Chronobiology Meets Work Life

*Chronotype-dependent nap behaviour and light exposure on work- and free days*

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______________________________
Joana L. Matera
Foreword

While writing this thesis ‘Chronobiology Meets Work Life: Chronotype-dependent nap behaviour and light exposure on work- and free days’, the idea grew to create a collage as front page, which combines the two research projects of my doctoral thesis. I realized that every person I showed the picture to, had different associations in regard to the meaning of the components. If this cover captures one’s imagination, the most important purpose of it will be fulfilled.

The first study investigates sleep-wake behaviour of shift workers. They are awake and asleep at alternating times of day, during light as well as during the dark phase, symbolized by the sun as well as by the moon and stars respectively. When speaking about chronotypes, there is a very common metaphor: the lark as an early bird symbolizing early chronotypes and the owl as a nocturnal bird displaying late chronotypes. Those two birds on the cover page symbolize chronotype differences amongst the study sample.

The second study analyses light profiles with regards to individuals’ internal time (again indicated as lark and owl). Light and darkness are the most important synchronizers for the biological clock, also for this study symbolization of day (sun) and night (moon and stars) bear a meaning. Furthermore, the spectral composition of light is important, illustrated as colour gradient between night and day.

Finally, I hope the cover page already aroused curiosity to read the outcome of my last 3½ years!

Joana L. Matera
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1 General Introduction

Life on earth is dominated by the daily 24-hour pattern of light and darkness. Every organism, ranging from eukaryotes to a complex organism carries an endogenous clock, which appears to have been a selection advantage during evolution. It seems as if this specific development made them able to predict the appearance of predators and sense the availability of food and with that essential energy, e.g. in terms of sunlight. The absence or presence of light and darkness provides temporal niches for cellular mechanisms such as DNA-replication, elongation or cell division, which are extremely light sensitive and conducted during dark phase. On the contrary, energy supply (at least for diurnal organisms) is most necessary during light phase.

In order to adapt to the naturally provided light-dark cycle, a time-measuring system is needed, an endogenous clock, comprising a self-sustaining and persistent oscillator, which synchronizes to environmental zeitgeber\(^1\) and is compensated against temperature changes. Entrainability\(^2\) of endogenous clocks ensures flexibility towards zeitgeber changes.

1.1 The Transcriptional-Translational Feedback Loop

The measurement of time is conducted by a so-called transcriptional-translational feedback loop; Fig. 1 provides a simplified overview. Transcription and translation of genes and proteins, hetero-dimerization, nucleus-cytoplasm-nucleus translocation, as well as two feedback loops are critical steps to maintain a nearly 24-hour rhythm (Vielhaber et al., 2000). In cells lacking a nucleus (e.g. erythrocytes), a 24-hour redox cycle and a rhythmic dimerization of peroxiredoxin has been described (O’Neill et al., 2011).

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\(^1\) German: time cue. Forcing oscillation which entrains biological rhythms.
\(^2\) The term entrainment is derived from the French word ‘entrainer’; carry over, sweep along; meaning the coupling of a self-sustained oscillator to a zeitgeber.
In humans four clock genes form the primary loop: \textit{Clock} (the equivalent in neurons is \textit{Npas2} (DeBruyne et al., 2007)), \textit{Bmal1}, \textit{Period1/2/3} (\textit{Per}) and \textit{Cryptochrome1/2} (\textit{Cry}). The positive branch of the primary feedback loop consists of Clock and Bmal1, which form a heterodimer in the cytoplasm (Gekakis et al., 1998; Reppert et al., 2001). Due to the histone acetyl transferase (HAT) activity of Clock, the Clock/Bmal1 complex is a transcription factor for many different genes. The HAT activity opens the gene locus of \textit{Per} and \textit{Cry}, allowing the RNA-polymerase to bind (Doi et al., 2006), which increases expression levels. In the cytoplasm casein kinase 1 δ or ε phosphorylates Per, either stabilizing or degrading the protein, depending on the location of phosphorylation (Keesler et al., 2000). The heterodimer of Per and Cry inhibit their own transcription (negative part of the feedback loop) by destroying the HAT activity of the Clock/Bmal1 complex, either by phosphorylation or conformational changes, leading to a re-condensing of the DNA-strand. Generally, \textit{Per} and \textit{Cry} levels are high during internal day, whereas \textit{Bmal1} and \textit{Clock} (or \textit{Npas2}) are expressed during internal night (Dardente et al., 2002; Reppert et al., 2001).

\begin{figure}
\centering
\includegraphics[width=\textwidth]{transcriptional_translational_feedback_loop.png}
\caption{Transcriptional-translational feedback loop. Positive feedback loop including \textit{Clock} and \textit{Bmal1} is indicated in green. Negative feedback regulation with Period (\textit{Per1/2/3}) and Cryptochrome (\textit{Cry}) is visualized with red arrows. The black arrow represents phosphorylation by casein kinase 1 δ or ε. Modified from: (Reppert et al., 2001).}
\end{figure}
Additionally, a second loop stabilizes the transcriptional-translational rhythm by regulating expression levels of Bmal1. The heterodimer Clock/Bmal1 or Npas2/Bmal1 binds not only to the promoter region of Cry and Per, but also enhances expression of RevErba and RORα (Guillaumond et al., 2005). These two proteins compete for the binding site (ROR element) in the promoter region of Bmal1. RORα activates, whereas RevErba inhibits transcription of Bmal1.

Because the oscillator ticks only in an approximately 24-hour rhythm with most clocks being slightly longer than 24 hours (on average 24.2 hours (Czeisler et al., 1999)), it is called circadian\(^3\) oscillator. This slightly longer rhythm requires a day-to-day correction in order to adapt to the naturally provided 24-hour day. This topic will be further addressed in chapter 1.3 ‘Entrainment’.

The transcriptional-translational feedback loop persists in every cell. It is understandable that a complex system consisting of cells, tissues and organs only works properly, if all cells are synchronized to the same phase. In order to assure synchronicity of all peripheral clocks, a superordinate system, a master clock, is required.

