, 629nm) in terms of selected subjective and objective parameters of vigilance. We hypothesized that short-wavelength/blue (455nm) light condition would be superior to green- and red-light conditions, reducing subjective levels of sleepiness, reducing reaction time to visual stimuli, and enhancing brain responses in regions associated with visuospatial attention. Using several electrophysiological measures (spectral analysis, ERP, eLORETA), not applied in previous studies, and objective measures of cognitive processing within the same subjects during cognitive load, we planned to provide further information regarding the alerting effects of short-wavelength light, contributing to future studies and potential applications in lighting or light-filtering technology.

Study 2 - Benefits of blocking blue light in the evening when used as an adjunct to CBT for patients with insomnia

A randomized controlled trial was run to assess the effect of CBT-I in combination with blue-light-blocking glasses (BB glasses) – a simple and easy-to-use intervention to block the adverse effects of evening exposure to blue-light. A CBT-I group with active glasses was compared with a CBT-I group wearing clear placebo glasses. We expected to find improvement in sleep parameters and psychiatric symptoms in both groups with a larger effect in the group with active filtering glasses.

Study 3 - Exploring evening and night exposure to light from media screens and potential benefits of adhering to "light hygiene" recommendations in a healthy population

This study aimed to test a healthy population for the use of screen-based devices during the evening and night hours and its association with subjectively perceived sleep quality and other sleep-related parameters. Additionally, we decided to compare groups of participants based on their use of blue-light filters and the amount of time they are exposed to electronic devices throughout the day,

90 minutes before their usual bedtime (which is hypothesized to be especially important because of sensitivity to suppression of melatonin levels) and during the night-time and examine the differences in their subjectively perceived sleep quality. These parameters, as their presence in current literature, is very sparse, are especially crucial for developing future interventions and strategies directly aimed at adhering to sleep (and light) hygiene recommendations with the potential to improve one's sleep. We hypothesized that longer screen exposure times would be associated with worse sleep quality. We also predicted that screen exposure 90 minutes before bedtime would be associated with worse outcomes on all sleep-related measures, while blue-light filtering would be associated with better outcomes.

3 Materials and Methods

3.1 Study 1

Study protocol: The experiment consisted of 3 different sessions and was conducted on three separate days, with a week in-between sessions. The subjects, in a randomized order, were exposed to the light of different wavelengths on each day of the experiment. Experimental sessions consisted of a 10-minute red light adaptation to reach a sensitivity baseline for ipRGCs (as mentioned by Chellappa and colleagues Chellappa et al. (2014)) and a 15-minute dark condition for the adaptation of rods and cones followed by a five minutes-long oddball task also in darkness. After the oddball task, the subject performed a PVT (Psychomotor Vigilance Task (Dinges & Powell, 1985)) on a computer screen After the PVT task, the lightbox was turned on, and the subject went through 3 oddball sessions followed by a 5 min resting-state EEG measurement and a PVT task after switching the lightbox off. The total length of the "under light" session was about 20 minutes, after which the experiment was concluded. In between administered tasks, the subjects were also asked to rate their level of subjective sleepiness using the adapted version of the Karolinska Sleepiness Scale at seven different timepoints during each session. The protocol of the study is depicted in the following figure (Fig 1).
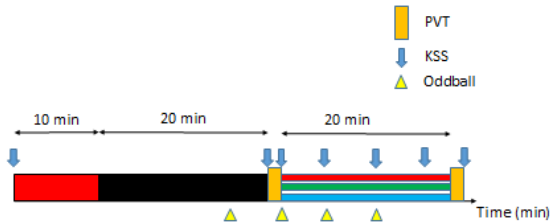

Fig 1. The protocol of the study. *Ten minutes of red light (629 nm) ipRGCs adaption followed by 20 minutes of the dark period (rod/cone adaptation), followed by approximately 20 minutes of exposure to one of three experimental lightning conditions. PVT, KSS, and Oddball measurements were conducted, as depicted in the figure.*

Participants: Twelve healthy (8 women and 4 men) volunteers between ages 24 and 32 (mean 27.3 years, SD = 2.38) were recruited and screened for severe neurological, psychiatric, and sleep disorders. The use of medication before the experiment was not allowed. All participants were nonsmokers and were instructed to refrain from consuming caffeine, alcohol, or other cognition-altering drugs during the 12-h period before the experimental sessions. None of them worked night shifts, nor has traveled across time zones in 4 weeks preceding the experiment. To minimize inter-individual variation in the circadian phase, individuals with extreme chronotypes were not accepted into the study.

Methods

Light exposure: Narrow-bandwidth light with short, medium or long wavelengths was delivered via custom-made lightbox device (Lightbox RGB 500, H. Medřický, LuxVitaEst, Prague, Czech Republic), 55x50x16cm in size, consisting of 14.4W RGB LEDs located on the sides and an acrylic board placed 30 cm away from the participant's eyes. The light was evenly distributed using a diffuser. The peak wavelengths for the short, medium and long-wavelength lights were 455nm, 508nm, and 629nm (Fig 2). The target irradiance density at the level of the eye was 14 $\mu W/cm^2$ for all light conditions (similar to (An, Huang, Shimomura, & Katsuura, 2009; Okamoto & Nakagawa, 2015)), with illuminance levels of 11.81 (455nm), 15.42 (508nm) and 29.48 lux for 629nm light. The illuminance level of the dark condition was 0.01 lux at the subjects' cornea.
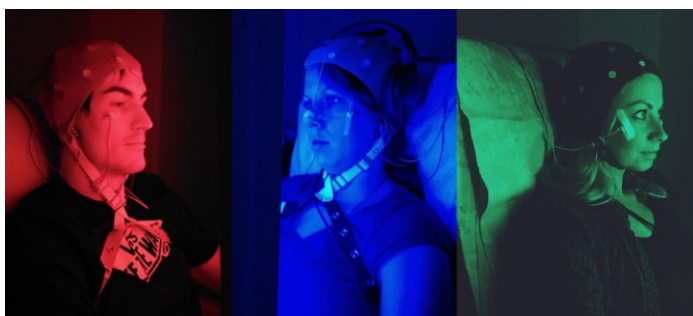

Fig 2. Lighting conditions used in the experiment (629, 455, 508 nm)

Actigraphy: The objective assessment of sleep and wake patterns was done using a wrist-worn actigraphic device with a tri-axial accelerometer (MotionWatch8, CamNTech, Cambridge, UK, www.camntech.com).

Sleepiness and reaction time measurements: Subjective sleepiness was measured by a translated version of the Karolinska Sleepiness Scale (KSS) (Akerstedt & Gillberg, 1990).

