

# *Acute effects of blue light on alertness*

*Results from a pilot study*

**Kine Marie A. Hillestad**



**MAPSYK330 / MAPSYK360, masterprogram i psykologi,**

**Studieretning: Atferd og Nevrovitenskap**

**ved**

**UNIVERSITETET I BERGEN**

**DET PSYKOLOGISKE FAKULTET**

**HØST 2022**

Antall ord: 14560

Veileder: Elisabeth Flo-Groeneboom Institutt for Klinisk psykologi

Biveileder: Louise Haugen Bjerrum Institutt for Klinisk psykologi og Lin Sørensen Institutt  
for biologisk og medisinsk psykologi

### **Abstract**

The discovery of a third-class retinal photoreceptors (ipRGCs) sensitive to the short wavelength light (from 460nm to 480nm) have influenced research on circadian rhythms over the last two decades, with increasing research focusing on the physiological and psychological effects of blue light and different colour temperatures during both daytime and nighttime. Meanwhile, research on daytime light exposure has given varying results. Piloting an experimental protocol, the acute effects of both monochromatic blue light ( $\lambda_{\max}$  479 nm) and dim light (<5 lux) were assessed in 12 healthy young subjects, during the morning hours. Chronotype and sleep prior to the test days were also assessed. Participants were exposed to 1 hour dim light (<5 lux) prior to testing for both light conditions. Alertness was measured using a psychomotor vigilance test (PVT) at three different times during the procedure. There was no significant effect of either blue or dim light on alertness, however there was a combined effect of alertness and dim light when total sleep time the night before dim light was accounted for, showing slower response time in the dim light condition.

**Keywords:** Circadian rhythm, light exposure, chronotype, attention

### Sammendrag

Oppdagelsen av en tredje type gangliecelle i retina, intrinsikt fotosensitive retinale ganglieceller (ipRGCs) som er sensitive til lys med kort bølgelengde (fra 460 til 480nm) har påvirket forskningen på cirkadiane rytmer de siste tiårene. Oppdagelsen har ført til mer forskning på fysiologiske og psykologiske effekter av blått lys og lys med ulike fargetemperaturer på dagtid og nattestid. Imidlertid har forskning på effekten av lys eksponering på dagtid gitt varierende resultater. I en pilot studie av en eksperimentell protokoll ble akutte effekter av både monokromatisk blått lys ( $\lambda_{\max}$  479 nm) og svakt lys (<5 lux) vurdert hos 12 friske unge forsøkspersoner. Aktigrafiske måling ble benyttet for å måle total søvn tid og søvn mønster samtidig som kronotype ble fastslått ved spørreskjema. Forsøkspersonene ble eksponert for 1 time svakt lys (<5 lux) før testing i begge lysforholdene. Oppmerksomhet/årvåkenhet ble målt ved hjelp av psykomotorisk årvåkenhets test (PVT) på tre forskjellige tidspunkt under prosedyren. Det var ingen signifikant effekt av verken blått eller svakt lys på årvåkenhet, men det var en kombinert effekt av årvåkenhet og svakt lys når total søvntid natten før ble tatt med.

**Keywords:** Circadian rhythm, light exposure, chronotype, attention

### **Acknowledgments**

I have taken an active part in collecting the data for this master thesis and ENLIGHT project since December 2021 an up to April 2022. I have administered the laboratory alone and together with my co-supervisor Louise Haugen Bjerrum and Oda Bugge Kambestad, getting the laboratory ready for testing, test running all the neurocognitive and emotional processing tests, collected data files, collected saliva samples, plotted data, and analyzed and scored the actigraphy data.

I would like to thank my main supervisor Elisabeth Flo-Groeneboom for her patient guidance, encouragement, advice, and great teamwork. I am very thankful for being trusted to take such a big part in administering the light laboratory, collecting data, analyzing actigraphy data and plotting data.

I would also like to thank my two co-supervisors Louise Haugen Bjerrum and Lin Sørensen. Special thank you to Louise for patiently teaching me the adequate skills needed for administering actigraphy watches and other relevant equipment, as well as guiding me in the right direction when working on my thesis. Thank you to Lin for helping me with data analyses.

Lastly, I would like to thank the entire ENLIGHT team for allowing me to be part of your research group.

## Table of Contents

Abstract .....	3
Sammendrag.....	4
Acknowledgments.....	5
Background .....	8
Circadian Clocks and Rhythms .....	9
The endogenous circadian rhythms.....	9
Measuring and describing the human circadian rhythm .....	13
Rest activity rhythms .....	14
Melatonin .....	14
Cortisol.....	16
Core body temperature.....	16
Sleep-wake regulation.....	17
The two-process model of sleep regulation .....	18
Sleep stages and assessment .....	20
Light and the human eye.....	21
Two visual systems .....	21
Retinohypothalamic tract .....	23
Artificial light.....	24
Acute non-image forming effects of light.....	25
Chronotype.....	28
Heritability, sex, and age.....	30
Alertness and Attention (Cognitive rhythms) .....	32
Circadian variations in alertness/ circadian rhythm of attention.....	33
Sleep deprivation, alertness, and attention.....	34

Aims and Hypotheses.....	36
Method .....	37
Ethical Consideration .....	37
Participants.....	37
Design .....	38
Procedure.....	39
Laboratory and Light conditions.....	40
Screening Tests, baseline- and outcome measures .....	41
Screening and baseline measurement .....	41
Study outcome measures.....	43
Randomization .....	47
Statistical Analyses .....	48
Results.....	49
Discussion .....	55
Conclusion.....	61
Reference list.....	62
Appendix.....	90

## **Background**

Research has shown that exposure to bright white light or blue-enriched light can elicit an acute alerting effect (Cajochen, 2007; Gooley et al., 2011; Rüger, Gordijn, Beersma, de Vries, & Daan, 2006). This effect has been demonstrated in laboratory-based studies documenting acute physiological (e.g., elevated core body temperature and increased EEG brain activity) and cognitive (improved performance on certain tests) changes (Badia, Myers, Boecker, Culpepper, & Harsh, 1991; Lowden, Åkerstedt, & Roger, 2004; Okamoto, Rea, Figueiro, 2014; Sahin & Figueiro, 2013; Viola, James, Schlangen, & Dijk, 2008). Although certain light conditions may enhance alertness, the effects are not consistently observed in high demanding tasks such as vigilance to response or alertness tasks. However, factors such as time of day and how well rested the participants were, may have contributed to the varying results. Some studies have employed strict protocols to control important variables such as sleep length and chronotype (Correa, Enrique, & Sanabria, 2014; Rahman, Flynn-Evans, Aeschback, Brainard, Czeisler, & Lockley, 2014), while other protocols have not followed up such potentially confounding variables (Smolders, de Kort, & Cluitmans, 2012). The aim of this Master's thesis was to investigate the effect of different light modalities on alertness while taking differences in chronotype and sleep history into consideration.

In the following background section, I will first provide a brief introduction on circadian rhythm and sleep and describe the two-process model of sleep regulation. Although not defined as acute, the effects of light on circadian rhythms and sleep regulation are still important to take into consideration when investigating the acute effects of light. Furthermore, I will describe the human light perception, as well as important circadian rhythm outcomes such as melatonin, cortisol, core body temperature and rest-activity-rhythms (RAR). I will subsequently describe



the variations in human chronotypes along with alertness and attention, and the role sleep deprivation and light plays on these outcomes.

### **Circadian Clocks and Rhythms**

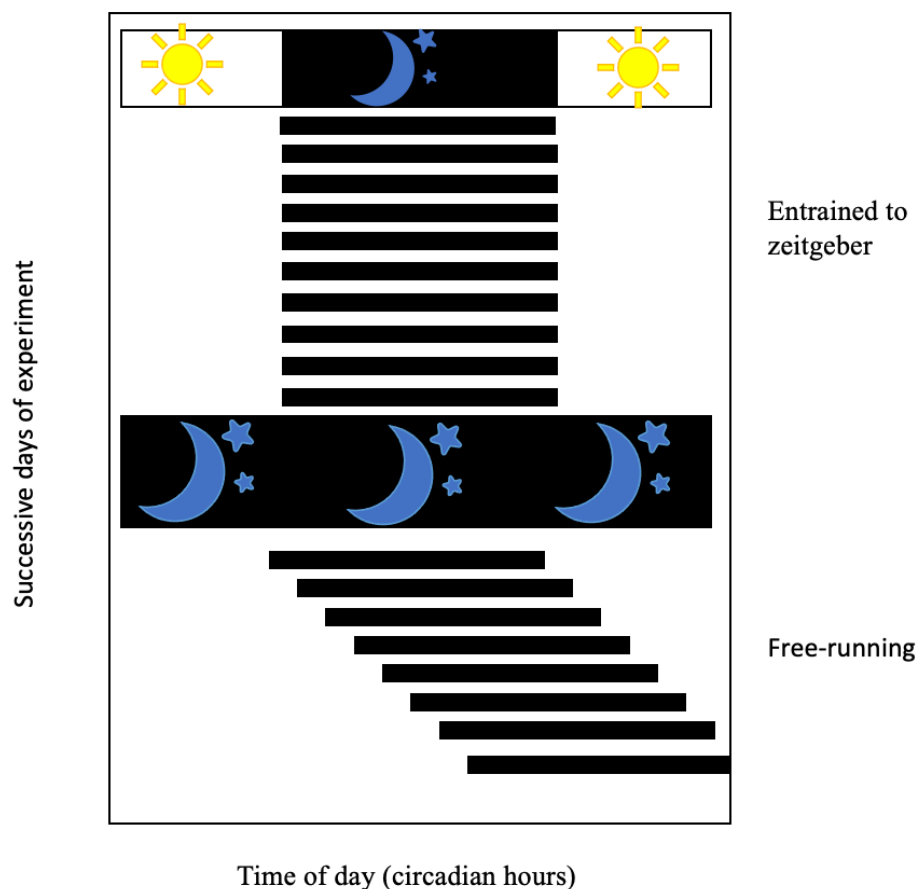
Entrained physiological rhythms in humans are a prerequisite for maintaining health (Lall, Atkinson, Corlett, Broadbridge, & Bonsall, 2012; Wehr, Wirz-Justice, Goodwin, Duncan, & Gillin, 1979). Physiological rhythms may be categorized depending on the length of the rhythm, such as ultradian (cycle of less than 24 hours), circadian (Circa= around, dies= day, i.e., approximately 24 hours), diurnal (night and day), infradian (more than 24 hours) and seasonal (e.g., variations between winter and summer) (Charrier, Olliac, Poubertoux, & Tordjman, 2017; Czeisler, Weitzman, Moore-Ede, Zimmerman, Knauer, 1980; Harding, Pompei, Bordonaro, McGillicuddy, Burmistrov, Sanchez, 2019; Ungar & Halberg, 1962). Longer rhythms, such as the female menstrual cycle of 28 days, are an example on infradian rhythm (Baker & Driver, 2006). Various bodily systems show oscillations in activity through the 24h day. This includes sleep and wakefulness, body temperature, hormonal secretion, systolic blood pressure, and other physiological parameters as well as psychological factors (Brzezinski, 1997; Czeisler & Buxton, 2017; Kleitman, 1933; Valdez, 2019; Waterhouse, Fukuda, & Morita, 2012).

#### **The endogenous circadian rhythms**

The circadian rhythms are set by both genetic and environmental factors (Charrier et al., 2017). Research shows that the endogenous circadian rhythms are close to, but not exactly 24-hours when an organism remains in a constant state, free of all time cues and with constant light and temperature conditions (Czeisler et al., 1999). Also, similar findings indicate that endogenous factors underpin the internal biological clock, which is responsible for an internal

time synchronization, and coordinating the circadian variations of biochemical, physiological, and behavioral parameters (Lowrey & Takahashi, 2011). Research on identical twins indicate that the biological clock has a genetic factor (Linkowsky et al., 1993).

The suprachiasmatic nucleus (SCN) of the hypothalamus, sometimes referred to as the “master clock” and “circadian pacemaker” is a key structure involved in controlling circadian rhythmicity (Moore, Speh & Leak, 2002). Circadian regulation of all biological functions is processed through direct or indirect signals between the SCN and different body organs and tissue throughout the day (Hasting, Reddy, & Maywood, 2003). Peripheral clock genes have been identified in every cell throughout the body, allowing each organ to maintain its own circadian rhythmicity and optimize its function according to environmental context (Charrier, Olliac, Roubertoux, & Tordjman, 2017). However, these clocks must be re-synchronized or entrained continuously through the SCN, which acts as a conductor (Charrier et al., 2017, Kalmbach et al., 2017; Vandewalle, Maquet, & Djik, 2009). The endogenous rhythm ( $\tau$ ) needs to adapt to the entraining stimuli (T, zeitgebers), e.g., the light-dark cycle (Duffy & Wright, 2005) to maintain an appropriate relationship between the body, the timing of sleep and wakefulness, and the societal time, as seen in Figure 1. This will ensure correct anticipation of and adaption to periodic changes. Without any external zeitgebers, the circadian rhythm would be a free-running rhythm, relying only on the endogenous rhythms of the internal clock. Research on free-running participants indicated the internal human daily phase to be about 24,2 hours (Czeisler et al., 1999). In line with this, research on blind participants that lack a functional retinohypothalamic tract show that their circadian rhythms drift and gradually delays day by day (Sack, Brandes, Kendall, & Lewy, 2000; Sack, Lewy, Blood, Keith, & Nakagawa, 1992).



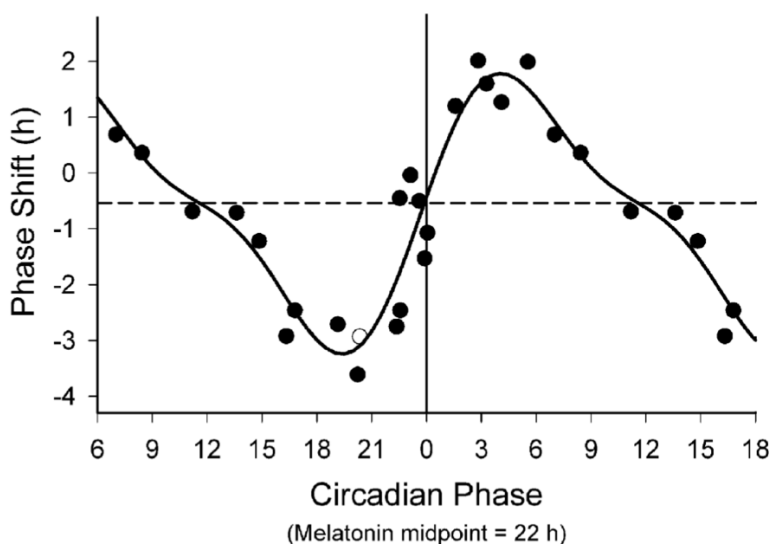
**Figure. 1 Entrainment of a circadian rhythm to light.** Upper part shows how circadian rhythms adjust their endogenous period ( $\tau$ ) to that of zeitgeber (T). Lower part shows circadian rhythm resume its endogenous period when in constant darkness (represented by the black bar in the center of actogram). Inspired by Golomberg, D., & Rosenstein, R, 2010.

### *The effects of light on the circadian entrainment*

Earth's rotation makes an exogenous contribution to the biological (circadian) rhythm in humans, making a daily light-dark cycle. Together with more modern environmental alterations such as work schedules, social demands, artificial light, and mealtimes, the period and phase of these rhythms undergo changes, synchronizing the endogenous timing system (Roenneberg et al., 2007; Valdez, 2019; Charrier et al., 2017).

Early research on entrainment estimated social interaction to be the primary environmental time cue (zeitgeber) (Mistlberger & Skene, 2004). However, research has shown

that light is the primary influential factor when adjusting  $\tau$  (endogenous rhythm) to the period of  $T$  (entraining stimuli) (Czeisler et al, 1989, Czeisler, Zeitzer, Brown, Djik, & Kronauer, 2000; Wright, Lack, & Kennaway, 2004). The effects of light on circadian entrainment shows a phase-response curve (PRC) (Czeisler et al., 1989; Khalsa, Jewett, Cajochen, & Czeisler, 2003), as shown in Figure.2. Light exposure close to the lowest point of the core body temperature (nadir) has the greatest phase shifting effects, affecting both magnitude and direction of the circadian rhythm (Khalsa et al., 2003; Lockley, Evans, Scheer, Brainard, Czeisler, & Aeschback, 2006). In addition to timing of the applied stimulus, higher intensity light (over 1000 lux) and blue light (~450nm) have a significantly stronger phase shifting effect than lower brightness and other wavelengths of the visible spectrum (Brainard et al., 2001; Cajochen et al., 2005; Rahman, et al., 2014). In a study by Khalsa et al., 2003, participants were exposed to 5000 lux and up to 10 000 lux for 6.7 hours at different points in their circadian cycle. As shown in Figure. 2, they found phase delay when light exposure was centered prior to the nadir of the core body temperature, and phase advance when light was centered after nadir.



**Figure 2. The PRC to the bright light stimulus.** The positive values show phase advances, and the negative show phase delays. Both are plotted against the timing of light exposure, either after or before nadir of the core body temperature. Adapted from Khalsa, S., Jewett, M., Cajochen, C., & Czeisler, C, 2003.

### **Measuring and describing the human circadian rhythm**

Since the endogenous rhythms are influenced by several external factors, the output rhythms needed for addressing internal biological time need to be studied under controlled experimental conditions (Duffy & Wright, 2005). The constant routine protocol was therefore developed to eliminate all periodical changes in behavior, in addition to maintaining a constant environment. The procedure usually requires constant ambient lighting levels and constant room temperature. It also aspires to eliminate sleep and associated behaviors such as eye closure and postural changes, to control food and fluid intake throughout the experimental procedure, and to maintain low levels of activity. These observations usually continue throughout an entire circadian cycle (Duffy & Wright, 2005).

Forced desynchrony protocol has also been widely used (Wever, 1980; Wright, Hull, & Czeisler, 2002; Wyatt, Cecco, Czeisler, & Dijk, 1999) in circadian research on humans and animals. The intent is to separate endogenous and activity related effects on daily rhythms (Strijkstra, Meerlo, & Beersma, 1999). In a forced desynchrony protocol, participants are placed on strict light-dark and rest-activity schedules that are either longer or shorter than the usual near 24 hours, making the endogenous circadian clock unable to entrain, allowing it to free run. This protocol was used by Czeisler et al., 1999, where they found that for people living under forced desynchrony protocols, their circadian phase was around 24.2 hours. They measured the interval between consecutive awakenings, and thereby showing that the endogenous rhythm, represented by the Greek letter tau ( $\tau$ ) were longer than the 24-hour light-dark cycle (Duffy & Wright, 2005).

Some of the outputs influenced by the SCN are used to assess circadian rhythms in research and clinical practice. Most notably, this includes the rest activity rhythm, melatonin, cortisol, and core body temperature.

### **Rest activity rhythms**

The rest-activity rhythm (RAR) reflects a complex interaction of both the endogenous circadian rhythms and the exogenous circadian entrainment cues (Waterhouse, Fukuda, & Morita, 2012). The pattern usually shows reduced activity and inactivity at night prior to and during sleep, and increased activity during the day in relation to wakefulness.

RAR is usually measured using wearable accelerometers, most often actigraphs, over multiple days (Ancoli-Israel, Cole, Alessi, Chambers, Moorcroft, & Pollak, 2003). The change in high and low activity are expressed through several outcomes such as total sleep time, wake after sleep onset, sleep onset latency (time it takes to fall asleep), and sleep efficiency (time in bed), in sleep research. In circadian research, RAR outcomes usually focus on rhythmic patterns and cover activity over multiple days as well as variability within each 24-h cycle, together with observation of peak and minimum activity and the difference between these activity periods (Ancoli-Israel et al., 2003; Smagula, Gujral, Capps, & Krafty, 2019). These RAR outcomes correlate with other rhythms related to the circadian rhythm, such as melatonin and core body temperature (Ancoli-Israel et al., 2003). Desynchronized RAR have been associated with fatigue and impairment in physical and cognitive performance (Oosterman, Van Someren, Vogels, Van Harten & Scerder, 2009; Tranah et al., 2011), while a strong RAR, i.e., clear distinction in activity patterns between active and inactive periods, have been associated with better health outcomes (Waterhouse et al., 2012).

### **Melatonin**

Melatonin is an indoleamine, also known as N-acetyl-5-methoxytryptamine and the “hormone of darkness”. It has been found in a variety of organisms such as bacteria, plants, and mammals (Zlotos, Jockers, Cecon, Rivara, & Witt-Enderby, 2014). It is synthesized and released primarily by the pineal gland, but also in some peripheral tissues, such as the retina

and the gut (Chen, Fichna, Bashashati, Li, & Storr, 2011; Weaver, Stehle, Stopa, & Reppert, 1993). The light stimuli are registered by retinal photoreceptors and conveyed to the SCN. In turn, the SCN regulates the rhythmic synthesis and secretion of melatonin from the pineal gland, through both direct and indirect projections (Morin, 1994; Moore, Speh, & Card, 1995). The melatonin is secreted into the blood stream and cerebrospinal fluid (the fluid around the brain & spinal cord), reaching distant organs (Sharman & Bondy, 2016). Melatonin production shows a clear circadian rhythm, with peak levels occurring at night, normally higher than 40 pg/ml and lower than 10 pg/ml during daytime (Wurtman, Axelrod, & Phillips, 1963; Lewy, Cutler, & Sack, 1999). However, light can acutely suppress melatonin synthesis when an individual is exposed to light during natural darkness (Lewy, Wehr, Goodwin, Newsome & Markey, 1980).

Gooley and colleagues (2011) performed a study where they compared one group that was exposed to indoor light (<200 lux) for 8 hours in the late evening with another group that was exposed to dim light (<3 lux) for 8 hours in the late evening. They found that compared to dim light, the indoor lighting suppressed melatonin onset in 99.0% of the participants and shortened the sleep duration by 90 minutes. Furthermore, exposure to indoor light during the usual hours of sleep suppressed melatonin levels by greater than 50% in most trials (Gooley et al., 2011).

Melatonin levels are usually measured by collecting blood or saliva samples repeatedly throughout 24 hours (Cajochen, Zeitzer, Czeisler, & Dijk, 2000; Cajochen et al., 2005). However, since the melatonin levels are directly affected by light, blood or saliva samples must be collected during dim light to ensure a reliable reflection of the endogenous rhythm of the SCN (Prayag, Najjar, & Gronfiner, 2019). This ensures a precise representation of the production and metabolism of melatonin levels, which again makes the timing of which melatonin starts to rise, dim light melatonin onset (DLMO), one of the most accurate markers for assessing circadian rhythm (Lewy & Sack, 1989). DLMO is a marker also widely used in

research on entrainment, and chronobiological disorders (Lewy & Sack, 1989; Pandi-Perumal et al., 2006). Using this method, research has shown that DLMO usually occurs 2-3 hours before habitual bedtime in healthy young adults with normally distributed sleep timing (Burgess & Eastman, 2008). Furthermore, the level of melatonin released at night differ between age and sex (Follenius et al., 1995).

### **Cortisol**

As opposed to melatonin, the diurnal cortisol level reaches its peak around wake-up time and its nadir around bedtime (Adam & Kumari, 2009). Cortisol is a steroid glucocorticoid hormone, product of the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis is a key component in stress adaptation and represents an important pathway where both social and physiological events impact biology and health (Adam, Quinn, Tavernier, McQuillan, Dahlke, & Gilbert, 2017). Daytime levels of cortisol are dependent on individual experiences, where short term activation has an adaptive function, and is crucial for everyday functioning. However, long-term activation of the system has shown negative mental and physical health outcomes (Herbert et al., 2006; Seeman, McEwen, Singer, Albert, & Rowe, 1997).

Since the level of cortisol follows a circadian rhythm, the levels vary from time of day. Therefore, to accurately measure the cortisol levels, saliva samples are usually collected four times throughout the day (Turpeinen & Härmäläinen, 2013).

### **Core body temperature**

The core body temperature follows a circadian rhythm with a peak in temperature around 21:00 and a low point, nadir, around 05:00 (Bjorvatn & Pallesen, 2008; Gilbert, van den Heuvel, Ferguson, & Dawson, 2004). Together with homeostatic and circadian processes, thermoregulatory processes also promote sleepiness and sleep propensity throughout the night



(Gilbert et al., 2004; Kräuchi, 2007). In addition, conscious factors such as physical activity, food intake and resting will influence the core body temperature and create fluctuations. However, most subtle day-to-day variations in thermoregulation are unconscious and controlled by the autonomic nervous system (van den Heuvel, Ferguson, Gilbert, & Dawson, 2004).

Monitoring the internal body temperature can be done in several ways, including esophageal temperature, oral temperature, and rectal temperature. Esophageal temperature, however, is a very invasive method not commonly used in research. Oral temperature is a non-invasive method, but the measurements are not always accurate. Rectal temperature on the other hand is the most accurate measure of CBT, and extensively used in research. However, it is an invasive method with prolonged response time (Moran & Mendal, 2002).

Taken together, when on a normal sleep-wake schedule, melatonin levels are highest, and CBT are lowest during nighttime (Gilbert et al., 2004; Weaver et al., 1993). Cortisol is low at habitual sleep onset and high at habitual wake time (Adam & Kumari, 2009). Together, these endogenous circadian rhythms are daily entrained to the 24-hour day by a combination of drives, such as timing of sleep-wake state, endogenous circadian pacemaker, posture, exercise, and environmental lighting (Haus, 2007).

### **Sleep-wake regulation**

The transition between wakefulness and sleep consists of a complex network of brain circuitry that elicit changes in motor control, cognition, consciousness, and brain activity (Mcginley et al., 2015). The wake-promoting system originating in the brainstem project to various structures, such as thalamus, basal forebrain, and other forebrain structures, through a dorsal and ventral pathway, which further excite the cortex and promotes wakefulness (Eban-Rothschild, Appelbaum, & Lecea, 2018). During sleep the ventrolateral and median preoptic

nuclei in the hypothalamus inhibit the arousal system through projections from the SCN (Gooley & Saper, 2017).

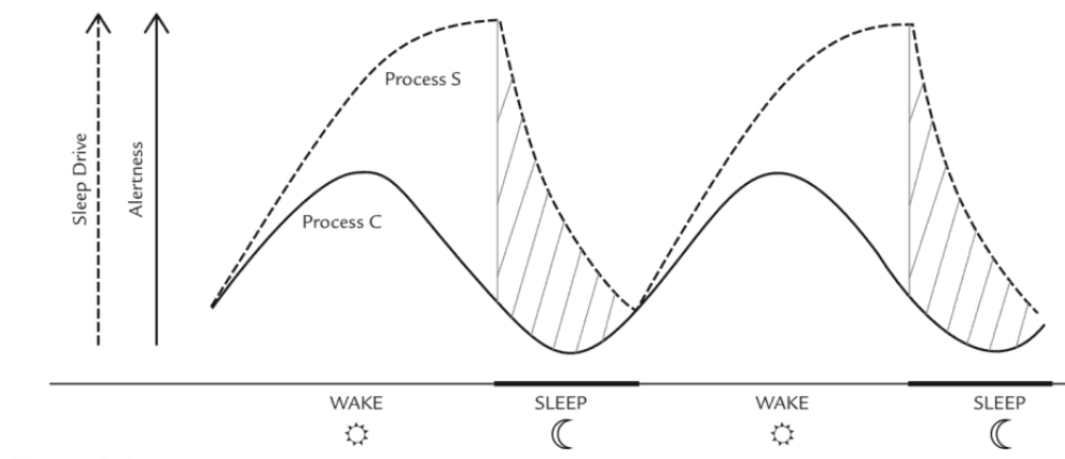
### **The two-process model of sleep regulation**

The two-process model of sleep proposed by Borbely, 1982, is central in the understanding of sleep-wake regulation. Although the model was originally developed as a model of sleep regulation, it has over the years expanded to include prediction of human waking alertness and performance (Borbely, Daan Wirz-Justice & Deboer, 2016). According to the model, there are two key interacting processes: the circadian (C) and the homeostatic (S) process (Borbely, 1982). Research indicates that the relationship between process C and S is not linear throughout the day, and that this relationship may affect a range of neurobehavioral events (Van Dongen & Dinges, 2003).