### 1.2 The ‘Master Clock’: Suprachiasmatic Nucleus

A small paired region of the anterior hypothalamus, the suprachiasmatic nucleus (SCN), is the location of our endogenous ‘master clock’. The SCN comprises only 20,000 neurons (Reppert et al., 2001). The major tasks of the SCN are 1) producing a stable endogenous rhythm, 2) active entrainment to time cues and 3) forwarding time information to the periphery in order to synchronize cellular clocks to the same phase.

The SCN itself can be divided into a core and a shell region. Gamma-amino butyric acid (GABA, one of the few inhibiting neurotransmitter of the mammalian brain) and gap junctions interconnect neurons within the SCN (Liu et al., 2000; van den Pol et al., 1993). The ventrolateral core neurons are mainly coupled via vasoactive intestinal peptide (VIP) and immediately phase shift to a new time

\(^3\) Circa: about, dies: day (Latin origin).
stimulus, *e.g.* after a transmeridian flight or an altered light-dark pattern in shift workers (Leak et al., 2001). The shell region is coupled via arginine vasopressin (AVP) (Meijer et al., 2012). Here the synchronization to a new light-dark pattern is slower. Depending on the width of the phase shift, a complete adaption takes a couple of days. Even under fully entrained conditions, SCN neurons fire in different phases (van Oosterhout et al., 2012), thus there is not 'the one' SCN output phase (Antle et al., 2005).

The output-neurons of the SCN are mostly GABAergic and therefore inhibitory (Chou et al., 2003). The SCN directly innervates only a few brain regions. One is the ventrolateral preoptic nucleus of the hypothalamus (VLPO), a circuit responsible for sleep initiation (Chou et al., 2002; Saper et al., 2005). But the vast majority of output neurons go to the ventral and dorsal SPZ (subparaventricular zone), dorsal to the SCN (Saper, 2013). Because of the inhibiting neurotransmitter GABA, the SPZ fires in anti-phase to the SCN. The SPZ is an important brain region for maintaining rhythms. Lesions of the vSPZ in mice lead to a loss of rhythmicity in locomotor activity, feeding and fasting cycle as well as sleep-wake patterns. Body temperature rhythm as well as melatonin secretion remained mainly unaffected, even if reduced in amplitude (Saper, 2013). Lesions of the dSPZ on the other hand resulted in a loss of rhythmicity in core body temperature. How exactly core body temperature is controlled needs to be elucidated, but research suggests that temperature modulation throughout the 24-hour day synchronizes peripheral clocks to the same phase (Buhr et al., 2010).

Only a few efferent neurons of the SCN directly control melatonin secretion. The darkness hormone melatonin gets secreted as soon as the SCN stops inhibiting neurons of the paraventricular nucleus of the hypothalamus (PVN). The PVN forwards its signal to the brainstem, which stimulates the pineal gland via the activating neurotransmitter noradrenalin (Karasek et al., 2006). GTP-binding proteins, localized in the cell membrane, activates adenylation cyclase, which synthetizes the cellular messenger cAMP from ATP. Elevated cAMP levels stimulate N-acetyltransferase activity and therefore the synthesis of melatonin from the amino acid tryptophan (Karasek et al., 2006). Within the human body,
nearly every tissue contains melatonin receptors. Hence melatonin is an important output, potentially also part of the synchronizing process of peripheral clocks, which is controlled by the SCN.

1.3 Entrainment

The intracellular oscillation of transcription and translation produces stable internal days with an approximately period length (τ) of 24 hours. In some individuals the oscillator length is longer, in others shorter than the zeitgeber cycle (T). This difference requires a day-to-day correction in order to prevent free-running. Free-running clocks are not entrained to a zeitgeber and run with their individual period length, so that rhythms of melatonin, cortisol and body temperature either successively advance or delay over the course of time. The term entrainment originates from the French word ‘entraîner’, meaning ‘to carry over’ or ‘to sweep along’. Entrainment is the active synchronization of the circadian oscillator to a zeitgeber (Roenneberg et al., 2013).

1.3.1 Entrainment by Light

When chronobiology was in child’s shoes, it was assumed that, different from all other animals, human beings were rather entrainable by social cues or even regular sounds and not by light (Wever, 1985). Evidence that social cues do not entrain biological clocks, emerged from observations in totally blind individuals, often displaying a free-running rhythm (Lewy et al., 1983; Lockley et al., 1997; Sack et al., 1992). Today it is known that light is the primary synchronizer of the mammalian clock. The mammalian eye contains, besides the well-known rods and cones, a third light receptor, the photosensitive retinal ganglion cells (Berson et al., 2002; Freedman et al., 1999). These receptors are most sensitive towards high frequent wavelengths of the blue spectrum, reaching its maximal sensitivity at 480nm (Brainard et al., 2001; Thapan et al., 2001). In blind individuals lacking the visual part of photo-perception, this non-visual pathway can still be functional, allowing synchronization (Lockley et al., 1997). If the non-
visual pathway is defective, but the visual system is fully intact, rods and cones take over for an accurate entrainment. With increasing age, the lens of the eye blurs and becomes yellowish. The blurred lens possibly filters blue wavelengths, so that light permeability is reduced. Yet, there is evidence that the biological system flexibly adapts to this progressive alteration and remains light sensitive comparable to younger persons (Benloucif et al., 2006; Gimenez et al., 2014; Najjar et al., 2014).