PVT (reaction time): After the oddball task in the dark, the subject performed a visual PVT task for the first time and at the end of the experiment (after 20 min of light exposure) for the second time, using the PEBL freeware (version 0.14, available at http://pebl.sourceforge.net/download.html) running the PEBL Perceptual Vigilance task, 20 stimulus trials in total.

EEG and ERP measurements: The subjects were sitting in an upright position in a chair with their eyes open. The EEG signal was registered from 21 Ag/AgCl scalp electrodes fixed on a cap, in positions following the International 10/20 system (Electro-Cap International, Inc., ECI).

P300: An auditory oddball paradigm with 120 standard (200 Hz, 40 ms, 75 dB SPL) and 30 target (500Hz, 40 ms, 75 dB SPL) tones were presented binaurally in a pseudo-random order (interstimulus interval, ISI = 1200 ms).

Power Spectra and eLORETA analysis: Welch method was used to perform the spectral analysis with data digitally filtered into six frequency bands: delta (0.5-3.5Hz), theta (4-7Hz), alpha 1 (7.5-9.5Hz), alpha 2 (10-12Hz), beta 1 (13-16Hz and 17-23Hz), beta 2 (24-34Hz) and gamma (35-50Hz) according to the conventional International Federation of Clinical Neurophysiology guidelines (Nuwer et al., 1998).
EEG connectivity analysis has been performed using the exact low-resolution electromagnetic tomography (eLORETA) software (publicly available free academic software at http://www.uzh.ch/keyinst/loreta.htm).

3.2 Study 2
Study protocol: Patients went through a standard CBT-I group therapy program. During the first CBT-I session, participants were asked to fill in the questionnaires and received actigraphs. The first week served as a baseline measurement as the first interventions were conducted at week 2. In the second session, patients were given either active blue-light blocking glasses (BB glasses) or placebo glasses. Patients in one group had the same type.

Participants: Forty-five patients diagnosed with insomnia were recruited at the Department of Sleep Medicine of the National Institute of Mental Health, Czech Republic, and enrolled in the CBT-I group program. Ethical approval was obtained from the local Ethical Committee. Insomnia diagnosis was established on the International Classification of Diseases, 10th edition (APA, 2013). Inclusion criteria were: a) minimum age of 18 years; b) absence of severe comorbid psychiatric, neurological or somatic disease; c) motivation to complete CBT-I program; d) stable usage of medication affecting sleep. Exclusion criteria were: a) interrupted CBT-I program; b) previous experience with CBT-I; c) night shifts. Thirty patients altogether (15 in each group) finished the study.

Methods

Subjective sleep measures: All patients were asked to complete a sleep diary every day during the therapy. Patients also completed a battery of self-reported questionnaires to assess sleep complaints and daytime symptoms at the beginning and the end of CBT-I.

The battery included the following questionnaires.
The Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989)
Insomnia Severity Index (ISI) (Bastien, Vallieres, & Morin, 2001)
Sheehan Disability Scale (SDS) (Sheehan, Harnett-Sheehan, & Raj, 1996)
Epworth Sleepiness Scale (ESS) (Johns, 1991).
Beck Depression Inventory-2 (BDI-II) (A. T. Beck, Ward, Mendelson, Mock, & Erbaugh, 1961)
Beck Anxiety Inventory (BAI): Beck Anxiety Inventory (BAI) (Aaron T. Beck & Steer, 1993).
Hyperarousal Scale (HAS) (Regestein, Dambrosia, Hallett, Murawski, & Paine, 1993).

Actigraphy: Patients received the devices (MotionWatch8, CamNTech, Cambridge, UK, www.camntech.com) at the beginning of CBT-I. Data were recorded continuously for 6 consecutive weeks before they were downloaded and analyzed by a researcher blinded to the experimental condition using MotionWare 1.4 software (CamNtech).

Interventions
CBT-I: The group CBT-I program was led by two trained psychologists. The length of the program was 6 weeks, with one two-hour session per week. One group consisted of 5 to 8 patients and one therapist. Each session had a specific structure according to the recommendations of the clinical manual for insomnia treatment (Morin & Espie, 2003). In the second week of the treatment, the sleep restriction was set up. Sleep restriction is one of the leading behavioral strategies used in CBT-I, aiming to reduce patients´ time spent in bed. Patients were recommended to spend the same amount of time in bed, as was their average TST during the previous week. The minimum length of TST was set up at 5 hours. This sleep window was titrated every week based on the following rule: if the sleep efficiency was higher than 85 %, the time in bed was prolonged by 15 minutes. Otherwise, time remained the same for another week.

Blue-light blocking glasses: For the active condition, the UVEX S1933X (U.S. certification ANSI Z87+ and CSA Z94.3) orange glasses were given to patients. Based on the used spectrum control technology, they were supposed to reduce up to 98 % of lights of blue wavelength. As the placebo condition, the UVEX S1900

(U.S. certification ANSI Z87+ and CSA Z94.3) clear glasses with no ability to filtrate blue light were used (Fig 3). Patients of both groups were instructed to wear the glasses 90 minutes before scheduled bedtime from week 2 till the end of the program. No adverse effects were reported by the patients.

Fig 3. Glasses used in the patient trial

3.3 Study 3

Study protocol: As a part of a broader questionnaire data collection, several sleep-related questionnaires were used in our study. We used Czech versions of all questionnaires, which were double-reverse translated from the originals. Permission from authors was obtained to translate and use the questionnaires.

Participants: A sample of 879 adults from the Czech Republic participated in an online survey aimed at exploring sleeping habits, chronotypes, and light hygiene. Participants were recruited via advertisement in a research center and via various social networks. Data collection was carried out between the years 2016 and 2018 using an online questionnaire platform. The selection criteria were habitual use of a mobile device during the evening or night hours and good general health according to screening questions (absence of severe health conditions and medication influencing sleep). Due to expected sleep disturbances (Krystal, 2012), we further excluded those with a history of psychiatric or severe neurological disorders (by a series of screening questions regarding present/past severe health conditions), those using psychiatric medication and people working shifts, leaving 696 participants (159 men and 538 women).