The homeostatic process S is a sleep-dependent process, in which sleep depth or the propensity of sleep increases at the onset of wakefulness and decreases during time spent sleeping. The S process has been linked to sleep quality, particularly deep sleep. Electroencephalography (EEG) has been used to record the brain's spontaneous electrical activity generated by the sleeping brain. EEG slow-wave activity (SWA) during non-REM (NREM) has been found to increase when participants are put through total sleep deprivation (SD) and partial SD (Dijk, Beersma, & Daan, 1987; Werth, Dijk, Achermann, & Borbely, 1996). Additionally, process S has been linked to a decrease in cognitive performance during time awake and increase in sleepiness (Schmidt, Collette, Cajochen, & Peigneux, 2007).

Process C is driven by the endogenous circadian rhythms and exogenous zeitgebers, and therefore follows a near 24-h rhythm, allowing the human body to sleep at nighttime. It works in opposition to process S, having lowest sleep propensity during the early evening, when process S sleep pressure is at its highest, and having its highest during the morning hours when

process S sleep pressure is lowest (Van Dongen & Dinges, 2003). This helps ensure that we do not wake up in the early morning hours or fall asleep in the early evening hours. This way the two systems work in opposition to each other throughout the day to consolidate periods of sleep and wakefulness (Schmidt et al., 2007).



**Figure 3. The two-process model of sleep regulation,** Process S shown by dotted lines and process C shown by solid lines. Adapted from Cheng, P., & Drake, C, 2016).

Despite their association, there is not a linear relationship between process S and process C. Interindividual differences can be observed in temporal disposition, especially in today's 24-hour society (Fuhr, Abreu, Pett, & Relógio, 2015; Bjorvatn & Pallesen, 2008). Work pressure, artificial light, food intake and social pressure all affect the relationship between these two processes and the circadian rhythm, which may result in daytime sleepiness and attentional deficits (Schmidt et al., 2007; Cajochen, 2007). The two-process model of sleep has been used extensively in research, and several amendments or additions to the original model have been suggested. In general, the two processes appear more interlinked and interdependent than originally suggested (Borbély et al., 2016).

### **Sleep stages and assessment**

Polysomnography (PSG) is a widely used multi-parameter measure of sleep and a diagnostic tool. It includes recording of electroencephalography (EEG), electromyogram (muscle response) and electrooculogram (eye movement) signals, as well as oxygen levels in your blood, heart rate and respiratory parameters (Iber, Ancoli-Israel, Chesson, & Quan, 2007). EEG allows researchers and clinicians to register the electrical signals produced by a multitude of communicating neurons, which gives a high temporal resolution (Burle, Spieser, Roger, Casini, Hasbrouchq, & Vidal, 2015). Humans go through phases of sleep, that are classified and defined by the PSG output. The two main sleep stages are rapid eye movement (REM) and non-rapid eye movement (NREM). NREM is further divided into three stages: N1; N2; and N3, according to the American Academy of Sleep Medicine (Iber et al., 2007). Each phase and stage of sleep is recognized by different EEG output, variations in muscle tone, and eye movement. N1 and N2 is referred to as light sleep, while N3 is referred to as deep sleep. N3 is characterized by high amplitude, low EEG frequency; also called slow wave sleep. REM sleep is characterized by lower amplitudes than N3, and higher EEG frequencies closer to waking state, in addition to rapid eye movement and muscle atonia. Throughout the night, NREM and REM sleep alternates in approximately 90-minutes cycles, and repeat throughout the night, usually 4-6 times (Brown, Basheer, McKenna, Strecker, & McCarley, 2012).

Even though PSG provides the most direct assessment of sleep, it is a comprehensive, time consuming and costly test that may cause discomfort and disturbed sleep. Hence, it is also common to use actigraphy and sleep diaries which are less invasive methods, often used together to monitor and quantify sleep wake patterns (Short, Gradisar, Lack, Wright, & Carskadon, 1012; Wolfson & Carskadon, 2003). Actigraphy is an objective method that still allow for some of the same measures as PSG; sleep onset latency (SOL, onset of sleep from when lights were turned off), sleep efficiency (SE, minutes of sleep divided by minutes in bed)

and wake after sleep onset (WASO, time awake after sleep onset to lights are on) by measuring limb movement. Actigraphy is a well-suited tool for research on circadian rhythms, as it can monitor sleep wake patterns for longer periods of time, and it allows the person to continue normal routines while monitored (Ancoli-Israel, Cole, Alessi, Chambers, Moorcroft, & Pollak, 2003).

### **Light and the human eye**

Light is essential for generating images of our environment and is detected by retinal photoreceptors, such as rods and cones that convey light information through the optic nerve. Light also elicits non-visual responses (non-image forming, NIF) through a third class of retinal photoreceptors called intrinsically photosensitive retinal ganglion cells (ipRGCs) (Provencio, Rodriguez, Jiang, Hayes, Moreira, & Rollag, 2000). Through these ipRGC cells, light can influence the circadian rhythm, arousal, attention, mood and cognitive processes (Cajochen, 2007; Hattar et al., 2006; Provencio et al., 2000; Prayag, Münch, Aeschbach, Chellappa, & Gronfier, 2019).

### **Two visual systems**

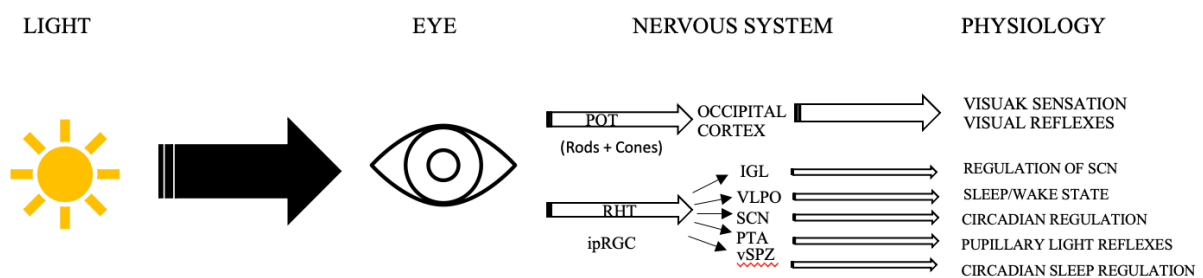
A duplex combination of rods and cones were long believed to be the only photoreceptive cells in the human retina. However, this was questioned when a study found that mice that were genetically modified to entirely lack rods and cones, showed signs of circadian entrainment and other NIF functions (Freedman et al., 1999). Together with research on visually blind humans (Czeisler et al., 1995), and macaque monkeys, with a very similar visual system to humans (Dacey et al., 2005), it was suggested that a third class of retinal photoreceptors was present. Consequently, ipRGCs was discovered approximately 20 years ago (Gamlin, McDougal, Pokorny, Smith, Yau, & Dacey, 2007; Hattar, Liao, Takao, Berson, & Yau, 2002;

Provencio et al., 2000). The photopigment melanopsin expressed by ipRGC, represent only 0.2% to 0.8% of all retinal ganglion cells (RGC) in humans, whereas the number seems to vary between 1-3% in rodents (Dacey et al., 2005; Hannibal, Hindersson, Ostergaard, Heegaard, Larsen, & Fahrenkrug, 2004). The ipRGCs respond to light independent of rods and cones. However, they also receive light information secondarily from rods and cones (Berson, Dunn, & Takao, 2002).

The two different systems detecting light in humans are shown in Figure 3. The first system is the classical visual system which uses mainly rods and cones and transforms light energy into electrical signals for both image forming and non-image forming visual functions (Schmidt, Chen, & Hattar, 2011). Rods are highly sensitive to light and show a  $\lambda_{max}$  sensitivity around 500 nm. They also play a crucial part in night vision. Cones are responsible for photopic vision (higher light intensity) and have high spatial acuity and color discrimination. There are three types of cones in the classical photopic system with different wavelength sensitivities. S-cones show a  $\lambda_{max}$  sensitivity around 420 nm, M-cones show a  $\lambda_{max}$  sensitivity around 535 nm and L-cones show a  $\lambda_{max}$  sensitivity around 565 nm (Bearson et al., 2002; Wald, 1945). The brain pathways of the classical visual system use the optic tract to project to subcortical nucleus, including the thalamic lateral geniculate nucleus (LGN), which receives information directly from ganglion cells. It also projects to the superior colliculus (SC) (Usrey & Alitto, 2015), and the lateral posterior pulvinar complex (Pul-LP), and thereafter reaching the primary visual occipital area (V1) as well as other neocortical regions engaged in dorsal and ventral visual attentional brain pathways (Kaas & Baldwin, 2019).

The second system is the non-image forming (NIF) system, consisting of rods and cones in addition to ipRGCs, which uses a light sensitive opsin called melanopsin, and are especially sensitive to light at the blue part of the spectrum (460-480nm) (Dacey et al., 2005; Gamlin et

al., 2007). This system relies on the luminance level of the surroundings to allow photoentrainment of the endogenous biological clock, and other biological systems like pineal melatonin secretion and pupillary light reflexes (Schmidt & Kofuji, 2008).



*Note. POT= Primary optic tract, RHT= retinohypothalamic tract, ipRGC= intrinsically photosensitive retinal ganglion cells, IGL= intergeniculate leaflets, VLPO= ventrolateral preoptic nuclei, SCN= suprachiasmatic nuclei, PTA= pretectal areas, vSPZ= ventral subparaventricular zones.*

**Figure 4. Light and non-visual responses.** Simplified explanation of the neuroanatomy that is responsible for visual and non-visual effects of light. Inspired by Hanifin, 2015.

### Retinohypothalamic tract

Research from rats first showed that projections from the retinal cells form the monosynaptic pathway, retinohypothalamic tract (RHT) (Moore & Lenn, 1972; Moore, Speh, & Card 1995), these findings have also been found in humans postmortem (Friedman, Johnson, Chorsky, & Stopa, 1991). The mammalian RHT is the primary neural projection involved in entraining the circadian rhythm to the environment (light-dark cycle), by transporting photic information from the retina to the hypothalamus, including direct projections to the SCN (Moore et al., 1995). The neural projections from the RHT are also involved in the suppression of melatonin production in response to light exposure (Klein & Moore, 1979).

Research on mice has shown that the ipRGCs have projections via the RHT throughout the brain, including ventrolateral preoptic nuclei (VLPO), which together with other brain

regions, like the lateral hypothalamus (LH) and the ascending arousal system, mediates sleep regulation and arousal (Lu, Bjorkum, Xu, Gaus, Shiromani, & Saper, 2002; Schmidt et al., 2011). It also projects to the ventral subparaventricular zone (vSPZ) of the hypothalamus, which is an important contributor to sleep regulation and locomotor activity (Moore & Danchenko, 2002; Schmidt et al., 2011). There have also been found projections to the intergeniculate leaflet (IGL) of the thalamus, which is involved in circadian regulation (i.e., phase shifting) through projections to the SCN (Morin, 1994; Morin, 2013). Additionally, there have been identified projections to the dorsomedial nucleus of the hypothalamus (DMH), a crucial component for behavioral and physiological circadian rhythms as feeding, drinking and body-weight regulation. Additionally, it has been found a connection between the DMH and locus coeruleus in monkeys, indicating that SCN sends projections to LC through DMH. The findings by Aston-Jones & Cohen, 2005 suggest that there is a SCN-DMH-LC circuit, possibly affecting the circadian regulation of both alertness and cognitive abilities (Usher, Cohen, Servan-Schreiber, Rajkowski, & Aston-Jones, 1999; Aston-Jones, Iba, Clayton, Rajkowski, & Cohen, 2007). Locus coeruleus is a nucleus in the brain known for its excitatory effect on large parts of the brain, promoting alertness (Aston-Jones & Cohen, 2005).

### **Artificial light**

Today people are typically more exposed to artificial light, and increasingly less exposed to daylight. Artificial light provides necessary illumination when natural light is not available and makes it possible to engage in tasks while being inside buildings (Klepeis et al., 2001). However, daylight consist of a wide range of wavelengths and have illuminance levels up to ~100.000 lux (Nicol, Wilson, & Chiancarella, 2006). Artificial light however usually contains less wavelengths, with an illuminance level around 500 lux, especially for indoor lightning (Nicol et al., 2006; Sinoo, van Hoof, & Kort, 2011).



Furthermore, research has shown that exposure to artificial light at sub-optimal times has adverse impacts on humans (Dominoni, Borniger, & Nelson, 2016; Valdez, 2019, Van Dongen & Dinges, 2003). Light exposure at the wrong time in the evening or at night can suppress melatonin secretion (Gooley et al., 2011) and even phase-shift the circadian rhythm (Khalsa, 2003; Lockley et al., 2006). Having electronic devices at disposal all the time makes exposure to blue enriched light a risk factor for sleep disturbances and may contribute to social jet lag (Roenneberg, Allebrandt, Merrow, & Céline, 2012). Contrarily, research has also indicated that artificial light can improve cognitive capacities, such as alertness and productivity (Cajochen, 2007). Light therapy has been used in treatment of seasonal affective disorder since the 1980s, and is today used as an antidepressant with the same efficacy as some antidepressant drugs. Light therapy is also used therapeutically in other psychiatric disorders with promising results (Dall'ave, Suzuki & Benedetti, 2015).

### **Acute non-image forming effects of light**

Melatonin suppression, mediated by ipRGCs projections to the SCN, is likely involved in some of the alerting effects seen by exposing participants to light at night (Gooley et al., 2011). However other possibilities should also be considered since research also shows that light exposure elicit alertness during daytime hours (Phipps-Nelson, Redman, Dijk & Rajaratnam 2003; Rüger, Gordijn, Beersma, de Vries, & Daan, 2006; Smolders, de Kort, & Cluitmans, 2012; Vandewalle et al., 2006), when melatonin levels are below 10 pg/ml (Lewy et al., 1999). Position emission tomography (PET) results from a study by Perrin et al., 2004 found that bright polychromatic light exposure suppressed melatonin and enhanced alertness. Conversely, through functional imaging they also found that the occipito-parietal attention network, involving the intraparietal sulcus had heightened activity in relation to light exposure (Perrin et al., 2004). Correspondingly, a functional magnetic resonance imaging (fMRI) study

by Vanderwalle et al., 2006 found increased subjective alertness, which correlated with heightened activity in the posterior thalamus, including pulvinar nucleus; involved in visual attention and regulation of alertness. Furthermore, during an auditory oddball task, light exposure increased activity in several cortical areas including parietal, temporal, occipital and insular areas (Vanderwalle et al., 2006). Nonetheless, the results from these two studies (Vanderwalle et al., 2006; Perrin et al., 2004) cannot be directly compared, due to the different experimental designs, and considerable differences in both spatial and temporal resolution.

A number of studies using a variety of methodologies have shown that acute and long term non-visual responses in humans are most sensitive to light of higher intensities and cooler color temperatures (Brainard et al., 2008; Rahman et al., 2014; Phipps-Nelson et al 2003). Accordingly, studies have found increased acute alerting effects using monochromatic light of wavelengths between 460 and 480 nm (Rahman et al., 2014; Revell, Arendt, Fogg, & Skene, 2006). These wavelengths correspond with the spectral sensitivity of the ipRGCs ( $\lambda_{\max}$  ~480 nm) that primarily mediates the non-visual responses. In a study by Rahman et al., 2014 participants remained in an environment free of time cues for 7 days. The first three days were baseline days and had a sleep-wake schedule based on their prior cycle, 8-hour:16-hour, followed by an initial 40-hour constant routine where the participants were asked to stay awake in constant dim light < 3lux. On day 6, the participants were randomly assigned to either 6.5-hours of monochromatic blue ( $\lambda_{\max}$  460nm) light or monochromatic green ( $\lambda_{\max}$  555 nm) light. To assess alertness, a 10-min auditory PVT was administered every 60 minutes during the 16-hour wake periods and in the start of the monochromatic light exposure, followed by every hour during light exposure and immediately upon light off. There were also polysomnographic recordings throughout the constant routine and light exposure episodes. Daytime 460nm light exposure significantly improved reaction times in auditory PVT and reduced attentional lapses together with improved EEG correlates of alertness, compared to

555-nm exposure. Contrastingly, there were no differences between the two spectral conditions in subjective sleepiness (Rahman et al., 2014). Furthermore, similar results have been found when participants are exposed to light during the biological night (Lockley et al., 2006, Sunde et al., 2020)

While some studies have shown that monochromatic light (460-480nm) can elicit acute alerting effects, there is still research that does not replicate these significant findings. Segal, Sletten, Flynn-Evans, Lockley, & Rajaratnam, 2016 investigated the wavelength-dependent sensitivity of acute alerting effects during daytime, after sleep restriction. Participants were sleep restricted to 5 hours in bed and 3 hours in bed at the laboratory, before being exposed to either narrowband blue light ( $\lambda_{\text{max}}$  458- 480 nm) or green light ( $\lambda_{\text{max}}$  551-555 nm) for 3 hours, which is remarkably less exposure than found in Rahman et al., 2014. This study, however, did not find any significant effects of light wavelength on auditory PVT or subjective sleepiness. Participants in the study by Segal et al., 2016 were exposed to light for a shorter duration, and exposed to less sleep restriction than participants in Rahman et al., 2014, which may correlate with some of the recent findings, suggesting that short term sleep restriction may interact with the circadian system and reduce the effectiveness of light during daytime, with regards to non-visual responses (Burgess, 2010).

Additionally, there has been a substantial amount of research on bright polychromatic light, suggesting that it can induce similar non-visual effects as monochromatic light (Smolders et al., 2012; Phipps-Nelson et al 2003; Leichtfried et al., 2015; Lafrance, Dumont, Lespérance, & Lambert, 1998). In a study by Phipps-Nelson et al., 2003 similar results were found when comparing two groups of either bright white light  $\sim$  1000 lx and dim light  $\sim$ 3 lux conditions. Following two nights of sleep restriction (5-hours each night), 8 hours of bright light improved reaction times on the PVT, showing a correlation between reduced subjective sleepiness and

improved PVT reaction times. Furthermore, reaction times on PVT decreased immediately after light onset. However, this was only an observed trend and not statistically significant.

Along with this, Smolders et al., 2012 tested the effects of two different illuminance levels (200 lx and 1000 lx) during office hours either in the morning or in the afternoon, for 1 hour, without any sleep restrictions. Participants showed reduced subjective sleepiness and shorter reaction times on PVT in the high illuminance group (1000 lx) for both morning and afternoon groups. However, the mentioned effects were most prominent in the morning group and the subjective measures were visible after only 10 minutes in 1000lx, showing an immediate effect independent of time-of-day exposure. Furthermore, a methodological issue when testing the effects of bright light vs dim light is the illuminance level used for the dim light condition. Researchers have found that half of the alerting effects of 9100 lux occurred at approximately 100 lux during early nighttime, indicating that 50 lux dim light condition might be too high and may elicit alertness enhancing effects (Cajochen, Zeitzer, Czeisler &, Dijk, 2000).

Most studies have used either monochromatic blue light with peak sensitivity  $\lambda_{\max}$  480 or polychromatic bright light ~1000 lux for studying the non-visual effects of light. However, effects have been documented for ordinary room light as well as dimmer light (Cajochen et al., 2000; Czeisler, Zeitzer, Brown, Dijk, & Kronauer, 2000).

## **Chronotype**

Chronotype is closely interrelated to the circadian rhythm. Our circadian rhythm can be altered by behavior, external pressures, and light, whereas chronotype refers to our preferred time of day to perform, sleep and wake, independent of environmental factors.

Morning-type (also known as larks), intermediate-type, and evening-type (also known as owls) are the three main chronotypes (Kalmbach et al., 2017) often measured using The

Morningness-Eveningness questionnaire (MEQ) by Horne and Östberg (Adan & Almirall, 1991). Morning-types, which are most active and alert in the morning and find it difficult to stay up late in evening, are considered to have an advanced sleep phase. Evening-types, which are most active and alert in the evening, making them stay up late and sleep late into the day, have a delayed sleep phase (Wittmann, Dinich, Merrow, & Roenneberg, 2006). Some evidence suggest that short circadian periods may play a role in extreme advanced sleep phases. Research also suggests that individuals with extreme delayed sleep phase may have circadian periods longer than 24.2h (Sack et al., 2007). Majority of people fall between these extreme chronotypes, 10% being morning-types, 80% being intermediate and 10% being evening-types (Wittmann et al., 2006). However, the chronotypes strongly depend on the light-dark situation, making people more inclined towards evening-type, when daylight is prolonged into the evening (Fabbian et al., 2016).

There is also an association between artificial light at night and chronotype. Vollmer et al, 2012 found that screentime was associated with chronotype, especially evening-type. Evening-types are characterized as being more active later at night, hence they are more likely to use electronic equipment later in the evening, exposing them for blue light emitting diode light (LED) which can delay their circadian clock, making their evening-type preference even more excessive (Vollmer, Michel, & Randler, 2012). Furthermore, adolescents living in brighter illuminated urban areas show a tendency for later chronotype. Artificial LAN seems to weaken the light-dark zeitgeber, thus affecting the circadian entrainment (Kantermann & Roenneberg, 2009).

Even though society is becoming more evening oriented by using artificial light, it is still best suited for the morning-types (Fabbian et al., 2016). Substantial sleep debt accumulates during the week for the evening-types who go to sleep late, controlled by the endogenous clock, and awake early, controlled by the external, societal clock (Roenneberg et al., 2007). This

accumulation of sleep debt is often retrieved during the weekends by expanding their sleep duration into the day (Roenneberg, Wirz-Justice, & Mellow, 2003). This misalignment is also called “social jet lag”, where the discrepancy between circadian and societal clock results in chronic sleep loss (Roenneberg et al., 2012).

Research has shown that sleep debt and long inertia times may decrease attention, performance and even memory consolidation (Karni & Sagi, 1993), as shown by higher accident rates due to decreased alertness and increased sleep inertia (Bonnet & Arand, 1995) as well as learning deficits among adolescents due to distributed sleep patterns (Carsadon et al., 2011). Correa, Molina, & Sanabria, 2014 tested 25 females with age ranging from 18-26 years, with extreme chronotypes, for driving performance at different times throughout the day. 17 placed in the morning-type group and 12 placed in the evening-type group. Each participant completed 2h session in two consecutive days, one at 8am and one at 8pm. They found that for the evening-types, there was a strong decrement in alertness and attention when they drove at their non-optimal time of day, i.e., morning sessions (8 am). Furthermore, they also found that for the morning-type group there were no differences in driving performance between the morning an evening session. These results correspond with an Italian study by Giannotti et al, 2002, in which high-school students who belonged to the evening-type showed more attention problems during the day, complained about sleepiness, and showed poorer school achievements than morning-type students.

### **Heritability, sex, and age**

Twin and family studies in the Unites States, Scandinavia, United Kingdom and Brazil have estimated the heritability of chronotype to be up to 50%, suggesting a strong polygenetic basis (Hur, Bouchard, & Lykken 1998; Barclay, Eley, Buysse, Archer, & Gregory, 2010; Koskenvuo, Hublin, Partinen, Heikkliä, & Kaprio, 2007; von Schantz et al., 2015).

However, chronotype does not solely rely on genetics and environmental factors (Vollmer et al., 2012; Hur et al., 1998); age is also a big contributor. Even though chronotype is considered to be a trait more so than a state, it has also been shown to gradually change through different phases of our lives (Kalmbach et al., 2017; Park, Kim, Shin, & Joo, 2020). Generally, a person's chronotype remains rather stable across shorter periods of time, either months or sometimes years. From birth to puberty, children are on average early chronotypes, progressively approaching evening-type through the beginning of puberty to where they reach their maximum in "lateness" around age 17-20. From there their chronotype slowly turns more morning oriented with increasing age (Randler & Engelke, 2019; Roenneberg et al., 2003). Later in life, around the age of 60, people generally become even earlier chronotypes than they were as children.

There are also some differences between men and women. Women seem to reach their maximum in lateness around 19.5 years, whereas men continue to delay their sleep until around 21 years (Adan & Vincenzo, 2002). Sex differences appear to persist throughout life, where men generally show a greater evening preference than women. However, this sex difference somewhat diminishes around the age of 50, which also correlates with the age where most women go through menopause (Greer, Sandridge, Chehabeddine, 2003; Hollander, Freeman, Sammel, Berlin, & Grisso, 2001). From this age, the differences between sexes are unclear with inconsistent results, but on average there is little difference in chronotype (Randler & Bausback, 2010; Roenneberg et al., 2007). Together, the age-dependent changes in chronotype, as well as the differences between gender, indicate that endocrine factors, may directly or in-directly, be involved in the changes of chronotype (Park, Matsumoto, Seo, Kang, Nagashima, 2002; Gau & Soong, 2003).

**Alertness and Attention (Cognitive rhythms)**

Attention is a crucial behavioral and cognitive process that makes it possible to selectively concentrate, respond to stimuli, and make efficient responses by processing and selecting incoming stimuli at any given time (Valdez, 2019). Humans are exposed to an enormous number of external stimuli continuously, and due to the finite number of stimuli the brain can process at once, humans are dependent on the ability to select and prioritize specific information for further processing, to respond adequately to the surroundings (Marois & Ivanoff, 2005)

There are four generally known types of attention that the human brain uses constantly throughout the day: 1) sustained attention; 2) selective attention; 3) divided attention; and 4) executive attention. Sustained attention, also known as vigilance and alertness, refers to our ability to continuously maintain alertness over time. Alertness and vigilance have been extensively studied with regards to homeostatic and circadian variations, with both constant routine, forced desynchronization and time of day protocols (Goel, Basner, Rao, & Dinges, 2013). Selective attention refers to the process of selecting relevant information, often referred to as a filtering process that allow us to tune in on critical information among vast number of stimuli. Divided attention is when we must split our attention across tasks. Since the brain has limited resources, dividing attention is difficult. Executive attention refers to our ability to regulate responses, particularly in conflict situations (Valdez, 2019).

The term “alertness” has been referred to in many ways, depending on research fields and context, and is frequently not defined (Oken, Salinsky, & Elsas, 2006). However, it has been used as the opposite of “sleepy”, as it is a common measure in research on circadian rhythm and sleep/wake regulation. It is measured by self-report questionnaires, such as the Karolinska Sleepiness Scale (Åkerstedt & Gillberg, 1990). Even though these self-reported measures are easy to administer, they are also susceptible to biases, and may correlate badly to



more objective correlates, such as psychomotor vigilance task. In most psychological studies, as well as the current study, the term “alertness” refers to a state of vigilance or sustained attention, which includes a person’s arousal level and their ability to sustain and maintain a certain level of cognitive performance (Oken et al., 2006), often measured by PVT.

### **Circadian variations in alertness/ circadian rhythm of attention**

There is a consensus in the literature that the homeostatic and circadian processes contribute to variations in alertness, executive functions and memory (Vandewalle et al., 2009; Carrier & Monk, 2000; Cajochen, Blatter & Wallach 2004; Valdez 2019) and it is well established that cognitive performance typically declines during the biological night and improves during the biological day (Zion & Sahochat, 2018). For a person who sleeps from 23:00 to 07:00, and with an intermediate chronotype, taken that the homeostatic and circadian process are working in synchrony, attention is usually at a low level in the morning, improves towards noon and decrease again at night, with the lowest level at dawn/early morning. However, we know that the homeostatic and circadian process is non-linear, and that several other conditions modulate the course of cognitive performance, such as chronotype, sleep deprivation, age, light, food intake and exercise (Giannotti et al., 2002; McHill, Hull, Wang, Czeisler, & Klerman, 2018).

Furthermore, subjective sleepiness has been correlated to behavioral alertness (vigilant attention) variables (Kaida et al., 2006). However, it is not comparable to level of alertness. A person reporting high levels of subjective sleepiness may also be alert and able to respond to stimuli (Shapiro et al., 2006). Additionally, subjective sleepiness refers to a person’s perceived state and correlates to different variables, such as mood, the need for sleep, sex, and decrease in cognitive performance (Shen, Barbera, & Shapiro, 2006). It shows a clear circadian rhythm

with high sleepiness in the morning, low sleepiness during daytime and increasing subjective sleepiness in the evening (Åkerstedt, Hallvig, & Kecklund, 2017).