The light information is forwarded via the retino-hypothalamic tract to the SCN. The SCN actively synchronizes to the given time cues. The core region of the SCN immediately adapts its phase to the light stimulus, which takes place on a molecular level. Being located directly above the optic chiasm, the core region of the SCN gets innervated by glutamergic neurons. Glutamate causes an opening of Ca²⁺ ion channels as well as an elevation of intracellular cAMP concentrations (Ding et al., 1998). Due to this, cAMP response element binding (CREB) is phosphorylated (Ginty et al., 1993), homodimerizes and binds to the cAMP response element in the promoter region. With that transcription of many different genes gets elevated, one of them is the clock gene Per1 (Shigeyoshi et al., 1997). Whereas a light stimulus immediately elevates expression levels of Per1, Cry levels adjust very slowly and in parallel to the sleep-wake behaviour during phase advancing (Reddy et al., 2002). On the contrary, Cry expression levels immediately adapt to a delayed light-dark pattern. Cry functions as a break in advancing entrainment processes (Reddy et al., 2002). This phenomenon is obvious during entrainment after a transmeridian flight. Adjustment to a later light-dark rhythm (as in westward flights) is quick, phase shifting the endogenous period 92 minutes later per day. Entrainment to an earlier phase (eastward flight) is slower, with only 50 minutes phase shift per day (Haus et al., 2013). Most clocks are slightly longer than 24 hours and therefore can more easily delay their phase; swimming with the current is easier than swimming against it.

The non-visual system differs in some aspects from the visual light perception. Since the circadian system integrates light intensities over a certain amount of time, the light history is very important. If only exposed to dim light
levels, the circadian oscillator will get increasingly sensitive towards light stimuli as compared to a day spent under bright sunlight. Additionally, blue spectral composition of light, high light intensities (bright artificial or sun light) and zeitgeber strength\(^4\) positively increase the effect of light on the biological system.

### 1.3.2 Entrainment Concepts

The two colleagues Pittendrigh and Aschoff had different concepts in regard to entrainment of circadian systems by light (Daan, 2000). Both concepts attempted to explain the different effects of light: a light stimulus in the early endogenous day causes an earlier output phase; light during the late internal day postpones the rhythm.

Aschoff's approach considered clocks under entrained conditions. His model postulated a velocity change after a bright light stimulus, either compressing or expanding internal period length. Following this 'Velocity Response Curve', acceleration or deceleration depended on internal time: morning light accelerates, whereas evening light retards velocity of the oscillator and therefore influences period length (Daan, 2000). On the contrary, Pittendrigh analysed responses of circadian systems under constant conditions. A light stimulus either causes a phase advance or a delay, depending on internal time, but the internal period length remained unaffected. Pittendrigh’s ‘Phase Response Curve’ (PRC) is still prevailing today (Czeisler et al., 1989; Jewett et al., 1997; Khalsa et al., 2003). Even though increasing light intensities enhance effects on a circadian system, an ‘Intensity Response Curve’ has never been properly described (Duffy et al., 2005).

In 2010, Roenneberg and colleagues published a concept, which does not make any assumptions in terms of velocity or phase changes (Ronneberg et al., 2010b). This concept is based on the property of the mammalian circadian system to integrate light signals at different circadian phases (Ronneberg et al., 2010a). The ‘Circadian integrative Response Characteristic’ (CiRC) not only

\(^4\) Difference of light intensities between light and dark phase.
Chapter 1: General Introduction

considers single light pulses, but rather light history over a course of time. Similar to Aschoff’s approach, it is based on entrained conditions. The ratio of integrated light exposure between compressing (internal forenoon) and expanding (internal afternoon) proportion determines the net-effect of light, either advancing or delaying the circadian system (Roenneberg et al., 2010a).

1.3.3 Entrainment by Other Factors

Besides light, also other factors function as zeitgeber for the circadian pacemaker. It was shown that metabolic conditions effects circadian rhythmicity by influencing intracellular redox states (Bass, 2012). The redox state of NADH and NADPH alters the DNA-binding affinity of the heterodimer Clock/Bmal1 (Mendoza, 2007) and can therefore influence the speed of the intracellular transcriptional-translational feedback loop (Sahar et al., 2012). Food furthermore entrains peripheral brain regions in SCN-ablated mice, traceable in food anticipatory activity. This activity is tightly synchronized to the feeding schedule and persists even in the absence of food (Saper, 2013; Stephan, 2002). The food entrainable oscillator (FEO) somehow feeds forward to the SCN. Yet, the FEO is not understood or even localized, but a lesion in the parabrachial nucleus of the brainstem could at least partly inhibit food anticipatory activity (Davidson et al., 2000).

Against the long prevailing believe that human circadian clocks are (compared to animals) only sensitive towards social zeitgebers, Duffy and colleagues demonstrated that not social cues, food or sleep timing, but only light entrain circadian clocks to a new schedule (Duffy et al., 1996). If the intrinsic oscillator cycles with a period length close to 24 hours and in similar phase to the zeitgeber cycle, weak synchronizers (e.g. food) will be sufficient for maintaining entrainment. Wide phase differences require strong synchronizing signals. Only light is a strong synchronizer for clocks with diverging phase or period length from the zeitgeber cycle (Duffy et al., 2009).
Visually blind individuals with functional photosensitive retinal ganglion cells (pRGC) or individuals without pRGC but intact rods and cones, entrain via normal light transduction. In totally blind individuals (lacking rods, cones and pRGC) melatonin was shown to be a strong synchronizer (Skene et al., 2007) and can prevent circadian oscillators in blinds from free-running (Sack et al., 1991).

1.4 Phase of Entrainment

So far, different entrainment concepts as well as zeitgebers are described. Not all clocks display the same phase of entrainment; they are differently embedded to the light-dark cycle. Phase of entrainment (Ψ) is the phase angle difference between zeitgeber and internal period and also called chronotype. People with a longer internal period length (τ>24 hours or late chronotypes) embed very late into the zeitgeber cycle, resulting in late melatonin onset or sleep times. In comparison, people with short endogenous periods (τ<24 hours, early chronotypes) show an earlier phase of entrainment with early hormone secretion (Duffy et al., 2001).

