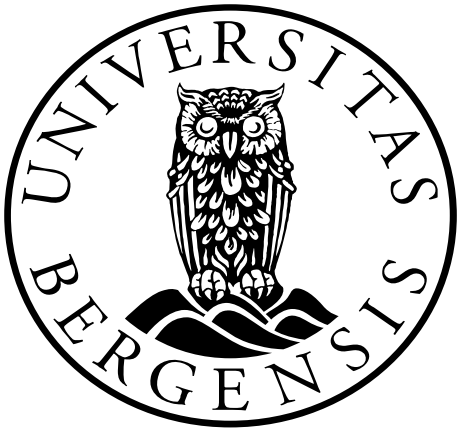
Daytime sleep after simulated night shift work, a polysomnographic study of the impact of working in blue-enriched and red-enriched narrow-bandwidth light.

Robin Bjorheim



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DAYTIME SLEEP IN SIMULATED NIGHT SHIFT AFTER BLUE AND RED LIGHT

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Abstract

One of every 5th person in Europe works night shift. Although research has shown negative effects of night shift on cognitive measures, work related accidents and health, little is known of the daytime sleep. Light on night shift induces effects on alertness and the regulation of sleep and wakefulness. The aim of our study was to characterize the daytime sleep when working night shift in two different wavelengths of light (blue-enriched 455 nm and red-enriched light 615 nm). Polysomnographic recording of the sleep were performed for one nighttime and the following sleep after simulated night shifts (23:00-07:00). Night shift consisted of computerized tasks in the laboratory in ceiling LED-luminaires. Day-time sleep showed a reduced total sleep time compared to night sleep. The time in N3 was preserved, at the expense of time in stage N1, N2 and REM sleep. There were no significant differences between day sleep blue and day sleep red. The sleep pressure, measured by slow wave activity (SWA), declined during sleep for both day-sleep and night-sleep. Significant higher SWA were found for day-sleep versus night-sleep. The dissipation of the sleep pressure, measured by and slow wave energy (SWE) were seen for both night and day-sleep as well as significant differences of day-sleep compared to night-sleep. These results contribute to the understanding of daytime sleep after working night shifts.

Keywords: night shift, day sleep, light exposure, slow wave activity

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Sammendrag

Hver femte europeer jobber nattskifte arbeid. Til tross for negative effekter av natteskift på kognitiv ytelse, arbeids-relaterte ulykker og helse, er lite kjent angående dagtidsøvn hos natteskift arbeidere. Lys på natteskiftet induserer effekter på årvåkenhet og reguleringen av søvn og våkenhet. Målet for denne studien var å karakterisere dagtidsøvnen etter å ha arbeidet natteskift i to ulike bølgelengder av lys (blå-beriket 455 nm og red-beriket lys 615 nm). Polysomnografisk måling ble benyttet under en natt og for den påfølgende søvnen etter simulert natteskift arbeid (23:00 – 07:00). Natteskift bestod av databaserte oppgaver i laboratoriet under takmonterte LED-belysning. Dagtids søvn viser redusert total søvnlengde sammenlignet med nattesøvn. Tiden i N3 var bevart, på bekostning av tid i stadiene N1, N2 og Rem søvn. Det var ingen signifikant forskjell mellom dagsøvn i blå-betingelse og rød-betingelse. Søvntrykket, som målt ved slow wave activity (SWA), ble redusert under søvn for både dagtid-søvn og nattesøvn. Signifikant høyere SWA var sett ved dagtid-søvn versus nattesøvn. Nedgang av søvntrykk, målt ved slow wave energi (SWE), var sett ved både natt- og dagtids-søvn på lik linje med signifikante forskjeller i dagtid søvn sammenlignet med nattesøvn. Disse resultatene bidrar til forståelsen for dagtidsøvn etter å ha arbeidet natteskift.

Forord

I would like to thank my main-supervisor Janne Grønli for everything that she has thought me, not only for my master thesis, but for the last 4 years. In the summer of 2017, I sent an email to Janne showing my interest in sleep research and asking if she needed a research assistant. Since then, I have been lucky enough to contribute to Bergen Stress and Sleep Group in the laboratory, journal clubs, meetings, seminars, and other activities. It has truly been an exciting journey thanks to Janne's significant ability to provide challenges at the appropriate level to enhance learning and further understanding.

I also want to thank my co-supervisor Torhild Thue Pedersen and in particular her involvement with the sleep script and analysis of data. She has also been very helpful whenever I need a pointer in the right direction when working on my thesis.

Lastly, I need to thank all the other members of Bergen Stress and Sleep group. They are truly great people to work with and I have learned a lot by being part of the group.

Innholdsfortegnelse

A normal day of the working week is for many people about an 8-hour workday occupying the first one-third of the 24 hour day. The next part is dedicated to leisure and the last one-third are normally devoted to sleep. Work and sleep are in this manner placed at two different times of the day, in the order of which is best suited to humans.

Night Shift Work

In many occupations, working hours exceed daytime and continue into the evening and night. In Norway, night shift is defined by law as work between 21:00 and 06:00 (Arbeidsmiljøloven, 2005). In the modern society, there is a need for working personnel during the night, for instance in healthcare and emergency work. According to Statistics Norway about 14 % of the working population in Norway are regular or occasionally night shift workers (StatisticsNorway, 2016). In the EU, 19 % of the working force reported to work at least one nightshift (2 hours or more between 22:00 and 05:00) the last month in 2015 (Eurofond, 2017).. This report showed higher enrollment of men on night shift (24 %) relative to women (14 %), indicating a gender difference in the occupational distribution of night shift (Eurofond, 2017).

Although a necessity, night shift is associated with a variety of work- and health-related problems. For long-time effects, research has linked night shift with metabolic disturbances, stroke, overweight and poorer sleep (Brown et al., 2009; Kecklund & Axelsson, 2016; Lee et al., 2017; Muecke, 2005). Due to the growing evidence of associations between night shift and cancer, the World Health Organization (WHO) concluded in 2019, that night shift work is probably carcinogenic (a Group 2A carcinogen) to humans (Erren, Morfeld, Groß, Wild, &

Lewis, 2019). Gastrointestinal disorders are also related to night shift according to a systematic review of articles in Medline form 1966-2009 (Knutsson & Bøggild, 2010).

More immediate effects seen at the workplace are higher risk of work accidents and lower cognitive performance (Åkerstedt, T., et al, 2005). An investigation of truck drivers found that truck crashes were increased in relation to increased time awake (Barger, L. K., et al, 2009).

According to Dawson and Reid, 24 hours without sleep are comparable with having a mean blood alcohol concentration of 0.10 % when concerning cognitive psychomotor performance (Dawson, D., Reid, K., 1997). This is of importance for the safety and performance of all work during night shift, for instance in healthcare and emergency services. Considering the safety of workers, patients, costumers and other people involved as well as the fellow road users when night shift workers are on their way home. A simulated driving study after night shift showed both an increase in number of driving off the road and a reduction in time to the first accident appears (Åkerstedt, T., et al, 2005).

Sleep deprivation, which often occur for night shift work, impairs attention and working memory. Other functions affected are memory and decision-making (Alhola, P., & Polo-Kantola, P, 2007). In addition, alertness and cognitive performance reaches a nadir in the early morning when night shift normally still are present (Åkerstedt, T, 2003).

Taken together, these studies show several negative health-related effects of night shift work. Minimizing the negative effects of working at night are important, not only for the workers involved, but also for the society. As stated of Folkard and Tucher, the safety and the productivity are reduced when working at night (Folkard & Tucker, 2003). There are several potential underlying factors. One strong candidate contributing to the work-related problems of night shift workers is poor sleep.

Although night shift workers report disturbed sleep, shorter sleep and increased subjective feeling of sleepiness, research is limited on the objective quality of sleep after working the night shift (Åkerstedt & Wright, 2009).

Sleep

Conceptualization of Sleep

Sleep is a complex process of physiological and behavioral changes which induce a behavioral state of unresponsiveness to the environment, due to reduced consciousness and increased threshold for sensory perception (Carskadon & Dement, 1989). This is a reversible process, assumed to operate in several animals (Anafi, Kayser, & Raizen, 2019). Sleep consists of two main categories: non-rapid eye-movement sleep (NREM) and rapid eye-movement sleep (REM). Sleep starts with NREM and will further progress into REM sleep and thereafter back to NREM sleep. A sequence of NREM-REM sleep is often referred to as a sleep cycle.

The normal cycle of wakefulness in the day and sleep during the night are not present from birth. As all parents know, an infant's first months are dedicated to sleep and eating. Short and random periods of sleep and wakefulness gradually grow into a more stable pattern of nighttime sleep and daytime wakefulness between the 2nd to 6th month of life (Parmelee, Wenner, & Schulz, 1964). Regulation of the sleep-wake cycle is in consequence developed in the first months of life and not innate from birth.

How sleep is regulated in a predictable and repetitive pattern has been under interest of investigation for a long time. This resulted in a conceptual model of sleep regulation in the late 80s, which three decades later, still stands as the leading model of sleep regulation.

The two-process model of sleep regulation

The two-process model of sleep regulation explains how sleep is regulated by the circadian- (C) and the homeostatic (S) -process (A. A. Borbély, 1982). The circadian component is relatively sleep independent, tracking time of day and sets the human body up for sleep and restitution at nighttime. The homeostatic component is sleep dependent. It refers to a build up of pressure for sleep as a consequence of time spent awake and in activity, and a decline in sleep pressure with time spent in sleep. Together, these two components will normally produce the highest pressure for sleep at nighttime for humans.

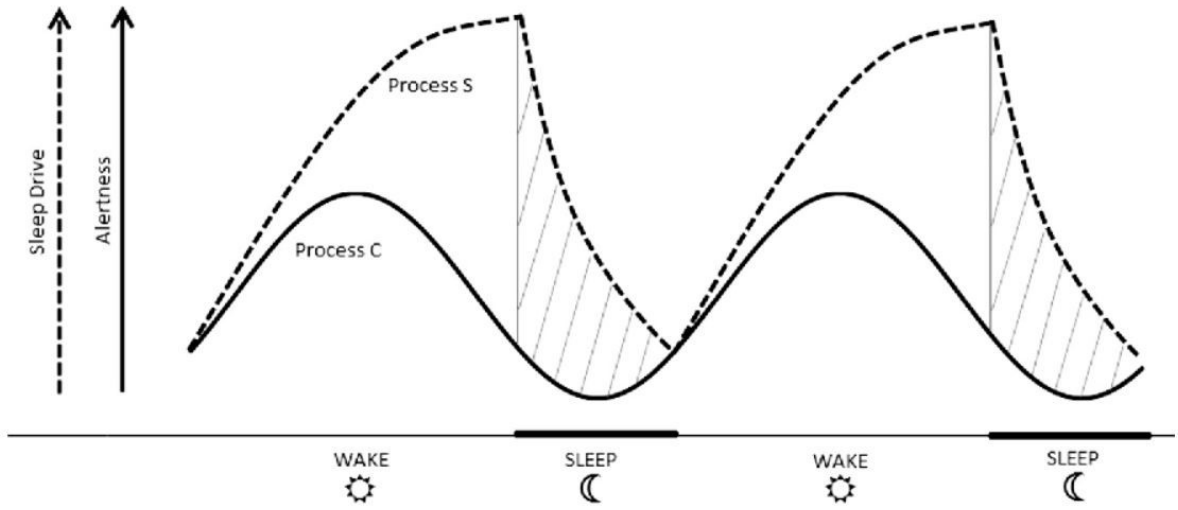


Figure 1 The two-process model of sleep regulation. Process S indicated by dotted lines and process C indicated by the solid line. Adapted form Cheng, P., & Drake, C, 2016).