Despite the useful contribution on alertness of subjective sleepiness scales, they are often used in company with cognitive performance tasks. A widely applied chronometric study used to assess cognitive alertness, vigilance and changes in cognitive performance is the Psychomotor Vigilance Task (PVT). PVT is based on simple reaction times to a visual or auditory stimuli that occur at random interstimulus intervals over a 5-to-10-minute period (Goel, Basner, & Dinges, 2015). Reaction times on PVT have shown a sensitivity related to homeostatic and circadian changes, such as daytime sleepiness and fatigue (Dinges & Powell, 1985; Lee, Bardwell, Ancoli-Israel, & Dimsdale, 2010). PVT activate frontoparietal attention networks and motor areas that are sensitive to circadian rhythmicity, and sleep deprivation has shown decreased activation in these areas, together with increased reaction time on PVT (Drummond et al., 2005).

### **Sleep deprivation, alertness, and attention**

Studies have shown that there is an observed decrease in attentional performance, variability in episodic memory recall and performance on logical reasoning tasks after total and partial sleep deprivation (Alhola & Polo-Kantola, 2007) and as the homeostatic sleep pressure increases, performance deficits increase (Doran, Van Dongen, & Dinges, 2001). In addition, there have been found large inter-individual differences on alertness under total and partial sleep deprivation, which seem to reflect a trait-like vulnerability (Van Dongen, Baynard, Maislin, & Dinges, 2004). Factors like ambient temperature, light exposure, physical activity, and environmental noise can also influence vigilant attention/alertness (Gabelhart & Van Dongen, 2017).

In a study by McHill et al., 2018, two groups of healthy individuals were compared for 32 days. One group was sleep restricted (5.6h sleep in a 24h day), whilst the control group had 8 hours of sleep. During time awake both groups completed the PVT for alertness. They found that for the control group, median reaction time and lapses of attention remained relatively stable across time spent awake, however, for the chronic sleep restricted group the median reaction time and lapses became increasingly impaired with time spend awake. Today millions of people suffer from insufficient sleep, either by extended wakefulness caused by workload, social pressure, or short sleep duration. Hence, this study found that chronic short sleep duration impairs neurobehavioral performance, without using extended wakefulness paradigm (McHill et al., 2018). Together with these findings, a phase effect has been discovered between morning-type students and better performance earlier in the day, whereas evening-types show better performance later in the day. This corresponds with the literature indicating that evening-type adolescents may be more exposed to sleep deprivation as they go to bed later in the evening but have the same obligation to start their day early, whereas morning-type adolescents, who go to sleep earlier in the evening, accumulates more sleep time (Roenneberg, 2012).

The decrease in vigilance or alertness has been a topic of interest since the 1950`s, with the accumulation of research leading to the lapse hypothesis (Williams, Lubin, & Goodnow, 1959). The hypothesis suggests that sleep deprivation causes moments of low responsiveness, initiating a “state instability”. This suggests that the increase in lapses on PVT during sleep deprivation is caused by moment-to-moment variability in attention, triggered by a complex interaction between the homeostatic sleep pressure and the endogenous circadian promotion of wakefulness together with the subject’s effort to perform (Doran et al., 2001).

## **Aims and Hypotheses**

Most studies investigating the alerting effects of light have been conducted at night or with strict protocols causing either sleep deprivation or free-running circadian rhythms. Although research indicates that different light modalities may enhance alertness at night, the results are inconclusive during daytime. There is little to no research on daytime light exposure, where participants chronotype has been assessed and actigraphy data reveal total sleep time night before light condition, together with a protocol where participants have not been exposed to sleep deprivation or a constant routine.

As adolescents and young adults are more and more exposed to artificial light and hence less exposed to natural daylight, there is room for research uncovering alertness decrement during daytime and the effects of different light modalities during daytime hours.

With this backdrop, the aim of this thesis is to investigate if monochromatic blue light has an effect on alertness, compared to dim light during the morning hours, with the following research questions:

1. Do different light modalities, i.e., monochromatic blue light 455 nm-60lux versus polychromatic dim light (<5 lux) have different acute effects on attention, as measured by PVT?
2. Is there an association between chronotype and attention measured with PVT during the morning hours?
3. Is there an association between prior total sleep time and attention measured by PVT during the morning hours?

Based on previous research (Phipps-Nelson, Redman, Dijk & Rajaratnam 2003; R ger, Gordijn, Beersma, de Vries, & Daan, 2006; Smolders, de Kort, & Cluitmans, 2012; Vandewalle et al., 2006) it is hypothesized that the monochromatic blue light would improve PVT

performance compared to dim light. It is also hypothesized that the effects of light would be affected by the participants' chronotype and sleep time, where a late chronotype and individuals with shorter total sleep time would yield worse response time on the PVT compared to those with earlier chronotypes and longer sleep time, respectively.

## **Method**

### **Ethical Consideration**

The Regional Ethics Committee "Prosjektet er godkjent av Regional Etisk Komite Sør-øst D (Rek, 2019/680)", see appendix I. All participants provided written consent before inclusion.

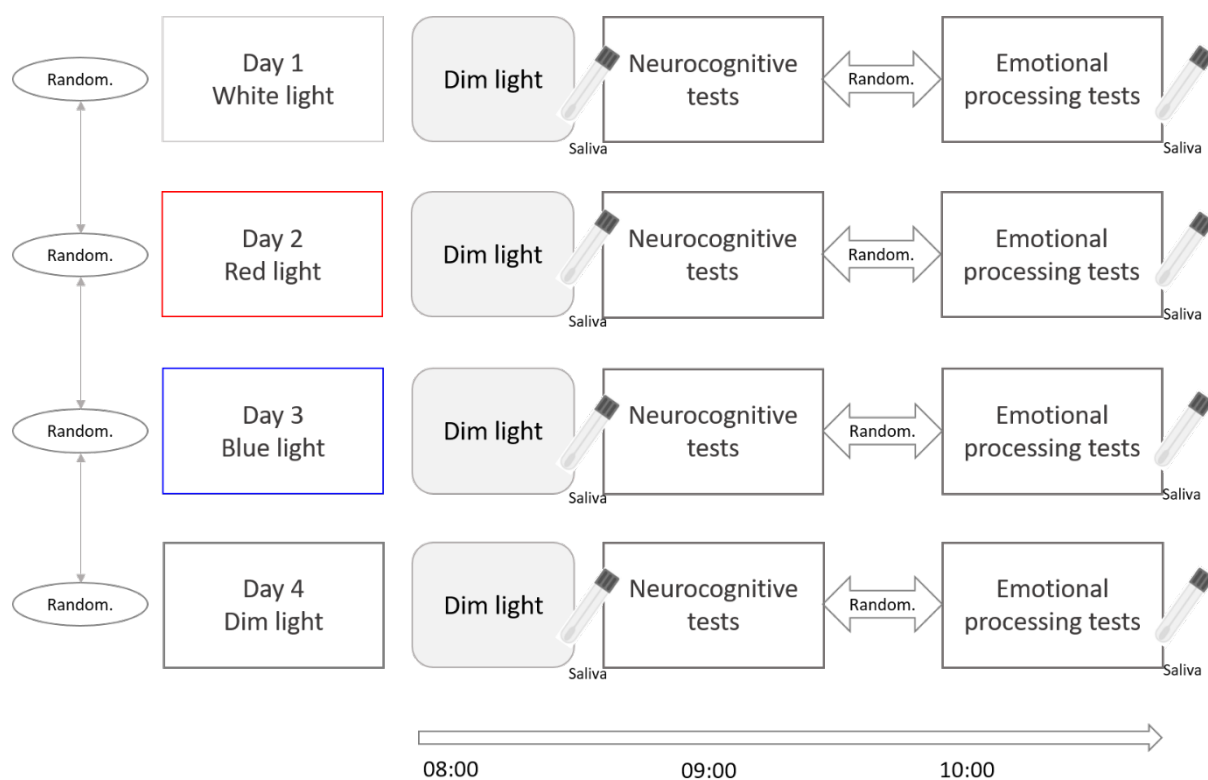
### **Participants**

30 participants were recruited in this study, through information given in lectures at the University of Bergen and through flyers posted on social media and on clipboards on campus, see appendix A. To participate in the study following criteria had to be met: age between 18-39, normal color vision (tested with 17-plate Ishihara Test of Color Deficiency) and agree to keep a stable circadian rhythm over the test weeks, including during the weekends. As this study was part of an ongoing experiment that also will include older adults and people with dementia participants was also screened using the C module of the Mini Mental State Examiner (Sheehan et al., 1998), on which they had to score above 26. Participants were excluded if they had any eye condition, were participating in another ongoing trial or had any condition contra-indicated to the intervention (e.g., psychosis or other mental disorder), as indicated by SCL-90 (Derogatis, Lipman, & Covi, 1973), and module C of the Mini (Sheehan et al., 1998). They were also excluded if they had travel over 3 time zones in the last three weeks and currently working night shifts.

## Design

The present pilot study is part of a larger experimental design, investigating the effects of different light modalities on cognitive performance, alertness, and emotional processing. The study has four different light conditions, and three different groups of participants, as described in the procedure section, however, only one group of participants were included in the current study. As shown in Figure 5, the light conditions and order of tests were randomized to mitigate systematic bias due to circadian timing, learning and test fatigue.

The present study focused on two light conditions, monochromatic blue and dim light, investigating the effects on alertness, as measured by the psychomotor vigilance task.



**Figure 5. Experimental condition and design.** Example of layout for experimental conditions and study design over the 4-day active study period. Noticeably, the order of light conditions and experimental testing will be randomized.

## Procedure

The experiments were conducted at the light laboratory, Bjørn Christiansens hus, Chirsties gate 12. The study started in November 2021, and data collection to the present study was closed in April 2022. After informing about the study in lectures and student areas, the individuals who were interested in participating contacted the researchers. Potential participants were invited to screening and baseline testing one week prior to the experiment. At the first meeting, during baseline, participants received information about the current study, as part of the informed consent letter which they had to sign, see appendix B and D. A researcher with health education was present to answer any question through the entire screening process. Participants who were included in the study arrived at the light laboratory for testing at 08:00 in the morning, for a total of four days (one per light modality), over a two-week period. Participants were instructed to wear blue light blocking goggles from the time they awoke, until arriving at the lab. The goggles were also used if they under any circumstances had to leave the laboratory during the experimental exercises. Participants were also instructed to not consume any caffeine, nicotine, foods, or liquids during experimental procedure, except for a 30-minute window where they were given snacks and water. Before the experimental procedure started, electrocardiogram (ECG) electrodes were placed on participants and a short briefing on the day's agenda was given verbally. During the experimental procedure we controlled for participants posture and gaze, however, during the 30 minutes rest period in the beginning they were free to direct their gaze at their own preferences.

The participants were exposed to dim light (<5 lux) for the first hour on all test days, and baseline saliva melatonin samples were collected using salivette tubes (Sarstedt AG & CO, Germany) towards the end of that hour. Snacks (fruit and nuts) were offered during the following 30 minutes they were exposed to the given light condition. After completing all tests new saliva melatonin samples were collected, see figure 6 for test day overview.

During the experimental session, participants had to complete two randomly assigned sets of tests, one testing the acute effects of light on cognitive performance, the other testing emotion recognition and processing. Details on the screening, baseline and experimental tests are provided in the “Screening Tests, baseline- and outcome measures” section.

Day 1: Red light			Day 2: Blue light		
60 min Dim light Melatonin Saliva sample	30 min	65 min Emotional recognition Psychomotor Vigilance task California Verbal Learning Task The Eriksen-Flanker task N-back test Melatonin Saliva sample	60 min Dim light Melatonin Saliva sample	30 min	65 min Psychomotor Vigilance task N-back test California Verbal Learning Task Emotional recognition The Eriksen-Flanker task Melatonin Saliva sample
Electrocardiogram			Electrocardiogram		
Day 3: Dim light			Day 4: White light		
60 min Dim light Melatonin Saliva sample	30 min	65 min The Eriksen-Flanker task California Verbal Learning Task Emotional recognition Psychomotor Vigilance task N-back test Melatonin Saliva sample	60 min Dim light Melatonin Saliva sample	30 min	65 min Emotional recognition N-back test Psychomotor Vigilance task The Eriksen-Flanker task California Verbal Learning Task Melatonin Saliva sample
Electrocardiogram			Electrocardiogram		

**Figure 6. Test day overview.** Example of 4 tests days where the order of light conditions and tests have been randomized

### Laboratory and Light conditions

The laboratory (30 m<sup>2</sup> room) was painted white to maximize the light intensity when needed and had no windows to avoid light contamination from the outside world. The room was air-conditioned and held a temperature of ~22°C except for a few days when the air-conditioner was turned off due to building maintenance. This caused a higher temperature in the room for a few testing days. The room was equipped with 20 standard ceiling-mounted LED-Luminaires (Module R 600 LED CCT/RGB MP; Glamox Luxo Lighting AB, Norway) (size: 60 x 60 cm), providing uniform illumination without producing glare. The room has five available test stations, separated by partition walls (white), with two LED luminaires suspended above each station and one Phillips Hue 7602031P7 lamp (Poland). The Phillips Hue lamps



provided dim white light (<5 lux). A filter foil (Metolight SGF-19; Asmetec, Germany) blocking all wavelengths <520 nm is fitted on the computer screens to avoid light contamination.

To ensure that the light conditions were correct, light was measured vertically, 120 cm above the floor, at each test station using a calibrated spectrometer (GL Spectics 1.0 T Flicker; GL Optic, Puszczkowo, Poland). Light conditions were then again controlled at one workstation at the beginning and the end of all experimental test days. Lightning parameters were calculated in agreement with the CIE S 026 Toolbox-version 1.049 (International Commission on Illumination, 2018). The larger ENLIGHT study had 4 different light conditions. Two different monochromatic conditions of blue ( $\lambda_{\max}$  455 nm, 60 lux) and red ( $\lambda_{\max}$  625 nm, 200 lux). The monochromatic light conditions were matched at photon flux level and had thus different lux values. Two different polychromatic conditions with white light would vary between high intensity ( $\approx$  1000 lux) and dim light (<5lux) The dim light condition had a Correlated Color Temperature of approximately 2974K.

### **Screening Tests, baseline- and outcome measures**

As this present pilot study is part of a larger experimental design, all participants underwent extensive screening, baseline measures and outcome measures. The current pilot study will focus on and elaborate on The Horne-Östberg Morningness-Eveningness Questionnaire (MEQ), Sleep diary and the Actigraphy. Meanwhile, to provide an overview of what participants were exposed to as part of the study, an overview of tests are provided.

#### **Screening and baseline measurement**

*International Physical Activity Questionnaire (IPAQ short)*, a brief 7-item questionnaire was used to map health-promoting physical activity (Craig et al., 2003). The questionnaire maps

the frequency of activities the prior week. Eyesight, -health and color/light perception was assessed by using a brief amnesic interview and by using the 17-plate *Ishihara Test of Color Deficiency*, see appendix G. Cognitive status was measured using *Mini-Mental State (MMSE)*. The MMSE is a validated cognitive functioning screening instrument which detects the severity of cognitive impairment on a 30-point scale (Folstein & Folstein, 1975). Scores above 26 were needed to further continue screening of the healthy young adults. Mental health status was assessed using the *checklist SCL-90*, which includes nine subcategories: Somatization, Obsessive-compulsive symptoms, Interpersonal, Depression, Anxiety, Hostility, Phobic anxiety, Paranoid thinking, and Psychoticism (Derogatis & Lipman, 1973). *The Wechsler Abbreviated Scale of Intelligence-Second Edition (WASI-II)* was used to assess baseline cognitive status (Wechsler, 2011). WASI-II is a newly revised version of the original Wechsler Abbreviated Scale, an accurate measure of IQ. Only two subtests were administered; Vocabulary, consisting of 42-items were the first four is picture tasks and the rest is presented in written and oral, and the Matrix reasoning, consisting of 35 items. In Matrix reasoning the task taker must complete a pattern of different geometric figures by choosing the correct missing matrix from the answer options (Wechsler, 2011). *The Toronto Alexithymia Scale (TAS-20)* measures the degree of emotional clarity and understanding. TAS-20 includes three subscales: 1) difficulty identifying emotions, 2) difficulty communicating emotions, and 3) externalizing thinking (Taylor, Bagby, & Parker, 2003). *The Mini-IPIP* was used to measure personality, covering the following five dimensions: extraversion, agreeableness, conscientiousness, neuroticism, and intellect/imagination (equal to the openness dimension) (Donnellan et al., 2006).

*The Horne-Östberg Morningness-Eveningness Questionnaire (MEQ)* was used to address participants circadian type (chronotype) (Adan & Almirall, 1991). MEQ is a self-assessment questionnaire based on questions about preferred rise time and bedtime, how one

feels after getting up in the morning, when subjective peak in performance during the day occurs and self-classification of chronotype. MEQ originally consist of 19 questions, however the current study used the short version developed by Adan & Almirall, 1991 consisting of 5 questions addressing individuals' preferences for bedtime and time of alertness (Adan & Almirall, 1991).

*A sleep diary* was handed out to the participants a week prior to the experiment, see appendix F. Participants was instructed to fill out the diary one week prior to the experiments and during the experiments. Instructions on how to use the sleep diary was provided in written form. The diary would record 10 sleep items: 1) Quality of day (Specifying how the day went); 2) Naps (all sleep periods outside of the night's sleep are noted, even if the naps were involuntary, for example, falling asleep in front of the television for 10 minutes); 3) Sleeping aids (all forms of sleeping pills, including over the counter, and alcohol intake, especially used as a sleeping agent); 4) Bedtime (both the timing going to bed and the time trying to fall asleep. Sometimes these times are the same); 5) Sleep time (best estimate of how long it took to fall asleep); 6) Number of awakenings (the number of remembered nightly awakening); 7) Duration of awakening (estimate of overall length of awakenings listen in questioned 6); 8) Awakening in the morning (the last awakening in the morning); 9) Rise time (the time of getting out of bed in that morning); and 10) Sleep quality.

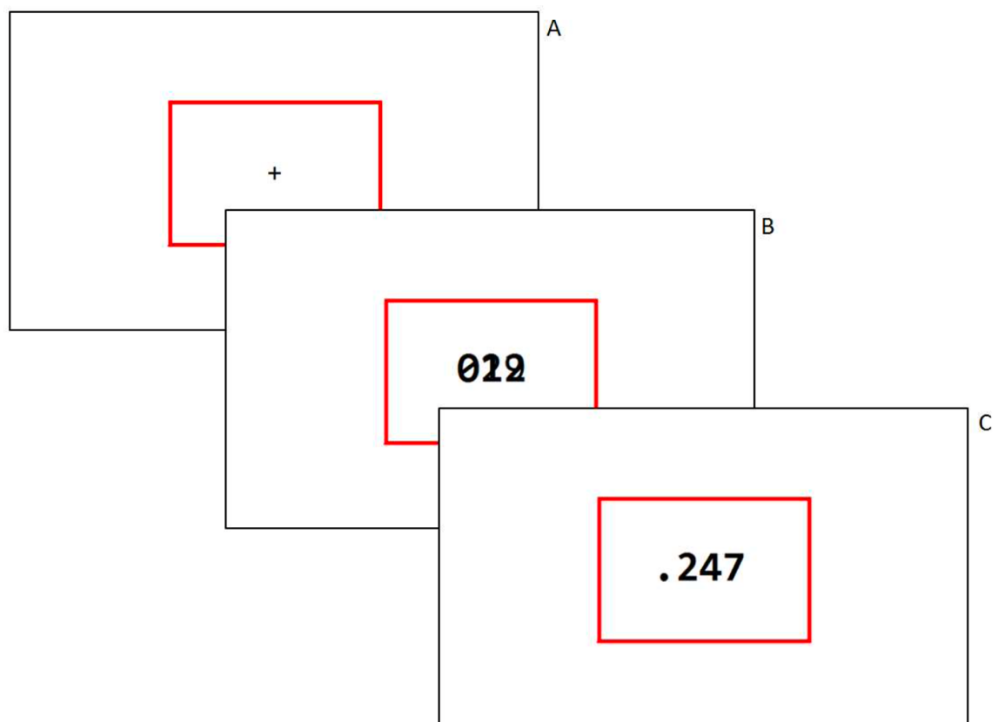
### **Study outcome measures**

As this study was part of a larger experimental protocol, i.e., the ENLIGHT study, participants were tested using several paradigms that will not be reported. The main outcome measures in the ENLIGHT study were the neuropsychological tests results, as well as alertness assessed by the PVT and emotional perception test results and Heart Rate Variability (HRV). The primary outcome in the present study is the Psychomotor Vigilance Task (PVT) (Loh,

Lamond, Dorrian, Roach, & Dawson, 2004). To provide insights into the whole experimental protocol that all participants completed, all outcome measures will be listed and briefly explained, while outcome measures used in the present study will be presented in greater detail.

*Saliva melatonin* levels were collected using Salivette® tubes (Sarstedt, Germany), and analyzed with enzyme-linked immunosorbent assay (ELISA), see appendix H. Melatonin levels were used to monitor changes in the light's non-visual neurological effects (Prayag, Najjar, & Gronfiner, 2019). To assess attention and cognitive inhibition, the *Erikson-Flanker task* (EFT) was administered (Luks et al., 2010). The *N-back task* was included as a working memory paradigm (Jaeggi, Buschkuhl, Perrig & Meier, 2010). *Emotion recognition and processing* was tested using emotion recognition and processing paradigms including emotion facial expressions (sadness, surprise, anger, fear, happy or neutral). The facial expressions were presented with different tasks to capture implicit and explicit processing of emotional stimuli (Koenig et al., 2019). In addition, two short questionnaires were administered, in all four light conditions, right after participants had completed the tests. These questionnaires assess the experience of lighting conditions (Flynn, Spencer, Martyniuk, & Hendrick, 1973; Smolders & de Kort, 2015) and pay potential eye discomfort or headache (Viola et al., 2008), see appendix E.

The psychomotor vigilance test (PVT) is a computer based neurobehavioral chronometric measure of individual reaction times (RTs) to stimuli occurring at random inter-stimulus intervals. PVT is usually administered visually or auditory, ranging from a standard 10-minute test to a 5-minute test (Loh et al., 2004). Subjects were instructed to respond to visual stimuli, with their dominant hand by pressing the space bar, when a digital stimulus appeared on the screen (shown in Figure 7)



**Figure 7. Example from a trail of visual psychomotor vigilance task. (A) no stimulus showing (B) stimulus occurring (C) Reaction time feedback. Adapted from Sunde, 2021**

The two primary outcome measures of PVT performance are usually the mean RT and lapses, defined as RT that exceed 500 ms or failure to react (Basner & Dinges, 2011). In the current study mean RT, mean lapses, mean fastest 10% RT and the mean slowest 10% RT will also be included in the analyses. Reaction time is intended to reveal the alertness (vigilance) (Loh et al., 2004). Lapses constitute measures of sleep deprivation on attention and vigilance, as well as fatigue (Lee, Bardwell, Ancoli-Israel, & Dimsdale, 2010). The PVT has shown to be suitable for repeated administration and is now considered the gold standard for neurobehavioral effects of sleep loss (Basner et al., 2018).

### *Measuring sleep*

Actigraphy was used in combination with sleep diaries to ascertain the participants sleep for one week prior to the experiments, and during the experiments. An actigraph provides

objective data, i.e., activity counts registered by an accelerometer, on the 24-hour sleep and wake activity. The actigraphs (Actiwatch Spectrum, Philips Respironics Inc., US) was placed by trained researchers on the participant's non-dominant wrist. The participants was instructed to push the event button on the watch at bed (when they turned out the lights for sleeping) and rise time (when they woke up and started the day). Participants was also handed an information sheet with a user manual, see appendix C. As limb movement is usually reduced during sleep as compared to an active wakeful state, activity counts as registered by the actigraphy has been used to ascertain sleep, and as such, validated as a useful tool (Marino et al., 2013). Data were recorded in 1 min epochs, and the wake threshold sensitivity was set to medium (40 activity counts per min), and time of inactivity for sleep onset and wake time was set to 10 min. Scoring of the actigraphy data was performed if event markers were missing or misplaced, in the Actiware software version 7 using the procedure for manual correction of actigraphic rest intervals developed by Austad & Follesøe, 2018, figure 8. To ensure inter-scorer reliability, all actigraphy recordings were scored by two different researchers, and compared to sleep diaries.

Outcomes measure extracted from the actigraphy data included: *Total sleep time* which showed total time in bed from the event button was pressed at night to the following morning. *Sleep efficiency* which is a measure of sleep quality. Total time sleeping from the event button was pressed to the next morning. *Sleep onset latency* is defined as the time from lights out to sleeping. *Wake after sleep onset* is defined as time awake after first sleep epoch has been registered.

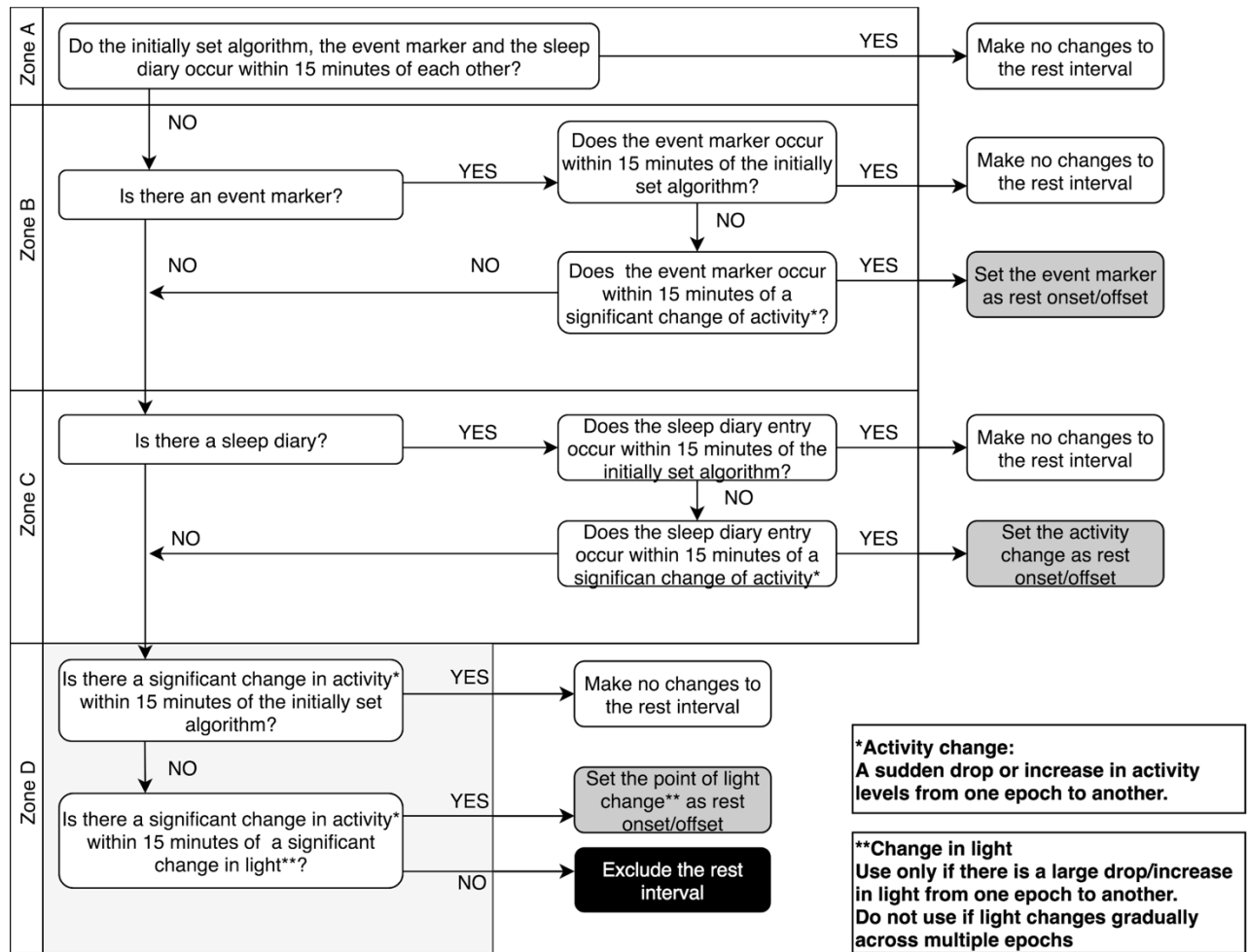


Figure 8. Standardized hierarchical approach. Adapted from Austad & Follesøe, 2018.