Methods

The Pittsburgh Sleep Quality Index (PSQI)(Buysse et al., 1989)
Fatigue Severity Scale (FSS) (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989)
Morningness-Eveningness Questionnaire (MEQ) (Horne & Ostberg, 1976)
Munich Chronotype Questionnaire (MCTQ) (Roenneberg, Wirz-Justice, & Merrow, 2003)

Screen exposure: Standardized questionnaires were complemented by custom-made questions and scales examining the length and timing of the evening

exposure to electronic devices (TV, PC, tablets, and phones). Visual analog scales with time descriptors (anchors) were used to mark the precise timing of this exposure, ranging from 4 P.M. till 4. AM (end-point defined by the participants' habitual bedtime). An example of the questions used: "*Mark exactly the times when you use the TV in the given time period*". By knowing the timing of evening exposure, we were able to determine whether or not the participant was exposed to artificial screen light 90 minutes before going to bed. Similar questions were used in previous studies (Becker & Lienesch, 2018; Bhat, Pinto-Zipp, Upadhyay, & Polos, 2018; Exelmans & Van den Bulck, 2017; Johansson, Petrisko, & Chasens, 2016; Woods & Scott, 2016). Furthermore, the length of exposure during night awakenings was gathered by simply asking the participants to estimate the time they spend on media devices while attending to various activities (sending messages, checking the time, working, watching videos or playing games) – "*If you wake up during the night, do you look at the screen of your device?*" and "*What are the activities that you perform?*". Additionally, we enquired about the use of various filters blocking short-wavelength light (both software and hardware) – "*Do you use any filters for blocking the blue-light spectrum of your screen?*"

4 Results

4.1 Study 1

Subjective sleepiness: Results of the 3x7 (3 light conditions x 7 timepoints) repeated measures ANOVA on mean KSS score (Fig 4) showed that there was a significant main effect of light color ($F_{(2,249)} = 5.178$, $p = 0.006$, Cohen's $f^2 = 0.002$) and timepoint ($F_{(6,245)} = 6.311$, $p<0.001$, Cohen's $f^2 = 0.165$), but no significant effect of interaction ($F_{(12,252)} = 0.298$, $p = 0.989$). Multiple comparisons post-hoc tests detected a significant difference between blue (455nm) and red (629nm) light conditions ($p = 0.005$), indicating that participants were less sleepy under blue than under red light conditions.
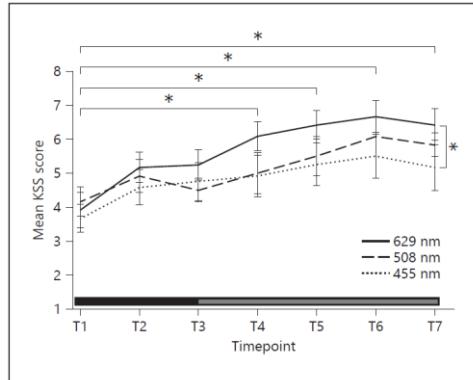
Fig 4. Mean subjective sleepiness as assessed by the translated KSS version. Higher scores indicate higher subjective sleepiness. Stars marks the significant difference between light conditions (p = 0.006) and timepoints (all p < 0.001). T4 represents the first measurement under light exposure, shortly after completing the first oddball task.

ERP P300 Analysis: Three aspects of the P300 component elicited by an oddball task were derived to assess brain cognitive function (amplitude, latency, and area under the curve – AUC). Firstly, we compared latencies of P300 responses (at Fz site) under light and dark conditions. Results in Figure 5 show the difference between latency during the baseline dark measurement and measurement under light conditions. Blue light (455nm) was the only lighting condition where subjects showed an improvement in latency, meaning reacting faster than under the dark condition. Results of the 3x3 (3 light conditions x 3 timepoints) repeated measures ANOVA on mean latency differences showed that there was a significant main effect of light color ($F_{(2,97)} = 3.720$, $p = 0.028$, Cohen's $f^2 = 0.006$) but no significant effect of ERP measurement ($F_{(2,97)} = 0.837$, $p > 0.05$), nor interaction between color and ERP ($F_{(4,100)} = 0.350$, $p > 0.05$).

Secondly, we analyzed the ERP P300 amplitude recorded over all EEG electrode sites and ERP measurements. At each EEG electrode site (Fz, Cz, Pz), the normalized P300 amplitude was averaged over all participants for each light condition. Unfortunately, 3x3 (3 light conditions x 3 timepoints) repeated-measures ANOVA on normalized P300 amplitude at each EEG electrode site failed to yield statistically significant results both for the absolute amplitude values (Fz – $F_{(2,99)} = 0.361$, $p = 0.939$; Cz – $F_{(2,99)} = 0.461$, $p = 0.881$; Pz – $F_{(2,99)} = 0.468$, $p = 0.876$) and the differences between the control measurement in the dark and under light exposure (Fz – $F_{(2,99)} = 0.363$, $p = 0.937$; Cz – $F_{(2,99)} = 0.294$, $p = 0.966$; Pz – $F_{(2,99)} = 0.459$, $p = 0.882$).
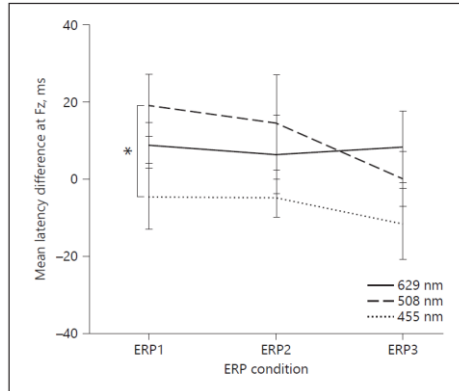
Fig 5. The difference between latencies of P300 response under light and dark condition. Negative values show the decrease of latency, positive an increase. Star represents a statistically significant difference between blue and green light conditions (p = 0.033).

Lastly, we calculated the mean AUC of P300 response (for Fz, Pz, and Cz electrodes) in all three light conditions during three different timepoints with 5 minutes in between oddball task administration as compared to AUC under control dark condition. A 4x3 repeated measures ANOVA shows a significant main effect of ERP condition ($F_{(3,130)}$ = 4.951, p = 0.003, Cohen's f^2 = 0.013), differences between 3 light conditions, however, failed to reach a statistical significance (p > 0.05).

eLORETA: For eLORETA analysis, we computed the difference of normalized absolute current density power between EEG during cognitive load (PVT) in the dark condition and all three experimental light conditions. No significant differences were observed.

Power spectrum analysis: A spectral analysis was carried out for all electrodes in the following frequency bands: delta (0.5-3.5Hz), theta (4-7Hz), alpha 1 (7.5-9.5Hz), alpha 2 (10-12Hz), beta 1 (13-16Hz and 17-23Hz), beta 2 (24-34Hz) and gamma (35-50Hz). The results were obtained as a difference between the absolute spectral power during cognitive load (PVT task) in dark and light conditions. Using the Kruskal-Wallis nonparametric test followed by Dunn-Bonferroni correction for adjusting to multiple comparisons, we found that blue (455 nm) light was the only experimental condition that led to an increase in absolute power. Results from all electrodes are to be found in Table 1, significant results being marked by bold letters.