The model will therefore serve as an explanation for why night workers report feeling sleepy at work and show reduced cognitive performance (Haidarimoghadam et al., 2017; Åkerstedt, 1998). Night shift workers will usually be awake for the majority of the day before going to work (normal sleep-wake pattern). When attending the night shift this will thus contribute to further buildup of the homeostatic pressure. When workers come home from their night shift the homeostatic pressure will be high as a result of the extended wake-time. This will be in the morning, a time of the day when the circadian process prepares the body for

daytime activities. The two processes of sleep regulation are in this case working in diverging directions, one promotes sleep and the other promotes wakefulness.

According to the model, daytime sleep will for this reason be of shorter duration. Studies of night shift workers have shown this to be true indicated by reduced total sleep time. (Matsumoto, 1978; Pires et al., 2009; Torsvall, Akerstedt, Gillander, & Knutsson, 1989).

Sleep homeostasis - process S

In the early part of this century the assumption was that sleep was regulated by the accumulation of toxins and bi-products of metabolism. The accumulation resulted in higher pressure for sleep, the more toxins and other substances present in the body. Kleitman argued against this assumption with the remark on observations where individuals sleep deprived for several days only experienced a periodic pressure of sleepiness at night with less sleepiness at daytime (A. A. Borbély, 2001). Despite this observation, the idea of a homeostatic pressure of sleep did not get neglected.

The sleeping brain generates brain waves which are detectable with the use of electroencephalography (EEG) recording. Deep NREM sleep has long been thought of as the most restorative part of sleep. This stage of sleep is often referred to as slow wave sleep (SWS) because the brain generates cortical slow brain waves. The intensity of slow waves per time unit are often referred to as slow wave activity (SWA). Sleep loss increases sleep pressure and SWA. Studies of both human subjects and rodents have shown an exponential increase in SWA when sleep deprived (Finelli, Baumann, Borbély, & Achermann, 2000). When human individuals were sleep deprived for 40.5 hours the sleep afterwards showed a progressively declining tendency (Borbély, A. A., et al. (1981). Such findings have led to the physiologically marker of homeostatic sleep pressure is often, and reliably, measured as SWA (Franken, Dijk, Tobler, & Borbély, 1991). In a review of the link between fatigue and safety there are evidence

of sleep homeostatic effects on impaired performance and increased accidents when sleep deprived, showing the negative effect of expanding the waketime (Williamson, A., et al, 2011).

As well as sleeping after sleep deprivation, reduction of sleep pressure can also be achieved with napping both before and during sleep deprivation. Participants experienced exponential decay of SWA and the characteristic declining slope of SWA over consecutive sleep cycles were altered when naps were taken in the evening. SWA within the nap did also increasingly occur the later the naps were scheduled (Werth, Dijk, Achermann, & Borbely, 1996). Taken together, these findings give reasons to assume a close relationship of the homeostatic process of sleep and SWA (Dijk, Brunner, & Borbely, 1990). When assessing the amount of SWA within a sleep period, the product of time in NREM sleep and SWA gives slow wave energy (SWE). Dissipation of SWE over the entire sleep episode will in this manner give insights on whether sleep pressure is reduced throughout the sleep (Skorucak, Arbon, Dijk, & Achermann, 2018).

Circadian regulation of sleep - process C

Circadian rhythms ("circa diem" is Latin for "about a day") are variations in biological processes with a repetitive interval of approximately 24-hours (Toh, 2008). This is an important feature of most organisms and keeps the body in advance of the external changes in the course of a day and across the seasons, independent of external cues (REF Russel foster a very short). The circadian regulation of sleep is, as mentioned, robust in spite of sleep deprivation (A. A. Borbély, 2001). The circadian drive for sleep promotes therefore sleep at night and wakefulness in the day.

When assessing circadian rhythms, the circadian phase (phi, ϕ) places a given event in time on a curve of the circadian cycle. Usually the lowest point are referred to as nadir and the highest point is called acrophase. One example of a circadian rhythm often used is core body

temperature. When core body temperature reach its nadir, the propensity to fall asleep is high (Lack, L. and Lushington, K. (1996),

For examination of the circadian process Kleitman developed a forced desynchrony protocol in the 60s. The protocol forces participants in a sleep-wake cycle much longer or shorter than the normal 24 hour rhythm. The large difference between normal rhythm and the forced protocol needs to be with enough desynchrony in order to not allow for entrainment and thereby be free-running (Morris, Aeschbach, & Scheer, 2012). In one experiment, eight young males were exposed to a forced desynchrony protocol of 28 hour rest-activity cycle. The rest were scheduled to 9.33 hours spent in bed with surrounding darkness and the timing of when sleep was scheduled varied across the experiment. No cues on time of day were present and participants lived in the laboratory for up to 36 days. Core body temperature was continually measured and sleep onset latency was recorded. Sleep onset latency was highest for the point of endogen circadian temperature which would correspond to about 22:00 hours under entrained conditions. Reduction in the time of sleep onset latency was seen in companion with a falling core body temperature. This shows a core temperature regulated by the circadian process (Dijk & Czeisler, 1994). Timing of sleep is clearly not only dependent on prior wake, but also on time of day. Presumably, this process facilitates sleep at the time when the organism gets the least use of being awake (Siegel, 2009). For humans this means activity during the day (diurnal) and rest during the night.

Measuring Sleep

Sleep stages and parameters

Neurons communicate by electrical and chemical signaling. When large numbers of neurons are active and communicate at the same time, we are able measure the voltage

fluctuations as brainwaves from outside of the scalp with the use of electroencephalography (EEG). EEG provides high temporal resolution but are limited on spatial resolution.

The frequency (Hz) of EEG measured are often divided into frequency-bands. According to the AASM manual (Berry RB, Brooks R, Gamaldo CE, Harding SM, Marcus C, Vaughn BV, 2012) the following definition are normally used staging the sleep: 0-3,99 Hz for delta-waves, 4-7,99 Hz for theta-waves, 8-13 Hz for alpha-waves, greater than 13 Hz for beta-waves.

Staging sleep requires a trained person which manually scores sequences of 30-seconds epochs. Beta-waves, and higher frequencies, are usually seen when the participant is active awake. When the individual goes into relaxed wakefulness with the eyes closed, brainwaves will often shift to alfa-waves. To score wakefulness, at least 50 % of the epoch must be of alfa-waves (or higher frequencies).

NREM are divided in three stages: N1, N2 and N3. The first stage of sleep (N1) is mostly seen as a transition from wake to sleep and sleep to wake. This stage is characterized by the slowing of EEG frequency relative to wakefulness with less than 50 % of the epoch duration as alpha activity. Sleep stage N2 includes EEG signals with no more than 20 % of epochs in slow wave frequency. This stage will often include sleep spindles and K-complexes of which are characteristic of the N2 stage. Sleep spindles are rapid bursts of low amplitude activity with frequencies of 7 - 14 Hz (De Gennaro, L. and M. Ferrara, 2003). The K-complexes are seen as sudden peaks of negative activity which are followed by an immediate positive peak (Colrain, I. M. (2005). The third stage (N3) are often referred to as deep sleep. N3 includes slow delta waves (<2Hz) for at least 20 % of the epoch.

The second main category of sleep is REM sleep, named by its characteristic rapid movement of the eyes. The stage includes low voltage, mixed frequency background EEG

signal with the appearance of saccadic eye movements and very low levels of muscle (submentalis) activity.

Sudden activations in the central nervous systems during sleep might occur and are called arousals. The nature of arousals are in debate, but are considered a marker of disruption of sleep (Halász, P., et al, 2004). A certain number of arousals are considered normal, whereas an increased number of arousals could be related to disturbed sleep. Arousals include increases in EEG frequency lasting for 3 seconds or longer but are only scored as arousal if there is 10 seconds of sleep prior to the event. If in REM sleep, the increase in EEG frequency must be accompanied by an increase in EMG (submentalis) for at least 1 second to qualify as arousal (REF: scholle 2005).

The AASM manual (American Academy of Sleep Medicine) recommends several sleep parameters to be reported, both for clinical and scientific use. Lights out are marked as a point in time (hh:mm) where the person allows herself or himself to fall asleep. Total recording time is defined as the total time from lights out to lights on (clock time the person awakened) and will indicate if the sleep episode was of normal length.

Sleep propensity serves as a useful indicator of the readiness to fall asleep and includes parameters as: Sleep onset latency (SOL), REM sleep latency and latency to N3. The propensity to fall asleep will normally be higher along with higher sleep pressure. Accordingly, sleep deprivation produces higher pressure for sleep and higher sleep propensity. This can for instance be seen as reduced SOL

SOL is defined as the time from lights out until the first epoch of sleep. REM sleep latency and latency to N3 is measured as time from sleep onset until the first epoch of REM sleep and N3, respectively. The latter signifies a need for deep sleep if the latency is short and may then be interpreted as a measure of high sleep pressure.

Consolidated sleep is a term related to the ability to maintain sleep without disruptions such as awakenings and arousals. The total minutes scored as wake taking place between first epoch of sleep and lights out are defined as wake after sleep onset (WASO). A practical measure of sleep efficacy is done by dividing total sleep time by total time in bed, giving the percentage of sleep in relation to the time spent in bed. Minutes awake, WASO, sleep efficiency, total number of arousals and arousal index are all measures which can be useful when assessing the ability to sustain sleep, also referred to as sleep consolidation.

Distribution of sleep stages

Normal human sleep consists of sleep cycles of around 90-110 minutes. Each cycle starts with NREM sleep and progress to REM sleep, and ends with a short or longer arousal/awakening. These cycles are repeated several times throughout the sleep episode. A normal night of sleep for adults is approximately 7,5 hours for weekdays and 8,5 hours on weekends (Carskadon & Dement, 1989).

The first one third of the sleep typically consists of more N3 (SWS) in the NREM sleep portions and less so for the last two third of the sleep. On the other side, longer REM sleep episodes are usually present in the last one third of the night (Carskadon & Dement, 1989).