**Randomization**

As illustrated by Figure 5, key features were randomized so that participants are their own controls. The randomized order of light condition will counter potential confounding effects as circadian phase, learning or fatigue. Randomization was created by using a sequence generator in the SPSS software.

Participants was not informed about the exact hypothesis for the different light conditions; however, it was not possible to shield researcher from the condition. As all tests are administered via pc and objectively recorded, it is reasonable to believe that the researchers have minimal influence on the participants performance.

## Statistical Analyses

All data was stored on a secure server at the University of Bergen (UiB, SAFE). All the statistical analyses were performed in IBM® SPSS® Statistic software for Mac, version 27 (IBM Corp., US).

Descriptive analyses were used to determine the mean and standard deviations for age, gender, and total sleep time and chronotype. Additionally, descriptive analyses were also used to determine mean and standard deviation for sleep efficiency, sleep onset latency and sleep after wake onset.

Four When using a General linear model repeated measures ANOVAs were conducted. For each analysis, response time from all three PVT sessions were entered (hence three levels). Also, for each of the four repeated measures ANOVAs, light condition was entered with two levels, i.e., blue, and dim light.

A General linear model repeated measures ANOVA was conducted to investigate the effect of light condition on alertness as measured by PVT. Alertness, was entered as the dependent variables and, light conditions, as the independent variable. A General linear model repeated measures ANOVA was also conducted to further look at effects of chronotype on alertness, with alertness as the dependent variable, light condition as the independent variable and using chronotype added as a covariate. Similarly, to look at the effects of prior total sleep time the night before blue light condition and alertness, a General linear model repeated measures ANOVA was conducted using alertness as the dependent variable, light condition as the independent variable and total sleep time night before blue light entered as a covariate. In the same manner, a General linear model repeated measures ANOVA was conducted to look at the effects of prior total sleep time the night before the dim light condition on alertness, using total sleep time before dim light as a covariate.

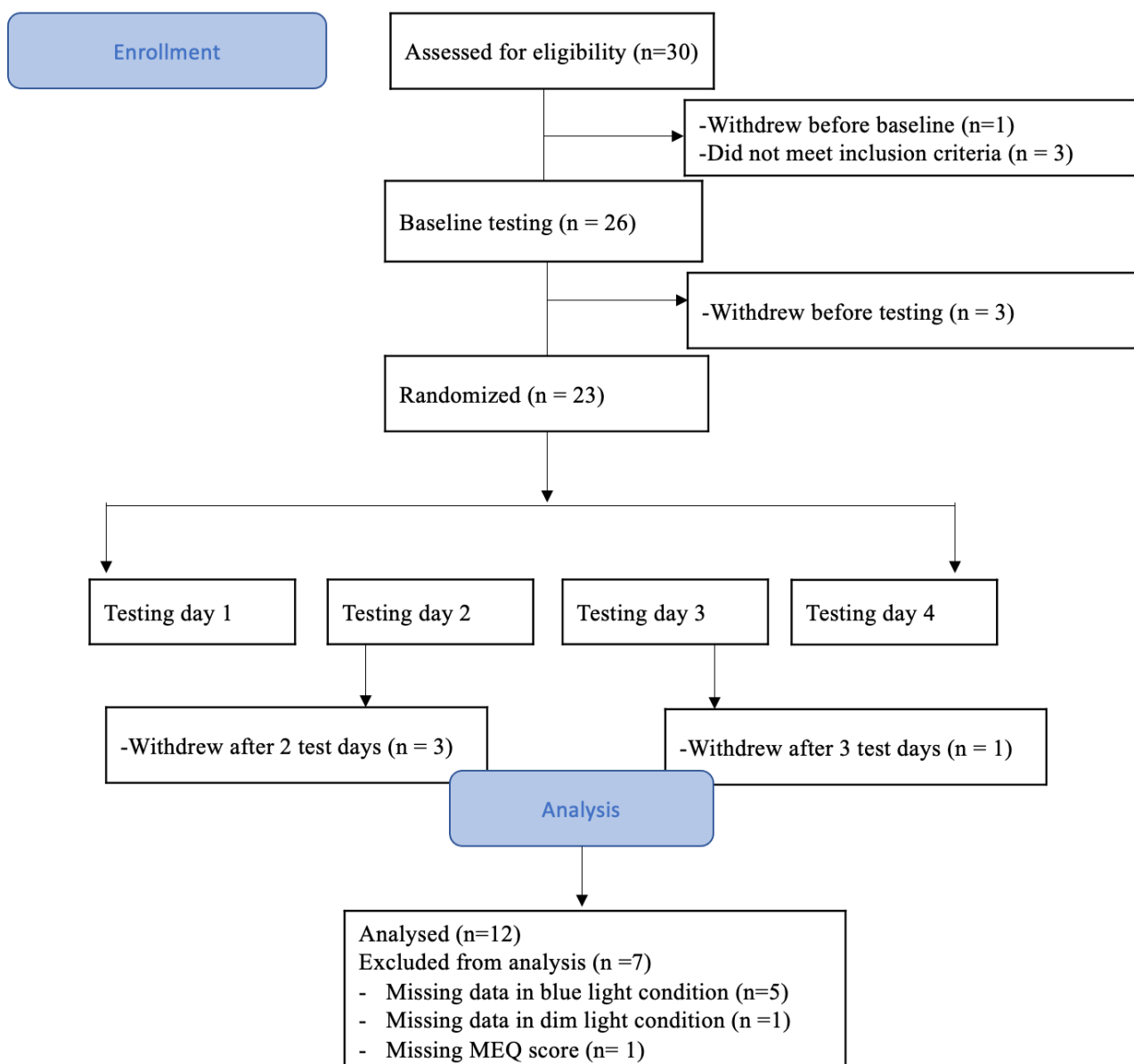


For all tests using a General linear model repeated measures ANOVA, the Mauchly's test of sphericity were used to ensure that the assumption of sphericity had not been violated.

### **Results**

Of the 30 individuals recruited, 1 withdrew before baseline testing and 3 did not meet the inclusion criteria. A total of 26 individuals completed baseline testing, while 3 withdrew before the baseline testing started, 3 withdrew after 2 test days and 1 withdrew after 3 test days. This left 19 participants who completed all test days (see flow chart figure 9). Out of these 19 remaining participants, 7 were excluded due to considerable missing data, which resulted in a sample of 12 participants (age  $22.41 \pm 3.06$ ).

In total 5 women and 7 males were included in the analysis ( $1.58 \pm 0.51$ ). Chronotype was measured in all 12 participants. Out of 12 participants, 8 ( $4 \pm .60$ ) were categorized as “moderately evening type” and 2 ( $4 \pm .60$ ) as “definitely evening type”, while only 2 ( $4 \pm .60$ ) were categorized as “neither type”, and no one were categorized as “morning type”.



**Figure 9.** Flow diagram for inclusion

Participants were asked to keep a stable circadian rhythm through the entire study, including the baseline week. Mean total sleep time during the baseline week was 6.7 hours (404.48 minutes  $\pm$ 27.69), mean sleep efficiency was 79.25% $\pm$ 4.47, mean sleep onset latency was 25.72 minutes $\pm$ 18.60 min and mean wake after sleep onset was 48.74 minutes $\pm$ 9.79. Total sleep time on the night before blue light condition was 5.9 hours (357.78 $\pm$  66.72 minutes), sleep

efficiency was  $78.93\% \pm 38.13$ , sleep onset latency was  $26.33 \text{ minutes} \pm 38.12$ , and wake after sleep onset was  $44.67 \text{ minutes} \pm 31.20$ . Total sleep time night before the dim light condition was 6.1 hours ( $368.04 \text{ minutes} \pm 110.90$ ), sleep efficiency was  $80.15\% \pm 7.49$ , sleep onset latency was  $25.50 \pm 21.89$ , and wake after sleep onset was  $45.17 \pm 22.20$ .

**Table 1:** *Descriptive sleep data from baseline and night before blue and dim light condition*

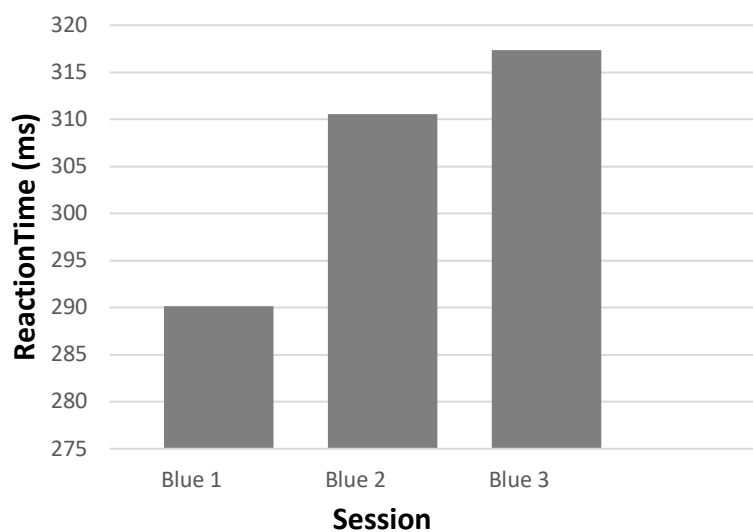
Sleep outcomes baseline week	n	Min	Max	Mean	Std. Dev
TST	12	352.00	445.57	404.48	27.69
Mean SE	12	72.41	87.00	79.25	4.47
Mean SOL	12	7.71	71.00	25.72	18.60
Mean WASO	12	34.29	67.43	48.74	9.79
Sleep outcomes night before blue light					
TST	12	238.00	509.00	357.79	66.73
SE	12	50.62	91.93	78.93	12.29
SOL	12	.00	133.00	26.33	38.13
WASO	12	7.00	107.00	44.67	31.19
Sleep outcomes night before dim light					
TST	12	264.00	647.00	368.04	110.91
SE	12	71.30	92.25	80.15	7.49
SOL	12	.00	64.00	25.50	21.89
WASO	12	18.50	89.00	45.17	22.20

*Note:* SE=Sleep efficiency, SOL=Sleep onset latency, Std. Dev=Standard deviation, TST=Total sleep time, WASO=Wake after sleep onset

Participants slept 13.56% (5.9 hours,  $357.78 \pm 66.72$  minutes) less the night before blue light compared to the baseline week ( $6.7 \text{ hours}, 404.48 \pm 27.69$  minutes), and 9.84%, ( $6.1 \text{ hours}, 368.04 \pm 110.90$  minutes) less the night before the dim light condition as compared to baseline week.

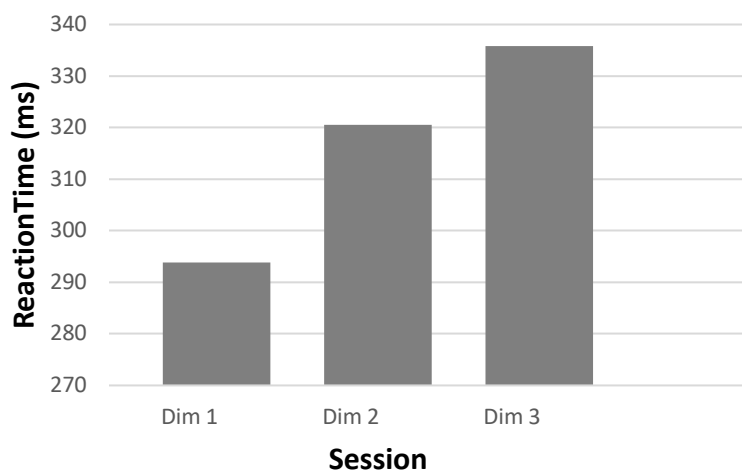
As shown in figure 10 and 11, the mean reaction time increased for each completed PVT session (in total 3 per test day) in both the blue and dim light condition. In the blue light condition the mean reaction time was 7.02% slower for the second session (mean reaction time 310.53 milliseconds $\pm$  44.12) compared to first session (mean reaction time 290.16 milliseconds $\pm$  35.15), and 3.71% slower on the third session (mean reaction time 317.35 milliseconds $\pm$  44.26) compared to first session.

In the dim light condition the mean reaction time was 9.11% slower for the second condition (mean reaction time 320.59 milliseconds $\pm$ 43.83), compared to the first condition (mean reaction time 293.81 milliseconds $\pm$ 38.63), and 14.31% slower on the third session (mean reaction time 335.86 milliseconds $\pm$ 53.95), compared to the first session.



**Figure 10.** Mean reaction time on PVT for blue light condition

*Note.* Blue 1= PVT session 1 blue light condition, Blue 2= PVT session 2 blue light condition, Blue 3= PVT session 3 blue light condition.

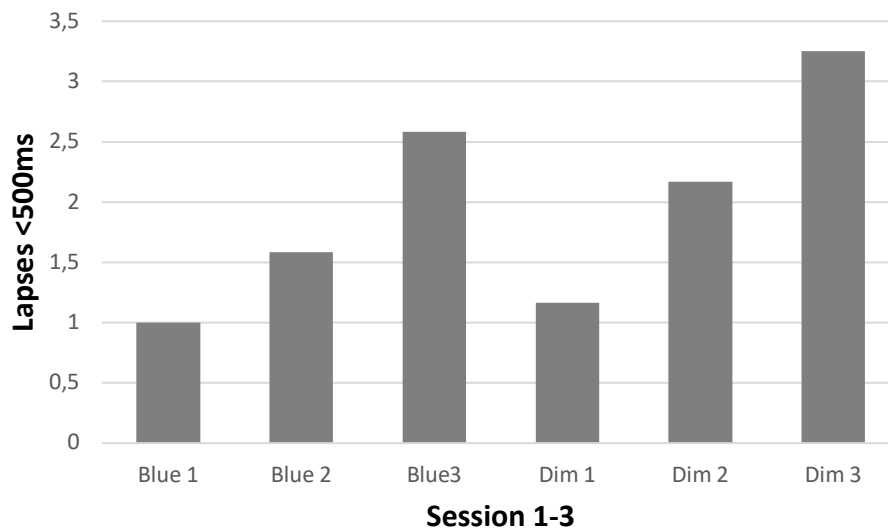


**Figure 11.** Mean reaction time on PVT for dim light condition

*Note.* Dim 1= session 1 dim light condition, Dim 2= session 2 dim light condition, Dim 3= session 3 dim light condition

Together with an increase in reaction time per PVT session, there was an increase in number of lapses <500 milliseconds on each PVT session in both light conditions, as seen in figure 12. In the blue light condition, mean number of lapses <500 milliseconds increased with 58% in the second session ( $1.58 \pm 1.92$ ), and 158% in the third session ( $2.58 \pm 2.23$ ) as compared to first session (mean number of lapses= $1.00 \pm 1.35$ ).

In the dim light condition, the second session ( $2.17 \pm 2.44$ ) showed a 85.47% increase in lapses compared to first session ( $1.17 \pm 1.47$ ), and a 177.78% increase when comparing the third session with first session.



**Figure 12.** Lapses <500ms per PVT session in blue and dim light condition  
*Note.* Blue 1= session 1, Blue 2= session 2, Blue 3= session 3, Dim 1= session 1, Dim 2= session 2, Dim 3= session 3.

First looking at the effects of different light modalities (i.e., monochromatic blue light, 455 nm-60 lux, versus polychromatic dim light, <5 lux) on alertness as measured by PVT, a repeated measures ANOVA was performed. The Mauchly's test of sphericity indicated that the assumption of sphericity had not been violated,  $X^2(2)=1.365$ ,  $p = .508$ . The analyses showed that the different light modalities did not have a significant effect on alertness, as measured by PVT ( $F(2,22)=1.424$ ,  $p = .262$ ,  $\eta^2 = .115$ ). However, there was a significant effect for session, indicating that test duration increased the participants' PVT response time, independent of light condition ( $F(2,22)= 11.156$ ,  $p = .001$ ,  $\eta^2 = .504$ )

Second, looking at the effect of chronotype on PVT, a repeated measure ANOVA was performed. The Mauchly's test of sphericity indicated that the assumption of sphericity had not been violated,  $X^2(2)=1.657$ ,  $p = .437$ . According to the analysis, there was no association between chronotype and alertness as measured by PVT ( $F(2,20)= 2.282$ ,  $p = .128$ ,  $\eta^2 = .186$ ). With regards to a potential effect of chronotype on the effects of light on alertness, there was

no significant effect ( $F(2,20) = .466, p = .634, \eta^2 = .045$ ), when chronotype was added in the repeated measures ANOVA.

Third, looking at the effect of prior total sleep time, the night before the monochromatic blue light condition, on PVT, a repeated measure ANOVA was performed. The Mauchly's test of sphericity indicated that the assumption of sphericity had not been violated  $X^2(2) = 1.729, p = .421$ . The analysis showed that there was no association between prior total sleep time the night before the monochromatic blue light condition and alertness as measured by PVT ( $F(2,20) = 2.042, p = .371, \eta^2 = .094$ ).

Lastly, a repeated measure ANOVA was also performed to look at the effect of prior total sleep time, the night before dim light condition, on PVT. The Mauchly's test of sphericity indicated that the assumption of sphericity had not been violated  $X^2(2) = .146, p = .929$ . The analysis showed that there was no association between prior total sleep time the night before the dim light condition and alertness as measured by PVT ( $F(2,20) = 1.028, p = .376, \eta^2 = .093$ ). However, a combined effect of PVT session number and light condition when total sleep time the night before dim light was included as a covariate was found ( $F(2,20) = 5.615, p = .012, \eta^2 = .360$ ), with increasingly longer response time for the dim light condition as compared to blue light condition (Figure 11).

## Discussion

The present pilot study examined acute alerting effects of light exposure in the morning hours. Participants were exposed to monochromatic blue (455 nm-60lux) and polychromatic dim light (<5 lux) under controlled laboratory conditions, and wore blue light blocking goggles before entering the laboratory. Based on previous research (Rahman et al., 2014; Revell, Arendt, Fogg, & Skene, 2006), it was anticipated that blue monochromatic light would show

alertness-enhancing properties on PVT, based on the short-wavelength sensitivity in the retina, as compared to dim light.

There were no significant effects of blue or dim light on alertness, as measured by PVT during daytime in this current study. This corresponds with a study by Segal et al., 2016, where subjects were exposed to narrowband blue light ( $\lambda_{\max}$  551-555nm) for 3 hours during daytime hours. They did not find any alertness enhancing effects, as measured with auditory PVT. They also had a control group exposed to 0lux, which gave similar results. However, subjects in that study were sleep restricted to that of 5 hours the night before testing. Adding to this, Badia et al., 2014 did not find any effects on alertness of either bright light (white light 5000-10000 lux) or dim light (50 lux). The subjects were not sleep restricted, although they had a limited sample size with only 4 subjects in the bright light condition and 4 subjects in the dim light condition. Also the dim light condition was considerably brighter than what is commonly used.

Even though studies have shown alertness enhancing effects of light during daytime, many studies have used protocols, such as sleep deprivation or constant routine (Segal et al., 2016; Rahman et al., 2014). In this pilot study, participants were asked to keep a stable circadian rhythm, but were free to go to bed at their desirable time. Thus, none of the participants in this study were purposely sleep deprived. Furthermore, empirical evidence shows that alerting effects of light are more readily observed during nighttime (Yoon, Jeong, Kwon, Kang & Song, 2002; Cajochen Zeitzer & Dijk, 2000), which may, in some part, be explained by the two-process model of sleep regulation. The circadian drive for sleep is highest at night, and therefore light may have higher opportunity to improve and enhance alertness. During the day, arousal levels are already high, due to the lower levels of the homeostatic drive for sleepiness (Achermann & Borbely, 1994; Borbely, 1982). The potential for improved alertness is lower, and it is possible that the current study lacked sufficient statistical power to observe alertness-enhancing effects of light on PVT.



The present pilot study opted to match the two monochromatic light conditions on photon flux level, yielding a relatively low lux in the blue light condition. This was also a means to investigate the light colour effect of blue and red light, while investigating effects of high light intensity in the 1000lux polychromatic light condition. However, it is possible that the blue light condition had too low intensity to discern any differences in alertness during the daytime.

There was a significant increase in reaction time related to the number of PVT tests independent of the different light modalities. Since the current study was part of a larger experimental design, each participant underwent several neurocognitive tests and emotional processing tests including the PVT. PVT tests were placed at the beginning of testing, in the middle and at the end. The slope of response time on PVT suggests a vigilance decrement because of increasing task duration (Lim et al., 2012). The PVT is based on the same target stimuli occurring at different time intervals, which may cause habituation to the stimulus (Oken, Salinsky & Elsas, 2006). However, due to the large number of test and possible habituation to the PVT, both boredom, motivational factors, fatigue, and cognitive demands may have acted as masking factors, and contributed to a decline in reaction time and increase in lapses on PVT.

The current study also looked at an association between chronotype and attention, as measured by PVT in the morning hours. Since testing was scheduled to start in the morning hours (08:00), we could expect some alertness decrement among the evening-types, as they were performing at their non-optimal time, attention wise (Correa et al, 2014; Giannotti et al, 2002; Wittmann et al., 2006). However, there were no significant effects between chronotype and attention. This is in contrast with the study by Correa et al., 2014, which found a strong alertness decrement when evening-type participants drove at their non-optimal time of day (i.e., morning time), and no difference in driving performance throughout the day for the morning-type group. Similar to the present pilot study, none of the participants in that study were exposed

to sleep deprivation prior to driving. Meanwhile, Correa and colleagues had a larger sample size ( $n=25$ ) and enough participants for each group extreme chronotype category (“definitely morningness”- “definitely eveningness”). The present study should probably have had a greater variance in chronotypes, to be able to detect potential effects of chronotype.

There was no association between total sleep time and attention in the current study. Participants slept less, both on the night before the blue light condition and the night before the dim light, as compared to the average total sleep time during baseline week. The results may indicate that even though participants slept less than the baseline before both light conditions, they were not sleep deprived to the extent that this alone impacted their alertness. Meanwhile, because of the low number of participants in this pilot study, it is not possible to rule out that the lack of significance is due to low statistical power. Interestingly, while we did not find significant effects of light on alertness or an effect of total sleep time on alertness, there was a significant effect of light on alertness, as measured by PVT when controlling for total sleep time the night before dim light, with increased response times for increased number of sessions in the dim light as compared to the blue light condition. On average, young adults report 7.5 to 8.5 hours of sleep per night during the week, including weekends (Sivertsen et al., 2019). In the current study, participants slept on average 6.1 hours the night before dim light, which is considerably less than the 7 to 9 hours of sleep that is recommended for adults (18-64 years) (Hirshkowitz et al., 2015). The results indicate that shorter than recommended sleep time combined with exposure to dim light the following day may cause a decrement in alertness/vigilance. The dim light condition in this pilot study was  $<5$  lux, which is considerably less than dim light used in some other studies. For example, using 50lux as a dim light condition, Badia et al., 1991, did not find any differential effects between 5000lux light condition and dim light during daytime assessments. However, the use of  $<5$ lux has been extensively used in the literature (Phipps-Nelson et al., 2003; Segal et al., 2016). The effects of sleep time in relation

to dim light only, is interesting. Although more analyses with a bigger sample is necessary, it is possible that lack of light has a bigger impact on performance following sleep deprivation, as compared to enhanced light.

There are some limitations to the pilot study that need to be considered. The sample size was relatively small due to reasons listed in Figure 8. Also, all participants were recruited through flyers at University of Bergen campuses and through lectures, causing a relatively young sample size, with age between 18 and 28 years. Research on chronotypes have shown larger age-dependent differences (Randler & Engelke, 2019), indicating that the current study could have benefitted from a larger sample size with a larger age span. Whether the results would have been different with older participants is not clear. Nonetheless, research has shown that older people become more morningness-oriented (Roenneberg et al., 2003). A more varied sample would thus likely yield a more diverse sample in terms of chronotype. In addition, research has shown age-related changes in physiological non-image forming responses mediated by the ipRGCs change (Herljevic, Middleton, Thapan & Skene, 2005). Thus, it will be of interest to investigate the potential effects of age when the larger ENLIGHT project has finished collecting data.

Several masking factors may have interfered with the results. Since the current study was part of a larger experimental design all participants underwent a large number of tests. As mentioned, a diverse set of variables such as boredom, motivation, energy intake posture, and cognitive demand may have interfered with alertness and contributed to decline in response time and incline in lapses on PVT. Meanwhile, it is a strength that the study employed the PVT, as it had been extensively used to ascertain light, circadian, and homeostatic influences on cognition (Lim & Dinges, 2008).

Prior light history has been suggested to impact direct effects of light exposure (Chang, Scheer, Czeisler, & Aeschback, 2013) and participants were therefore instructed to use blue

light blocking goggles from awakening to arriving at the laboratory. However, there is no way to detect whether participants used these goggles as instructed. Nevertheless, all participants were exposed to 1 hour dim light (<5lux) in the beginning of the procedure, which would have been expected to increase the efficacy of the upcoming light exposure.

Participants were not restricted from caffeine before entering the laboratory, however, they could not consume any caffeine after arriving to the laboratory and during testing. Research indicate that caffeine shows effects on psychomotor functions and can influence a range of cognitive functions and alertness (Beaven & Ekström, 2013). Since the decomposition time for caffeine is several hours, this may have influenced the results as participants did not have to report daily consumption of caffeine before testing. Meanwhile, individuals have a varying dependence of caffeine. Restricting participants from consuming any caffeine before testing would likely have a great impact on the results as well.

Even though participants were instructed to keep a stable circadian rhythm, they were not asked to stay away from electronic devices late in the evening. Research has shown that exposure to artificial light at night or late in the evening may cause disrupt sleep, and especially phase delay the nadir of the circadian rhythm, and thereby also change the timing of REM sleep. Since most spontaneous awakening happens under REM sleep (Czeisler, Weitzman, Moore-Ede, Zimmerman, & Knauer, 1980), the reduced REM sleep in individuals exposed to artificial light during the evenings may impact alertness in the following morning (Chang, Aeschbach, duffy, & Czeisler, 2015).

The different light conditions used in the pilot study were monochromatic blue light (455 nm-60lux) and dim light (<5lux) suitable for experimental use, but not common in everyday life. However, these extreme light conditions were used to evoke effects of light on alertness in an experimental paradigm, the use for everyday light applications will have to be further studied following results from the larger ENLIGHT study.

### **Conclusion**

This pilot study has contributed to the research field by investigating the acute alerting effects of different light modalities on alertness. However, no alerting effects were found as an effect of light exposure on PVT. Nonetheless, a significant effect was found, showing that reaction time on PVT increased throughout each test session independent of light condition. This finding further supports the time-on-task effect, showing that extended demands on the attention system may cause decline in performance over time.

These results further show that there were no significant effect of prior total sleep time on alertness. However, there was a significant effect of light on alertness, as measured by PVT, when controlling for total sleep time the night before dim light condition. This may indicate that less than recommended sleep time may not affect the daytime alertness alone. However, even a relatively small reduction in sleep time combined with low (<5lux) illuminance during wakefulness, might negatively impact performance reliant on alertness. Meanwhile, as this was a pilot study with a low n, the results will have to be confirmed with a bigger sample.