	0.5–3.5 Hz		4–7 Hz		7.5–9.5 Hz		10–12 Hz		13–16 Hz		17–23 Hz		24–34 Hz		35–50 Hz	
	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p
AFz	2.326	0.313	3.767	0.152	0.032	0.984	1.087	0.581	0.078	0.962	4.734	0.094	4.551	0.103	6.572	**0.037**
C3	4.222	0.121	4.821	0.090	1.581	0.454	3.623	0.163	1.947	0.378	0.839	0.657	5.844	0.054	6.569	**0.037**
C4	1.676	0.433	1.650	0.438	1.195	0.550	1.146	0.564	0.275	0.871	0.137	0.934	2.515	0.284	6.842	**0.033**
Cz	1.483	0.476	0.734	0.693	0.059	0.971	0.920	0.631	0.236	0.889	0.734	0.693	2.128	0.345	5.140	0.077
F3	1.443	0.486	1.842	0.398	1.740	0.419	1.902	0.386	3.659	0.160	1.427	0.490	2.533	0.282	6.650	**0.036**
F4	2.302	0.316	1.659	0.428	2.902	0.234	2.041	0.360	0.560	0.756	3.586	0.166	7.074	**0.029**	5.407	0.067
F7	0.263	0.877	0.920	0.631	4.194	0.123	1.191	0.551	2.542	0.281	0.722	0.697	2.324	0.313	6.695	**0.035**
F8	0.551	0.759	4.114	0.128	0.698	0.705	0.470	0.791	1.488	0.475	0.020	0.990	2.113	0.348	0.650	0.722
Fp1	0.272	0.873	1.218	0.544	2.011	0.366	0.362	0.834	1.195	0.550	1.227	0.542	0.956	0.620	2.601	0.272
Fp2	1.542	0.463	0.168	0.919	0.344	0.842	0.921	0.631	2.596	0.234	2.907	0.234	3.826	0.148	3.407	0.182
Fz	0.254	0.881	1.713	0.425	0.074	0.964	1.095	0.579	0.474	0.789	2.000	0.368	6.245	**0.044**	8.410	**0.015**
O1	2.018	0.365	4.330	0.115	1.135	0.567	1.101	0.577	1.113	0.573	0.114	0.945	2.929	0.231	10.074	**0.006**
O2	1.560	0.458	2.096	0.351	1.686	0.430	1.230	0.541	2.584	0.275	3.977	0.137	2.000	0.368	3.689	0.158
P3	3.173	0.205	0.695	0.706	1.389	0.499	0.150	0.928	0.114	0.945	1.856	0.395	3.815	0.148	2.128	0.345
P4	0.821	0.663	0.344	0.842	0.110	0.947	0.0656	0.720	0.770	0.680	2.186	0.335	1.389	0.499	3.047	0.218
Pz	0.655	0.721	0.342	0.743	0.470	0.791	0.011	0.995	0.290	0.865	0.086	0.958	2.281	0.320	2.024	0.363
T3	8.140	**0.017**	6.632	**0.036**	7.646	**0.022**	5.734	0.057	2.284	0.319	6.529	**0.038**	7.893	**0.019**	6.168	**0.046**
T4	6.505	**0.039**	5.680	0.058	7.749	**0.021**	3.788	0.150	1.743	0.418	3.839	0.147	7.074	**0.029**	6.601	**0.037**
T5	4.992	0.082	4.815	0.090	2.137	0.344	1.545	0.462	0.500	0.779	3.317	0.208	5.640	0.060	6.245	**0.044**
T6	2.182	0.336	1.938	0.379	0.799	0.671	0.119	0.942	0.814	0.666	4.194	0.123	3.718	0.156	6.302	**0.043**

Table 1. Results of absolute EEG power density for all electrodes. The results were obtained as a difference between the absolute spectral power during cognitive load (PVT task) in dark and blue-light conditions. "p" represents adjusted p-value. All significant results point towards higher EEG power density under the blue-light condition as compared to darkness.

Summary of the results

- Blue light (455nm) had the strongest effect in suppressing the subjective feeling of sleepiness as compared to green (508nm) or red (629nm) light
- No significant differences were found for reaction times measured by PVT
- An increase in power density under several electrodes, mostly in higher beta (F4, Fz, T3, T4) and gamma bands (Afz, C3, C4, F3, F7, Fz, O1, T3, T4, T5, T6) was observed only in blue-light (455nm) compared to dark condition during cognitive load
- A decrease in P300 latency was observed under blue (455nm) light
- No differences between light conditions in terms of the localization of neural activity using eLORETA were detected

4.2 Study 2

Pre- to post-treatment differences between groups: Differential values for questionnaire scores (pre- minus post-treatment value) were calculated, reflecting the change in scores reached after finishing CBT-I groups (as compared to baseline). Differences for both groups were then compared (using a GLM), finding a statistically significant difference in BAI score [$F(1, 22) = 6.389$, p = 0.019, Cohen's $d = 1.26$], with a larger decline in anxiety score in the active group (6.73±4.15) as compared to the placebo group (5.91±4.32). Differences in all other questionnaire scores were found to be insignificant and can be found in Table 2.

Following analyses of questionnaire scores, a comparison of the differential values of both objective and subjective sleep parameters in active and placebo groups was carried out. A statistically significant difference was found for subjective total sleep time [$F(1, 22) = 8.565$, p = 0.008, Cohen's $d = 0.91$], resulting in approximately 44 minutes longer TST in the active group as compared to the placebo group. Differences in all other sleep parameters were found to be insignificant and are shown in Table 3.

Effect of intervention in each group: The change between pre- and post-treatment scores for each group separately was assessed using paired-sampled t-tests. The results are to be found in Table 4. For both active and placebo groups, a significant difference was found for the following questionnaires: ISI, PSQI and SDS, and sleep parameters: subjective WASO and subjective sleep efficiency.

Furthermore, in the active group only, a significant reduction was observed in HAS score (41.60±8.40 vs. 36.93±10.02), (t=2.90, p=0.012, Cohen's d=0.75), BDI-II score (15.13±12.04 vs. 9.20±9.03), (t=3.66, p=0.003, Cohen's d=0.95) and BAI score (10.80±5.88 vs. 6.47±4.03), (t=3.67, p=0.003, Cohen's d=0.95), while subjective TST was prolonged (369.14±48.93 min. vs. 406.02±50.16 min.), (t=-2.73, p=0.018. Cohen's d = -0.76). In the placebo group, a significant reduction of objective TST was observed (378.79±49.46 min. vs. 352.13±37.17 min.), (t=2.58, p=0.024, Cohen's d=0.72).