How clocks embed to a 24-hour light-dark cycle depend on individuals’ sensitivity towards the zeitgeber, genetic inheritance, age, sex and light exposure. Among a population the phase of entrainment, here measured as corrected mid-sleep on free days, is approximately normally distributed (see Fig. 2): the majority displays an intermediate chronotype. Only very few clocks are embedded very late/early into the external 24-hour day (Ronneberg et al., 2007a).
Fig. 2. German chronotype-distribution. Chronotype, as MSF, was derived from MCTQ entries, n=72,400. From: Roenneberg, personal communication, state: 02.2013.

1.4.1 Measuring Phase of Entrainment

Since Aschoff and Pittendrigh, there is still an on-going discussion about the assessment of chronotype under entrained or rather constant conditions, for a detailed disquisition see (Ronneberg et al., 2013). Constant routine and forced desynchrony eliminate masking effects of light, activity and food intake (or even sleep) on circadian output rhythms in order to measure the unmasked cycle length of the oscillator. In constant routine protocols, participants are kept awake for a minimum of 48 hours. Forced desynchrony protocols consist of extremely short (<20h) or long (>28h) light-dark patterns, which are both beyond the range of entrainment. In this protocol sleep is permitted. In both protocols circadian phase and period length is assessed via core body temperature, cortisol or melatonin onset (Duffy et al., 2002b). Because core body temperature rhythms are sensitive towards physical activity or food intake, both is restricted in constant routine and forced desynchrony. Melatonin is highly sensitive towards light that is why both protocols are conducted in dim light. Dim light melatonin onset (DLMO) can be measured in saliva, blood or urine, sampled for more than 24 hours minimum (Lewy et al., 1999). But these conditions (as constant dim light, food and sleep restriction) were never a selection criterion in evolution. As far as we know, life on earth developed under the 24-hour cycle of light and darkness.
Less invasive and complex are questionnaires for measuring the behavioural component of the circadian clock under entrained conditions. General advantages of questionnaire-based chronotype assessment are the non-invasiveness, easy availability, cheap costs as well as short duration of assessment. There are many different questionnaires available all enquiring sleep-wake habits. The most prominent one is the Morningness-Eveningness Questionnaire (MEQ) (Horne et al., 1976), but there are many more, such as the Circadian Type Inventory (Di Milia et al., 2005), the Preferences Scale (Smith et al., 2002), the Composite Scale of Morningness (CSM) (Smith et al., 1989) and the Diurnal Type Scale (Torsvall et al., 1980).

In both of the following studies, the Munich Chronotype Questionnaire (MCTQ) developed by Roenneberg and colleagues was used for chronotype assessment (Roenneberg et al., 2003). In comparison to the other questionnaires the MCTQ does not ask for diurnal preference, it determines phase of entrainment as midpoint of sleep on free days, corrected for oversleep, due to accumulated sleep loss during the preceding workweek (MSF_{sc}). In rotational shift workers sleep patterns change drastically throughout the schedule. In order to determine shift workers’ chronotype, the MCTQ provides a shift work version, the MCTQ_{Shift} (Juda et al., 2013b). Questionnaire-based chronotype assessment is very accurate and correlates with biological markers. The MSF_{sc} correlates with clock gene expression of *Per1, 2* and *RevErba* as well as with melatonin profiles (Novakova et al., 2013). Yet, the small risk remains that participants’ MSF_{sc} does not project the internal phase of entrainment. Very seldom is the phenomenon of ‘internal desynchrony’, where sleep-wake behaviour is uncoupled from other circadian outputs as core body temperature or hormone secretion.

### 1.4.2 Chronotype and Genetics

The predisposition of being rather early or late is inherited (Jones et al., 1999). Early chronotypes display a shorter and late chronotypes a longer internal period length (Duffy et al., 2001).
Very short intrinsic period lengths were shown to be associated with a mutation in the Per2 gene. This mutation causes an under-phosphorylation of Per2 by casein kinase 1 δ or ε, which in turn weakens stabilization and promotes degradation of Per2 (Keesler et al., 2000). A short cycle length of the oscillator is the consequence, visible in an advanced sleep phase syndrome (Hamet et al., 2006). Not equally understood is the association between genes and the delayed sleep phase syndrome (Osland et al., 2011). Furthermore, the long repeat allele of a Per3 polymorphism has been associated with earlier and the short allele with later chronotypes (Archer et al., 2003).

1.4.3 Chronotype and Light

Life is the most important synchronizer of circadian clocks. Besides light no other zeitgeber is able to synchronize the SCN (Duffy et al., 1996). Before the invention of artificial light, we spent most of our time awake outside during photoperiod. Nowadays our life moved inside biologically ‘dark’ buildings, with light intensities of less than 500lx. In comparison, at a cloudy day light intensities of 10,000lx and on sunny days of more than 100,000lx can be measured.

By turning artificial light on and off, human beings actively create their own light-dark cycles with unnatural long and high light exposures in the evening (Wright et al., 2013). Given too little and poorly timed entrainment signals, the clock does not synchronize properly to the light-dark cycle. Indeed it was shown that few time spent outside was related to late chronotypes (Roenneberg et al., 2007c). On the contrary, increasing light intensities during the day and reduced light during internal night improved entrainment. Participants of this ‘camping study’ showed a tight adjustment to sunrise and sunset as well as an advancing in phase of entrainment (Wright et al., 2013).

How the clock embeds to the light-dark cycle is highly dependent on longitude (time zone). Roenneberg and colleagues showed that the population of Germany is entrained to sunrise, with eastern inhabitants being exactly 36 minutes (the time the sun needs to move from east to west) earlier chronotypes than western inhabitants (Roenneberg et al., 2007b).
Furthermore, it was shown that people living in urban regions experience less light as compared to their rural neighbours and display an averagely later chronotype (Roenneberg et al., 2013).

1.4.4 Chronotype, Age and Sex

Chronotype displays a clear age-dependency. Both cross-sectional and longitudinal studies showed that children are generally early chronotypes, but successively become later chronotypes during their adolescence (Crowley et al., 2014; Gau et al., 2003; Roenneberg et al., 2004). On average, the turning point is at the age of 19 for women and 21 for men. From then on chronotype progressively advances until elderly end up at a chronotype comparable to their young grandchildren, see Fig. 3 (Roenneberg et al., 2004). Generally, females are slightly earlier chronotypes than males (Adan et al., 2002).