**Reference list**

- Adam, E. K., & Kumari, M. (2009). Assessing salivary cortisol in large-scale, epidemiological research. *Psychoneuroendocrinology*, *34*(10), 1423-1436. <https://doi.org/10.1016/j.psyneuen.2009.06.011>
- Adam, E. K., Quinn, M. E., Tavernier, R., McQuillan, M. T., Dahlke, K. A., & Gilbert, K. E. (2017). Diurnal Cortisol Slopes and Mental and Physical Health Outcomes: A Systematic Review and Meta-analysis. *Psychoneuroendocrinology*, *83*, 25-41. <https://doi.org/10.1016/j.psyneuen.2017.05.018>
- Adan, A., & Almirall, H. (1991). Horne & Östberg morningness-eveningness questionnaire: A reduced scale. *Personality and individual differences*, *12*(3), 241-253. [https://doi.org/10.1016/0191-8869\(91\)90110-W](https://doi.org/10.1016/0191-8869(91)90110-W)
- Adan, A., & Natale, V. (2002). Gender differences in morningness-eveningness preference. *Chronobiology international*, *19*(4), 709–720. <https://doi.org/10.1081/cbi-120005390>
- Alhola, P., & Polo-Kantola, P. (2007). Sleep deprivation: Impact on cognitive performance. *Neuropsychiatr Dis Treat*, *3*(5), 553-567.
- Ancoli-Israel, S., Cole, R., Alessi, C., Chambers, M., Moorcroft, W., & Pollak, C. P. (2003). The role of actigraphy in the study of sleep and circadian rhythms. *Sleep*, *26*(3), 342-392. <https://doi.org/10.1093/sleep/26.3.342>
- Aschoff, J., & Pohl, H. (1978). Phase relations between a circadian rhythm and its zeitgeber within the range of entrainment. *Naturwissenschaften*, *65*(2), 80-84. <https://doi.org/10.1007/BF00440545>
- Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function : Adaptive gain and optimal performance. *Annu Rev Neurosci*, *28*(1), 403-450. <https://doi.org/10.1146/annurev.neuro.28.061604.135709>

- Aston-Jones, G. S., Iba, M., Clayton, E., Rajkowski, J., & Cohen, J. (2007). The locus coeruleus and regulation of behavioral flexibility and attention: clinical implications. 196-235. <https://doi.org/10.1017/CBO9780511544156.008>
- Badia, P., Myers, B., Boecker, M., Culpepper, J., & Harsh, J. R. (1991). Bright light effects on body temperature, alertness, EEG and behavior. *Physiol Behav*, 50(3), 583-588. [https://doi.org/10.1016/0031-9384\(91\)90549-4](https://doi.org/10.1016/0031-9384(91)90549-4)
- Baker, F. C., & Driver, H. S. (2006). Circadian rhythms, sleep, and the menstrual cycle. *Sleep Med*, 8(6), 613-622. <https://doi.org/10.1016/j.sleep.2006.09.011>
- Barclay, N. L., Eley, T. C., Buysse, D. J., Archer, S. N., & Gregory, A. M. (2010). DIURNAL PREFERENCE AND SLEEP QUALITY: SAME GENES? A STUDY OF YOUNG ADULT TWINS. *Chronobiol Int*, 27(2), 278-296. <https://doi.org/10.3109/07420521003663801>
- Basner, M., & Dinges, D. F. (2011). Maximizing Sensitivity of the Psychomotor Vigilance Test (PVT) to Sleep Loss. *Sleep*, 34(5), 581-591. <https://doi.org/10.1093/sleep/34.5.581>
- Basner, M., Hermosillo, E., Nasrini, J., McGuire, S., Saxena, S., Moore, T. M., . . . Dinges, D. F. (2018). Repeated Administration Effects on Psychomotor Vigilance Test Performance. *Sleep*, 41(1), 1. <https://doi.org/10.1093/sleep/zsx187>
- Beaven, C. M., & Ekstrom, J. (2013). A Comparison of Blue Light and Caffeine Effects on Cognitive Function and Alertness in Humans. *PLoS One*, 8(10), e76707-e76707. <https://doi.org/10.1371/journal.pone.0076707>
- Berson, D. M., Dunn, F. A., & Takao, M. (2002). Phototransduction by Retinal Ganglion Cells That Set the Circadian Clock. *Science*, 295(5557), 1070-1073. <https://doi.org/10.1126/science.1067262>

- Bjorvatn, B., & Pallesen, S. (2008). A practical approach to circadian rhythm sleep disorders. *Sleep Med Rev, 13*(1), 47-60. <https://doi.org/10.1016/j.smr.2008.04.009>
- Bonnet, M. H., & Arand, D. L. (1995). We are chronically sleep deprived. *Sleep, 18*(10), 908–911. <https://doi.org/10.1093/sleep/18.10.908>
- Borbely, A. (1978). Effects of light on sleep and activity rhythms. *Prog Neurobiol, 10*(1), 1-31. [https://doi.org/10.1016/0301-0082\(78\)90018-7](https://doi.org/10.1016/0301-0082(78)90018-7)
- Borbely, A. A. (1982). “A two process model of sleep regulation.” *Human Neurology 1*(3): 195-204.
- Borbely, A. A., & Achermann, P. (1999). Sleep homeostasis and models of sleep regulation. *J Biol Rhythms, 14*(6), 557-568.
- Borbely, A. A., Daan, S., Wirz-Justice, A., & Deboer, T. (2016). The two-process model of sleep regulation: a reappraisal. *J Sleep Res, 25*(2), 131-143. <https://doi.org/10.1111/jsr.12371>
- Brainard, G. C., Hanifin, J. P., Greeson, J. M., Byrne, B., Glickman, G., Gerner, E., & Rollag, M. D. (2001). Action Spectrum for Melatonin Regulation in Humans: Evidence for a Novel Circadian Photoreceptor. *J Neurosci, 21*(16), 6405-6412. <https://doi.org/10.1523/JNEUROSCI.21-16-06405.2001>
- Brainard, G. C., Sliney, D., Hanifin, J. P., Glickman, G., Byrne, B., Greeson, J. M., . . . Rollag, M. D. (2008). Sensitivity of the Human Circadian System to Short-Wavelength (420-nm) Light. *J Biol Rhythms, 23*(5), 379-386. <https://doi.org/10.1177/0748730408323089>
- Brown, R. E., Basheer, R., McKenna, J. T., Strecker, R. E., & McCarley, R. W. (2012). CONTROL OF SLEEP AND WAKEFULNESS. *Physiol Rev, 92*(3), 1087-1187. <https://doi.org/10.1152/physrev.00032.2011>



- Brzezinski, A. (1997). Melatonin in Humans. *N Engl J Med*, 336(3), 186-195.  
<https://doi.org/10.1056/NEJM199701163360306>
- Burgess, H. J. (2010a). Partial Sleep Deprivation Reduces Phase Advances to Light in Humans. *J Biol Rhythms*, 25(6), 460-468. <https://doi.org/10.1177/0748730410385544>
- Burgess, H. J. (2010b). Partial Sleep Deprivation Reduces Phase Advances to Light in Humans. *J Biol Rhythms*, 25(6), 460-468. <https://doi.org/10.1177/0748730410385544>
- Burgess, H. J., & Eastman, C. I. (2008). Human Tau in an Ultradian Light-Dark Cycle. *J Biol Rhythms*, 23(4), 374-376. <https://doi.org/10.1177/0748730408318592>
- Burle, B., Spieser, L., Roger, C., Casini, L., Hasbroucq, T., & Vidal, F. (2015). Spatial and temporal resolutions of EEG: Is it really black and white? A scalp current density view. *Int J Psychophysiol*, 97(3), 210-220.  
<https://doi.org/10.1016/j.ijpsycho.2015.05.004>
- Cajochen, C. (2007). Alerting effects of light. *Sleep Med Rev*, 11(6), 453-464.  
<https://doi.org/10.1016/j.smr.2007.07.009>
- Cajochen, C., Blatter, K., & Wallach, D. (2004). Circadian and sleep-wake dependent impact on neurobehavioral function. *Psychologica Belgica*, 44(1-2), 59-80.  
<https://doi.org/10.5334/pb.1017>
- Cajochen, C., Münch, M., Kriebel, S., Kräuchi, K., Steiner, R., Oelhafen, P., . . . Wirz-Justice, A. (2005). High Sensitivity of Human Melatonin, Alertness, Thermoregulation, and Heart Rate to Short Wavelength Light. *J Clin Endocrinol Metab*, 90(3), 1311-1316. <https://doi.org/10.1210/jc.2004-0957>
- Cajochen, C., Reichert, C. F., Maire, M., Schlangen, L. J. M., Schmidt, C., Viola, A. U., & Gabel, V. (2019). Evidence that homeostatic sleep regulation depends on ambient lighting conditions during wakefulness. *Clocks & Sleep (Online)*, 1(4), 517-531.  
<https://doi.org/10.3390/clockssleep1040040>

- Cajochen, C., Zeitzer, J. M., Czeisler, C. A., & Dijk, D.-J. (2000). Dose-response relationship for light intensity and ocular and electroencephalographic correlates of human alertness. *Behav Brain Res, 115*(1), 75-83. [https://doi.org/10.1016/S0166-4328\(00\)00236-9](https://doi.org/10.1016/S0166-4328(00)00236-9)
- Carrier, J., & Monk, T. H. (2000). CIRCADIAN RHYTHMS OF PERFORMANCE: NEW TRENDS. *Chronobiol Int, 17*(6), 719-732. <https://doi.org/10.1081/CBI-100102108>
- Carskadon, M. A. P. (2011). Sleep in Adolescents: The Perfect Storm. *Pediatr Clin North Am, 58*(3), 637-647. <https://doi.org/10.1016/j.pcl.2011.03.003>
- Carskadon, M. A., Acebo, C., & Seifer, R. (2001). Extended nights, sleep loss, and recovery sleep in adolescents. *Archives italiennes de biologie, 139*(3), 301–312.
- Chang, A.-M., Aeschbach, D., Duffy, J. F., & Czeisler, C. A. (2015). Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next-morning alertness. *Proc Natl Acad Sci U S A, 112*(4), 1232-1237. <https://doi.org/10.1073/pnas.1418490112> (From the Cover)
- Chang, A.-M., Scheer, F. A. J. L., Czeisler, C. A., & Aeschbach, D. (2013). Direct Effects of Light on Alertness, Vigilance, and the Waking Electroencephalogram in Humans Depend on Prior Light History. *Sleep, 36*(8), 1239-1246. <https://doi.org/10.5665/sleep.2894>
- Charrier, A., Olliac, B., Roubertoux, P., & Tordjman, S. (2017). Clock Genes and Altered Sleep-Wake Rhythms: Their Role in the Development of Psychiatric Disorders. *Int J Mol Sci, 18*(5), 938. <https://doi.org/10.3390/ijms18050938>
- Chellappa S. L. (2021). Individual differences in light sensitivity affect sleep and circadian rhythms. *Sleep, 44*(2), zsaa214. <https://doi.org/10.1093/sleep/zsaa214>

- Chen, C.-Q., Fichna, J., Bashashati, M., Li, Y.-Y., & Storr, M. (2011). Distribution, function and physiological role of melatonin in the lower gut. *World Journal of Gastroenterology*, *17*(34), 3888-3898. <https://doi.org/10.3748/wjg.v17.i34.3888>
- Cheng, Philip & Drake, Christopher. (2016). Shift Work and Work Performance. 10.1093/acprof:oso/9780190217662.003.0002.
- Correa, Á., Molina, E., & Sanabria, D. (2014). Effects of chronotype and time of day on the vigilance decrement during simulated driving. *Accid Anal Prev*, *67*, 113-118. <https://doi.org/10.1016/j.aap.2014.02.020>
- Craig, C. L., Marshall, A. L., Sjoström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., . . . Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*, *35*(8), 1381-1395. <https://doi.org/10.1249/01.MSS.0000078924.61453.FB>
- Czeisler, C., Zeitzer, J. M., Brown, E., Dijk, D. J., & Kronauer, R. (2000). Sensitivity of the human circadian pacemaker to nocturnal light: melatonin phase resetting and suppression. *J Physiol*, *526*(3), 695-702. <https://doi.org/10.1111/j.1469-7793.2000.00695.x>
- Czeisler, C. A., & Buxton, O. M. (2017). Chapter 35 - Human Circadian Timing System and Sleep-Wake Regulation. In (Sixth Edition ed., pp. 362-376.e365). Elsevier Inc. <https://doi.org/10.1016/B978-0-323-24288-2.00035-0>
- Czeisler, C. A., Duffy, J. F., Shanahan, T. L., Brown, E. N., Mitchell, J. F., Rimmer, D. W., . . . Kronauer, R. E. (1999). Stability, Precision, and Near-24-Hour Period of the Human Circadian Pacemaker. *Science*, *284*(5423), 2177-2181. <https://doi.org/10.1126/science.284.5423.2177>
- Czeisler, C. A., Kronauer, R. E., Allan, J. S., Duffy, J. F., Jewett, M. E., Brown, E. N., & Ronda, J. M. (1989). Bright Light Induction of Strong (Type 0) Resetting of the

Human Circadian Pacemaker. *Science*, 244(4910), 1328-1333.

<https://doi.org/10.1126/science.2734611>

Czeisler, C. A., Shanahan, T. L., Klerman, E. B., Martens, H., Brotman, D. J., Emens, J. S., . . .

. Rizzo, J. F. (1995). Suppression of Melatonin Secretion in Some Blind Patients by Exposure to Bright Light. *N Engl J Med*, 332(1), 6-11.

<https://doi.org/10.1056/NEJM199501053320102>

Czeisler, C. A., Weitzman, E. d., Moore-Ede, M. C., Zimmerman, J. C., & Knauer, R. S.

(1980). Human Sleep: Its Duration and Organization Depend on its Circadian Phase. *Science*, 210(4475), 1264-1267. <https://doi.org/10.1126/science.7434029>

Dacey, D. M., Liao, H.-W., Peterson, B. B., Robinson, F. R., Smith, V. C., Pokorny, J., . . .

Gamlin, P. D. (2005). Melanopsin-expressing ganglion cells in primate retina signal colour and irradiance and project to the LGN. *Nature*, 433(7027), 749-754.

<https://doi.org/10.1038/nature03387>

Dallaspezia, S., Suzuki, M., & Benedetti, F. (2015). Chronobiological Therapy for Mood

Disorders. *Curr Psychiatry Rep*, 17(12), 1-11. <https://doi.org/10.1007/s11920-015-0633-6>

Deboer, T. (2018). Sleep homeostasis and the circadian clock: Do the circadian pacemaker

and the sleep homeostat influence each other's functioning? *Neurobiol Sleep Circadian Rhythms*, 5, 68-77. <https://doi.org/10.1016/j.nbscr.2018.02.003>

Derogatis, L.P., Lipman, R.S., Covi, L. SCL-90:an outpatient psychiatric rating scale-preliminary report. *Psychopharmacology bulletin*. 1973;9(1):13-28.

Dijk, D. J., Beersma, D. G. M., & Daan, S. (1987). EEG Power Density during Nap Sleep:

Reflection of an Hourglass Measuring the Duration of Prior Wakefulness. *J Biol Rhythms*, 2(3), 207-219. <https://doi.org/10.1177/074873048700200304>

- Dinges, D. F., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., . . . Pack, A. I. (1997). Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. *Sleep, 20*(4), 267-277. <https://doi.org/10.1093/sleep/20.4.267>
- Dinges, D.F., Powell, J.W. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods, Instruments, & Computers 17*, 652–655 (1985). <https://doi.org/10.3758/BF03200977>
- Dominoni, D. M., Borniger, J. C., & Nelson, R. J. (2016). Light at night, clocks and health: from humans to wild organisms. *Biol Lett, 12*(2), 20160015-20160015. <https://doi.org/10.1098/rsbl.2016.0015>
- Donnellan, M. B., Oswald, F. L., Baird, B. M., & Lucas, R. E. (2006). The Mini-IPIP Scales: Tiny-Yet-Effective Measures of the Big Five Factors of Personality. *Psychol Assess, 18*(2), 192-203. <https://doi.org/10.1037/1040-3590.18.2.192>
- Doran SM, Van Dongen HP, Dinges DF. Sustained attention performance during sleep deprivation:evidence of state instability. *Arch Ital Biol.* 2001;139(3):253-67. Doi:10:4449/AIB.V139I3.503
- Drummond, S. P. A., Bischoff-Grethe, A., Dinges, D. F., Ayalon, L., Mednick, S. C., & Meloy, M. J. (2005). The neural basis of the psychomotor vigilance task. *Sleep, 28*(9), 1059-1068. <https://doi.org/10.1093/sleep/28.9.1059>
- Duffy, J. F., & Wright, K. P. (2005). Entrainment of the Human Circadian System by Light. *J Biol Rhythms, 20*(4), 326-338. <https://doi.org/10.1177/0748730405277983>
- Eban-Rothschild, A., Appelbaum, L., & de Lecea, L. (2018). Neuronal Mechanisms for Sleep/Wake Regulation and Modulatory Drive. *Neuropsychopharmacology, 43*(5), 937-952. <https://doi.org/10.1038/npp.2017.294>

- Erlend, S., Torhild, P., Jelena, M., Eirunn, T., Janne, G., Anette, H., . . . Ståle, P. (2020). Alerting and Circadian Effects of Short-Wavelength vs. Long-Wavelength Narrow-Bandwidth Light during a Simulated Night Shift. *Clocks & Sleep (Online)*, 2(37), 502-522. <https://doi.org/10.3390/clockssleep2040037>
- Fabbian, F., Zucchi, B., De Giorgi, A., Tiseo, R., Boari, B., Salmi, R., . . . Manfredini, R. (2016). Chronotype, gender and general health. *Chronobiol Int*, 33(7), 863-882. <https://doi.org/10.1080/07420528.2016.1176927>
- Flynn JE, Spencer TJ, Martyniuk O, Hendrick C. Interim Study of Procedures for Investigating the Effect of Light on Impression and Behavior. *Journal of the Illuminating Engineering Society*. 1973;3(1):87-94.
- Follesø, H. S., Austad, S. B., Olsen, A., & Saksvik-Lehouillier, I. (2021). The development, inter-rater agreement and performance of a hierarchical procedure for setting the rest-interval in actigraphy data. *Sleep medicine*, 85, 221-229. <https://doi.org/10.1016/j.sleep.2021.07.025>
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*, 12(3), 189-198. [https://doi.org/10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)
- Follenius M, Weibel L, Brandenberger G. 1995. Distinct modes of melatonin secretion in normal men. *J Pineal Res*. 18:135–40.
- Freedman, M. S., Lucas, R. J., Soni, B., von Schantz, M., Muñoz, M., David-Gray, Z., & Foster, R. (1999). Regulation of Mammalian Circadian Behavior by Non-rod, Non-cone, Ocular Photoreceptors. *Science*, 284(5413), 502-504. <https://doi.org/10.1126/science.284.5413.502>

- Friedman, D. I., Kelly Johnson, J., Chorsky, R. L., & Stopa, E. G. (1991). Labeling of human retinohypothalamic tract with the carbocyanine dye, DiI. *Brain Res*, *560*(1), 297-302.  
[https://doi.org/10.1016/0006-8993\(91\)91246-W](https://doi.org/10.1016/0006-8993(91)91246-W)
- Fuhr, L., Abreu, M., Pett, P., & Relogio, A. (2015). Circadian systems biology: When time matters. *Comput Struct Biotechnol J*, *13*(C), 417-426.  
<https://doi.org/10.1016/j.csbj.2015.07.001>
- Gabehart, R. J., & Van Dongen, H. P. A. (2017). Circadian Rhythms in Sleepiness, Alertness, and Performance. 388-395.e385. <https://doi.org/10.1016/B978-0-323-24288-2.00037-4>
- Gaggioni, G., Maquet, P., Schmidt, C., Dijk, D.-J., & Vandewalle, G. (2014). Neuroimaging, cognition, light and circadian rhythms. *Front Syst Neurosci*, *8*, 126-126.  
<https://doi.org/10.3389/fnsys.2014.00126>
- Gamlin, P. D. R., McDougal, D. H., Pokorny, J., Smith, V. C., Yau, K.-W., & Dacey, D. M. (2007). Human and macaque pupil responses driven by melanopsin-containing retinal ganglion cells. *Vision Res*, *47*(7), 946-954.  
<https://doi.org/10.1016/j.visres.2006.12.015>
- Gau, S. F., & Soong, W. T. (2003). The transition of sleep-wake patterns in early adolescence. *Sleep*, *26*(4), 449-454. <https://doi.org/10.1093/sleep/26.4.449>
- Giannotti, C. (2002). Hölder ratio of solutions of elliptic equations with a point on the boundary. *Journal of mathematical analysis and applications*, *273*(2), 249-261.  
[https://doi.org/10.1016/S0022-247X\(02\)00204-4](https://doi.org/10.1016/S0022-247X(02)00204-4)
- Gilbert, S. S., van den Heuvel, C. J., Ferguson, S. A., & Dawson, D. (2004). Thermoregulation as a sleep signalling system. *Sleep Med Rev*, *8*(2), 81-93.  
[https://doi.org/10.1016/S1087-0792\(03\)00023-6](https://doi.org/10.1016/S1087-0792(03)00023-6)

- Goel, N., Basner, M., & Dinges, D. F. (2015). Phenotyping of Neurobehavioral Vulnerability to Circadian Phase During Sleep Loss. *Methods Enzymol*, 552, 285-308.  
<https://doi.org/10.1016/bs.mie.2014.10.024> (Methods in Enzymology)
- Golombek, D. A., & Rosenstein, R. E. (2010). Physiology of Circadian Entrainment. *Physiol Rev*, 90(3), 1063-1102. <https://doi.org/10.1152/physrev.00009.2009>
- Gooley, J. J., Chamberlain, K., Smith, K. A., Khalsa, S. B. S., Rajaratnam, S. M. W., Van Reen, E., . . . Lockley, S. W. (2011). Exposure to Room Light before Bedtime Suppresses Melatonin Onset and Shortens Melatonin Duration in Humans. *The journal of clinical endocrinology and metabolism*, 96(3), E463-E472.  
<https://doi.org/10.1210/jc.2010-2098>
- Gooley, J. J., & Saper, C. B. (2017). Anatomy of the Mammalian Circadian System. 343-350.e344. <https://doi.org/10.1016/B978-0-323-24288-2.00033-7>
- Greer, W., Sandridge, A. L., & Chehabeddine, R. S. (2003). The frequency distribution of age at natural menopause among Saudi Arabian women. *Maturitas*, 46(4), 263-272.  
[https://doi.org/10.1016/S0378-5122\(03\)00215-9](https://doi.org/10.1016/S0378-5122(03)00215-9)
- Hannibal J, Hindersson P, Ostergaard J, Georg B, Heegaard S, Larsen PJ and Fahrenkrug J (2004) Melanopsin is expressed in PACAP-containing retinal ganglion cells of the human retinohypothalamic tract. *Invest Ophthalmol Vis Sci* 45:4202-4209
- Hanifin, J. P. (2015). Circadian, Neuroendocrine and Neurobehavioral Effects of Polychromatic Light in Humans. In: ProQuest Dissertations Publishing.
- Harding, C., Pompei, F., Bordonaro, S. F., McGillicuddy, D. C., Burmistrov, D., & Sanchez, L. D. (2019). The daily, weekly, and seasonal cycles of body temperature analyzed at large scale. *Chronobiol Int*, 36(12), 1646-1657.  
<https://doi.org/10.1080/07420528.2019.1663863>



- Hastings, M. H., Reddy, A. B., & Maywood, E. S. (2003). A clockwork web: circadian timing in brain and periphery, in health and disease. *Nat Rev Neurosci*, *4*(8), 649-661.  
<https://doi.org/10.1038/nrn1177>
- Hattar, S., Kumar, M., Park, A., Tong, P., Tung, J., Yau, K.-W., & Berson, D. M. (2006). Central projections of melanopsin-expressing retinal ganglion cells in the mouse. *J. Comp. Neurol*, *497*(3), 326-349. <https://doi.org/10.1002/cne.20970>
- Hattar, S., Liao, H. W., Takao, M., Berson, D. M., & Yau, K. W. (2002). Melanopsin-Containing Retinal Ganglion Cells: Architecture, Projections, and Intrinsic Photosensitivity. *Science*, *295*(5557), 1065-1070.  
<https://doi.org/10.1126/science.1069609>
- Haus, E. (2007). Chronobiology in the endocrine system. *Adv Drug Deliv Rev*, *59*(9), 985-1014. <https://doi.org/10.1016/j.addr.2007.01.001>
- Herbert, J., Goodyer, I. M., Grossman, A. B., Hastings, M. H., De Kloet, E. R., Lightman, S. L., . . . Seckl, J. R. (2006). Do Corticosteroids Damage the Brain? *J Neuroendocrinol*, *18*(6), 393-411. <https://doi.org/10.1111/j.1365-2826.2006.01429.x>
- Herljevic, M., Middleton, B., Thapan, K., & Skene, D. J. (2005). Light-induced melatonin suppression: age-related reduction in response to short wavelength light. *Exp Gerontol*, *40*(3), 237-242. <https://doi.org/10.1016/j.exger.2004.12.001>
- Hirshkowitz, M., Whiton, K., Albert, S. M., Alessi, C., Bruni, O., DonCarlos, L., . . . Adams Hillard, P. J. (2015). National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*, *1*(1), 40-43.  
<https://doi.org/10.1016/j.sleh.2014.12.010>
- Hollander, L. E., Freeman, E. W., Sammel, M. D., Berlin, J. A., Grisso, J. A., & Battistini, M. (2001). Sleep quality, estradiol levels, and behavioral factors in late reproductive age

- women. *Obstet Gynecol*, 98(3), 391-397. [https://doi.org/10.1016/S0029-7844\(01\)01485-5](https://doi.org/10.1016/S0029-7844(01)01485-5)
- Hur, Y. M., Bouchard, T. J., & Lykken, D. T. (1998). Genetic and environmental influence on morningness-eveningness. *Personality and individual differences*, 25(5), 917-925. [https://doi.org/10.1016/S0191-8869\(98\)00089-0](https://doi.org/10.1016/S0191-8869(98)00089-0)
- Iber, C., Ancoli-Israel, S., Chesson, A. L., & Quan, S. F. (2007). The New Sleep Scoring Manual-The Evidence Behind The Rules. *Journal of clinical sleep medicine*, 3(2), 107-107. <https://doi.org/10.5664/jcsm.26812>
- Jaeggi, S. M., Buschkuhl, M., Perrig, W. J., & Meier, B. (2010). The concurrent validity of the N-back task as a working memory measure. *Memory*, 18(4), 394-412. <https://doi.org/10.1080/09658211003702171>
- Jewett, M. E., Cajochen, C., Khalsa, S. B. S., & Czeisler, C. A. (2003). A phase response curve to single bright light pulses in human subjects. *J Physiol*, 549(3), 945-952. <https://doi.org/10.1113/jphysiol.2003.040477>
- Kaida, K., Takahashi, M., Åkerstedt, T., Nakata, A., Otsuka, Y., Haratani, T., & Fukasawa, K. (2006). Validation of the Karolinska sleepiness scale against performance and EEG variables. *Clin Neurophysiol*, 117(7), 1574-1581. <https://doi.org/10.1016/j.clinph.2006.03.011>
- Kalmbach, D. A., Schneider, L. D., Cheung, J., Bertrand, S. J., Kariharan, T., Pack, A. I., & Gehrman, P. R. (2017). Genetic Basis of Chronotype in Humans: Insights From Three Landmark GWAS. *Sleep*, 40(2). <https://doi.org/10.1093/sleep/zsw048>
- Kantermann, T., & Roenneberg, T. (2009). Is Light-at-Night a Health Risk Factor or a Health Risk Predictor? *Chronobiol Int*, 26(6), 1069-1074. <https://doi.org/10.1080/07420520903223984>