	N (Active/Placebo)	Active	Placebo	F	Sig.	Effect size
ISI	15/12	6.73 ± 4.15	5.91 ± 4.32	0.048	0.828	0.19
PSQI	15/12	4.20 ± 3.89	4.17 ± 2.89	0.258	0.617	0.01
ESS	14/12	0.57 ± 3.46	0.08 ± 2.50	1.443	0.243	0.16
SDS	15/12	8.77 ± 9.60	6.17 ± 8.80	0.073	0.789	0.28
HAS	15/12	4.66 ± 6.23	3.42 ± 9.38	0.020	0.889	0.16
BDI	15/12	5.93 ± 6.27	2.00 ± 4.65	1.694	0.207	0.71
BAI	15/12	4.33 ± 4.57	−0.91 ± 3.67	6.389	**0.019**	**1.26**

Table 2. Comparison of questionnaire differential values between Active and Placebo group. Mean (±SD) of ifference in questionnaire scores pre- and post-CBT-I group program in groups of patients with "active" filtering glasses and "placebo" glasses. F values, statistical significance, and effect sizes (Cohen's d) are provided. Positive values indicate a decrease in scores post-treatment. ISI = Insomnia Severity Index, PSQI = Pittsburgh Sleep Quality Index, ESS = Epworth Sleepiness Scale, SDS = Sheehan Disability Scale, QOL = Quality of Life, HAS = Hyperarousal Scale, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory

	N (Active/Placebo)	Active	Placebo	F	Sig.	Effect size
SOL Subj. (min.)	13/14	18.39 ± 25.05	34.30 ± 61.67	1.444	0.242	0.33
SOL Obj. (min.)	15/13	3.63 ± 8.43	5.81 ± 12.34	0.968	0.335	0.21
TST Subj. (min.)	13/14	−36.88 ± 48.68	7.04 ± 47.50	8.565	**0.008**	**0.91**
TST Obj. (min.)	15/13	9.75 ± 37.32	26.66 ± 37.24	0.024	0.878	0.45
WASO Subj. (min.)	13/14	23.32 ± 38.46	12.94 ± 20.44	0.675	0.420	0.33
WASO Obj. (min.)	15/13	6.45 ± 25.21	9.99 ± 22.76	0.066	0.800	0.15
SE Subj. (%)	13/14	−15.49 ± 12.83	−10.43 ± 10.26	3.535	0.073	0.44
SE Obj. (%)	15/13	−1.21 ± 3.94	−1.27 ± 3.06	0.066	0.800	0.02
Subj. sleep quality	13/14	−0.38 ± 1.07	−0.82 ± 1.14	0.281	0.601	0.40
Morning alertness	13/14	−0.18 ± 0.80	−0.49 ± 1.12	0.015	0.905	0.32

Table 3. Comparison of differential values of sleep parameters between Active/Placebo group. Mean (±SD) of difference in scores of objectively (actigraphy) and subjectively rated sleep parameters pre- and post-CBT-I group program in groups of patients with "active" filtering glasses and "placebo" glasses. Negative values depict an increase in the presented variables. F values, statistical significance, and effect sizes (Cohen's d) are provided. SOL = Sleep Onset Latency, TST = Total Sleep Time, WASO = Wake After Sleep Onset, SE = Sleep Effectivity.

	Active (n = 15)						Placebo (n = 15)				
Sleep parameter	Pre-treatment	Post-treatment	t	P-value	ES	Sleep parameter	Pre-treatment	Post-treatment	t	p Value	ES
Questionnaires						Questionnaires					
ISI	17.27 ± 5.42	10.53 ± 3.36	6.29	**0.000**	**1.60**	ISI	16.83 ± 2.98	10.92 ± 3.42	4.75	**0.001**	**1.37**
PSQI	12.60 ± 4.36	8.40 ± 12.39	4.18	**0.001**	**1.08**	PSQI	13.08 ± 3.42	8.92 ± 3.20	5.00	**0.000**	**1.44**
ESS	8.71 ± 3.79	8.14 ± 4.19	0.62	0.547	0.17	ESS	5.17 ± 3.59	5.08 ± 3.53	0.12	0.910	0.03
SDS	18.97 ± 11.34	10.20 ± 6.76	3.54	**0.003**	**0.91**	SDS	14.92 ± 10.31	8.75 ± 8.11	2.43	**0.034**	**0.70**
HAS	41.60 ± 8.40	36.93 ± 10.02	2.90	**0.012**	**0.75**	HAS	35.5 ± 10.13	32.08 ± 11.28	1.26	0.233	0.36
BDI	15.13 ± 12.04	9.20 ± 9.03	3.66	**0.003**	**0.95**	BDI	11.83 ± 9.00	9.83 ± 9.38	1.49	0.164	0.43
BAI	10.80 ± 5.88	6.47 ± 4.03	3.67	**0.003**	**0.95**	BAI	10.42 ± 7.56	11.33 ± 9.99	−0.86	0.407	−0.25
Sleep diaries						Sleep diaries					
SOL (min.)	36.80 ± 27.01	18.41 ± 6.15	2.65	**0.021**	**0.73**	SOL (min.)	59.77 ± 62.30	25.48 ± 23.53	2.08	0.058	0.56
TST (min.)	369.14 ± 48.93	406.02 ± 50.16	−2.73	**0.018**	**−0.76**	TST (min.)	382.73 ± 69.27	375.69 ± 49.32	0.56	0.588	0.15
WASO (min.)	43.95 ± 41.94	20.63 ± 11.81	2.17	**0.049**	**0.61**	WASO (min.)	43.78 ± 30.64	30.83 ± 22.92	2.37	**0.034**	**0.63**
SE (%)	74.59 ± 12.63	90.09 ± 4.28	−4.35	**0.001**	**−1.21**	SE (%)	74.67 ± 11.30	85.09 ± 9.07	−3.80	**0.002**	**−1.02**
Actigraphy						Actigraphy					
SOL (min.)	12.47 ± 15.12	8.83 ± 9.83	1.67	0.117	0.43	SOL (min.)	18.12 ± 12.31	12.31 ± 11.74	1.69	0.115	0.47
TST (min.)	359.97 ± 52.18	350.22 ± 47.50	1.01	0.329	0.26	TST (min.)	378.79 ± 49.46	352.13 ± 37.17	2.58	**0.024**	**0.72**
WASO (min.)	100.78 ± 26.54	94.33 ± 29.35	0.99	0.339	0.34	WASO (min.)	112.45 ± 33.24	102.46 ± 31.60	1.58	0.140	0.44
SE (%)	74.53 ± 6.21	75.74 ± 5.67	−1.19	0.254	−0.31	SE (%)	73.68 ± 5.47	74.95 ± 5.99	−1.49	0.161	−0.41

Table 4. *Effect of intervention within each group.* Results of the paired-samples t-tests are presented for a group with "active" filtering glasses and "placebo" glasses. t-values, statistical significance, and effect sizes (Cohen's d) are provided. ISI = Insomnia Severity Index, PSQI = Pittsburgh Sleep Quality Index, ESS = Epworth Sleepiness Scale, SDS = Sheehan Disability Scale, QOL = Quality of Life, HAS = Hyperarousal Scale, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, SOL = Sleep Onset Latency, TST = Total Sleep Time, WASO = Wake After Sleep Onset, SE = Sleep Effectivity.