![Chronotype chart](image)

Fig. 3. Age- and sex-dependency of chronotype. Grey areas display significant differences between males (open circles, grey line) and females (filled circles, black line). From: (Roenneberg et al., 2004).

1.4.5 Excursus: Chronotype, Personality and Lifestyle

The association of chronotype and personality has been often discussed. Psychological diseases or mood disorders (e.g. anxiety, neuroticism, major depressive disorders) are often attributed to late chronotypes (Kitamura et al., 2010; Mecacci et al., 1998). Late chronotypes are found to be more extroverted
and suffer more often from sleep complaints as insomnia and nightmares (Larsen, 1985; Merikanto et al., 2012). Research found late chronotypes displaying a less regular and unhealthier lifestyle (Fleig et al., 2009; Monk et al., 2004; Sato-Mito et al., 2011). Food choices were of poorer quality and general calorie uptake was elevated. Furthermore, being a late chronotype was associated with less physical activity, increased uptake of alcohol and cigarette consumption (Urban et al., 2011).

All these findings can be explained with increased circadian misalignment and curtailed sleep, both seen in late chronotypes during workweek. Most studies do not account for circadian misalignment or sleep duration. Our rigid ‘industrial society’ (working times or general code of conduct) forces late chronotypes to live against their circadian clock during workweek (e.g. terminating sleep in the middle of the biological night). High circadian misalignment and reduced sleep durations are the result. It is questionable, if those findings persisted when late chronotypes could sleep and live according to their internal rhythm. A reason why chronotype has a significant effect in models could be that ‘chronotype’ combines many features, as short sleep duration, high social jetlag and poor sleep quality during workweek. When corrected for circadian misalignment or sleep, what most studies neglect, chronotypes would potentially lose strength within a model. Therefore it is doubtful, whether diurnal lateness was the actual causation for these psychological disorders or lifestyle alterations.

1.5 Sleep-Wake Regulation

In 1982, several researchers such as Aschoff, Daan, Achermann and Borbély developed the two-process model of sleep. The model explains timing of sleep and wakefulness throughout the 24-hour day, regulated by the interaction of two processes (Borbély, 1982). Sleep pressure homeostatically builds up with increasing time of wakefulness and reduces during sleep (process S). Many investigations aimed to identify the homeostatic component. An accumulation of adenosine in the basal forebrain is – besides many other molecules discussed,
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e.g. interleukins, TNFα, growth hormone releasing hormone, nitric oxide or lactate – the most accepted one (Porkka-Heiskanen, 2013).

The circadian component provides ‘sleep gates’ throughout the 24-hour day (process C), in most individuals during dark phase and twelve hours after individual midnight. Since phase of entrainment differs between individuals, also timing of sleep shows inter-individual differences, from very early to very late sleep times. The SCN regulates sleep and wakefulness by innervating sleep promoting and wakefulness promoting circuits with reciprocal inhibition (Saper et al., 2001; Saper et al., 2010). Neurons of the ventrolateral preoptic nucleus of the hypothalamus (VLPO) are active during sleep and send inhibitory GABAergic projections to wakefulness promoting brain regions. Some neurons of SCN directly innervate the VLPO, but most afferent neurons derive from the wakefulness promoting dorsomedial hypothalamus (DMH) (Chou et al., 2002). During night, inhibitory signals from SCN and DMH decreases, thus VLPO neurons become active. The interaction of VLPO and the arousal system functions similar to a ‘flip-flop’ switch mechanism (Saper et al., 2001).

Most efferent neurons of the SCN project to the ventral SPZ. The vSPZ forwards the signal besides others to the dorsomedial hypothalamus (DMH), which promotes wakefulness via orexin comprising neurons (Chou et al., 2003; Saper et al., 2005). Via VLPO and DMH innervations, the SCN controls sleep and wake state (Chou et al., 2002).

Fig. 4 displays the interaction of both processes. High levels of sleep pressure will initiate sleep at any time (e.g. after night shifts), but as soon as sleep pressure levels decrease, the circadian component takes over. Enhanced circadian drive for sleep and high levels of sleep pressure ensure consolidated sleep, as indicated as striped area in Fig. 4 (Dijk et al., 1994; Dijk et al., 2002). Also the occurrence of sleep stages underlies process S and C. Whereas slow wave sleep (SWS) is driven by sleep pressure and most prominent in the beginning of the night, rapid eye movement (REM) sleep is under circadian control, with an increasing REM-sleep propensity during morning hours (Dijk et al., 1995).
Fig. 4. Two-process model of sleep. Interaction of homeostatic build-up of sleep pressure (process S) and the circadian component (process C) determine timing of sleep, here indicated by striped area. Please note that sleep times and durations are highly individual. Modified from (Achermann et al., 1992).

If sleep-wake cycles were only modulated only by the sleep homeostatic component, a nap would shift us to a later phase. Additionally, we would also awake fully refreshed after a night and be most sleepy in the evening. Factually, people feel tired after waking up and alert two hours before their habitual bedtime (during the so called wake-maintenance-zone or forbidden-sleep-zone) (Lavie, 1986). Increasing build-up of sleep pressure shortens sleep latency\(^5\). But the circadian component interferes with sleep initiation, providing sleep gates where sleep latency is short. Shortest sleep latencies coincide with sleep propensities during biological night and midday (Carskadon et al., 1987; Richardson et al., 1982). On the other hand, low levels of sleep inertia\(^6\) coincide with circadian drive for wakefulness and low levels of sleep pressure. In the morning hours, the circadian process initiates wakefulness at low levels of homeostatic sleep pressure. Based on that, the two-process model was extended by a third dimension, process W, which describes alertness and sleepiness throughout the 24-hour day (Åkerstedt et al., 1997) and therefore modulates sleep inertia. Sleep inertia is smallest when self-awaken and highest when being awaken from slow wave sleep (Ikeda et al., 2010; Tassi et al., 2000). Normally, it lasts less than 30 minutes, but in sleep-deprived persons it can persist up to four hours (Tassi et al., 2000). With the help of this model the progression of

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\(^5\) Duration needed to fall asleep.