- Karni, A., & Sagi, D. (1993). The time course of learning a visual skill. *Nature*, *365*(6443), 250-252. <https://doi.org/10.1038/365250a0>
- Klein, D. C., & Moore, R. Y. (1979). Pineal N-acetyltransferase and hydroxyindole-O-methyltransferase: control by the retinohypothalamic tract and the suprachiasmatic nucleus. *Brain Res*, *174*(2), 245-262.
- Kleitman, N. (1933). STUDIES ON THE PHYSIOLOGY OF SLEEP: VIII. Diurnal Variation in Performance. *The American journal of physiology*, *104*(2), 449-456. <https://doi.org/10.1152/ajplegacy.1933.104.2.449>
- Klepeis, N. E., Nelson, W. C., Ott, W. R., Robinson, J. P., Tsang, A. M., Switzer, P., . . . Engelmann, W. H. (2001). The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. *Journal of exposure science & environmental epidemiology*, *11*(3), 231-252. <https://doi.org/10.1038/sj.jea.7500165>
- Koenig, J., Parzer, P., Haigis, N., Liebmann, J., Jung, T., Resch, F., & Kaess, M. (2021). Effects of acute transcutaneous vagus nerve stimulation on emotion recognition in adolescent depression. *Psychol. Med*, *51*(3), 511-520. <https://doi.org/10.1017/S0033291719003490>
- Koskenvuo, M., Hublin, C., Partinen, M., Heikkilä, K., & Kaprio, J. (2007). Heritability of diurnal type: a nationwide study of 8753 adult twin pairs. *J Sleep Res*, *16*(2), 156-162. <https://doi.org/10.1111/j.1365-2869.2007.00580.x>
- Krauchi, K. (2007). The thermophysiological cascade leading to sleep initiation in relation to phase of entrainment. *Sleep Med Rev*, *11*(6), 439-451. <https://doi.org/10.1016/j.smr.2007.07.001>

- Lafrance, C., Dumont, M., Lespérance, P., & Lambert, C. (1998). Daytime Vigilance after Morning Bright Light Exposure in Volunteers Subjected to Sleep Restriction. *Physiol Behav*, *63*(5), 803-810. [https://doi.org/10.1016/S0031-9384\(97\)00538-6](https://doi.org/10.1016/S0031-9384(97)00538-6)
- Lall, G. S., Atkinson, L. A., Corlett, S. A., Broadbridge, P. J., & Bonsall, D. R. (2012). Circadian entrainment and its role in depression: a mechanistic review. *J Neural Transm (Vienna)*, *119*(10), 1085-1096. <https://doi.org/10.1007/s00702-012-0858-z>
- Lee, I.-S., Bardwell, W. A., Ancoli-Israel, S., & Dimsdale, J. E. (2010). Number of Lapses during the Psychomotor Vigilance Task as an Objective Measure of Fatigue. *J Clin Sleep Med*, *6*(2), 163-168. <https://doi.org/10.5664/jcsm.27766>
- Leichtfried, V., Mair-Raggautz, M., Schaeffer, V., Hammerer-Lercher, A., Mair, G., Bartenbach, C., . . . Schobersberger, W. (2015). Intense illumination in the morning hours improved mood and alertness but not mental performance. *Appl Ergon*, *46*, 54-59. <https://doi.org/10.1016/j.apergo.2014.07.001>
- Lewy, A. J., Cutler, N. L., & Sack, R. L. (1999). The Endogenous Melatonin Profile as a Marker for Circadian Phase Position. *J Biol Rhythms*, *14*(3), 227-236. <https://doi.org/10.1177/074873099129000641>
- Lewy, A. J., & Sack, R. L. (1989). The Dim Light Melatonin Onset as a Marker for Circadian Phase Position. *Chronobiology international*, *6*(1), 93-102. <https://doi.org/10.3109/07420528909059144>
- Lewy, A. J., Wehr, T. A., Goodwin, F. K., Newsome, D. A., & Markey, S. P. (1980). Light Suppresses Melatonin Secretion in Humans. *Science*, *210*(4475), 1267-1269. <https://doi.org/10.1126/science.7434030>
- Lim, J., & Dinges, D. F. (2008). Sleep Deprivation and Vigilant Attention. *Ann N Y Acad Sci*, *1129*(1), 305-322. <https://doi.org/10.1196/annals.1417.002> (Annals of the New York Academy of Sciences)

- Lim, J., Ebstein, R., Tse, C.-Y., Monakhov, M., Lai, P. S., Dinges, D. F., & Kwok, K. (2012). Dopaminergic Polymorphisms Associated with Time-on-Task Declines and Fatigue in the Psychomotor Vigilance Test. *PLoS One*, 7(3), e33767-e33767. <https://doi.org/10.1371/journal.pone.0033767>
- Linkowski, P., Van Onderbergen, A., Kerkhofs, M., Bosson, D., Mendlewicz, J., & Van Cauter, E. (1993). Twin study of the 24-h cortisol profile: evidence for genetic control of the human circadian clock. *American Journal of Physiology - Endocrinology And Metabolism*, 264(2), 173-181. <https://doi.org/10.1152/ajpendo.1993.264.2.E173>
- Lockley, S. W., Evans, E. E., Scheer, F. A. J. L., Brainard, G. C., Czeisler, C. A., & Aeschbach, D. (2006). Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans. *Sleep*, 29(2), 161-168. <https://doi.org/10.1093/sleep/29.2.161>
- Loh, S., Lamond, N., Dorrian, J., Roach, G., & Dawson, D. (2004). The validity of psychomotor vigilance tasks of less than 10-minute duration. *Behavior research methods, instruments, & computers : a journal of the Psychonomic Society, Inc*, 36(2), 339-346. <https://doi.org/10.3758/bf03195580>
- Lowden, A., Åkerstedt, T., & Wibom, R. (2004). Suppression of sleepiness and melatonin by bright light exposure during breaks in night work. *J Sleep Res*, 13(1), 37-43. <https://doi.org/10.1046/j.1365-2869.2003.00381.x>
- Lowrey, P. L., & Takahashi, J. S. (2011). Genetics of Circadian Rhythms in Mammalian Model Organisms. *Adv Genet*, 74, 175-230. <https://doi.org/10.1016/B978-0-12-387690-4.00006-4> (Advances in Genetics)
- Lu, J., Bjorkum, A. A., Xu, M., Gaus, S. E., Shiromani, P. J., & Saper, C. B. (2002). Selective Activation of the Extended Ventrolateral Preoptic Nucleus during Rapid Eye

- Movement Sleep. *J Neurosci*, 22(11), 4568-4576.  
<https://doi.org/10.1523/JNEUROSCI.22-11-04568.2002>
- Luks, T. L., Oliveira, M., Possin, K. L., Bird, A., Miller, B. L., Weiner, M. W., & Kramer, J. H. (2010). Atrophy in two attention networks is associated with performance on a Flanker task in neurodegenerative disease. *Neuropsychologia*, 48(1), 165-170.  
<https://doi.org/10.1016/j.neuropsychologia.2009.09.001>
- Marino, M., Li, Y., Rueschman, M. N., Winkelman, J. W., Ellenbogen, J. M., Solet, J. M., . . . Buxton, O. M. (2013). Measuring Sleep: Accuracy, Sensitivity, and Specificity of Wrist Actigraphy Compared to Polysomnography. *Sleep*, 36(11), 1747-1755.  
<https://doi.org/10.5665/sleep.3142>
- Marois, R., & Ivanoff, J. (2005). Capacity limits of information processing in the brain. *Trends Cogn Sci*, 9(6), 296-305. <https://doi.org/10.1016/j.tics.2005.04.010>
- McGinley, Matthew J., Vinck, M., Reimer, J., Batista-Brito, R., Zaghera, E., Cadwell, Cathryn R., . . . McCormick, David A. (2015). Waking State: Rapid Variations Modulate Neural and Behavioral Responses. *Neuron*, 87(6), 1143-1161.  
<https://doi.org/10.1016/j.neuron.2015.09.012>
- McHill, A. W., Hull, J. T., Wang, W., Czeisler, C. A., & Klerman, E. B. (2018). Chronic sleep curtailment, even without extended (>16-h) wakefulness, degrades human vigilance performance. *Proc Natl Acad Sci U S A*, 115(23), 6070-6075.  
<https://doi.org/10.1073/pnas.1706694115>
- Mistlberger, R. E., & Skene, D. J. (2004). Social influences on mammalian circadian rhythms: animal and human studies. *Biol. rev*, 79(3), 533-556.  
<https://doi.org/10.1017/S1464793103006353>
- Moore, R. Y., & Lenn, N. J. (1972). A retinohypothalamic projection in the rat. *J. Comp. Neurol*, 146(1), 1-14. <https://doi.org/10.1002/cne.901460102>

- Moore, R. Y., Speh, J. C., & Leak, R. K. (2002). Suprachiasmatic nucleus organization. *Cell Tissue Res*, 309(1), 89-98. <https://doi.org/10.1007/s00441-002-0575-2>
- Moore, R. Y., Speh, J. C., & Patrick Card, J. (1995). The retinohypothalamic tract originates from a distinct subset of retinal ganglion cells. *J. Comp. Neurol*, 352(3), 351-366. <https://doi.org/10.1002/cne.903520304>
- Moran, D. S., & Mendal, L. (2002). Core Temperature Measurement: Methods and Current Insights. *Sports Med*, 32(14), 879-885. <https://doi.org/10.2165/00007256-200232140-00001>
- Morin, L. P. (1994). The circadian visual system. *Brain Research Reviews*, 19(1), 102-127. [https://doi.org/10.1016/0165-0173\(94\)90005-1](https://doi.org/10.1016/0165-0173(94)90005-1)
- Morin, L. P. (2013). Neuroanatomy of the extended circadian rhythm system. *Exp Neurol*, 243, 4-20. <https://doi.org/10.1016/j.expneurol.2012.06.026>
- Nicol, F., Wilson, M., & Chiancarella, C. (2006). Using field measurements of desktop illuminance in European offices to investigate its dependence on outdoor conditions and its effect on occupant satisfaction, and the use of lights and blinds. *Energy and buildings*, 38(7), 802-813. <https://doi.org/10.1016/j.enbuild.2006.03.014>
- Okamoto, Y., Rea, M. S., & Figueiro, M. G. (2014). Temporal dynamics of EEG activity during short- and long-wavelength light exposures in the early morning. *BMC Res Notes*, 7(1), 113-113. <https://doi.org/10.1186/1756-0500-7-113>
- Oken, B. S., Salinsky, M. C., & Elsas, S. M. (2006). Vigilance, alertness, or sustained attention: physiological basis and measurement. *Clin Neurophysiol*, 117(9), 1885-1901. <https://doi.org/10.1016/j.clinph.2006.01.017>
- Oosterman, J. M., van Someren, E. J. W., Vogels, R. L., van Harten, B., & Scherder, E. J. A. (2009). Fragmentation of the rest-activity rhythm correlates with age-related cognitive

- deficits. *J Sleep Res*, *18*(1), 129-135. <https://doi.org/10.1111/j.1365-2869.2008.00704.x>
- Pandi-Perumal, S. R., Smits, M., Spence, W., Srinivasan, V., Cardinali, D. P., Lowe, A. D., & Kayumov, L. (2007). Dim light melatonin onset (DLMO): A tool for the analysis of circadian phase in human sleep and chronobiological disorders. *Prog Neuropsychopharmacol Biol Psychiatry*, *31*(1), 1-11. <https://doi.org/10.1016/j.pnpbp.2006.06.020>
- Park, M., Kim, S. A., Shin, J., & Joo, E.-J. (2020). Investigation of gene-gene interactions of clock genes for chronotype in a healthy Korean population. *Genomics & informatics*, *18*(4), 38.31-38.39.
- Park, Y. M., Matsumoto, K., Seo, Y. J., Kang, M. J., & Nagashima, H. (2002). Changes of sleep or waking habits by age and sex in Japanese. *Percept Mot Skills*, *94*(3), 1199-1213. <https://doi.org/10.2466/PMS.94.2.1199-1213>
- Perrin, F., Peigneux, P., Fuchs, S., Verhaeghe, S., Laureys, S., Middleton, B., . . . Dijk, D.-J. (2004). Nonvisual Responses to Light Exposure in the Human Brain during the Circadian Night. *Curr Biol*, *14*(20), 1842-1846. <https://doi.org/10.1016/j.cub.2004.09.082>
- Phipps-Nelson, J., Redman, Dijk, D. J., & Rajaratnam, S. M. W. (2003). Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. *Sleep*, *26*(6), 695-700. <https://doi.org/10.1093/sleep/26.6.695>
- Prayag, A. S., Jost, S., Avouac, P., Dumortier, D., & Gronfier, C. (2019). Dynamics of Non-visual Responses in Humans: As Fast as Lightning? *Front Neurosci*, *13*, 126-126. <https://doi.org/10.3389/fnins.2019.00126>



- Prayag, A. S., Münch, M., Aeschbach, D., Chellappa, S. L., & Gronfier, C. (2019). Light Modulation of Human Clocks, Wake, and Sleep. *Clocks Sleep, 1*(1), 193-208.  
<https://doi.org/10.3390/clockssleep1010017>
- Prayag, A. S., Najjar, R. P., & Gronfier, C. (2019). Melatonin suppression is exquisitely sensitive to light and primarily driven by melanopsin in humans. *J Pineal Res, 66*(4), e12562-n/a. <https://doi.org/10.1111/jpi.12562>
- Provencio, I., Rodriguez, I. R., Jiang, G., Hayes, W. P., Moreira, E. F., & Rollag, M. D. (2000). A Novel Human Opsin in the Inner Retina. *J Neurosci, 20*(2), 600-605.  
<https://doi.org/10.1523/JNEUROSCI.20-02-00600.2000>
- Rahman, S. A., Flynn-Evans, E. E., Aeschbach, D., Brainard, G. C., Czeisler, C. A., & Lockley, S. W. (2014). Diurnal Spectral Sensitivity of the Acute Alerting Effects of Light. *Sleep, 37*(2), 271-281. <https://doi.org/10.5665/sleep.3396>
- Randler, C., & Bausback, V. (2010). Morningness-eveningness in women around the transition through menopause and its relationship with climacteric complaints. *Biological rhythm research, 41*(6), 415-431.  
<https://doi.org/10.1080/09291010903407631>
- Randler, C., & Engelke, J. (2019). Gender differences in chronotype diminish with age: a meta-analysis based on morningness/chronotype questionnaires. *Chronobiol Int, 36*(7), 888-905. <https://doi.org/10.1080/07420528.2019.1585867>
- Revell, V. L., Arendt, J., Fogg, L. F., & Skene, D. J. (2006). Alerting effects of light are sensitive to very short wavelengths. *Neurosci Lett, 399*(1), 96-100.  
<https://doi.org/10.1016/j.neulet.2006.01.032>
- Roenneberg, T., Allebrandt, Karla V., Mellow, M., & Vetter, C. (2012). Social Jetlag and Obesity. *Curr Biol, 22*(10), 939-943. <https://doi.org/10.1016/j.cub.2012.03.038>

- Roenneberg, T., Kuehnle, T., Juda, M., Kantermann, T., Allebrandt, K., Gordijn, M., & Merrow, M. (2007). Epidemiology of the human circadian clock. *Sleep Med Rev*, *11*(6), 429-438. <https://doi.org/10.1016/j.smr.2007.07.005>
- Roenneberg, T., Wirz-Justice, A., & Merrow, M. (2003). Life between Clocks: Daily Temporal Patterns of Human Chronotypes. *J Biol Rhythms*, *18*(1), 80-90. <https://doi.org/10.1177/0748730402239679>
- Ruger, M., Gordijn, M. C. M., Beersma, D. G. M., de Vries, B., & Daan, S. (2006). Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure. *Am J Physiol Regul Integr Comp Physiol*, *290*(5), R1413-1420. <https://doi.org/10.1152/ajpregu.00121.2005>
- Sack, R. L., Auckley, D., Auger, R. R., Carskadon, M. A., Wright, K. P., Vitiello, M. V., & Zhdanova, I. V. (2007). Circadian rhythm sleep disorders: Part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm : An American academy of sleep medicine review. *Sleep*, *30*(11), 1484-1501.
- Sack, R. L., Brandes, R. W., Kendall, A. R., & Lewy, A. J. (2000). Entrainment of Free-Running Circadian Rhythms by Melatonin in Blind People. *N Engl J Med*, *343*(15), 1070-1077. <https://doi.org/10.1056/NEJM200010123431503>
- Sack, R. L., Lewy, A. J., Blood, M. L., Keith, L. D., & Nakagawa, H. (1992). CIRCADIAN-RHYTHM ABNORMALITIES IN TOTALLY BLIND PEOPLE - INCIDENCE AND CLINICAL-SIGNIFICANCE. *The journal of clinical endocrinology and metabolism*, *75*(1), 127-134. <https://doi.org/10.1210/jcem.75.1.1619000>
- Sahin, L., & Figueiro, M. G. (2013). Alerting effects of short-wavelength (blue) and long-wavelength (red) lights in the afternoon. *Physiol Behav*, *116*, 1-7. <https://doi.org/10.1016/j.physbeh.2013.03.014>

- Schmidt, C., Collette, F., Cajochen, C., & Peigneux, P. (2007). A time to think: Circadian rhythms in human cognition. *Cogn Neuropsychol*, *24*(7), 755-789.  
<https://doi.org/10.1080/02643290701754158>
- Schmidt, T. M., Chen, S.-K., & Hattar, S. (2011). Intrinsically photosensitive retinal ganglion cells: many subtypes, diverse functions. *Trends Neurosci*, *34*(11), 572-580.  
<https://doi.org/10.1016/j.tins.2011.07.001>
- Schmidt, T. M., & Kofuji, P. (2008). Novel insights into non-image forming visual processing in the retina. *Cellscience*, *5*(1), 77-83.
- Seeman, T. E., McEwen, B. S., Singer, B. H., Albert, M. S., & Rowe, J. W. (1997). Increase in urinary cortisol excretion and memory declines: MacArthur studies of successful aging. *J Clin Endocrinol Metab*, *82*(8), 2458-2465.  
<https://doi.org/10.1210/jc.82.8.2458>
- Segal, A. Y., Sletten, T. L., Flynn-Evans, E. E., Lockley, S. W., & Rajaratnam, S. M. W. (2016). Daytime Exposure to Short- and Medium-Wavelength Light Did Not Improve Alertness and Neurobehavioral Performance. *J Biol Rhythms*, *31*(5), 470-482.  
<https://doi.org/10.1177/0748730416659953>
- Shapiro, C. M., Auch, C., Reimer, M., Kayumov, L., Heslegrave, R., Huterer, N., . . . Devins, G. M. (2006). A new approach to the construct of alertness. *J Psychosom Res*, *60*(6), 595-603. <https://doi.org/10.1016/j.jpsychores.2006.04.012>
- Sharman, E. H., & Bondy, S. C. (2016). Melatonin: A Safe Nutraceutical and Clinical Agent.
- Shen, J., Barbera, J., & Shapiro, C. M. (2006). Distinguishing sleepiness and fatigue: focus on definition and measurement. *Sleep Med Rev*, *10*(1), 63-76.  
<https://doi.org/10.1016/j.smr.2005.05.004>
- Sheehan, DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a

- structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The journal of clinical psychiatry*. 1998.
- Short, M. A., Gradisar, M., Lack, L. C., Wright, H., & Carskadon, M. A. (2012). The discrepancy between actigraphic and sleep diary measures of sleep in adolescents. *Sleep Med*, 13(4), 378-384. <https://doi.org/10.1016/j.sleep.2011.11.005>
- Sinoo, M. M., van Hoof, J., & Kort, H. S. M. (2011). Light conditions for older adults in the nursing home: Assessment of environmental illuminances and colour temperature. *Building and environment*, 46(10), 1917-1927. <https://doi.org/10.1016/j.buildenv.2011.03.013>
- Smagula, S. F., Gujral, S., Capps, C. S., & Krafty, R. T. (2019). A Systematic Review of Evidence for a Role of Rest-Activity Rhythms in Dementia. *Front Psychiatry*, 10, 778-778. <https://doi.org/10.3389/fpsy.2019.00778>
- Smolders, K. C. H. J., & de Kort, Y. A. W. (2014). Bright light and mental fatigue: Effects on alertness, vitality, performance and physiological arousal. *Journal of environmental psychology*, 39, 77-91. <https://doi.org/10.1016/j.jenvp.2013.12.010>
- Smolders, K. C. H. J., de Kort, Y. A. W., & Cluitmans, P. J. M. (2012). A higher illuminance induces alertness even during office hours: Findings on subjective measures, task performance and heart rate measures. *Physiol Behav*, 107(1), 7-16. <https://doi.org/10.1016/j.physbeh.2012.04.028>
- Strijkstra, A. M., Meerlo, P., & Beersma, D. G. M. (1999). Forced desynchrony of circadian rhythms of body temperature and activity in rats. *Chronobiol Int*, 16(4), 431-440. <https://doi.org/10.3109/07420529908998718>
- Taylor, G. J., Bagby, R. M., & Parker, J. D. A. (2003). The 20-Item Toronto Alexithymia Scale: IV. Reliability and factorial validity in different languages and cultures. *J Psychosom Res*, 55(3), 277-283. [https://doi.org/10.1016/S0022-3999\(02\)00601-3](https://doi.org/10.1016/S0022-3999(02)00601-3)

The circadian system of man—Results of experiments under temporal isolation: by Rutger A.

Wever. 276 pp. 1979. Springer-Verlag, Berlin. DM 98, \$53.90. (1980). *Comparative biochemistry and physiology. A, Comparative physiology*, 67(3), 532-532.

[https://doi.org/10.1016/S0300-9629\(80\)80040-5](https://doi.org/10.1016/S0300-9629(80)80040-5)

Tranah, G. J., Blackwell, T., Stone, K. L., Ancoli-Israel, S., Paudel, M. L., Ensrud, K. E., . . .

Yaffe, K. (2011). Circadian activity rhythms and risk of incident dementia and mild cognitive impairment in older women. *Ann Neurol*, 70(5), 722-732.

<https://doi.org/10.1002/ana.22468>

Turpeinen, U. P. D., & Hämäläinen, E. M. D. (2013). Determination of cortisol in serum, saliva and urine. *Best Pract Res Clin Endocrinol Metab*, 27(6), 795-801.

<https://doi.org/10.1016/j.beem.2013.10.008>

Ungar, F., & Halberg, F. (1962). Circadian Rhythm in the in vitro Response of Mouse Adrenal to Adrenocorticotrophic Hormone. *Science*, 137(3535), 1058-1060.

<https://doi.org/10.1126/science.137.3535.1058>

Usher, M., Cohen, J. D., Servan-Schreiber, D., Rajkowski, J., & Aston-Jones, G. (1999). The Role of Locus Coeruleus in the Regulation of Cognitive Performance. *Science*,

283(5401), 549-554. <https://doi.org/10.1126/science.283.5401.549>

Valdez, P. (2019). Circadian Rhythms in Attention. *Yale J Biol Med*, 92(1), 81-92. (Focus: Attention Science)

van den Heuvel, C. J., Ferguson, S. A., Gilbert, S. S., & Dawson, D. (2004). Thermo regulation in normal sleep and insomnia: the role of peripheral heat loss and new applications for digital thermal infrared imaging (DITI). *Journal of thermal biology*, 29(7-8), 457-461. <https://doi.org/10.1016/j.jtherbio.2004.08.014>

Van Dongen, H. P. A., Baynard, M. D., Maislin, G., & Dinges, D. F. (2004). Systematic interindividual differences in neurobehavioral impairment from sleep loss: Evidence

of trait-like differential vulnerability. *Sleep*, 27(3), 423-433.

<https://doi.org/10.1093/sleep/27.3.423>

Van Dongen, H. P. A., & Dinges, D. F. (2003). Investigating the interaction between the homeostatic and circadian processes of sleep-wake regulation for the prediction of waking neurobehavioural performance. *J Sleep Res*, 12(3), 181-187.

<https://doi.org/10.1046/j.1365-2869.2003.00357.x>

Vandewalle, G., Baeteau, E., Phillips, C., Degueldre, C., Moreau, V., Sterpenich, V., . . .

Maquet, P. (2006). Daytime Light Exposure Dynamically Enhances Brain Responses.

*Curr Biol*, 16(16), 1616-1621. <https://doi.org/10.1016/j.cub.2006.06.031>

Vandewalle, G., Maquet, P., & Dijk, D.-J. (2009). Light as a modulator of cognitive brain

function. *Trends Cogn Sci*, 13(10), 429-438. <https://doi.org/10.1016/j.tics.2009.07.004>

Viola, A. U., James, L. M., Schlangen, L. J. M., & Dijk, D.-J. (2008). Blue-enriched White

Light in the Workplace Improves self-reported Alertness, Performance and Sleep Quality. *Scand J Work Environ Health*, 34(4), 297-306.

<https://doi.org/10.5271/sjweh.1268>

Vollmer, C., Michel, U., & Randler, C. (2012). Outdoor Light at Night (LAN) Is Correlated With Eveningness in Adolescents. *Chronobiol Int*, 29(4), 502-508.

<https://doi.org/10.3109/07420528.2011.635232>

von Schantz, M., Taporoski, T. P., Horimoto, A. R. V. R., Duarte, N. E., Vallada, H., Krieger,

J. E., . . . Pereira, A. C. (2015). Distribution and heritability of diurnal preference

(chronotype) in a rural Brazilian family-based cohort, the Baependi study. *Sci Rep*,

5(1), 9214-9214. <https://doi.org/10.1038/srep09214>

Wald, G. (1945). Human Vision and the Spectrum. *Science*, 101(2635), 653-658.

<https://doi.org/10.1126/science.101.2635.653>

- Waterhouse, J., Fukuda, Y., & Morita, T. (2012). Daily rhythms of the sleep-wake cycle. *J Physiol Anthropol*, 31(1), 5-5. <https://doi.org/10.1186/1880-6805-31-5>
- Weaver, D. R., Stehle, J. H., Stopa, E. G., & Reppert, S. M. (1993). Melatonin receptors in human hypothalamus and pituitary : implications for circadian and reproductive responses to melatonin. *J Clin Endocrinol Metab*, 76(2), 295-301. <https://doi.org/10.1210/jc.76.2.295>
- Wechsler D. Wasi-II: Wechsler abbreviated scale of intelligence: PsychCorp;2011.
- Wehr, T. A., Wirz-Justice, A., Goodwin, F. K., Duncan, W., & Gillin, J. C. (1979). Phase Advance of the Circadian Sleep-Wake Cycle as an Antidepressant. *Science*, 206(4419), 710-713. <https://doi.org/10.1126/science.227056>
- Werth, E., Dijk, D. J., Achermann, P., & Borbely, A. A. (1996). Dynamics of the sleep EEG after an early evening nap : experimental data and simulations. *American journal of physiology. Regulatory, integrative and comparative physiology*, 40(3), R501-R510.
- Wever, R. (1966). The duration of re-entrainment of circadian rhythms after phase shifts of the Zeitgeber A theoretical investigation. *Journal of theoretical biology*, 13, 187-201. [https://doi.org/10.1016/0022-5193\(66\)90016-6](https://doi.org/10.1016/0022-5193(66)90016-6)
- Williams, H. L., Lubin, A., & Goodnow, J. J. (1959). Impaired performance with acute sleep loss. *Psychological monographs*, 73(14), 1-26. <https://doi.org/10.1037/h0093749>
- Wittmann, M., Dinich, J., Mellow, M., & Roenneberg, T. (2006). Social Jetlag: Misalignment of Biological and Social Time. *Chronobiol Int*, 23(1-2), 497-509. <https://doi.org/10.1080/07420520500545979>
- Wolfson, A. R., & Carskadon, M. A. (2003). Understanding adolescent's sleep patterns and school performance: a critical appraisal. *Sleep Med Rev*, 7(6), 491-506. [https://doi.org/10.1016/S1087-0792\(03\)90003-7](https://doi.org/10.1016/S1087-0792(03)90003-7)

- Wright, H. R., Lack, L. C., & Kennaway, D. J. (2004). Differential effects of light wavelength in phase advancing the melatonin rhythm. *J Pineal Res*, *36*(2), 140-144.  
<https://doi.org/10.1046/j.1600-079X.2003.00108.x>
- Wright, K. P., Jr., Hull, J. T., & Czeisler, C. A. (2002). Relationship between alertness, performance, and body temperature in humans. *Am J Physiol Regul Integr Comp Physiol*, *283*(6), 1370-1377. <https://doi.org/10.1152/ajpregu.00205.2002>
- Wurtman, R. J., Axelrod, J., & Phillips, L. S. (1963). Melatonin Synthesis in the Pineal Gland: Control by Light. *Science*, *142*(3595), 1071-1073.  
<https://doi.org/10.1126/science.142.3595.1071>
- Wyatt, J. K., Cecco, A. R.-D., Czeisler, C. A., & Dijk, D.-J. (1999). Circadian temperature and melatonin rhythms, sleep, and neurobehavioral function in humans living on a 20-h day. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, *277*(4), 1152-1163. <https://doi.org/10.1152/ajpregu.1999.277.4.R1152>
- Yoon, I. Y., Jeong, D. U., Kwon, K. B., Kang, S. B., & Song, B. G. (2002). Bright light exposure at night and light attenuation in the morning improve adaptation of night shift workers. *Sleep*, *25*(3), 351-356. <https://doi.org/10.1093/sleep/25.3.351>
- Zion, N., & Shochat, T. (2018). Cognitive functioning of female nurses during the night shift: The impact of age, clock time, time awake and subjective sleepiness. *Chronobiol Int*, *35*(11), 1595-1607. <https://doi.org/10.1080/07420528.2018.1497642>
- Zlotos, D. P., Jockers, R., Cecon, E., Rivara, S., & Witt-Enderby, P. A. (2014). MT1 and MT2 Melatonin Receptors: Ligands, Models, Oligomers, and Therapeutic Potential. *J. Med. Chem*, *57*(8), 3161-3185. <https://doi.org/10.1021/jm401343c>
- Åkerstedt, T., & Gillberg, M. (1990). Subjective and Objective Sleepiness in the Active Individual. *Int J Neurosci*, *52*(1-2), 29-37.  
<https://doi.org/10.3109/00207459008994241>



Åkerstedt, T., Hallvig, D., & Kecklund, G. (2017). Normative data on the diurnal pattern of the Karolinska Sleepiness Scale ratings and its relation to age, sex, work, stress, sleep quality and sickness absence/illness in a large sample of daytime workers. *J Sleep Res*, 26(5), 559-566. <https://doi.org/10.1111/jsr.12528>

## Appendix

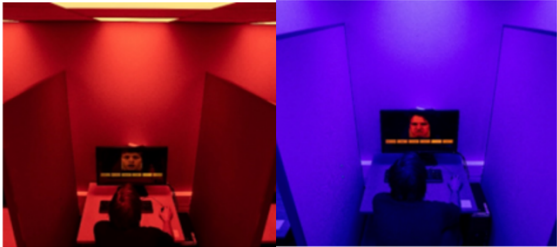
### A. Recruitment flyer

**KAN LYS FÅ DEG TIL Å PRESTERE BEDRE?**  
Vil du bidra i spennende forskning på lys?  
Deltagere søkes til lysstudie

**Hva handler studien om?**  
ENLIGHT prosjektet ønsker å undersøke hvordan ulike former for lys påvirker kognisjon og humør

**Hva skal du gjøre?**  
Møte opp på lab for testing 4 ganger, deltagelsen tar omtrent 3 timer hver gang  
(08:00-11:00)  
Holde stabil døgnrytme i løpet av en 3-ukers periode

**Du kan delta dersom du**  
Er mellom 18 og 40 år  
Har normalt fargesyn  
Ikke har noen psykiske eller neurologiske lidelser



Fotograf: Eivind Senneset

**DU VIL BLI KOMPENSERT MED 1000KR FOR DELTAGELSEN**

Er du interessert i å delta, eller har du noen spørsmål?  
Email: [Oda.Kambestad@uib.no](mailto:Oda.Kambestad@uib.no)  
Telefon: 960 13 673

## B. Information to participants about the experimental period



UNIVERSITETET I BERGEN

Institutt for klinisk psykologi

Kjære deltaker,

Tusen takk for at du vil delta i studien!