Summary of the results

- A combination of CBT-I + blue-light blocking glasses was more effective in ameliorating patients' symptoms than CBT-I + placebo glasses
- The use of BB glasses was associated with significantly increased subjective TST and decreased subjective SOL
- BB glasses were further associated with no decline in objective TST (as opposed to the placebo group)
- The use of BB glasses was associated with a reduction of anxiety
- The use of BB glasses was associated with a reduction of depressive symptoms
- The use of BB glasses was associated with lower levels of hyperarousal

4.3 Study 3

We used a general linear model to assess the effects of cumulative screen exposure on selected sleep (PSQI, sleep length, sleep latency) and sleep-related parameters (FSS, social jet-lag, sleep inertia, tendency to wake up before alarm). The results are summarized in Table 5.

As we can see, statistical differences were found for morning inertia (F=1.518, p=0.019, η^2=0.141), meaning the more exposed the participants were, the less alert and more tired they felt the next morning. More hours of exposure were also associated with prolonged sleep latency on workdays (F=1.433, p=0.038, η^2=0.135). No significant associations were found for the remaining variables.

When comparing groups based on the exposure 90 minutes before bedtime (summary in Table 6), significant differences were found for sleep inertia (F=4.455, p<0.001, Cohen's d=0.45) meaning that participants that did not expose themselves to the light of device screens felt more alert and less tired the next morning. They were also more likely to wake up before the scheduled alarm clock (Z=-2.976, p =0.003, Cohen's d=0.30). Furthermore, social jet-lag (as measured by MCTQ) and fatigue (as measured by FSS) were greater in the group of participants that used electronic devices before going to bed (Z=-3.902, p<0.001, Cohen's d=0.22 and Z=-2.157, p= 0.032, Cohen's d= 0.15 respectively). Although subjective sleep quality (PSQI) did not differ between these two groups, we found significant differences for the PSQI components (Table 7), in particular, components 4 (habitual sleep efficiency) and 7 (daytime dysfunction). Sleep efficiency score was higher (indicating lower %) in the non-exposure group (Z=-2.753, p=0.006, Cohen's d=0.28) while daytime dysfunction was worse in the pre-sleep exposure group (t=3.931, p <0.001, Cohen's d=0.40). All these differences remained statistically significant after controlling for age, except for the total FSS score.

The next analysis was focused on screen exposure on mobile devices during the night (after falling asleep). We divided the sample into three groups: no screen use

during sleep (N=403), light use (N=46), and time checking (N=247). After running ANOVA, we observed significant differences for the following variables (Table 6 and 7): PSQI total score (F=3.733, p=0.024, Cohen's d=0.16) and components 1 – Subjective sleep quality (F=3.859, p=0.022, Cohen's d=0.08), 2 – Sleep latency (F=3.508, p=0.031, Cohen's d= 0.09), 5 – Sleep disturbances (F=3.683, p=0.026, Cohen's d=0.07) and 7 – Daytime dysfunction (F= 4.657, p=0.01, Cohen's d=0.10) and FSS scores (F=7.623, p=0.001, Cohen's d=0.52).

Furthermore, when analyzing sub-items of the PSQI's 5th component (Sleep disturbance), we found significant differences in the number of night awakenings (F=4.628, p=0.01 f=0.11), troubles falling asleep (F=3.783, p=0.023, f=0.09) and bad dreams (F=7.301, p=0.001, f=0.13). After running post-hoc (LSD) tests, we found universal results for all variables: a significant difference between those that did not expose themselves to screens during night time and those that regularly checked the time on their screens, with worse outcomes in these sub-items in those that checked the time on their screens. No differences were found between groups of time-checkers and light users or light users and those that did not use screens. All these differences remained statistically significant after controlling for age (ANCOVA), except for PSQI component 7 (daytime dysfunction).

Lastly, we analyzed the use of blue-light filters, according to an answer to a simple question: whether participants did or did not use a specific filter for filtering blue-light on their screens. Only 10.6% of the sample (N=74) reported using filters, while 622 participants did not. The most prevalent means of filtering blue light were f.lux (Windows) and Twilight (Android) software. No significant differences were observed for all sleep-related variables mentioned in the previous analyses. A statistical trend was found for the duration of sleep on workdays (489 vs. 461 minutes, t=3.595, p=0.058, Cohen's d=0.23), meaning those that used blue-light filters slept in average approximately 28 minutes longer on a workday than those that did not use any means of filtering blue-light (Table 6). No other differences were observed.

	Sleep Inertia	Sleep latency-Workday	Sleep latency-Freeday	Sleep on Workdays	Sleep on Freedays	Wake Before Alarm	PSQI	FSS	SJL
F	1.518	1.433	0.776	1.047	1.186	0.948	0.723	0.947	0.909
sig.	**0.019**	**0.038**	0.854	0.394	0.197	0.572	0.912	0.573	0.644

Table 5. Effect of cumulative light exposure on sleep and sleep-related parameters. Significant results are shown in bold. PSQI – Pittsburgh Sleep Quality Index total score, FSS – Fatigue Severity Scale, SJL – Social jet-lag, Sleep on Workdays/Freedays – sleep duration