\(^6\) A phenomenon of feeling not refreshed after a full night of sleep or after a nap.
alertness levels even throughout subsequent night shifts can be predicted (Folkard et al., 1999).

In our everyday life sleep timing is not only controlled by homeostatic sleep pressure or by circadian rhythms, also social obligations (e.g. household, taking care of children or pets) or working times determine when we can go to sleep or have to wake up. Thus, sleep begin, end and duration may differ between work- and free days. Individuals’ sleep need is independent of chronotype. Due to early working times, many people (generally later chronotypes) accumulate sleep loss during the workweek, which is compensated on free days (Roepke et al., 2010; Taillard et al., 1999). On the other hand early chronotypes stay awake far too long on weekends due to social demands and accumulate sleep deprivation and social jetlag. Furthermore, early chronotypes are associated with an increased vulnerability to sleep loss. Several studies showed poorer performances of early chronotypes under sleep deprivation and a generally faster build-up of sleep pressure (Maire et al., 2013; Mongrain et al., 2006; Mongrain et al., 2007; Taillard et al., 2003).

1.6 Shift Work: Living Against the Biological Clock

During the years of the industrial revolution (beginning in the late 18th century), an increasing number of people started to work at night. Since the invention of artificial light by Thomas A. Edison, working around the clock was possible and saver than previous lighting systems (such as candles or gas lighting). Today almost 20% of the industrial population work rotational or permanent shifts and asked for working times besides ‘9 to 5’, numbers are even higher (Stevens et al., 2011). Shift work is associated with high social jetlag (a measurement of living against the biological clock) as well as an elevated risk for many diseases, likely emerging from circadian disruption and chronic sleep deprivation. Shift work research is susceptible to difficulties with respect to the study design. Most studies simulate shift work in the laboratory, with some protocols differing widely from real life. Only few studies are conducted in the field, where heterogeneity between setting impair comparability (Kantermann et al., 2010).
1.6.1 Shift Work and Social Jetlag

Analysing the sleep-wake behaviour on work- and free days, in most cases a huge discrepancy in timing and duration becomes apparent. On workdays, even normal office workers stay up in the middle of their biological night in order to go to work, whereas on free days sleep episodes are generally longer and begin later. It seems, as if the person lives in different time zones on work- and free days (Roenneberg et al., 2013). This is even worse in shift workers, ‘flying’ east (before a morning shift), west (after a night shift) and back home again (during evening shifts and free days). Activity or sleep at the wrong internal time of day causes jetlag-like symptoms. Whereas normal jetlag is only temporary, improving after a readjustment of the biological clock to the new time zone, social jetlag\(^7\) is chronic (Wittmann et al., 2006). It is a measurement of the extent to which someone is living against the biological clock on workdays compared to free days. Furthermore, it quantifies how much sleep is taken within or beside the individual circadian ‘sleep window’.

In shift workers, social jetlag is extremely high due to the fact that shifts are covering the 24-hour day (Juda et al., 2013a). For an early chronotype on night shifts, it can be up to seven hours (compared to that, a late type has three hours of social jetlag). On morning shifts, early chronotypes shift their sleep only by one hour, whereas late types suffer from four hours of social jetlag (Juda et al., 2013a).

Social jetlag was found to increase the likelihood of being a smoker, the consumption of caffeine-containing beverages (e.g. coffee and energy-drinks) as well as alcohol uptake (Adan, 1994; Wittmann et al., 2006). The stimulating effects of nicotine and caffeine facilitate to overcome sleepiness, whereas alcohol improves the ability to fall asleep and is used to promote earlier and easier sleep onset. Furthermore, each hour of social jetlag increases the probability of becoming obese by 30% (Roenneberg et al., 2012). A recent study found, even if conducted in non-shift workers that high levels of social jetlag was correlated with metabolic unhealthy obese individuals as well as elevated levels of glycated

\(^7\) Neologism; ‘social’: the effect is caused by occupational and social dues; ‘jetlag’: wakefulness- and sleep on work- and free days appear like living in different time zones.
haemoglobin⁸ (Parsons et al., 2014). This study underlines the tremendous effects of living against the biological clock on metabolism and health.

1.6.2 Shift Work and Health

High consumption of alcohol, nicotine and caffeine is common among shift workers (Fido et al., 2008). But an unhealthy lifestyle alone cannot explain the long list of impairments and severe illnesses shift work is associated with, e.g. among others cardio-vascular diseases, diabetes mellitus type II, gastrointestinal diseases, sleep disorders as insomnia, shift work disorder and sleep apnoea, psychological disorders as major depression disorder or anxiety disorder, as well as cancer (Di Milia et al., 2013; Esquirol et al., 2011; Faraut et al., 2013; Haus et al., 2013; Koller, 1983; Monk et al., 2013; Scott et al., 1997).

The fatal aspects of shift work mainly result from a permanent sleep deprivation as well as circadian disruption (misalignment of the internal circadian clock and external environment or behaviour, but mostly of the sleep-wake cycle in relation to the biological night) (Arendt, 2010; Baron et al., 2014). Circadian disruption sleep deprivation and adversely timed light exposure are associated with many different physiological changes, which possibly promote the development of the mentioned pathologies, explained in the following chapters.

A recently conducted study attempted to reduce circadian disruption and sleep deprivation (Vetter et al., 2015). Shift workers were assigned according to their internal time to different shift sequences. The most strenuous shift was eliminated, so that earliest chronotypes worked no night shifts and latest chronotypes within the given distribution, worked no morning shifts. Sleep duration during workweek was lengthened in the chronotype-adjusted shift schedule. Although the number of consecutive shifts was elevated within the chronotype-adjusted schedule, social jetlag remained stable or even decreased.