Nedenfor gis en oversikt over hva som skal skje før og under de fire test-dagene i lyslaboratoriet ved Det psykologiske fakultet, *Christies gate 12* (bak lille Lungegårdsvannet og KODE 2).

### Kartlegging av døgnrytme før og underveis i eksperimentperioden

Fra og med én uke før den første testdagen i lyslaboratoriet og til og med siste testdag skal du ha på deg en aktivitetsklokke (aktigraf) som måler søvn- og aktivitetsrytme (døgnrytme), samt fylle ut en søvndagbok. I hele eksperimentperioden skal du holde en stabil døgnrytme der du legger deg og står opp til omtrent samme tid hver dag – inkludert i helgene. Siden testdagene starter kl. 08:00 er det viktig at disse dagene ikke utgjør et avvik i døgnrytmen. *Søvndagbok, instruksjoner om hvordan du skal bruke aktigrafen og din personlige test-timeplan finner du i mappen du har fått utlevert.*

### Før du ankommer lyslaboratoriet om morgenen på test-dager

- På testdager tar du på deg de oransje brillene du har fått utdelt med en gang du våkner. Disse skal du ha på deg helt frem forskeren ber deg ta de av på lyslaben.
- Sørg for å spise en god frokost før du drar hjemmefra.
- Du kan innta din vanlige morgen-dose med koffein (og/eller nikotin), men det vil ikke være mulig å innta koffein og/eller nikotin underveis i testingen.
- Ta med utfylt søvndagbok.
- Med utgangspunkt i helsevesenets retningslinjer for smittevern kan du ikke ha med følge når du møter opp til testing i lyslaboratoriet.

### Hva skal skje underveis i testingen i lyslaboratoriet?

Når du ankommer Det psykologiske fakultet i *Christies gate 12* vil du bli møtt av en forsker som tar deg med opp på lyslaboratoriet i 5.etg. og forteller deg hva som skal skje underveis. På hver av de fire test-dagene i lyslaboratoriet (se din personlige eksperiment-timeplan) vil du gjennomføre nevropsykologiske tester i ulike lysbetingelser. Før testene begynner vil du sitte i *svak belysning*. Her blir elektroder blir til brystet ditt. Elektrodene skal måle hjerteaktivitet underveis i testingen. I denne perioden vil du også ha tilgang til lett underholdning slik som radio og småprat med forskerne. Du er også velkommen til å ta med strikke-/hekletoy og liknende, men det vil ikke være tillatt å bruke mobiltelefon. Du vil så bli sittende i én av lysbetingelsene i *30 minutter* før testingen starter. Testingen tar ca. *60 minutter*. Du vil bli tilbudt vann og litt snacks underveis. Med forbehold om variasjon er det estimert at du hver test-dag vil være ferdig mellom kl. 11:30 og 12:00.

### Smitteverntiltak i forbindelse med studiedeltakelse

Noen dager før du kommer til testing på Lyslaben sender vi deg en sms med kontrollspørsmål for COVID-19. Dagen før testing vil du få tilsendt en ny sms med de samme COVID-19-kontrollspørsmålene. Dersom du har fått bekreftet COVID-19-smitte, er i karantene eller mistenker COVID-19-smitte, må du *melde avbud til en av forskerne i studien*. Kontaktinformasjon finner du på side 3.



## UNIVERSITETET I BERGEN

*Institutt for klinisk psykologi*

---

### Spesifikke smitteverntiltak på Lyslab

1. Alle parter bekrefter at de er symptomfrie på gjennomføringsdagen.
2. Alle parter holder 1 meter avstand på lab-rommet, også når man entrer og forlater rommet.
3. Alle parter bruker munnbind. Forsøksledere bruker i tillegg til munnbind også visir, samt hansker der det er nødvendig.
4. Alt utstyr som berøres av forsøkspersoner, dørhåndtak og lignende blir forsvarlig rengjort mellom hver forsøksperson. Forsøksledere har ansvar for å desinfiserende utstyr i rommet, slik som arbeidspult, tastatur, mus, skjerm, instrumenter, papirskjema, skrivesaker etc.

### Generelle smitteverntiltak

Vi oppfordrer deg til å følge myndighetenes anbefalinger til enhver tid:

1. Hold deg hjemme om du er syk, og respekter gjeldende regler for karantene og isolasjon. Bestill test dersom du mistenker COVID-19-smitte.
2. Ha rene hender, unngå å ta deg til ansiktet.
3. Hold minst én meters avstand til andre enn dem du lever med til vanlig.

Du bør teste deg for COVID-19 dersom du:

- har nyoppstått luftveisinfeksjon eller andre symptomer på COVID-19 (slik som sår hals, rennende nese og hoste, muskelsmerter og generell sykdomsfølelse, feber eller frysninger, hodepine, tung pust, magesmerter, kvalme og noen ganger diaré, nedsatt smaks- og luktesans)
- har hatt nærkontakt med en som er smittet (det vil si nærmere enn to meter i mer enn 15 minutter)
- har vært på reise i et land eller region med mye smitte de siste ti dagene
- har vært på fest der smittevernreglene ikke er fulgt (vent 3-5 dager eller test deg med en gang om du får symptomer)
- av andre grunner mistenker COVID-19-smitte

Du kan avtale test uten henvisning fra fastlege. Det er gratis å ta test ved kommunenes testtilbud: Bergen Legevakt, teststasjonen på Festplassen, teststasjonen i Fyllingsdalen (Spelhaugen) og teststasjonen på Flesland (for reisende som ankommer fra utlandet).

Hovedregelen er at du må holde deg hjemme til du får prøvesvar. Unntaket er om du har testet deg, uten at du har symptomer, vært utsatt for smitte, er i karantene eller mistenker smitte av andre grunner. Er du student eller ansatt ved UiB og har fått påvist COVID-19? Meld fra til UiB ved bruk av meldeskjemaet på <https://www.uib.no/korona/134449/informasjon-til-deg-som-er-student-ved-uib>

Er du "vanlig" forkjølet eller syk med luftveissymptomer, må du holde deg hjemme til du er frisk, selv om du har tatt COVID-19-test og svaret er negativt. Om du har blitt symptomfri mens du venter på testsvar, må du likevel holde deg hjemme til du får svaret. Du kan omgås normalt med dem du bor med, de trenger ikke være i karantene.

Og igjen, takk for at du ønsker å delta i studien!

Ikke nøl med å ta kontakt dersom du har noen spørsmål. Kontaktinformasjon finner du på neste side.



UNIVERSITETET I BERGEN

*Institutt for klinisk psykologi*

---

**Kontaktinformasjon:**

Louise Bjerrum  
Stipendiat ved Det psykologiske fakultet  
Universitetet i Bergen  
Mobil: +47 99 56 33 98  
E-post: [louise.bjerrum@uib.no](mailto:louise.bjerrum@uib.no)

Oda Bugge Kambestad  
Vitenskapelig assistent ved Det psykologiske fakultet  
Universitetet i Bergen  
Mobil: +47 98 54 45 07  
E-post: [oda.kambestad@uib.no](mailto:oda.kambestad@uib.no)

## C. Actigraphy information given to participants

DATO:

### AKTIGRAF

Kjære deltaker,

Du har nå fått en *aktigraf* på håndleddet. Denne skal være på til du er ferdig med deltakelse i studien.

#### Hva er en aktigraf?

En aktigraf måler hvor mye en person er i bevegelse og hvor mye lys som er i rommet. På den måten kan vi si noe om døgnrytmen i søvn- og våkenhetsmønsteret.

#### Hvordan foregår måling med aktigraf?

Aktigrafen er plassert rundt håndleddet på den ikke-dominante armen (altså venstre arm hos høyrehendte).

Plasser den gjerne over genseren du har på deg, eller brett opp genser/jakke slik at klokken kan registrere lyset. Hvis klokken oppleves som visuelt forstyrrende kan du dekke klokken ved å brette over genser/skjorte.

- La aktigrafen være på til vi innhenter den etter endt forsøk
- Aktigrafen må være på 24 timer i døgnet, også når du dusjer eller bader
- Aktigrafen er helt vanntett

### VIKTIG – HVER MORGEN OG KVELD

Hold inne den venstre knappen i 2 sekunder:



- Hver gang du skrur av lyset for å sove **om kvelden**
- Hver gang du står opp av sengen **om morgenen**

Du slår ikke av aktigrafen ved å trykke på knappen. Trykk heller to ganger enn ingen

Takk for at du følger instruksjonene!

Ta gjerne kontakt om du lurer på noe.

Louise Bjerrum  
Stipendiat ved Det psykologiske fakultet  
Universitetet i Bergen  
Mobil: 96 01 36 73  
E-post: [louise.bjerrum@uib.no](mailto:louise.bjerrum@uib.no)

Oda Bugge Kambestad  
Forskningsassistent ved Det psykologiske fakultet  
Universitetet i Bergen  
Mobil: 96 01 36 73  
E-post: [oda.bugge.kambestad@gmail.com](mailto:oda.bugge.kambestad@gmail.com)

## D. Information sheet and consent form



UNIVERSITETET I BERGEN

Institutt for klinisk psykologi

### Forespørsel om deltakelse i forskningsprosjektet

«Lysets effekt på prestasjon og humør»

Kjære .....

Vi kontakter deg fordi vi ønsker å gjennomføre en studie om lys og hvordan det kan påvirke fungering og humør hos personer med tidlig påvist kognitiv svikt, friske eldre og friske voksne. Tidligere studier har vist at lysbehandling har en positiv effekt på søvn, fungering, humør og livskvalitet. Denne studien ønsker å finne ut hvilke egenskaper med lyset som påvirker vår fungering.

Nedenfor gis en oversikt over hva studien innebærer. Ta den tiden du trenger til å avgjøre om du ønsker å delta. Diskuter gjerne vår forespørsel med forskere i studien og familien din.

#### Hva innebærer studien?

I studien vil vi teste deg med anerkjente kliniske spørreskjemaer for å vurdere eventuell grad av kognitiv svikt og mental og fysisk helse. Du vil ha på en «aktigraf», et aktivitetsarmbånd som måler søvn- og aktivitetsrytme. Du vil få en grundig klinisk undersøkelse av forskere med helsebakgrunn.

I løpet av studien vil du gjennomføre nevrokognitive tester og emosjonelle tester som går over fire dager. Testene blir gjennomført under ulike lysbetingelser. Før testen vil du sitte i svært svak belysning sammen med en av forskerne. Du vil i denne tiden ha tilgang til mat og lett underholdning som brettspill, lydbøker, radio og/eller småprat med forskerne som er med deg den dagen.

Vår forskergruppe vil undersøke om lysbetingelsene innebærer fordeler for personer med og uten påvist kognitiv svikt, som økt fokus og bedre humør. Det understrekes at lysbehandling regnes som ikke-invasiv, og at lyset ikke er forventet å innebære bivirkninger eller ubehag. Studien vil starte med måling av søvn én uke før testing. I denne perioden vil du bli bedt om å sove normalt og ikke reise over flere enn tre tidssoner. Testingen vil pågå i fire halve dager. Under disse dagene vil måleutstyr bli montert på brystkassen for å måle hjerterate til stimuli. Enkelte vil oppleve mild kløe, men disse måleredskapene er ikke forbundet med risiko for forsøkspersonen.

Siden prosjektet krever at man stiller på lab fire dager i tillegg til én dag med screening vil alle deltagere godtgjøres med til sammen 800 NOK. Deltagere får 400 NOK etter de to første eksperimentelle dagene er gjennomført og 400 NOK etter endt eksperiment.

#### Hva skjer med sensitive opplysninger?

Informasjonen som registreres skal kun brukes i studiens hensikt. I studiens analyser vil alle opplysninger behandles uten navn og fødselsnummer eller andre direkte identifiserbare opplysninger.

Gateadresse:  
Christies gate 12

Postadresse:  
5015 BERGEN

**UNIVERSITETET I BERGEN***Institutt for klinisk psykologi*

---

Ved eventuell fare for COVID-19-smitte vil din kontaktinformasjon også kunne benyttes til smittesporing.

**Frivilligdeltakelse**

Det er helt frivillig å være forsøksperson i studien og delta på testene vi vil gjennomføre. Du kan når som helst, uten å oppgi noen grunn, trekke tilbake samtykke til å delta.

*Dersom du ønsker å delta, undertegner du samtykkeerklæringen på neste side.*

**Ansvarlige**

Studien vil bli gjennomført av stipendiat Louise Bjerrum, og forskningsassistent Oda Bugge Kambestad, ved Institutt for klinisk psykologi, Universitetet i Bergen

Prosjektansvarlig er Elisabeth Flo-Groeneboom, psykolog og professor ved Institutt for klinisk psykologi, Universitetet i Bergen.

Når du signerer vedlagte informasjonsskjema, bekrefter du at du har mottatt dette informasjonsbrevet og at du ønsker å delta i denne undersøkelsen.

Ta gjerne kontakt med oss dersom du har spørsmål eller kommentarer, på telefonnummer oppgitt under.

Vennlig hilsen

---

Elisabeth Flo-Groeneboom  
Professor  
Institutt for klinisk psykologi  
Universitetet i Bergen  
Tlf: +47 55 58 88 85/93\_04\_64\_92

---

Gateadresse:  
Christies gate 12

Postadresse:  
5015 BERGEN



**UNIVERSITETET I BERGEN***Institutt for klinisk psykologi*

---

## Samtykke til deltakelse i studien

### INFORMASJONSSKJEMA

Jeg gir med dette mitt samtykke til å delta i studien for å undersøke lysets effekt på prestasjon og humør. Jeg har lest og forstått informasjonsskrivet til studien.

Jeg er klar over at forskerteamet ønsker å registrere sensitive opplysninger om mulige sykdommer og testresultater. Opplysninger behandles konfidensielt og kun informasjon som er nødvendig for studien vil bli innhentet.

Jeg er klar over at samtykket er frivillig og at jeg når som helst kan trekke samtykket tilbake uten ytterligere forklaring.

.....  
Signatur

.....  
Sted/Dato

.....  
Navn i blokkbokstaver

---

Gateadresse:  
Christies gate 12

Postadresse:  
5015 BERGEN

## E. Evaluation of light condition, eye strain and headache

Dato: \_\_\_\_\_

ID-nr.:

Lysbetingelse:

---

Svar med å *sette ring rundt* tallet som du synes er rett for hvert ledd i skjemaet under.

I hvilken grad synes du lyset er... (*eller gjør rommet...*):

---

Utrivelig	1	2	3	4	5	6	7	Trivelig
Ubehagelig	1	2	3	4	5	6	7	Behagelig
Forstyrrende	1	2	3	4	5	6	7	Ikke-forstyrrende
Blendende	1	2	3	4	5	6	7	Ikke-blendende
Uklart	1	2	3	4	5	6	7	Klart
Varmt	1	2	3	4	5	6	7	Kaldt
Dempet	1	2	3	4	5	6	7	Sterkt
Avslappende	1	2	3	4	5	6	7	Oppkvikkende
Ikke egnet til å arbeide i	1	2	3	4	5	6	7	Egnet til å arbeide i

---

Dato: \_\_\_\_\_

ID-nr.: I hvilken grad opplever du følgende symptomer på nåværende tidspunkt? (*Sett kryss*)

Symptom	Fraværende	Fornemmelse	Moderat	Kraftig
Irritabilitet				
Hodepine				
Anstrengelse av øynene				
Generelt ubehag i øynene				
Tretthet i øynene				
Vanskelig å fokusere				
Vanskelig å holde konsentrasjonen				
Uskarpt/tåketete syn				

## F. Sleep diary

ID-NR:

©Bjørn Bjorvann

### SØVNDAGBOK

Spørsmål 1 og 2 fylles ut før sengetid, resten av skjemaet fylles ut om morgenen. Husk å notere dato.

	Eksempel: 01.01.18	Tirsdag	Onsdag	Torsdag	Fredag	Lørdag	Søndag	Mandag
Hvordan har du fingern på dagtid? 1 = veldig bra, 2 = bra, 3 = middels, 4 = dårlig, 5 = veldig dårlig	4							
Har du tatt en eller flere hørebrunder i løpet av dagen? Noter tidspunktene for alle blundene.	16:00-16:30 og 18:15-18:30							
Tok du sovemedisin og/eller alkoholljelp for å sove? Noter medikament og dose, samt evt alkoholinntak	5 mg Imovane 1 glass rødvin							
Hvilket klokkeslett gikk du til sengs?	22:30							
Når prøvde du å sove (angit klokkeslettet)?	23:00							
Hvor lang tid tok det før du sovnet?	45 min							
Hvor mange ganger våknet du i løpet av natten?	3							
Hvor lenge var du våken totalt i løpet av disse nattlige oppvåkningene (angit omtrent hvor lenge du var våken)?	90 min							
Når våknet du opp om morgenen uten å få sove igjen?	06:15							
Noter tidspunktet for din endelige oppvåkning.								
Når stod du opp?	06:40							
Hvordan var siste natts søvn totalt sett: 1 = veldig lett, 2 = lett, 3 = middels, 4 = dyp, 5 = veldig dyp	1							

**Husk å trykke på knappen på aktiografen din hver gang du legger deg til å sove og når du våkner om morgenen!**



## G. Ishihara's test for colour Deficiency

Deltakernr.:

### Ishihara's Tests for Colour Deficiency, 24 Plates Edition ©Kanehara Trading Inc., 2017

#### Før administrering av testen

1. Sjekk lysforholdene i rommet. Platene leses best i rom med god tilgang på dagslys. Elektrisk lys bør derfor likne så mye som mulig på dagslys. Sjekk at armaturene på lyslab er satt til scene nr. 12 i hvitt lys (gir tilnærmet lik 500 fotopisk lux på øyenivå).
2. Platene holdes 75 cm fra deltakeren, og bør tiltes slik at vinkelen på platen er i linje med synsvinkelen.
3. Plate 1-15 vises én etter én. Deltakerens oppgave er å si hvilket tall som står på hver av platene – svaret bør avgis innen tre sekunder.

#### Resultater

##### Plate 1-7

	1	2	3	4	5	6	7
Svar							

##### Plate 8-15

	8	9	10	11	12	13	14	15
Svar								

#### Referanseskårer

Under er en oversikt over typisk svarrespons på plate 1-15 hos en person med normalt fargesyn, en person med nedsatt fargesyn i form av rød-grønn-fargeblindhet, og en person med total fargeblindhet. X indikerer at platen ikke kan leses hos i den respektive gruppen.

Plate	Normalt fargesyn	Nedsatt fargesyn: rød-grønn-fargeblindhet	Total fargeblindhet
1	12	12	12
2	8	3	X
3	29	70	X
4	5	2	X
5	3	5	X

Deltakernr.:
--------------

6	15	17	X
7	74	21	X
8	6	X	X
9	45	X	X
10	5	X	X
11	7	X	X
12	16	X	X
13	73	X	X
14	X	5	X
15	X	45	X

**Tolkning**

- 13 eller flere plater leses korrekt → Normalt fargesyn
- 9 eller færre plater leses korrekt → Rød-grønn-fargeblindhet
- I tilfeller med 9 eller færre plater lest korrekt: hva angår plate 14 og 15 regnes det kun som abnormt dersom plate 14 leses som 5 og plate 15 leses som 45 OG at svarene på disse to avgis langt raskere enn svarene på plate 9 og 10.

**Resultat**

	X
Normalt fargesyn	
Nedsatt fargesyn: rød-grønn-fargeblindhet	
Total fargeblindhet	

**Eventuelle kommentarer:**


---



---



---



---



---

## H. Protocol for saliva samples



UNIVERSITETET I BERGEN

Institutt for klinisk psykologi

Prosjekt: ENLIGHT (Exploring new and optimal light conditions to improve cognition, mood, and health in people with dementia, prosjektnr. 275305)

Prosjektleder: Elisabeth Flo-Groeneboom, Professor, Institutt for klinisk psykologi, Universitetet i Bergen  
Ansvarlige for spyttprøvetaking: Louise Bjerrum (ph.d.-stipendiat), Oda Bugge Kambestad (vitenskapelig assistent), Kine Marie Andersen Hillestad (masterstudent)

### Smittevern

Spyttprøver tas med Salivette® (Sarstedt, Tyskland). Av smittevernhensyn vil Salivette®-prøvene bli forhåndsmerket med etiketter som tåler løsemiddel (sprit) og -80 grader (Brady EMEA, Belgia). Disse to kravene til merking av spyttprøver følges av flere laboratorier ved UiB og Haukeland universitetssykehus. ENLIGHT-prosjektgruppen har rådført seg med avdelingsingeniør Ingeborg Brønstad ved Klinisk Institutt 1, Det medisinske fakultet, og overingeniør Nina Harketstad ved Institutt for biologisk og medisinsk psykologi (IBMP), Det psykologiske fakultet. Begge er involvert i analyse av spyttprøver i ulike prosjekter. Spyttprøvene i ENLIGHT vil bli analysert av Nina Harketstad, under en sikkerhetsbenk som sikrer en trygg håndtering av spyttprøver som inneholder mulige SARS-CoV 2-virusvarianter.

### Protokoll for spyttprøvetaking

Spyttprøvene er organisert i to bokser; én boks brukes til transport av spyttprøver fra Lyslab til kjøleskap etter prøvetaking, en annen boks blir brukt til oppbevaring av spyttprøver i kjøleskap på Søvnlab, Christies gate 12, 5.etg. Oppbevaringsboksen blir også brukt til transport av spyttprøver fra kjøleskap til Biolaben på IBMP der Nina Harketstad legger prøvene på frys før de analyseres. Spyttprøvene bør transporteres til Nina Harketstad innen 2-3 dager etter prøvetaking. Spyttprøvene kan oppbevares i kjøleskap i maksimum én uke.

Tomme Salivette®-rør klar til spyttprøvetaking står plassert i et stativ i rommet deltakeren skal avlegge spyttprøve. Deltakerne skal selv ta spyttprøven. Forsøksledere ansvarlige for spyttprøvetaking vil dermed aldri være i direkte kontakt med prøven, men skal likevel bruke engangshansker egnet for laboratorier, munnbind type II-R og visir, samt holde minst én meters avstand til forsøkspersoner til enhver tid.

1. Forsøksleder gir grundig demonstrasjon av spyttprøvetaking ved bruk av et Salivette®-demo-rør.
2. Deltaker desinfiserer hender, tar Salivette®-prøve fra stativet, tar av lokket heller swab i munnen uten at munnen berører spyttprøve-røret.
3. Deltaker lar swab ligge inni munnen i angitt tid. NB! swab skal IKKE tygges på.
4. Deltaker fører swab tilbake i Salivette®-røret kun ved hjelp av tenner (munn skal ikke være i direkte kontakt med Salivette®-røret).
5. Deltaker setter på lokket på Salivette®-røret og setter prøven i egnet stativ.
6. Deltaker desinfiserer prøven og stativet med desinfiserende serviett utlevert av forsøksleder.



UNIVERSITETET I BERGEN

*Institutt for klinisk psykologi*

---

7. Deltaker legger desinfisert Salivette®-prøve i en plastlomme, desinfiserer utsiden av plastlommen med desinfiserende serviett og legger plastlommen i anvist transportboks.
8. Deltaker desinfiserer hender.
9. Forsøksleder frakter transportboks til kjøleskap, tar ut oppbevaringsboks og heller Salivette®-prøven over i oppbevaringsboks som deretter plasseres tilbake i kjøleskap.
10. Forsøksleder desinfiserer håndtak på kjøleskap, kaster engangshansker og desinfiserer hender.



## I. Authorization



---

<b>Region:</b> REK sør-øst D	<b>Saksbehandler:</b> Finn Skre Fjordholm	<b>Telefon:</b> 22 84 58 21	<b>Vår dato:</b> 17.02.2020	<b>Vår referanse:</b> 2019/680
			<b>Deres dato:</b>	REK sør-øst D

Vår referanse må oppgis ved alle henvendelser

Elisabeth Flo  
Universitetet i Bergen

### 2019/680 Effekten av ulike lysbetingelser på kognisjon og humør

**Forskningsansvarlig:** Universitetet i Bergen  
**Prosjektleder:** Elisabeth Flo

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av

Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst D) i møtet 08.05.2019. Vurderingen er gjort med hjemmel i helseforskningsloven § 10.