	Sleep Inertia	Sleep latency—Workday	Sleep latency—Freeday	Sleep on Workdays	Sleep on Freedays	Wake before alarm	PSQI	FSS	SJL
Differences by exposure 90 minutes before bedtime									
No (N = 130)	5.05±1.69	12.79±14.92	16.52±18.06	459.46±118.33	515.79±88.38	1.40±0.49	6.74±2.31	29.40±13.15	0.83±1.10
Yes (N = 341)	4.31±1.60	12.61±12.37	14.25±12.23	468.71±127.84	523.45±122.60	1.26±0.44	6.78±2.43	32.27±12.83	1.28±1.11
Stat. test	4.455	0.130	1.561	-0.7161	-0.650	-2.976	-0.144	-2.157	-3.902
Sig.	**<0.001**	0.896	0.119	0.474	0.516	**0.003**	0.885	**0.032**	**<0.001**
Effect size	0.45	0.01	0.15	0.08	0.07	0.30	0.02	0.22	0.15
Differences by character of night time exposure									
No screen use (N = 403)	4.64±1.66	11.38±10.58	13.57±12.81	460.47±116.36	516.36±106.02	1.31±0.46	6.49±2.34	31.49±12.93	1.09±1.11
Time checking (N = 247)	4.38±1.69	13.58±13.60	15.68±14.59	468.63±131.12	515.70±103.29	1.26±0.44	7.01±2.31	35.47±12.14	1.19±1.38
Light use (N = 46)	4.78±1.77	12.98±17.90	12.98±17.90	466.11±126.07	502.83±98.26	1.36±0.49	6.78±2.64	31.91±13.94	0.98±0.88
Stat. test	2.266	2.542	1.909	1.306	0.349	0.350	3.733	7.623	0.931
Sig.	0.104	0.079*	0.149	0.705	0.705	0.272	**0.024**	**0.001**	0.395
Effect size	0.1	0.28	0.27	0.35	0.33	0.04	0.16	0.52	0.06
Differences by use of blue-light filters									
No (N = 622)	4.57±1.71	12.07±12.38	14.08±12.86	460.70±122.60	513.70±100.78	1.31±0.46	6.73±2.32	32.99±12.92	1.13±1.20
Yes (N = 74)	4.50±1.47	13.92±11.86	16.86±16.92	489.18±117.67	528.11±131.58	1.23±0.42	6.35±2.67	32.39±12.30	0.99±1.23
Stat. test	0.334	-1.220	-1.905	3.595	-1.122	-1.320	1.321	0.384	0.912
Sig.	0.739	0.223	0.090*	0.058*	0.262	0.187	0.187	0.701	0.362
Effect size	0.04	0.15	0.18	0.23	0.12	0.18	0.15	0.05	0.11

Table 6. Summary of comparative statistics. Mean values of item scores or total scores and their SD are shown, comparing groups of participants by the presence/absence of screen exposure 90 minutes before bedtime, use of blue-light filters, and exposure to screens during night awakenings. Significant results are shown in **bold**. Stars (*) represent results where a statistical trend was observed. PSQI – Pittsburgh Sleep Quality Index, FSS – Fatigue Severity Scale, SJL – Social jet-lag.

	PSQI #1 (Sleep Q.)	PSQI #2 (Sleep lat.)	PSQI #3 (Sleep dur.)	PSQI #4 (Sleep eff.)	PSQI #5 (Sleep dis.)	PSQI #6 (Sleep med.)	PSQI #7 (Dayt. dysf.)
Differences by exposure 90 minutes before bedtime							
No (N = 130)	0.91±0.72	0.88±0.87	0.37±0.60	1.91±1.44	1.18±0.46	0.11±0.51	1.38±0.80
Yes (N = 341)	1.01±0.74	0.90±0.83	0.41±0.67	1.49±1.50	1.19±0.48	0.07±0.30	1.70±0.79
Stat. test	1.777	0.072	0.375	7.619	0.158	1.567	15.451
Sig.	0.183	0.788	0.540	**0.006**	0.691	0.211	**<0.001**
Effect size	0.13	0.02	0.06	0.28	0.02	0.09	0.40
Differences by character of nighttime exposure							
No screen use (N = 403)	0.89±0.73	0.79±0.79	0.39±0.66	1.75±1.48	1.13±0.45	0.05±0.32	1.48±0.79
Time checking (N = 247)	1.03±0.74	0.95±0.86	0.45±0.75	1.59±1.50	1.22±0.48	0.08±0.33	1.67±0.78
Light use (N = 46)	1.11±0.77	1.00±0.84	0.35±0.56	1.37±1.51	1.26±0.49	0.04±0.21	1.65±0.82
Stat. test	3.859	3.508	0.949	1.891	3.683	1.029	4.657
Sig.	**0.022**	**0.031**	0.388	0.152	**0.026**	0.358	**0.010**
Effect size	0.08	0.09	0.04	0.09	0.07	0.23	0.10
Differences by use of blue-light filters							
No (N = 622)	0.96±0.73	0.85±0.82	0.42±0.70	1.70±1.48	1.18±0.47	0.05±0.28	1.57±0.80
Yes (N = 74)	0.95±0.82	0.93±0.86	0.28±0.56	1.42±1.51	1.09±0.44	0.16±0.52	1.51±0.80
Stat. test	0.014	0.591	2.822	2.291	2.415	8.330	0.305
Sig.	0.907	0.446	0.093	0.131	0.121	0.074	0.581
Effect size	0.01	0.09	0.22	0.18	0.20	0.26	0.08

Table 7. Summary of comparative statistics of single PSQI components. Mean values of item scores or total scores and their SD is displayed, comparing groups of participants by the presence/absence of screen exposure 90 minutes before bedtime, use of blue-light filters, and exposure to screens during night awakenings. Significant results are shown in bold. The 7 components are: Subjective sleep quality, Sleep latency, Sleep duration, Habitual sleep efficiency, Sleep disturbances, Use of sleeping medication, and Daytime dysfunction.

Summary of the results

- A significant association between screen exposure length and sleep inertia was found
- An association was also found for sleep latency on workdays, with longer latencies in those exposing themselves more to the light of media screens
- Exposure to artificial screen light 90 minutes before sleep was associated with increased sleep inertia in the mornings and a tendency to rely on the alarm clock to wake up in the morning
- Exposure to artificial screen light 90 minutes before sleep was associated with higher scores in PSQI's daytime dysfunction component
- Frequent time-checking at night was associated with an increase in night awakenings, higher prevalence of bad dreams and higher PSQI total score (with significant differences in components 1 – subjective sleep quality, and 5 – sleep disturbances) and FSS scores
- The use of blue-light filters was associated (stat. trend) with increased duration of sleep on workdays and lower number of night awakenings

5 Summary and Conclusions

Three studies have been carried out as a part of this dissertation. In the first study, an EEG laboratory experiment, shows that short-wavelength (blue) light is capable of promoting vigilance in a group of healthy volunteers. Its alertness-enhancing properties have been confirmed in both subjective and objective measures: a decrease in one's subjective feeling of sleepiness, shorter latency of P300 response, and increased power density in higher beta and gamma bands. In the second study, a trial on insomnia patients showed that the combination of standard cognitive-behavioral therapy program with blue-light blocking glasses was more effective in enhancing subjective sleep quality and reducing symptoms of anxiety, depression, and hyperarousal compared to CBT-I with placebo glasses. And finally, the third study, an online questionnaire survey, showed a negative association between evening and night screen exposure and our sleep and potential benefits of adhering to "light hygiene" recommendations, such as filtering blue light spectrum or avoiding screen exposure in the evening and night hours.