Night-time sleep has been rigorously researched. This has led to identification of some patterns generally seen in normal night sleep. Sleep stage N1 makes up for only 2-5 %, whereas around 45-55 % of total sleep is dedicated to N2. The last 50 % are roughly divided between N3 and REM with about 25 % each. Less than 5 % of the time spent in bed will normally be wakefulness (Carskadon & Dement, 1989).

Daytime sleep

Sleep at daytime is not as deliberately investigated as night sleep. Nevertheless, a handful of studies have been performed and there seems to be some recurring patterns. Brazilian bus-drivers working shifts showed significantly reduced sleep length and sleep efficacy, with more N1 sleep when sleeping at daytime. For the younger drivers there were also less REM sleep and slightly more minutes of N3 when sleeping in the day compared to sleeping at night (Pires et al., 2009). Another study conducted by Torsvall revealed reduced sleep length of more than 2 hours for day sleep when compared to night sleep. This unfolded as reduced N1, N2 and REM sleep. Time spent in SWS was conserved and constituted significantly increased when presented as a percentage of total sleep. Total time awake was also increased (Torsvall et al., 1989). Two years after publication of this article, the same group of participants were subjects in another study. This field study investigated differences between three types of shiftwork (morning, day and night shift) with the same results on total sleep time, N2, N3, REM sleep and SWS of night shift workers as the previous study (Akerstedt, Kecklund, & Knutsson, 1991).

Light's impact on sleep

Light and photoreception

Our ability to see the surroundings are only made possible by light. For humans, the spectrum of visible light is in the range of 400 – 700 nanometers (nm). All materials reflect and absorb light waves to different degrees (Bear, 2016). When the light waves reach the eye's retina it activates different photoreceptor cells via opsin, a light sensitive protein. The cells responsible for forming images are rods and cones. When activated by light these cells further signal to retina ganglion cells (RGC) with axons forming the optic nerve, where the signals are transmitted further to the brain (Hattar, Liao, Takao, Berson, & Yau, 2002).

In parallel, another group of cells in the retina is activated by light, the intrinsically photosensitive retinal ganglion cells (ipRGC), responsible for non-image forming responses to light. The ipRGC cells uses another light sensitive opsin, called melanopsin. The sensitivity to light for these cells is for this reason reactive to a smaller specter of light waves than rods and cones with an absorption peak at around 480 nm (the blue light specter) (Panda, S., et al, 2005). The ipRGC forms a direct nerve path, known as the retionohypothalamic tract, to the suprachiasmatic nucleus in the brain. This part of the brain is sometimes referred to as the masterclock because of its role in synchronizing internal biological clocks in our circadian system (Paul & Brown, 2019). The non-image forming system is in consequence the driver for synchronization of biological clocks, regulation of melatonin, pupil size and locomotor behavior (Hattar et al., 2002).

The iPRGC cells also signal both directly and indirectly to other hypothalamic areas. Signals are sent to the ventral lateral preoptic area (VLPO) known for its role in sleep regulation and arousal. Sleep is promoted by this area when neurotransmitter systems of the VLPO are active and thereby inhibition of ascending arousal systems. On the other side, when the same systems are not inhibited, alertness is promoted (Lok, R., et al. (2018). Locus coeruleus are a nucleus in the brain affected by ipRGCs, also related to alertness. Level of arousal was increased when experimentally injection of excitatory agents were used to activate locus coeruleus (Aston-Jones, G., & Cohen, J. D. (2005).

At first it was assumed that ipRGCs were operating separately from conventional rods and cones. Most experiments have therefore used either blue-enriched light or bright light in their experimental intervention (Lok, Smolders, Beersma, & de Kort, 2018). Newer experiments indicate a more flexible system where the ipRGCs and the rods and cones are able to share information when needed (Vandewalle, Maquet, & Dijk, 2009). This explains how the

circadian system both are responsive to lower levels of light and a broader spectrum of wavelengths than assumed in earlier experimental interventions.

Circadian entrainment

Even though the circadian system is able to keep track of time with the absence of external cues, the system uses external information for adjusting the internal environment in synchrony with the external environment. This process is known as entrainment. Without external information the individual would be in free-running, relying solely on the internal clock. Research on free-running participants indicates the internal human daily phase to be about 24,2 hours (Czeisler et al., 1999). The length of the human circadian period also varies due to individual differences (chronotypes). Some difference between the internal circadian period and the external period are likely to be present and thereby a daily adjustment takes place as entrainment.

Information of the external light environment serves as the most important time cue (zeitgeber) (Duffy & Wright, 2005). Light has been recognized to have different effects on sleep depending on timing of exposure. Light in the morning gives advancing effects on circadian rhythms and light in the evening provides delaying effects on circadian rhythms (Alexander A. Borbély, 1978). Timing of light is for this reason important to consider when investigating wakefulness and sleep.

Effects of Light on Wakefulness and Sleep

Light exposure at daytime is generally thought of as positive for circadian entrainment, for stay awake and for being sleepy in the evening. Hence, a growing interest for light exposure as a treatment for several psychological disorders and other health related problems. When

institutionalized elderly people were exposed to 2 hours of morning light (6000 – 8000 lux) for two weeks, sleep was improved. The participants showed 1 hour shorter SOL, 1.73 hours less wakefulness and 1.03 hours more sleep (Fetveit, Skjerve, & Bjorvatn, 2003).

There are also one example of a study with light treatment for demented patients with no effect on sleep length, but with increased sleep consolidation (Ancoli-Israel, Martin, Kripke, Marler, & Klauber, 2002). In accordance with this, the same author did a project on patients with Alzheimer's disease where both bright light (2500 lux) in morning and in the evening gave more consolidated sleep (longer maximum sleep bouts) at night (Ancoli-Israel et al., 2003). A study on normal healthy individuals reports improvement of subjective rating in both sleep quality and sleep duration after blue light exposure at daytime in an office setting (Viola, James, Schlangen, & Dijk, 2008). In sum, light exposure in the morning or in the daytime may serve positive effects on sleep.

Light exposure in the evening or at night might provide another effect on sleep. A field-study conducted on elderly people applied light exposure at evening time in a home setting. The regression analysis revealed significant associations of the amount of evening light prolonging subsequent SOL (Obayashi et al., 2014). This and similar findings inspired research on limiting the exposure for blue light in the evening. However, Heath and colleges did not find any effect on SOL and slow-rolling eye movements when filtering out blue-light from tablet screens (Heath et al., 2014). In line with this, Grønli et al. also did not find that exposure to the blue-light from iPad screens for 30 minutes before bedtime to impact on sleep duration and SOL compared to controls reading in a book. This study did however find effects on EEG parameters, where SWA was delayed and the quality impared (Grønli et al., 2016). The further question of investigation is in this manner the impact of light on brainwaves during sleep.

When focusing on EEG frequencies studies of light's impact on sleep are scarce. To our knowledge, the first experiment on this matter was conducted by Cajochen in 1992 (Cajochen,

Dijk, & Borbely, 1992). Here, eight male subjects were exposed to bright light at 2 500 lux or dim light at 6 lux for three hours before bedtime at two different days. Both slow-wave activity (SWA; 0,75-1,00 Hz) and REM sleep was reduced in the first 90 minutes of sleep when exposed to bright light. Thereafter the experiment revealed an increase in SWA (0,25-2,00 Hz) for the time-interval of 270-360 minutes into the sleep period. The authors interpreted this as an immediate suppression of SWA and REM sleep as a result of exposure to bright light, with a rebound effect later to make up for the lost SWA, but not for REM sleep.

A similar tendency was seen when Münch compared blue light (460 nm) with green light (550 nm) exposure for two hours before sleep (Munch et al., 2006). SWA was slightly reduced (not significant) and REM sleep was significantly reduced for the first part of sleep. There was a significant increase later for the time interval 180 – 270 minutes into sleep in the SWA spectrum and not for REM which had a significant reduction also in this part of the sleep episode.

Other studies have also found what seems to be an acute suppression of SWA for the first 90 minutes of sleep after light exposure (Chellappa et al., 2013; Cho, Joo, Koo, & Hong, 2013; Zhang, Wang, Wang, Qu, & Huang, 2017), but failed to find a rebound effect later. A possible explanation for the lack of rebound effect in these studies might be because of different light procedures, for example intensity, wavelength and time-length of exposure.

The effects of different wavelengths of light on the circadian system, wakefulness and sleep are however not fully understood. For years, red light has been used at night to prevent interruption of the circadian rhythms. The assumption was that longer wavelengths did not have activating effects on ipRGCs. Some studies have found increased sleep propensity when exposed to red light before sleep (Meijden et al., 2018). A study from 2017 however, suggest that red light exceeding the intensity of 10 lux negatively impact the following sleep in rats

(Zhang et al., 2017). Consequetly, there are reasons to believe that not only blue-light, but also red-light exposure before sleep is able to produce disturbing effects on sleep quality.

Effect of Light Exposure in Night Shift Work

As described, light influences sleep in a variety of ways. One of the practical tips we in the sleep community promotes for the public are in this manner, to reduce light exposure before bedtime. Even though a fairly simple advice to follow for most people, for some groups of the society this will not be an option. Most nightshift workers, for instance, are in need of light for doing their jobs. Research on night shift workers and manipulation of light have shown promising results when examining how light is able to enhance wakefulness and cognitive performance at work. Control room workers (N = 30) were, after baseline with the existing light condition, exposed to both 17 000 K (Kelvin) and 6 500 K blue-enriched white light. Shift durations were for one week (12 hours a day) each, seperated with 14 days (Motamedzadeh, Golmohammadi, Kazemi, & Heidarimoghadam, 2017). On the other hand, some research shows different results when assessing both subjective and objective sleepiness (Sletten et al., 2017). The study conducted by Sletten used two light conditions, one of 17 000 K, 89 lux and one condition of standard whit light 4 000 K, 84 lux. The light exposure on night shift does therefore not always provide enhancing effects on performance, emphasizing the importance of further investigation.

Recent results from our own laboratory have shown when participants worked in short-wavelength light (455 nm, 60 lux) at night the cognitive performance was better and they felt less sleepy compared to working in long-wavelength light (625 nm, 196 lux) (Sunde et al., 2020). The experiment was set up with a simulated night shift starting at 23:00 h and ended at 06:45 h for two consecutive nights. The work shift was simulated by giving participants five bouts of computer-based tests including The Karolinska Sleepiness Scale (KSS), Positive and

Negative Affect Schedule (PANAS), a 2-min computerized Digit Symbol Substitution Test (DSST), and a 10-min computerized Psychomotor Vigilance Task (PVT). PANAS revealed no effect of light conditions on mood, whereas PVT showed faster reaction time and DSST more correct responses in short-wavelength light. The implication of these results is to use light as an enhancer of performance on nightwork. Although light exposure at night might be a useful enhancer of cognitive performance, these implications come with a caveat. Only little is known of how night shift workers sleep when their shift is finished, and they are back home in their own bed. As described in the section of daytime sleep, there are indications of altered daytime sleep in night shift workers.