#### Prosjektleders prosjektbeskrivelse

*Demens er en progressiv sykdom med funksjonstap og ulike atferds- og psykologiske symptomer ved demens (APSD). Omlag 90% opplever APSD og søvnproblemer i løpet av sykdomsforløpet. De kausale mekanismene bak sammenhengen mellom døgnrytme, søvn, kognitiv fungering og APSD er ennå ikke kjent. Bruk av lys er en lovende behandling, og mangelen på systematiske og grunnleggende studier med mennesker med demens gjør dette til et viktig forskningsfelt. ENLIGHT-prosjektet vil undersøke hvordan lys påvirker kognisjon, humør og døgnrytme, samt å belyse hvordan dette kan anvendes i en klinisk kontekst. ENLIGHT har 4 målsetninger. 1) Teste effekten av ulike lysbetingelser på kognitiv prestasjon hos personer med demens 2) Teste effekten av ulike lysbetingelser på humør hos personer med demens 3) Teste effektene av lysromterapi hos eldre med demens som bor hjemme 4) Studere implementeringen av den nevnte behandlingen og støtte planene for at nevnte behandling kan bli et standard tilbud*

#### Vurdering

Saken ble første gang behandlet av REK sør-øst D i møtet den 8.5.2019. Komiteen fant at den foreliggende informasjonen ikke var tilstrekkelig til å fatte vedtak, og valgte å rette flere spørsmål til prosjektleder. Saken ble utsatt, og prosjektleder ble bedt om å svare på følgende spørsmål innen seks måneder:

1) Komiteen savner et klart definert endepunkt og suksesskriterier og ber om at dette klargjøres. Hvor stor må forskjellen være for at dette kan tenkes innført?

2) Samtykkeskrivet til pårørende må reformuleres slik at man henvender seg til pårørende og ikke pasient. Det vil for eksempel si at første setning i avsnittet «Hva innebærer studien» må det stå «I studien vil vi teste pasienten med anerkjente kliniske spørreskjema ...» i stedet for «I studien vil vi teste deg med anerkjente kliniske spørreskjema».

Vedlagt prosjektleders tilbakemelding fulgte en revidert protokoll, der det er tatt inn en lengre diskusjon og redegjørelse for hva som vil være å anse som endepunkt og suksesskriterium for intervensjonen.

Videre er det lagt ved et nytt informasjonsskriv for del 1 og 2. Det nye skrevet inneholder mindre informasjon enn det som ble lagt ved søknaden, og komiteen ber om at den nye versjonen forkastes, og at den versjonen som ble sendt inn sammen med søknaden blir brukt i prosjektet. Når dette er fylt ut med navn, kan det sendes til REK til orientering.

Det er også sendt inn reviderte informasjonsskriv for del 3. Komiteens merknad om informasjonsskrivet er etterfulgt, i tillegg til at det er foretatt enkelte, mindre endringer.

Det omsøkte prosjektet skal undersøke hvordan lys påvirker kognisjon, humør og døgnrytme hos personer med demens. Videre skal det belyses hvordan kunnskap om dette temaet kan anvendes i en klinisk kontekst. Det skal rekrutteres 34 deltakere som alle er eldre med demens og en kontrollgruppe bestående av 34 eldre uten demens og 34 unge friske voksne. Deltakerne skal fylle ut en rekke spørreskjemaer. Del 1 og 2 er lab-basert over to dager, og vil undersøke den umiddelbare effekten av ulike lysforhold. Deltagelse innebærer måling av søvn og aktivitet i uken forut for undersøkelsen. I del 3 vil behandlingsgruppen få installert terapilys i oppholdsrommet og kontrollgruppen vanlig lys i en periode på 16 uker. Det vil bli tatt spyttprøver fra deltakerne som destrueres innen to måneder, det vil ikke bli gjort genetiske undersøkelser. Det skal innhentes samtykke fra samtlige deltakere. I de tilfellene hvor deltakeren ikke er samtykkekompetent vil det innhentes samtykke fra pårørende.

Komiteen har vurdert søknaden og har ingen innvendinger til at studien gjennomføres som beskrevet i søknad, tilbakemelding fra prosjektleder og protokoll.

#### **Vedtak**

REK har gjort en helhetlig forskningsetisk vurdering av alle prosjektets sider. Prosjektet godkjennes med hjemmel i helseforskningsloven § 10.

Vi gjør samtidig oppmerksom på at etter ny personopplysningslov må det også foreligge et behandlingsgrunnlag etter personvernforordningen. Det må forankres i egen institusjon.

Godkjenningen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad, tilbakemelding fra prosjektleder og protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2023. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 31.12.2028. Forskningsfilen skal oppbevares atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Dersom man ønsker å foreta vesentlige endringer i forhold til formål, metode, tidsløp eller organisering, skal søknad sendes til den regionale komiteen for medisinsk og helsefaglig forskningsetikk som har gitt forhåndsgodkjenning. Søknaden skal beskrive hvilke endringer som ønskes foretatt og begrunnelsen for disse, jf. helseforskningsloven § 11.

Søker skal sende sluttmelding til REK sør-øst D på eget skjema senest seks måneder etter godkjenningsperioden er utløpt, jf. helseforskningsloven § 12.

REKs vedtak kan påklages, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sør-øst D. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst D, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Med vennlig hilsen

Finn Wisløff  
Professor em. dr. med.  
Leder

Finn Skre Fjordholm  
rådgiver

Kopi: [post@uib.no](mailto:post@uib.no)

**J. Descriptive statistics age, gender and chronotype****Descriptive Statistics**

	N	Minimum	Maximum	Mean	Std. Deviation
kjønn	12	1,00	2,00	1,5833	,51493
alder	12	18,00	28,00	22,4167	3,05877
Valid N (listwise)	12				

**Statistics**

chronotype

N	Valid	12
	Missing	0
Mean		4,0000
Median		4,0000
Std. Deviation		,60302
Minimum		3,00
Maximum		5,00

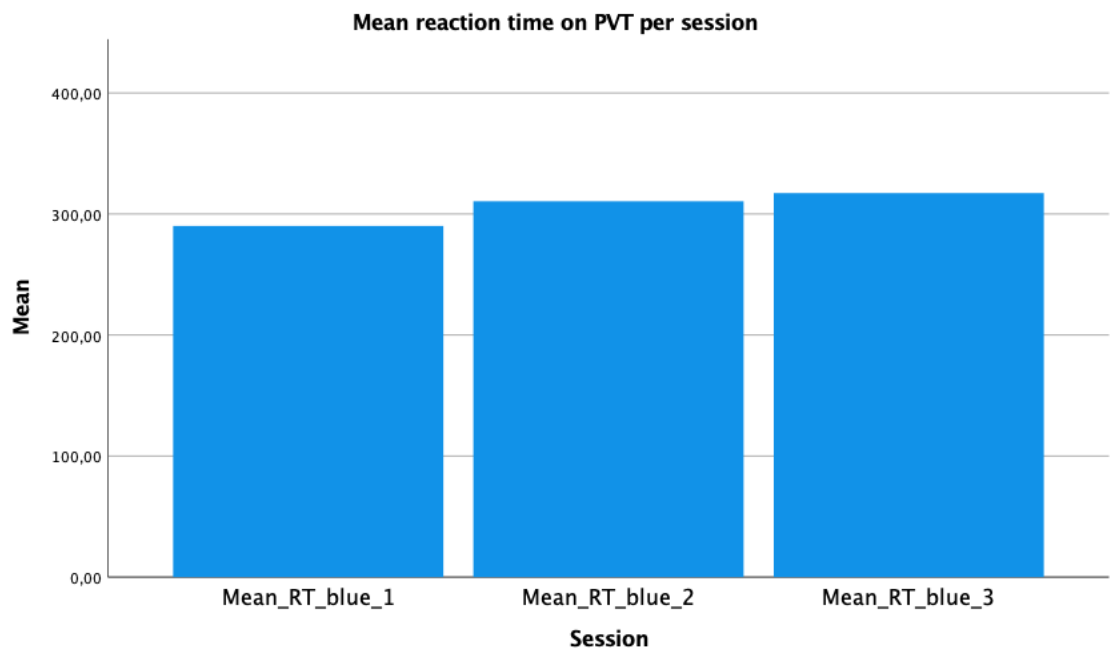
**chronotype**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	neither	2	16,7	16,7	16,7
	mod evening	8	66,7	66,7	83,3
	def evening	2	16,7	16,7	100,0
	Total	12	100,0	100,0	

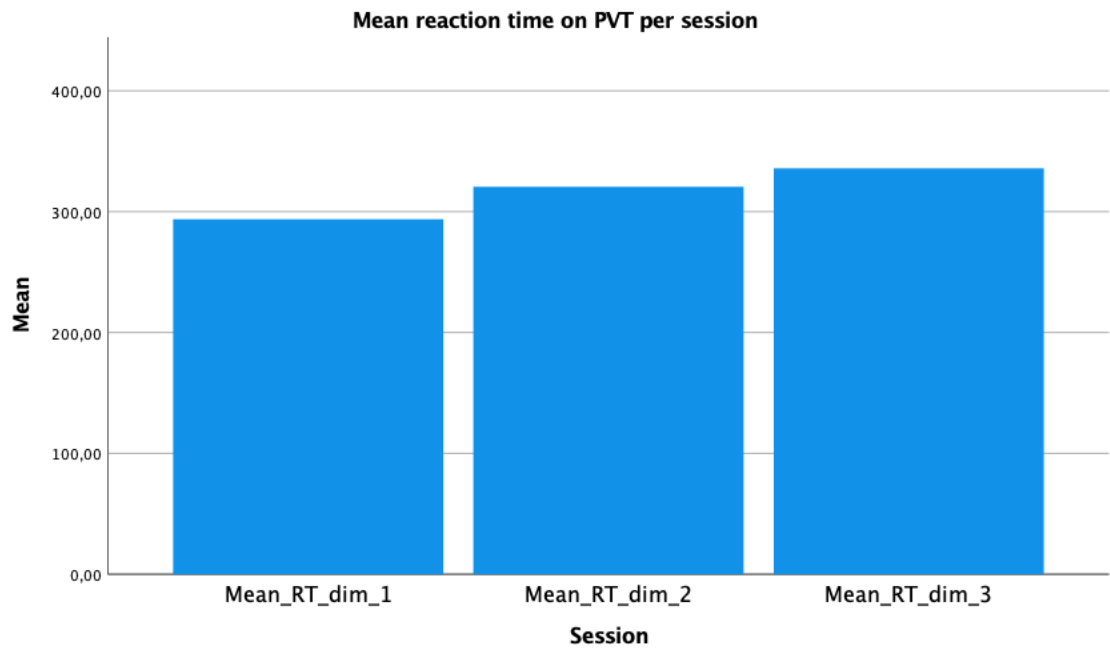
**K. Descriptive statistics from actigraphy data**

<b>Descriptive Statistics</b>					
	N	Minimum	Maximum	Mean	Std. Deviation
BL_TST1	12	352,00	445,57	404,4762	27,69288
MEAN_SE_BL	12	72,41	87,00	79,2513	4,46963
MEAN_SOL_BL	12	7,71	71,00	25,7222	18,59688
MEAN_WASO_BL	12	34,29	67,43	48,7381	9,79376
Total sleep time natt til blå lysbetingelse	12	238,00	509,00	357,7917	66,72857
Sleep efficiency natt til blå lysbetingelse	12	50,62	91,93	78,9283	12,29441
Sleep onset latency natt til blå lysbetingelse	12	,00	133,00	26,3333	38,13215
Wake after sleep onset natt til blå lysbetingelse	12	7,00	107,00	44,6667	31,19246
Total sleep time natt til dim lysbetingelse	12	264,00	647,00	368,0417	110,90751
Sleep efficiency natt til dim lysbetingelse	12	71,30	92,25	80,1483	7,48587
Sleep onset latency natt til dim lysbetingelse	12	,00	64,00	25,5000	21,88607
Wake after sleep onset natt til dim lysbetingelse	12	18,50	89,00	45,1667	22,19985
Valid N (listwise)	12				

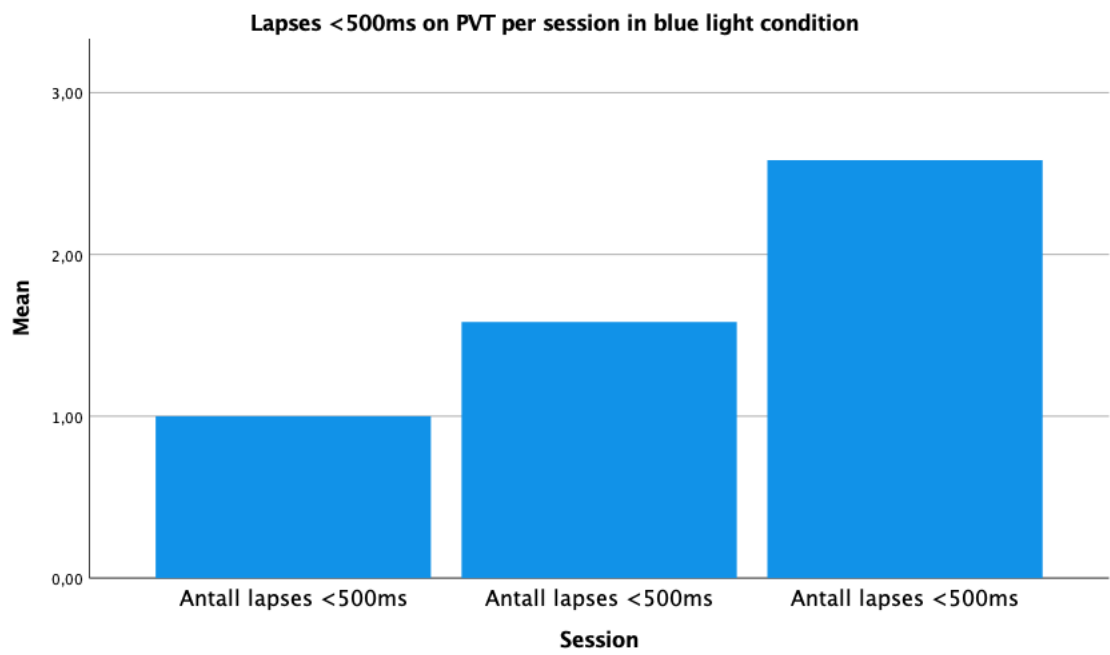
**L. Mean reaction time graph blue light condition graph**



**M. Mean reaction time dim light condition graph**

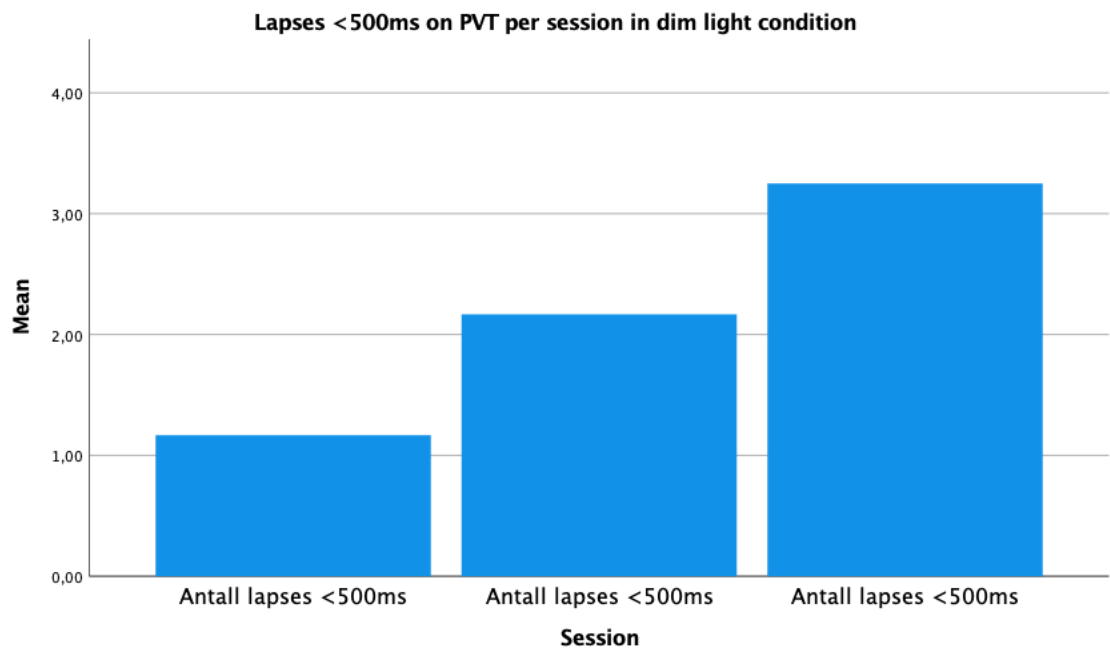


**N. Lapses <500ms for blue light condition graph**





**O. Lapses <500ms for dim light condition graph**



**P. Repeated measures ANOVA colour and session**

**Mauchly's Test of Sphericity<sup>a</sup>**

Measure: MEASURE\_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon <sup>b</sup>		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
colour	1,000	,000	0	.	1,000	1,000	1,000
session	,873	1,354	2	,508	,888	1,000	,500
colour * session	,873	1,356	2	,508	,887	1,000	,500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

- a. Design: Intercept  
Within Subjects Design: colour + session + colour \* session
- b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

**Tests of Within-Subjects Effects**

Measure: MEASURE\_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
colour	Sphericity Assumed	2075,415	1	2075,415	1,948	,190	,150
	Greenhouse-Geisser	2075,415	1,000	2075,415	1,948	,190	,150
	Huynh-Feldt	2075,415	1,000	2075,415	1,948	,190	,150
	Lower-bound	2075,415	1,000	2075,415	1,948	,190	,150
Error(colour)	Sphericity Assumed	11719,638	11	1065,422			
	Greenhouse-Geisser	11719,638	11,000	1065,422			
	Huynh-Feldt	11719,638	11,000	1065,422			
	Lower-bound	11719,638	11,000	1065,422			
session	Sphericity Assumed	15016,904	2	7508,452	11,156	<,001	,504
	Greenhouse-Geisser	15016,904	1,775	8459,040	11,156	<,001	,504
	Huynh-Feldt	15016,904	2,000	7508,452	11,156	<,001	,504
	Lower-bound	15016,904	1,000	15016,904	11,156	,007	,504
Error(session)	Sphericity Assumed	14806,563	22	673,026			
	Greenhouse-Geisser	14806,563	19,528	758,232			
	Huynh-Feldt	14806,563	22,000	673,026			
	Lower-bound	14806,563	11,000	1346,051			
colour * session	Sphericity Assumed	666,581	2	333,290	1,424	,262	,115
	Greenhouse-Geisser	666,581	1,775	375,549	1,424	,263	,115
	Huynh-Feldt	666,581	2,000	333,290	1,424	,262	,115
	Lower-bound	666,581	1,000	666,581	1,424	,258	,115
Error(colour*session)	Sphericity Assumed	5148,605	22	234,027			
	Greenhouse-Geisser	5148,605	19,524	263,701			
	Huynh-Feldt	5148,605	22,000	234,027			
	Lower-bound	5148,605	11,000	468,055			

## Q. Repeated measures ANOVA session, light and chronotype

### Mauchly's Test of Sphericity<sup>a</sup>

Measure: MEASURE\_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon <sup>b</sup>		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
colour	1,000	,000	0	.	1,000	1,000	1,000
session	,951	,450	2	,798	,953	1,000	,500
colour * session	,832	1,657	2	,437	,856	1,000	,500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + MEQ\_score

Within Subjects Design: colour + session + colour \* session

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

### Tests of Within-Subjects Effects

Measure: MEASURE\_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
colour	Sphericity Assumed	300,011	1	300,011	,274	,612	,027
	Greenhouse-Geisser	300,011	1,000	300,011	,274	,612	,027
	Huynh-Feldt	300,011	1,000	300,011	,274	,612	,027
	Lower-bound	300,011	1,000	300,011	,274	,612	,027
colour * MEQ_score	Sphericity Assumed	782,882	1	782,882	,716	,417	,067
	Greenhouse-Geisser	782,882	1,000	782,882	,716	,417	,067
	Huynh-Feldt	782,882	1,000	782,882	,716	,417	,067
	Lower-bound	782,882	1,000	782,882	,716	,417	,067
Error(colour)	Sphericity Assumed	10936,755	10	1093,676			
	Greenhouse-Geisser	10936,755	10,000	1093,676			
	Huynh-Feldt	10936,755	10,000	1093,676			
	Lower-bound	10936,755	10,000	1093,676			
session	Sphericity Assumed	5627,488	2	2813,744	4,668	,022	,318
	Greenhouse-Geisser	5627,488	1,907	2951,073	4,668	,024	,318
	Huynh-Feldt	5627,488	2,000	2813,744	4,668	,022	,318
	Lower-bound	5627,488	1,000	5627,488	4,668	,056	,318
session * MEQ_score	Sphericity Assumed	2751,301	2	1375,650	2,282	,128	,186
	Greenhouse-Geisser	2751,301	1,907	1442,791	2,282	,131	,186
	Huynh-Feldt	2751,301	2,000	1375,650	2,282	,128	,186
	Lower-bound	2751,301	1,000	2751,301	2,282	,162	,186
Error(session)	Sphericity Assumed	12055,262	20	602,763			
	Greenhouse-Geisser	12055,262	19,069	632,182			
	Huynh-Feldt	12055,262	20,000	602,763			
	Lower-bound	12055,262	10,000	1205,526			
colour * session	Sphericity Assumed	114,582	2	57,291	,233	,794	,023
	Greenhouse-Geisser	114,582	1,712	66,924	,233	,761	,023
	Huynh-Feldt	114,582	2,000	57,291	,233	,794	,023
	Lower-bound	114,582	1,000	114,582	,233	,640	,023
colour * session * MEQ_score	Sphericity Assumed	229,389	2	114,695	,466	,634	,045
	Greenhouse-Geisser	229,389	1,712	133,980	,466	,606	,045
	Huynh-Feldt	229,389	2,000	114,695	,466	,634	,045
	Lower-bound	229,389	1,000	229,389	,466	,510	,045
Error(colour*session)	Sphericity Assumed	4919,216	20	245,961			
	Greenhouse-Geisser	4919,216	17,121	287,318			
	Huynh-Feldt	4919,216	20,000	245,961			
	Lower-bound	4919,216	10,000	491,922			

## R. Repeated measures ANOVA session light and total sleep time before blue light condition

### Mauchly's Test of Sphericity<sup>a</sup>

Measure: MEASURE\_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon <sup>b</sup>		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
colour	1,000	,000	0	.	1,000	1,000	1,000
session	,865	1,308	2	,520	,881	1,000	,500
colour * session	,825	1,729	2	,421	,851	1,000	,500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + BLUE\_TST

Within Subjects Design: colour + session + colour \* session

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

### Tests of Within-Subjects Effects

Measure: MEASURE\_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
colour	Sphericity Assumed	604,710	1	604,710	,569	,468	,054
	Greenhouse-Geisser	604,710	1,000	604,710	,569	,468	,054
	Huynh-Feldt	604,710	1,000	604,710	,569	,468	,054
	Lower-bound	604,710	1,000	604,710	,569	,468	,054
colour * BLUE_TST	Sphericity Assumed	1096,568	1	1096,568	1,032	,334	,094
	Greenhouse-Geisser	1096,568	1,000	1096,568	1,032	,334	,094
	Huynh-Feldt	1096,568	1,000	1096,568	1,032	,334	,094
	Lower-bound	1096,568	1,000	1096,568	1,032	,334	,094
Error(colour)	Sphericity Assumed	10623,070	10	1062,307			
	Greenhouse-Geisser	10623,070	10,000	1062,307			
	Huynh-Feldt	10623,070	10,000	1062,307			
	Lower-bound	10623,070	10,000	1062,307			
session	Sphericity Assumed	690,707	2	345,354	,471	,631	,045
	Greenhouse-Geisser	690,707	1,762	392,064	,471	,608	,045
	Huynh-Feldt	690,707	2,000	345,354	,471	,631	,045
	Lower-bound	690,707	1,000	690,707	,471	,508	,045
session * BLUE_TST	Sphericity Assumed	150,007	2	75,004	,102	,903	,010
	Greenhouse-Geisser	150,007	1,762	85,148	,102	,881	,010
	Huynh-Feldt	150,007	2,000	75,004	,102	,903	,010
	Lower-bound	150,007	1,000	150,007	,102	,756	,010
Error(session)	Sphericity Assumed	14656,555	20	732,828			
	Greenhouse-Geisser	14656,555	17,617	831,946			
	Huynh-Feldt	14656,555	20,000	732,828			
	Lower-bound	14656,555	10,000	1465,656			
colour * session	Sphericity Assumed	387,062	2	193,531	,830	,450	,077
	Greenhouse-Geisser	387,062	1,702	227,364	,830	,435	,077
	Huynh-Feldt	387,062	2,000	193,531	,830	,450	,077
	Lower-bound	387,062	1,000	387,062	,830	,384	,077
colour * session * BLUE_TST	Sphericity Assumed	485,905	2	242,952	1,042	,371	,094
	Greenhouse-Geisser	485,905	1,702	285,425	1,042	,363	,094
	Huynh-Feldt	485,905	2,000	242,952	1,042	,371	,094
	Lower-bound	485,905	1,000	485,905	1,042	,331	,094
Error(colour*session)	Sphericity Assumed	4662,700	20	233,135			
	Greenhouse-Geisser	4662,700	17,024	273,891			
	Huynh-Feldt	4662,700	20,000	233,135			
	Lower-bound	4662,700	10,000	466,270			

## S. Repeated measures ANOVA session light and total sleep time before dim light condition

### Mauchly's Test of Sphericity<sup>a</sup>

Measure: MEASURE\_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon <sup>b</sup>		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
colour	1,000	,000	0	.	1,000	1,000	1,000
session	,909	,858	2	,651	,917	1,000	,500
colour * session	,984	,146	2	,929	,984	1,000	,500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + DIM\_TST

Within Subjects Design: colour + session + colour \* session

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

### Tests of Within-Subjects Effects

Measure: MEASURE\_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
colour	Sphericity Assumed	482,854	1	482,854	,415	,534	,040
	Greenhouse-Geisser	482,854	1,000	482,854	,415	,534	,040
	Huynh-Feldt	482,854	1,000	482,854	,415	,534	,040
	Lower-bound	482,854	1,000	482,854	,415	,534	,040
colour * DIM_TST	Sphericity Assumed	94,603	1	94,603	,081	,781	,008
	Greenhouse-Geisser	94,603	1,000	94,603	,081	,781	,008
	Huynh-Feldt	94,603	1,000	94,603	,081	,781	,008
	Lower-bound	94,603	1,000	94,603	,081	,781	,008
Error(colour)	Sphericity Assumed	11625,035	10	1162,503			
	Greenhouse-Geisser	11625,035	10,000	1162,503			
	Huynh-Feldt	11625,035	10,000	1162,503			
	Lower-bound	11625,035	10,000	1162,503			
session	Sphericity Assumed	4770,230	2	2385,115	3,553	,048	,262
	Greenhouse-Geisser	4770,230	1,833	2602,001	3,553	,053	,262
	Huynh-Feldt	4770,230	2,000	2385,115	3,553	,048	,262
	Lower-bound	4770,230	1,000	4770,230	3,553	,089	,262
session * DIM_TST	Sphericity Assumed	1379,973	2	689,987	1,028	,376	,093
	Greenhouse-Geisser	1379,973	1,833	752,729	1,028	,371	,093
	Huynh-Feldt	1379,973	2,000	689,987	1,028	,376	,093
	Lower-bound	1379,973	1,000	1379,973	1,028	,335	,093
Error(session)	Sphericity Assumed	13426,590	20	671,329			
	Greenhouse-Geisser	13426,590	18,333	732,375			
	Huynh-Feldt	13426,590	20,000	671,329			
	Lower-bound	13426,590	10,000	1342,659			
colour * session	Sphericity Assumed	1860,586	2	930,293	5,643	,011	,361
	Greenhouse-Geisser	1860,586	1,968	945,288	5,643	,012	,361
	Huynh-Feldt	1860,586	2,000	930,293	5,643	,011	,361
	Lower-bound	1860,586	1,000	1860,586	5,643	,039	,361
colour * session * DIM_TST	Sphericity Assumed	1851,462	2	925,731	5,615	,012	,360
	Greenhouse-Geisser	1851,462	1,968	940,652	5,615	,012	,360
	Huynh-Feldt	1851,462	2,000	925,731	5,615	,012	,360
	Lower-bound	1851,462	1,000	1851,462	5,615	,039	,360
Error(colour*session)	Sphericity Assumed	3297,143	20	164,857			
	Greenhouse-Geisser	3297,143	19,683	167,514			
	Huynh-Feldt	3297,143	20,000	164,857			
	Lower-bound	3297,143	10,000	329,714			