Altogether, our data represent a valuable contribution to current sleep and chronobiology research as they enhance understanding of the blue light's effects on human sleep and cognition, employing up-to-date unique research designs with a potential to lead to the development of new lighting or light-filtering systems and applications for healthy sleep promotion in both the general and clinical populations.

The EEG experiment provided further evidence that narrow-bandwidth short-wavelength (blue) light is capable of improving both subjective perception of one's levels of sleepiness and also to boost cortical activity related to cognitive tasks as measured by EEG power spectra and ERP P300 parameters. This shows that EEG recording and especially the use of event-related potentials, is a valid

source of information when it comes to measuring neurophysiological reactions to different light sources. The limitations of this study lie mainly in the small sample size, which could have been the reason for no significant differences in current density measured by eLORETA. Nevertheless, using a design with monochromatic lights of different colors but the same irradiance density brought additional information about the biological effect of these three short/medium/long wavelength-lights and corresponds to the recent methodological recommendations of Prayag and colleagues (Prayag et al., 2019). This is also in line with suggestions of recent review studies, where for instance, Katsuura and Lee appeal to build a truly adapted artificial environment based on the biological characteristics of human beings (Katsuura & Lee, 2019). Similarly, Bourgin & Hubbard believe that a more detailed spectral management of lights could also be applicable to many daily living conditions, far beyond simply the workplace or the home, allowing us to also better adapt to situations like transmeridian travel or shift-work (Bourgin & Hubbard, 2016).

Our second study, a combined psychotherapeutic and chronotherapeutic (BB glasses) intervention, showed to be more effective in enhancing subjective sleep quality and reducing symptoms of anxiety, depression, and hyperarousal in insomnia patients compared to intervention with placebo glasses. This was one of the few studies that focused on a clinically-relevant sample (in addition to (Esaki et al., 2016; Esaki et al., 2017; Henriksen et al., 2016; Shechter, Kim, St-Onge, & Westwood, 2018; Zimmerman et al., 2019)) and the first study to have used blue-light blocking glasses in addition to a standardized psychotherapeutic intervention. Our study showed that wearing blue-light blocking glasses in the evening may help reduce the phase-delaying effect of light and facilitate an improvement in various subjective and objective sleep parameters, depressive and anxiety symptoms, and hyperarousal, alleviating most of the symptoms that insomnia patients struggle with. Application of this easy-to-use and cheap tool could lead to additional indications of light interventions as a complementary and innocuous treatment to help patients with sleep or other psychiatric symptoms, as proposed by Blume et al. (Blume et al., 2019).

Our third study showed that above-average exposure to screens of media devices was associated with sleep inertia, suggesting that light in the evening may not only increase cortical arousal during evening hours but can influence one's alertness the following morning as well. Furthermore, being exposed to media screens was associated with prolonged sleep latency on workdays, more daytime dysfunction, more night awakenings, and sleep disturbances, and higher fatigue scores. On the other hand, the use of blue-light filters was associated with increased sleep duration and fewer night awakenings. All these results point towards worse sleep and daytime functioning in those who expose themselves to artificial light in the evenings and at nights and possible benefits of blocking the blue part of the light spectrum. The main benefits of this particular study lie in the relatively high number of participants and a broad spectrum of sleep and sleep-related questionnaires used. Unlike previous studies, we have explicitly focused on

the length and timing of screen exposure, which in return brought impressive results further applicable for healthy sleep promotion, not only in a healthy population but in patient populations as well. Although recent literature review found a lack of high-quality evidence to support using blue-light blocking to improve sleep quality (Lawrenson, Hull, & Downie, 2017), two of our studies clearly show the benefits of blocking or avoiding artificial light in the evening and night hours. The effects of the absence of artificial light exceeded mere improvements in sleep. Enhancement of daytime functioning and decline in depressive and anxiety symptoms has been shown. Incorporating recommendations regarding appropriate light exposure into the practices of sleep hygiene may, therefore, help to promote public health and prevent disease, as initially proposed by Erren & Reiter (Erren & Reiter, 2009).

Furthermore, these results also add to the potential of creating „circadian-friendly" lighting systems, incorporating suggestions from recent studies (Canazei et al., 2019; Okkels et al., 2020; Scott et al., 2019) or newly-studied metamere light (Allen, Hazelhoff, Martial, Cajochen, & Lucas, 2018; de Zeeuw et al., 2019) to promote new designs of lighting systems that do not lead to chronodisruption.

Several limitations of studies for this thesis have already been mentioned and mainly include small sample sizes and limited ability to control for all possible confounding variables. These are also the recommendations from a recent review (Tahkamo, Partonen, & Pesonen, 2019) that calls for repeated measure designs, and also, systematic reviews on other light-induced health concerns, as well as meta-analyses of any adverse health impacts, to further clarify the scientific evidence on impacts of light on human health. Also, other factors that influence the effects of light should be considered, such as chronotype, circadian phase, homeostatic state, prior light history, and genetic disposition, as they may obscure its effects on sleep and cognition. Recently, suggestions have also been made to validly measure and compare the biological effects of light and light filters, and novel physiologically relevant and retinally referenced frameworks for quantifying have been published (Prayag et al., 2019; Spitschan, Lazar, & Cajochen, 2019). Future studies should, therefore, keep better track of these factors and take them into account when evaluating the effects of light exposure (Souman, Tinga, Te Pas, van Ee, & Vlaskamp, 2018).

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7 Publications of the Graduant

Original papers related to this dissertation:

In English:

Šmotek, M., Vlček, P., Saifutdinova, E., & Kopřivová, J. (2019). Objective and Subjective Characteristics of Vigilance under Different Narrow-Bandwidth Light Conditions: Do Shorter Wavelengths Have an Alertness-Enhancing Effect?. *Neuropsychobiology*, *78*(4), 238–248. https://doi.org/10.1159/000502962 **(IF 1.675)**

Janků, K., **Šmotek, M.**, Fárková, E., & Kopřivová, J. (2020). Block the light and sleep well: Evening blue light filtration as a part of cognitive-behavioral therapy for insomnia. *Chronobiology international*, *37*(2), 248–259. https://doi.org/10.1080/07420528.2019.1692859 **(IF 2.562)**

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In Czech:

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Other publications:

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Janků, K., **Šmotek, M.**, Fárková, E., Miletínová, E., Kopřivová, J. Blue light blocking glasses and CBT-I: effect on subjective and objective sleep quality, *Sleep Medicine*, Volume 64, Supplement 1, 2019, Page S174, ISSN 1389-9457

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