In 1991, Dawson and Campbell exposed participants to 4 hours of light (clock time 24:00-04:00) at 6000 lux during night shift work and dim light (<200 lux) throughout the rest of the shift. Compared to the controls (dim light the entire night shift) the light exposure gave positive effects on daytime sleep resulting in 62 minutes longer sleep time and 52 minutes reduced WASO (Dawson & Campbell, 1991). The results of this experiment are in contradiction with the results of Torsvall (Torsvall et al., 1989) and Åkerstedt (Akerstedt et al., 1991), presented above. All three studies examined daytime sleep after night shift work whereas only Dawson and Campbell actively manipulated the light conditions.

In today's research, with the increasingly use of different light manipulations at night shift the question therefore remains, will light manipulations further impact on the already altered daytime sleep for night shift workers?

Aims and Hypotheses

Every night shift worker goes home to sleep when their shift has ended. Nevertheless, there have been few scientific experiments to examine the daytime sleep of simulated night shift workers. We have also failed to find studies of night shift work when light is manipulated with measures of both SWA and SWE for daytime sleep. There is therefore little known of the sleep quality of night shift workers after shift work has ended. Our goal is to bring new knowledge of the daytime sleep of night shift workers. A population associated with less sleep and several health issues, most likely due to poorer sleep.

The aim of this thesis is to characterize the daytime sleep when working night shift in two different wavelengths of light (blue: 455 vs red:615 nm). Specifically, I am to answer the following questions:

If sleep-wake quantity and quality are different in

1. day sleep (blue and red condition) compared to night sleep,
2. Day sleep blue condition is different from day sleep red condition

Based on earlier research (Akerstedt, Kecklund, & Knutsson, 1991; Pires et al., 2009; Torsvall, Akerstedt, Gillander, & Knutsson, 1989) it is hypothesized that total sleep time is reduced when comparing daytime sleep with night time sleep. Time spent in N3 is expected to be preserved but increased when expressed as a percentage of TST. Time in stage N2 and REM sleep is expected to be reduced.

Sleep propensity is hypothesized to be higher for daytime sleep due to the preceding sleep deprivation. This will be examined through the parameters of SOL and latencies to REM and N3 which all are predicted to be shorter in accordance with earlier research on sleep deprivation (Elmenhorst et al., 2008; Vgontzas, A. N., Zoumakis, E., Bixler, E. O., Lin, H.

M., Follett, H., Kales, A., & Chrousos, G. P. (2004). Sleep consolidation will also be assessed. For this, time spent awake (in minutes), WASO, number of arousals, arousal index is used. More consolidated sleep is predicted for sleep deprived daytime sleepers when compared to night time sleep, producing less time spent awake and lower WASO, number of arousals and arousal index.

For quality of deep sleep EEG frequencies analyzed as SWA and SWE are used. Based on earlier research SWA is predicted to be higher for daytime sleep relative to night time sleep because of the sleep deprivation prior to daytime sleep which will produce higher levels of sleep pressure (Borbély, A. A., et al. (1981). SWA and SWE are expected to expose a general declining tendency throughout the sleep in all conditions due to the reduction of sleep pressure taking place as sleep progresses as seen for earlier research (Franken, Dijk, Tobler, & Borbély, 1991).

According to earlier research of Münch, Cajochen and Chellappa we also predict a suppression of SWA in the frontal derivation at the beginning of sleep (presumably at the 60- or the 120-minute datapoint). Although many studies have found effects of blue light on sleep there are also studies indicating that red light produces similar types of effects. We have in this manner not solid enough evidence to predict stronger effects for one of the conditions when comparing daytime sleep of the blue-light and the red-light condition. The direction of our hypothesis is in consequence open ended for this hypothesis.

Method

Ethical Consideration

The Regional Committee for Medical and Health Research Ethics in Western Norway approved the study (2016/1903). All participants provided written informed consent before inclusion. Hence, the study was in accordance with the declaration of Helsinki.

Participants

A total number of 21 participants were included in this study. Participants were recruited through flyers, emails and information given in lectures at the University of Bergen. When assigning an interest for participating one was provided with an online survey for further screening. This process included participants which met the following criteria: age between 19-30 years, a body mass index (BMI) under 30 and self-reported health at the score of good to excellent (including no relevant or current history of psychiatric-, neurological-, cardiovascular-, lung disease, sleep diseases or disorders, eye diseases or disorders. The participants had normal color vision, tested with the use of 17-plate Ishihara Test for Color Deficiency. Participants did not use any medication, except for oral contraceptives. The females did not breastfeed and were not pregnant. Their usual menstrual cycle length and last menses onset were reported, and menstrual phase (follicular, luteal) were estimated in accordance with Vidafar (Vidafar et al., 2018).

Participating required no transmeridian travelling the last month before and during the experiment, as well as no night work. Chronotype was assessed by the short Morningness-Eveningness Questionnaire (Adan & Almirall, 1991), and no extreme chronotypes were found. Alcohol was prohibited to use 3 days prior and during the experiment, caffeine for 1 week prior

and during the experiment and tobacco use 2 hours prior and during the experiment. Normal sleep duration was self-reported to be in the range of 6-10 hours per night. This was further confirmed with polysomnographic recording of the night sleep (baseline nights). Participants received a gift card when completing the study protocol.

Design

The study was registered at ClinicalTrails.gov (NCT03203538), investigating how light intervention could improve adaptation to night shift work. The experiment was conducted at high latitudes (~ 60 °N) in the autumn (October 2018) and winter (March 2019) which provides limited exposure to daylight in the evening and the morning (prior to and after night shifts).

The intervention design was a repeated measures in a counterbalanced crossover design. Participants verified to adhere to the sleep criteria (timing of sleep and sleep length, measured by sleep diary and actigraphy) three days before the first simulated night shift, except from the third day where habitual bedtime was postponed with 1h due to melatonin saliva sampling.

A one-night ambulatory polysomnographic recording of their sleep was performed one night (night sleep) between the study protocols, and after each of the two night shifts, when participants went home to sleep without any restrictions (day sleep). The simulated night shift, at two different timepoints was separated by 4 weeks.

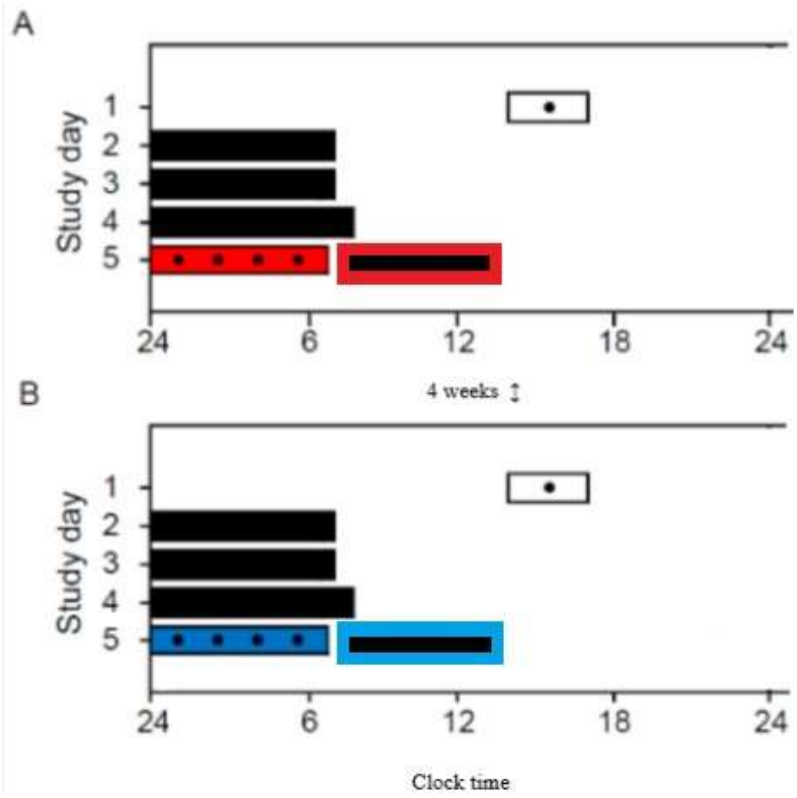


Figure 2: Raster plot of the simulated night shift protocol (adapted from Sunde 2020). Two single night shifts were performed in the laboratory from 23:00h to 06:45h (clock time plotted on horizontal lines). 4 weeks separated the sessions (indicated by space between panel A and B) in a counterbalanced design. Panel A illustrate the week of short-wavelength narrow-bandwidth light exposure (visually seen as red light. Panel B illustrates the week of long-wavelength narrow-bandwidth light exposure (visually seen as blue light). White bars indicate enrollment and practice session (3 days before the first night shift only). Black bars indicate assumed sleep periods at night-time. Colored bars indicate night shifts performed in the laboratory. Black bars with colored outline indicate assumed sleep periods at daytime. Black dots indicate test bouts.

Procedure

Three days before the first simulated night shift, the participants practiced performance tasks similar to tasks given during the experimental night shifts. Actigraphs and sleep diary were given with instruction for use. For this session, the participants were exposed to a standard illumination (~4000 K) approximately 200 lx at eye level (measured in vertical plane, at 120 cm height). The participants had no restrictions on light exposure or activities before the start of the study protocol but were asked to keep normal sleep habits and were prohibited from taking naps the day before night shift.

The shift started at 23:00h and ended at 06:45h with groups of four to eight participants per group. Prior to the start of the night shift, at 23:30h, subjective measures of visual comfort (symptoms of headache and eye strain) and evaluation of lighting conditions were assessed (see Sunde et al., 2020). The night shift work consisted of a total of five test bouts, each enduring for about 20 minutes. The test bouts included measure of subjective sleepiness (Karolinska Sleepiness Scale, KSS); measure of sustained attention (Psychomotor Vigilance Task, PVT and Digit Symbol Substitution Test, DSST). Participants used noise cancelling headsets (BOSE QuietComfort 25, BOSE, USA), to avoid disturbance during testing.

Several short breaks were given (~10-15 minutes) where participants were able to do quiet activities (for example talking and reading). Water and toilet breaks *ad libitum*, the latter implied walking through a hallway in dimmed lights. Besides this, participants remained seated at their desk in front of a computer. Standardized meals (~200 kcal) were arranged at approximately 02:00h and 05:00h, all other foods and drinks were prohibited. Observations from a researcher in the laboratory ensured compliance to the protocol. After the simulated night shifts the PSG equipment was checked and the participants went home to sleep. For further details I will direct the reader to Sunde 2020 (Sunde et al., 2020), as the focus of my thesis are outcomes on daytime sleep.