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⁸ Indicator for poorly of controlled blood glucose levels, as seen in people suffering from diabetes.
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Working inline with the biological rhythm also positively affected subjective parameters as sleep quality and wellbeing. (Vetter et al., 2015).

1.6.2.1 Sleep Deprivation

Chronic sleep reduction is a major aspect in shift workers. Sleep duration after night shifts and before morning shifts are on average two hours shorter, than a normal night sleep (Torsvall et al., 1989). Late chronotypes cannot fall asleep before a morning shift early enough to get enough sleep, but can sleep long after night shifts. Early chronotypes on the contrary suffer most from reduced sleep after night shifts (Juda et al., 2013a). The biological clock would awake them as soon as sleep pressure reached moderate levels.

After sleep deprivation, impaired cognitive performance and elevated sleepiness may lead to an increased injury risk (Åkerstedt et al., 2011). The exact relationship needs to be elucidated, but chronic sleep curtailment has an impact on mood, which could be an initial step for the development of major depression disorder. Indeed shift work was shown to increase the lifetime risk for major depressive disorders (Scott et al., 1997). Besides sleep deprivation, also aberrant light patterns (as seen in shift workers) could tremendously influence mood, at least in mice, showing a more depression-like behaviour (Bedrosian et al., 2013; Legates et al., 2012; Monteggia et al., 2012).

More is known about physiological changes. Chronic sleep reduction leads to alterations of the immune system, i.e. an up-regulation of neutrophil and leucocyte counts, C-reactive protein (CRP), diverse interleukins as IL-6 and the tumour necrosis factor alpha (TNFα) (Faraut et al., 2012; Meier-Ewet et al., 2004). High numbers of neutrophils are known to damage coronary arteries by proteolysis, which can initiate the development of several cardio-vascular diseases. Furthermore, the regulation of neuroendocrine secretion is altered. Secretion of growth hormone and prolactin is coupled to sleep. Shifted sleep timings also change timing of secretion and with that the whole cascade controlled by these hormones. Although cortisol is under circadian control und should not be affected by sleep deprivation, evening cortisol levels are elevated
and the overall amplitude is reduced in shift workers (Berry, 2012). Since cortisol regulates among others blood pressure, high levels potentially result in chronic hypertension, which can promote severe cardio-vascular diseases. Indeed, shift work and especially sleep deprivation was shown to be a risk factor for hypertension (Gholami-Fesharaki et al., 2013; Mullington et al., 2009; Tochikubo et al., 1996). Besides cortisol, also the secretion of the two hunger regulating endocrines leptin and ghrelin is impaired. Sleep restriction decreases the satiety hormone leptin, secreted by adipocytes (Scheer et al., 2009), whereas hunger stimulating hormone ghrelin, secreted by stomach cells, is elevated (Spiegel et al., 2004). This alteration leads to higher energy uptake and also an altered food preference towards fatty and carbohydrate-rich nourishments. Both conceivably result in overweight, the development of sleep apnoea or diabetes mellitus type II (Knutson et al., 2007; Nedeltcheva et al., 2014). The altered glucose metabolism, as a result of sleep deprivation, even increases the risk for the pathology of diabetes. After only three nights of restricted sleep, glucose tolerance as well as insulin sensitivity was dramatically reduced, leading to elevated blood glucose levels (Scheer et al., 2009). This is a major precursor for developing diabetes type II.

1.6.2.2 Circadian Disruption

Sleep deprivation as well as circadian disruption was shown to alter the regulation of blood transcriptome and metabolome (Archer et al., 2014; Davies et al., 2014; Moller-Levet et al., 2013). Especially DNA-repair mechanisms and transcriptional proteins (*e.g.* RNA-polymerase, DNA-elongation, ribosomes and so on) were down-regulated. Accumulating mutations, due to reduced DNA-repair mechanisms, are one critical step for cell aging and the development of cancer. Additionally, clock gene expression is altered after circadian disruption (Haus et al., 2013). Besides sustaining a circadian rhythm, clock genes have many different functions within the cell. For instance, Per2 acts as a tumour prevention factor in cells generally, but especially in breast tissue (Fu et al., 2002; Xiang et al., 2008; Yang et al., 2009). Disturbed clock gene expression potentially impair this tumour repressive function. Furthermore, DNA-methylation is under
circadian control. Altered clock gene expression negatively impact DNA-methylation (Bonsch et al., 2007). Tumour suppressing and preventing genes are shut quiet via methylation in tumour cells. It seems as if circadian disruption enables tumour development (Haus et al., 2013).

Shift work disorder (SWD) is commonly seen in rotational shift workers. SWD is associated with high levels of sleepiness during wakefulness and frequent episodes on insomnia and poor sleep quality ratings, depending on the shift schedule and type of shift. Working or sleeping at times of day, when others are not awake or already asleep potentially negatively affects family and social life (Harrington, 2012). This in turn impairs mood and general shift work tolerance.

Food intake when glucose tolerance is low, potentially lead to the development of diabetes or overweight, as already described in chapter 1.6.2.1. During a night shift protocol, participants’ daily energy expenditure was reduced, which may increase the risk of gaining overweight (McHill et al., 2014).
Circadian disruption are the two main biological consequences of shift work, which in turn may lead to various health problems.
risk factors for the development of several physical and psychological diseases (indicated by purple circles). Even though this figure is an oversimplification and does not show every possible connection, it illustrates the various consequences of sleep loss and circadian disruption by visualizing pathways of pathogenesis. Napping and light treatment are beneficial countermeasures against sleep curtailment and circadian misalignment.

### 1.6.2.3 Light Exposure

Besides sleep deprivation and circadian disruption, insufficient and poorly timed light exposure are risk factors for the development of diseases.