Laboratory and Light

The laboratory used for nightshifts was air-conditioned, held a temperature of ~22 °C, had no windows and occupied an areal of 30 m^2. 20 LED-luminaires (Modul R 600 LED CCT/RGB MP; Glamox Luxo Lighting AB, Gothenburg, Sweden; size 60 X 60 cm were mounted in the ceiling, separated to produce uniform illumination of the rom. There were eight similar desk spaces with partition walls for separation. At every desk there were identical computers fitted with screen filter foil (Metolight SFG-10; Asmetec, Kirchheimbolanden,

Germany) in order to block all light wavelengths under 520 nm. With the use of a spectroradiometer (GL Spectis 1,0 T; GL Optic, Puszczykowo, Poland) light conditions were assessed at three times (beginning, middle and at the end) under the experimental procedure. Measurements were performed in vertical plane at eye level (120 cm height) facing the same direction as when the participants were seated at desk spaces. Lighting parameters were calculated in agreement with the CIE S 026 Toolbox-version 1.049 (International Commission on Illumination, 2018). When immersed in the performance tasks we controlled for participants' posture and gaze, at all other times participants were free to direct their gaze after their own preferences. For this reason, the reported light levels reflect approximate light exposure at eye level. Photon density was measured as similar for the two light conditions, both with lower than 15 nm half-peak bandwidth (FIGURE?).

Linear mixed model was used to examine stability of light exposure. Factors included were: Group (six groups of participants), Light (short-wavelength vs. long-wavelength), Time (beginning, middle and end of shift night). The interaction Light by Time were entered as fixed factors. We found a significant effect of Light ($F_{1,54}$ = 1087.44; $p < 0.001$) where the short-wavelength light shows higher irradiance (EMM = 125; SE = 1 μW/cm^2) relative to the long-wavelength light (EMM = 82; SE = 1 μW/cm^2). No significant effects of Time ($F_{2,54}$ = 1.07; p = 0.351) or the Light by Time interaction ($F_{2,54}$ = 0.27; p = 0.765), were revealed.

Polysomnography

The polysomnographic data were monitored using SOMNOmedics PSG+ ambulatory devices (SOMNOmedics, GmbH, Randersacker, Germany). The six EEG electrodes (CNSAC Gold Cup EEG electrodes, MedShop GmbH, Austria) were placed according to the international 10–20 system (F3:M2, F4:M1, C3:M2, C4:M1, O1:M2, O2:M1). EEG data were stored at 256 Hz. The analogue low-pass filter was limited to 35 Hz and the high-pass filter to

0.2 Hz. Electrooculogram (EOG) electrodes was recorded from outer canthus of both eyes approximately 1 cm lateral and 1cm above (E2) or below (E1) the midline, with M2 as reference electrode. Electromyogram (EMG) was recorded with submental electrodes with a reference electrode placed on mentalis muscle.

A registered polysomnographic technologist (RPSGT) staged visually the sleep in 30 sec epochs (wake, N1, N2, N3 and REM sleep) using Domino software, version 2.9.0, and according to the AASM Manual for the Scoring of Sleep and Associated Events, version 2.6 (Berry RB, Brooks R, Gamaldo CE, Harding SM, Marcus C, Vaughn BV, 2012), blinded to the light conditions.

Sleep parameters extracted from the PSG recordings includes: Total sleep time, latency to sleep (minutes from trying to sleep to the first sleep epoch), latency to REM sleep (minutes from sleep onset to the first epoch of REM sleep), latency to N3 (minutes from sleep onset to the first epoch of N3), sleep efficiency, arousals per hour, wake after sleep onset (WASO), time- and percentage of time spent in each sleep stage (N1, N2, N3, REM sleep).

EEG power spectrum analysis were calculated offline using Fast Fourier Transformation (FFT) for unfiltered EEG signals. The EEG power spectra were calculated during N3 sleep in the frequency band 1-4 Hz, from each of three EEG derivations (F4:M1, C4:M1, O2:M1).

Statistical analyses

Linear mixed models were used to best include all available data in a dataset with missing values on single data points. For differences in sleep parameters, ‘recording’ (night sleep and day sleep) was set as fixed effects and participants as a random effect. For analyses of SWA and SWE in N3, in frontal, central, and occipital cortex, LMM was used with

recording, time (60 min, 120 min, 180, min, 240 min, 300 min, 360 min) and their interactions as fixed effects, and participants as a random effect.

When main effects and interaction effects reached significance, any differences were assessed with Least Significant Difference (LSD) tests. Means and SEM were calculated using descriptive statistics.

All statistical analyses were performed with the use of IBM® SPSS® Statistics software for Windows (Version 25.0. Armonk, NY: IBM Corp). GraphPad Prism 9.1.0 for Windows (GraphPad Software, San Diego) was used for all figures.

Results

Participants

21 individuals were recruited. None of the participants withdrew but when performing sleep scoring, 6 were excluded for the blue-condition and 4 were excluded for red-condition due to technical issues. This resulted in N = 16 (age 21.87 ± 2.30, 4 males) for the blue-condition and N = 17 (for the red-condition (age 22.19 ± 1.68, 5 males). The baseline night sleep recordings of these participants (N = 8) showed large individual differences and in consequence sleep efficacy yielded abnormal sleep. We therefore included 12 night-sleep recordings of another experiment performed with identical procedure of the current experiment. Night sleep recordings included 21 individuals (N = 21, age 22.00 ± 1.84, 6 males).

Night Sleep

Night sleep showed a typical sleep architecture with values expected for nighttime sleep. The mean minutes of TIB was 499.70 for night sleep. Total sleep time was 442.06 ± 18.22 min (7.37 hours), and sleep efficiency was 88,33% +/-1,94. SOL was 22.00 ± 5.49 mins, latency to N3 43.52 ± 30.90 mins and REM sleep latency 98.23 ± 15.26 mins.

Time spent in awake was 57.63 ± 9.18 mins (11.53 % of TIB), time spent in N1 was 29,25 ± 3,30 (6,6 % of TST), N2 180,38 ± 12,47 min (40,2 % of TST), N3 117,55 ± 7,42 min (27.5 % of TST), and REM sleep 114.9 ± 8.29 min (25,6 % of TST).

Markers of sleep consolidation showed WASO of 36.13 ± 8.65 min (7,2 % of TIB), total number of arousals was 38.25 ± 4.58, and an arousal index of 7.62 ± 0.86/hour.

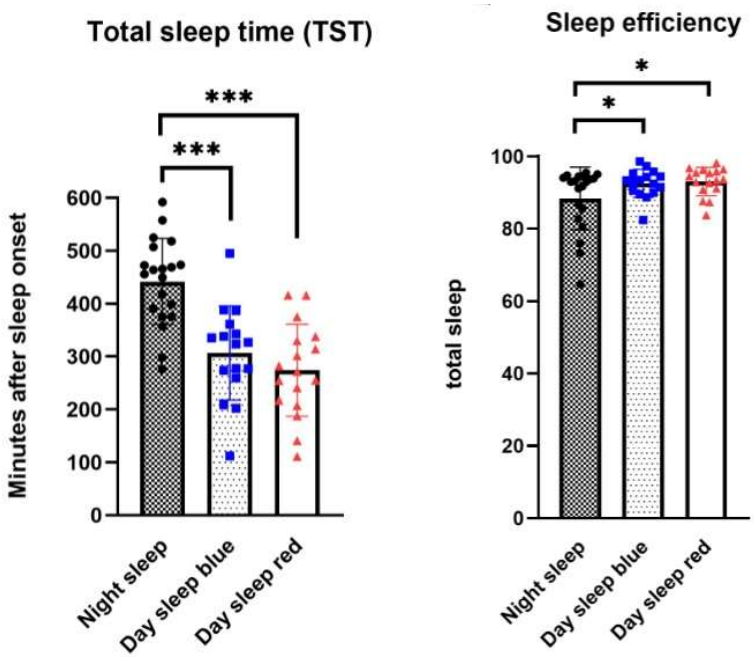
Conditional Increase in Sleep Propensity and Sleep Consolidation

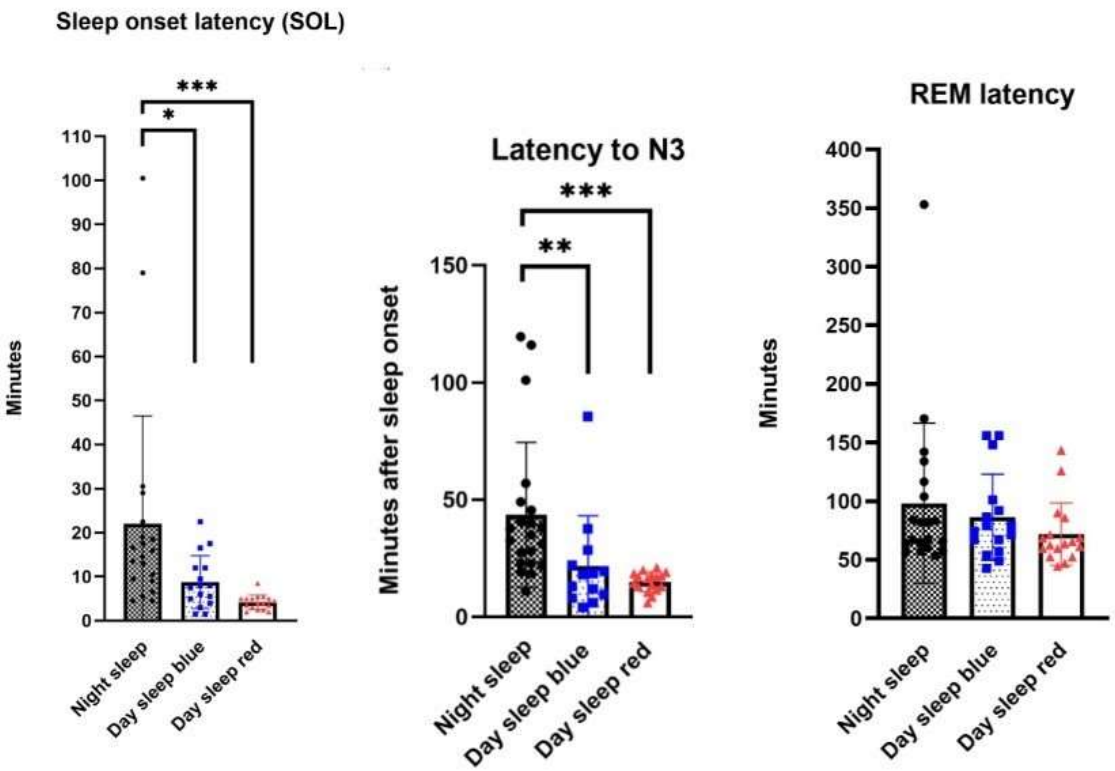
The mean minutes of TIB was 330.86 minutes for blue condition and 293.97 minutes for red condition. Total sleep time was shorter than night sleep ($F(2, 30.30) = 21{,}31$, $p < .001$), both in day sleep blue 306.78 ± 22.23 min (-135.90 minutes, $p < .001$) and day sleep red 274.03 ± 21.10 minutes (-165.56 minutes, $p < .001$). Sleep efficiency was 4,2 % higher in day sleep blue condition ($p = .049$) and 4,7 % higher in day sleep red condition ($p = .024$), relative to night sleep ($F(2, 50) = 3.29$), $p = .046$ (see figure x). Sleep architecture indicated higher sleep propensity than during night sleep. SOL was significantly shorter in day sleep compared to night sleep ($F(2, 44.59) = 7{,}07$, $p = .011$), where day sleep blue was 13,61 minutes shorter ($p = .011$) and day sleep red 18,21 minutes shorter ($p = .001$). The latency to deep sleep (N3) (($F(2, 50) = 8{,}68$, $p = .001$) was 22.32 minutes shorter ($p = .005$) and 28.55 minutes shorter ($p < .001$), in day sleep blue and day sleep red, respectively, compared to night sleep. This finding suggests a fast move to the restorative sleep stage. The REM latency was not significantly different from night sleep ($F(2, 50) = 1{,}32$, $p = .276$).

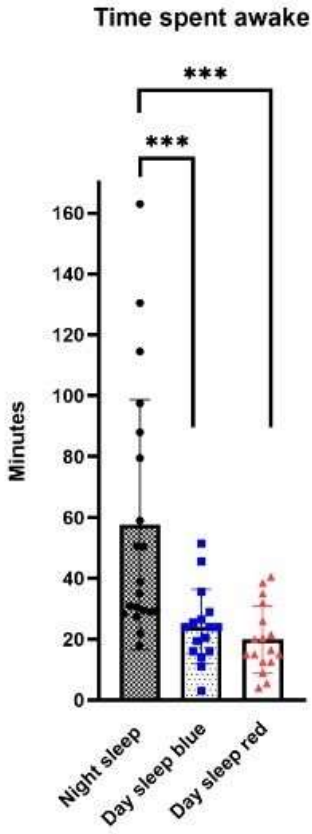
DAYTIME SLEEP IN SIMULATED NIGHT SHIFT AFTER BLUE AND RED LIGHT

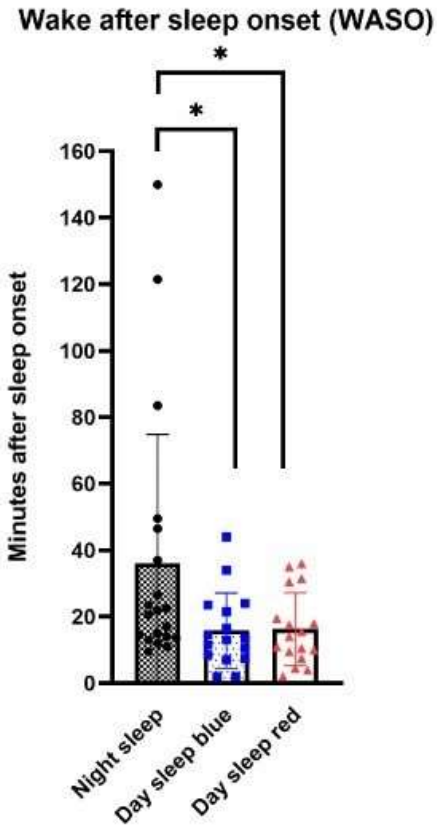
Sleep was more consolidated after night shift as minutes awake was significantly reduced (F (2, 50) = 11.02, p < .001), -33.53 ± 9.03 minutes (blue, p = .001) and -37.68 ± 8.88 minutes (red, p <.001). Similarly, findings were found for WASO (F (2, 41.29) = 3,95, p = .027) with a reduction of -20.40 ± 8.48 minutes (blue, p = .020) and -19.97 ± 8.34 minutes (red, p = .021). Number of arousals were only significant lower (F (2, 24.59) = 4,87, p = .017 for day sleep red (-15.44 ± 5.53, p = .009), but not in day sleep blue condition (-1.93 ± 5.53, p = .729). This was evident also in the arousal index (number arousal per hr in sleep) (F (2, 28.16) = 5,93, p = .007), as day sleep blue showed significant lower index than night sleep (4.54 ± 0.50/h, p = .005) and not so for day sleep red (5.97 ± 0.57/h, p = .764).

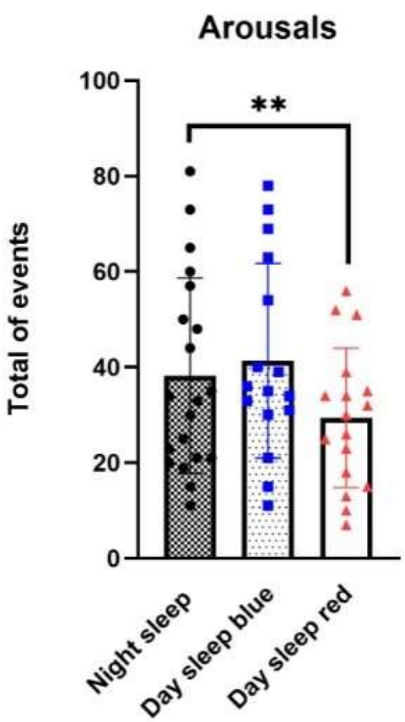
There were no significant differences in day sleep parameters between working night shift in blue- or red-light.




Sleep onset latency (SOL)
Minutes
***
*
110
100
90
80
70
60
50
40
30
20
10
0
Night sleep
Day sleep blue
Day sleep red
Latency to N3
Minutes after sleep onset
***
**
150
100
50
0
Night sleep
Day sleep blue
Day sleep red
REM latency
Minutes
400
350
300
250
200
150
100
50
0
Night sleep
Day sleep blue
Day sleep red


Time spent awake
***
***
Minutes
0
20
40
60
80
100
120
140
160
Night sleep
Day sleep blue
Day sleep red


Wake after sleep onset (WASO)
*
*
Minutes after sleep onset
0
20
40
60
80
100
120
140
160
Night sleep
Day sleep blue
Day sleep red


Arousals
**
Total of events
0
20
40
60
80
100
Night sleep
Day sleep blue
Day sleep red

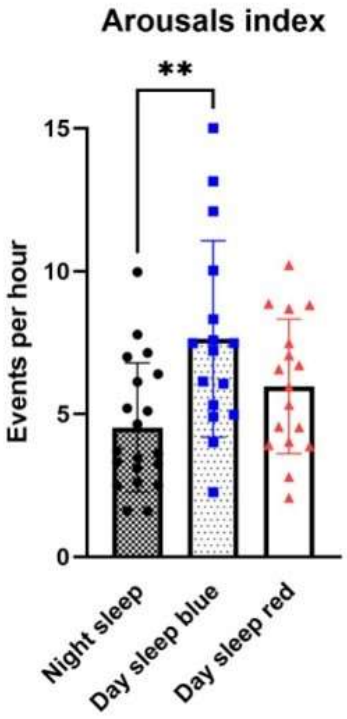

Arousals index
**
Events per hour
0
5
10
15
Night sleep
Day sleep blue
Day sleep red

Figure 3. Sleep parameters. Data from night sleep (n = 21) and day sleep after simulated night shift work in red (n = 17) and blue (n = 16) condition. The values are in minutes, expressed as mean ± SEM. ***p<0.001, ** p<0.01, *p < 0.05, compared to night sleep. Arousals are expressed as total of events and arousal index as events per hour. There were no significant differences between the two day-sleep conditions.

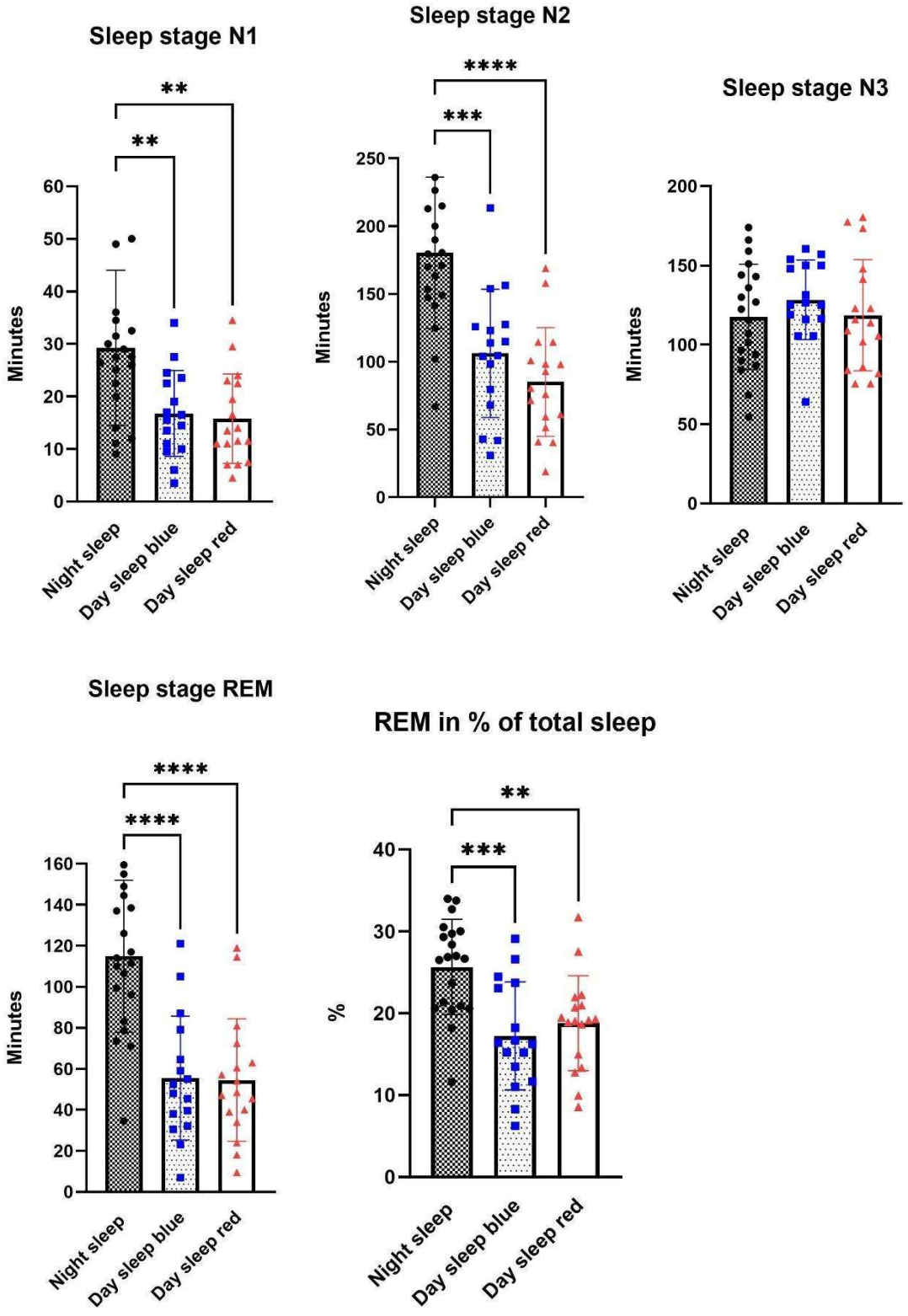
Sleep stages

Time spent in minutes in the light NREM sleep stages (N1: F (2, 21.00) = 10,76, p = .001) and (N2: F (2, 25.88) = 22,81, p <.001) and in REM sleep (F (2, 25.34) = 22,37, p < .001) were significantly reduced for both day sleep blue and day sleep red, compared to night sleep. N1 for blue condition was 17.80 ± 2.73 minutes (-11.90 minutes in difference, p = .001) and for red condition 15.80 ± 2.69 minutes (-13.90 minutes in difference, p < .001) compared to night sleep. Time spent in N2 for blue condition was 110.99 ± 11.83 minutes (-73.34 minutes in difference, p < .001) and for red condition 89.28 ± 11.58 minutes (-93.05 minutes in difference, p < .001), compared to night sleep. For REM sleep, the mean time spent after working in the blue condition was 56.71±7.87 minutes (-55.87 minutes in difference, p < .001) and for red condition 59.30 ± 7.72 minutes (-53.28 minutes in difference, p < .001) compared to night sleep.

Time spent in stage N3 was preserved in the day sleep compared to night sleep (F (2, 36.59) = 0,42, p = 0.66), with 125.59 ± 7.85 minutes (+8.45 minutes in difference, p = .410) in blue light condition and 117.84 ± 7.62 minutes (+0.70 minutes in difference, p = .945) in red light condition.

When comparing sleep stages in percent of total sleep time, N2 (F (2, 27.53) = 10,74, p < .001 and REM sleep (F (2, 26.45) = 11,57, p < .001) were significantly reduced in day sleep for both light conditions compared to night sleep (N2: blue -6.31 %, p = .007 and red -10.11 %, p < .001, REM: blue -7.70 %, p < .001 and red -5.03 %, p = .004). The opposite pattern was

observed for percentage spent in N3 (F (2, 29.00) = 20,61, p < .001), where both day sleep was >15 % higher compared to night sleep (blue: +15,73 %, p < .001 and red: +16,94 %, p < .001).



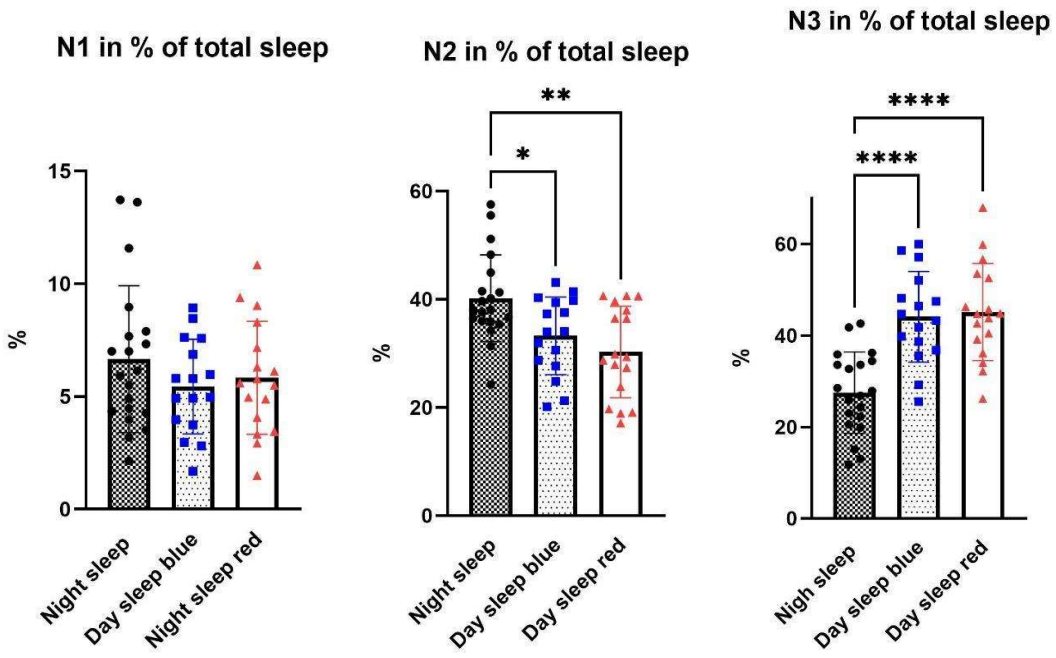


Figure 4. Sleep stages. Data from night sleep (n = 21) and day sleep after simulated night shift work in red (n = 17) and blue (n = 16) condition. The values are in minutes and percentages of total sleep, expressed as mean ± SEM. ***p<0.001, ** p<0.01, *p < 0.05, compared to night sleep. There were no significant differences between the two day sleep conditions.

Slow Wave Parameters in N3

Whether night shift in different light conditions changes the homeostatic sleep pressure was then examined. Here, EEG power density for the slow waves (1-4 Hz) in N3 was averaged in 60-min intervals, in all three cortical regions (frontal, central and occipital). Due to the shortened sleep length during day sleep, 6 intervals (a total of 360 sleep minutes) was included in this analysis.

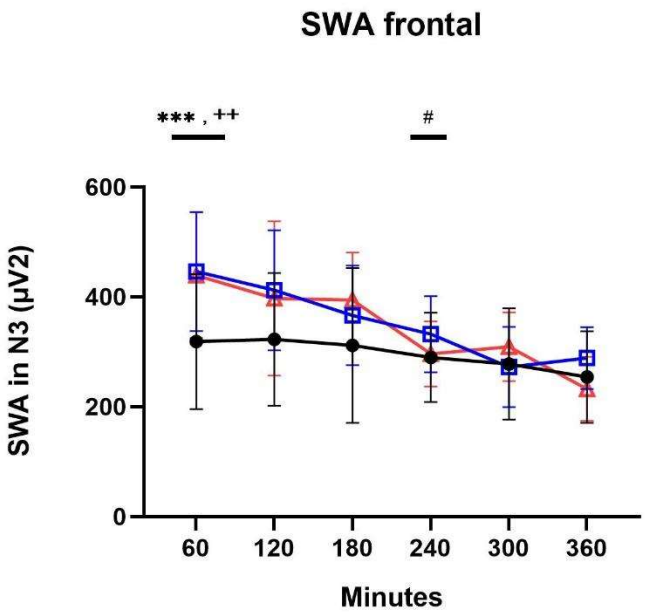
Slow Wave Activity (SWA)

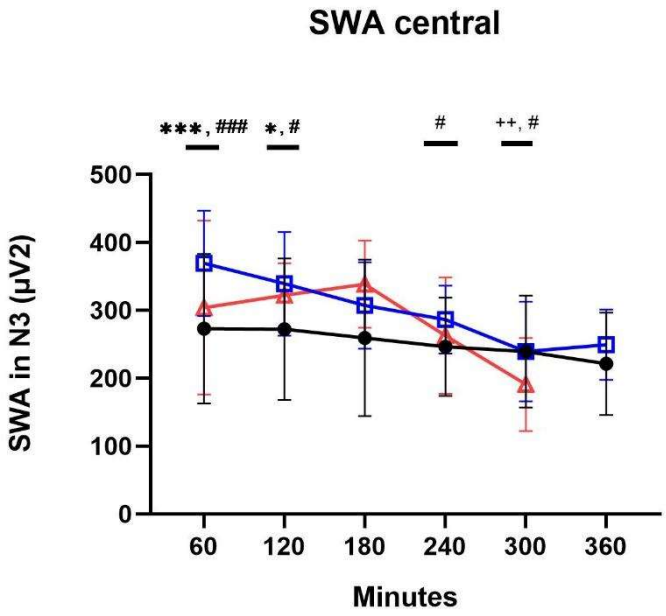
In line with a homeostatic sleep regulation, and consistent with studies on sleep loss (Chellappa et al., 2013; Munch et al., 2006), SWA in the frontal cortex yielded main effects for

'recording' (F (2, 195.47) = 4.64, p = .011) and 'time' (F (5, 182.29) = 22.61, p < .001). In all recordings, the sleep pressure (SWA) was highest the first 60 minutes and declined during time in sleep. SWA the first 60 minutes was higher both in day sleep blue (+77.63 μV^2, p > .001) and day sleep red (+68,24 μV^2, p = .002) compared to night sleep. In both day sleep groups SWA was higher than night sleep throughout the sleep period, but it did not reached accepted significance (p's> .054). After 4hrs of sleep (240 minutes), day sleep blue showed significant higher SWA than day sleep red (+60,40 μV^2, p = .011).

At the central derivation, SWA yielded effects for 'recording' (F (2, 184.93) = 9.02, p < .001, Time (F (5, 166.80) = 15.74, p < .001 and interaction of 'recording' * 'time' (F (9, 166.80) = 2.11, p = .031. Day sleep blue showed higher SWA, both compared to night sleep and day sleep red at the first 60 minutes (+75.33 μV^2, p < .001 and +75,47 μV^2, p < .001, respectively) and after 120 minutes in sleep (+44.80 μV^2, p = .017 and +48.22 μV^2), p =.025, respectively). As seen in the frontal cortex, day sleep blue showed higher SWA than day sleep red at the 240-minute interval (p = .039), a difference persisting also at the 300-minute interval (p = .046). Moreover, towards the end of the sleep period, day sleep red exhibited higher SWA than night sleep at 300-minute interval (p = .009).

Occipital SWA yielded main effect for 'time' (F (5, 167.95) = 7.45, p < .001), with the highest amount of SWA the first 60 minutes. There were no significant differences in SWA across recordings.


SWA frontal
***, ++
#
SWA in N3 (µV2)
600
400
200
0
60
120
180
240
300
360
Minutes


SWA central
***, ###
*, #
#
++, #
SWA in N3 (µV2)
500
400
300
200
100
0
60
120
180
240
300
360
Minutes

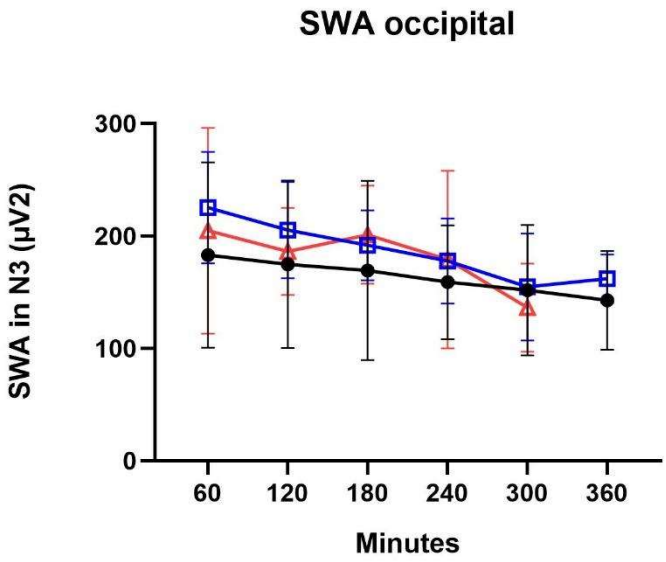


Figure 5. SWA in N3 across cortical regions. Data from night sleep (n = 21) and day sleep after simulated night shift work in red (n = 17) and blue (n = 16) condition. The values are in μV^2, expressed as mean. ***p<0.001, ** p<0.01, *p < 0.05, for blue light condition compared to night sleep, +++ p<0.001, ++ p<0.01, +p < 0.05, for red light condition compared to night sleep and ### p<0.001, ## p<0.01, #p < 0.05, for blue light condition compared to red light condition.

Slow Wave Energy (SWE)

Total SWA generated in stage N3 during the sleep period can be quantified with SWE.

Frontal SWE yielded main effects for 'recording' (F (2, 205.57) = 3.79, p = .024), 'time' (F (5, 185.77) = 18.81, p < .001 and interaction of recording * 'time' (F (10, 185.27) = 3.17, p = .001). Day sleep blue showed significantly higher SWE across the first 120 minutes of sleep compared to night sleep +46,90 %, p<0.001 and +29,35 %, p=0.20), whilst day sleep red exhibited higher SWE across the first 60 minutes of sleep (+53,15 %, p < .001). After 4 hours of day sleep (240 mins) SWE was similar to night sleep (blue: -14,30 %, red: -36,47 %).

At the central derivation, SWE yielded main effects for 'recording' (F (2, 201.20) = 3.93, p = .021, 'time' (F (5, 187.83) = 19.76, p > .001 and interaction of recording * time (F (10, 187.18) = 3.36, p > .001). Day sleep blue revealed significantly higher SWE during the

first 120 minutes of the sleep compared to night sleep (+47,37 %, p < .001 and +29,29 %, p = .018). Day sleep red showed higher SWE during the first 60 minutes compared to night sleep (+52,85, p < .001).

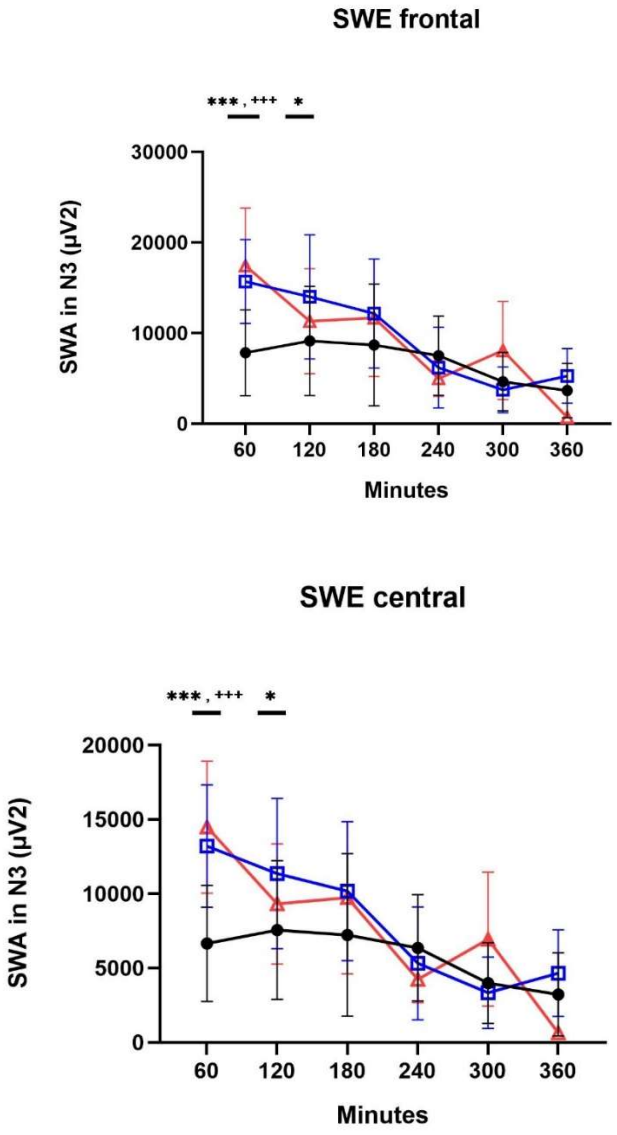


Figure 6. SWE in N3 across cortical regions. Data from night sleep (n = 21) and day sleep after simulated night shift work in red (n = 17) and blue (n = 16) condition. The values are in μV^2, expressed as mean. ***p<0.001, ** p<0.01, *p < 0.05, for blue light condition compared to night sleep, +++ p<0.001, ++ p<0.01, +p < 0.05, for red light condition compared to night sleep and ### p<0.001, ## p<0.01, #p < 0.05, for blue light condition compared to red light condition.

Discussion

Sleep was more than 2 hours shorter during daytime compared to nighttime. The lost sleep-time affected time spent in all stages of sleep, with one exception, N3 sleep. These results are much in accordance with both Torsvall and Åkestedt (Akerstedt, Kecklund, & Knutsson, 1991; Torsvall, Akerstedt, Gillander, & Knutsson, 1989).

When comparing sleep stages in percentage of total sleep the percentage of N3 were > 15 % larger for both daytime conditions than night sleep. Torsvall showed a SWS percentage for daytime sleep after night shift to be of 24 % whereas our participants had 44 % for blue- and 45 % for red-condition (Torsvall, L., et al, 1989). The relative high percentage (almost half the sleep episode) in N3 indicates a high homeostatic pressure for sleep. One possible explanation for the difference of our own and the study of Torsvall might be our prohibition of napping prior to and during night shift. The Torsvall paper reports of both napping before and during the night shift, with SWS being a great part of total naptime. Our participants did not get the opportunity for reducing sleep pressure until falling asleep after the night wok and would in consequence be in high demand for SWS. Taken together, our own and the research of Torsvall could serve as investigation of the difference in sleep pressure when night shift workers are allowed to nap versus not allowed to nap, emphasizing the importance of napping when working the night shift.

The homeostatic pressure for sleep was further investigated through SWA and SWE. Our hypothesis stated an expectation of suppressed SWA in start of the sleep period with a possible rebound effect later in the sleep episode. The results rejected this hypothesis, contradictory to earlier research (Cajochen, Dijk, & Borbely, 1992; Chellappa et al., 2013; Munch et al., 2006. One important difference between the current experiment and the earlier research used in forming our hypothesis might be accountable for the diverging results. In lack of research on the daytime sleep of night shift workers after working in manipulated light

environment, we needed to form our hypothesis based on research of light exposure in the evening, before participants entered normal night-sleep. The sleep deprivation of ~ 24 hours in our experiment may have provided a sleep pressure high enough to override the possibly SWA suppressing effects of light exposure before sleep. This is also supported when taking SWE into account. The SWE presents a declining curve in both day-sleep conditions throughout the sleep episode for all three cortical EEG derivations. The night-sleep condition, however, exhibits a slight increase of SWE from 60- to 120-minutes before declining throughout the sleep period. The difference of SWE between day-sleep and night-sleep are high for the first part of the sleep period and relatively small for the second part of sleep. These differences most likely reflect the homeostatic pressure for sleep, which are higher for sleep deprived day-time sleepers, but are reduced in the first part of sleep considering that N3 sleep predominantly manifests in this part and less for the second part of sleep.

No significant difference between SWE in the two day-sleep conditions were found but the curves clearly show two different patterns. The blue light-condition displays a more or less stable decline until the 300 – 360-minute interval, where it rises a little in all three cortical derivations.

The results also confirm the assumption stated by Skoruack, that the increase of SWA in response to sleep deprivation are dependent on the cortical region (Skorucak, Arbon, Dijk, & Achermann, 2018). Both the frontal SWA and central SWA derivations are significantly higher for day-time sleep compared to night-time sleep, but the SWA occipital derivation did not show significant differences.

As seen, the number of minutes in N3 sleep were about the same for day-time sleep compared to nigh-time sleep even tough sleep were reduced by more than 2 hours. When sleep is compromised, studies show that N3 sleep are consistently preserved, which may serve as a strong argument for the importance of the brain and body getting sufficient amounts of N3 sleep

(Tononi & Cirelli, 2014; Vyazovskiy & Harris, 2013; Xie et al., 2013). It is tempting to suggest that deep sleep has been prioritized at the expense of other sleep stages though there are also other possible explanations. One of which the reduced levels of stage N2 and REM sleep might be explained by the reduced length of total sleep. Time spent in REM sleep and stage N2 sleep are both known to be dependent on the length of sleep (Agnew & Webb, 1973) and therefore the sleep length itself could be the reason for the reduction of these two stages. In addition, the timing of REM sleep has also been shown to be delayed with light exposure (Cajochen, Krauchi, Danilenko, & Wirz-Justice, 1998).

There are limitations of our study that need to be considered. Most of our participants were females. For the health sector this are transferable with 78 % of night shift workers in Europe being female. But in general, the European night workers reports to consist of more males than females (Eurofond, 2017). Participants were mostly recruited trough the University and for this reason a selection of young and healthy individuals. Whether the same results would be present in an older population are not clear. Studies have shown indications to age differences in response to light exposure (Münch et al., 2011).

We have not controlled for the exposure of light when participants leave the experimental procedure. There are for instance studies indicating a positive effect when shielding nightshift workers for light on way home form night shift (Santhi, Duffy, Horowitz, & Czeisler, 2005). On the other hand, the experimental procedure closely resembles the real night shift situation with all the potential influencing effects of light before and after work.

The light exposure used in our procedure are of narrow-bandwidth blue (455 nm) and red (625 nm) which is suitable for experimental use only. These conditions are not useful to implement directly in normal night shift situations and goes at the expense of the ecological validity of our results. We have chosen such extreme light conditions in order to evoke light

effects in the following sleep. We will in consequence encourage the reader to take this into considerations when interpreting the results of our study.

In conclusion, our results have shown that day-time sleep after simulated night shift work compared to night sleep has reduced TST, N1, N2 and REM sleep, whereas N3 sleep is preserved. SWA and SWE were higher for day-time sleep in comparison to night sleep and declined during sleep for both day-sleep and night-sleep.

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