A result of our industrial society is an increasing light pollution: light from commercials, shop lightings or from street lamps enter bedrooms (Pauley, 2004). There is an on-going discussion in regard to the severity of nightly light pollution. Since the eyelid filters more than 80% of light and the eyeballs are rolled upwards during slow wave sleep, negative effects of this light should be minimal (Kantermann et al., 2009).

Light at night and its negative effects on melatonin secretion has long been discussed as risk factor for the development of cancer. Furthermore, many findings speak in favour to this close association. Mainly every tissue comprises melatonin receptors (in breast tissue about 80% of the cells exhibit melatonin receptors) and melatonin stimulates the hypothalamus and therefore controls hormone secretion. Thus, melatonin is meant to have a widespread and diverse effect in the human body. Melatonin itself is an anti-oxidant and reduces oxidative stress, emerging from the respiration chain in mitochondria (Johns et al., 2014). Free oxygen radicals highly damage the cell, increase aging and cause DNA-mutations (Muftuoglu et al., 2014). Shift workers experiencing light at night display reduced melatonin levels and a high morbidity of breast cancer. Especially earlier chronotypes and women working night shifts before their first pregnancy displayed an increased risk (Hansen et al., 2012; Menegaux et al., 2013). Colon cancer, prostate cancer in men and breast cancer in women are the most prevalent forms of cancer among shift workers (Kelleher et al., 2014; Sigurdardottir et al., 2012). Additionally, blind individuals, without any suppression of melatonin, seldom suffer from breast cancer and melatonin
administration reduced tumour growth at least in animals (Blask et al., 1999; Feychtig et al., 1998; Pauley, 2004). Melatonin suppression by light during internal night causes elevation of oestrogen levels. Especially for women during or after menopause, high oestrogen concentrations are a risk factor for the development of breast cancer (Anbalagan et al., 2015). It is noteworthy that the direct link between light at night, melatonin and the development of cancer is still missing in humans.

Light comprising blue wavelengths can immediately suppress melatonin. Although night shift workers were exposed to light at night, some studies showed that melatonin is not necessarily reduced (Dumont et al., 2012; Goichot et al., 1998; Grundy et al., 2011; Peplonska et al., 2012).

Besides inappropriate timing, also too little light exposures are meant to be harmful. In the last years, the impact of vitamin D as risk factor for tumour development was of increasing interest. The production of vitamin D, which is per definition not vitamin, but rather a hormone, is initiated by sunlight. Today it is known that many tissues produce vitamin D, where it functions as an extracellular signal to coordinate apoptosis and cell differentiation, by controlling the transcription of many different genes (Fleet et al., 2012; Picotto et al., 2012). In tumour cells, these control mechanisms are altered or even destroyed. Shift workers are generally less exposed to sunlight, leading to a vitamin D deficiency. Several studies implied a close relation of vitamin D levels and tumour growth (Ahonen et al., 2000; Engel et al., 2010; Garland et al., 1989).

1.6.3 Countermeasures

Reducing the adverse effects of shift work is subject of many different studies. Different countermeasures are proposed in order to reduce shift work-related diseases. Most important countermeasures discussed are taking a nap, scheduled light-dark exposure as well as the intake of medication or stimulants.
1.6.3.1 Napping

Taking a nap is a powerful countermeasure against sleep deprivation and potentially against sleep loss-associated health risks common in shift workers, see Fig. 5. Acute sleep deprivation increased numbers of leucocytes and neutrophils in blood samples. It was shown that a 30-minute nap ameliorates neutrophils and leucocyte counts to baseline levels, comparable to a ten-hour recovery sleep (Faraut et al., 2011). Furthermore, napping improved elevated cortisol and high IL-6 levels (Vgontzas et al., 2007). Taking a nap before or during night shifts improved performance and sleepiness levels (Bonnet, 1990; Lumley et al., 1986; Ruggiero et al., 2013). Lower sleepiness in turn minimizes accident and injury risks (Åkerstedt et al., 2011). Studies recommend taking a nap between three and four o’clock, when the circadian component provides a second sleep window and the homeostatic build-up of sleep pressure is already elevated. This combination provides high sleep propensity, during which sleep latency is short, making it easy to doze of (Dijk et al., 1995).

1.6.3.2 Light

Folkard showed that only 3% of permanent night shift workers displayed a fully adapted melatonin rhythm to the inverse sleep-wake pattern and 21% at least showed a partly adjustment (Folkard, 2008). These small numbers of adjusted shift workers are mostly a result of free days, which cause a re-synchronization of the biological clock towards the natural light-dark cycle. In permanent shift schedules, a partly adaption of the biological clock is recommended, so that melatonin secretion, circadian provided sleep gates and actual sleep timing at least partly coincide (Smith et al., 2012). With bright light and shielding from light at certain times, the biological clock can be successively shifted and with that circadian misalignment and potentially also its severe health effects can be reduced (Boivin et al., 2005). Most important is to remain this sleep-wake, light-dark pattern also on free days, in order to prevent re-adjustment. Frequent re-adjustment has been shown to be associated with reduced reaction time and frontal lobe atrophy (Karatsoreos, 2014). Thus, adjustment within a rotational schedule is not recommended.
Melatonin suppression during night shifts can be reduced by yellowish illumination of the work place or by increasing the zeitgeber strength between light and dark phase.

1.6.3.3 Substance Intake

Many shift workers take hypnagogues in order to initiate sleep (e.g. before morning shifts) or maintain sleep (e.g. after night shifts). With that at least sleep deprivation is reduced, although circadian misalignment is not. The intake of hypnagogues is often accompanied by side effects and an increased risk for addiction. Melatonin administration after night shifts was shown to be beneficial for sleep initiation, but could not improve alertness during the upcoming night (Sharkey et al., 2001). Since melatonin shifts the clock, accurate timing of melatonin intake is needed. Melatonin intake is only recommended in permanent schedules in order to adjust circadian rhythms to e.g. permanent night shifts. This potentially reduces circadian misalignment and therefore positively impacts the development of diseases. Generally, in rotating shift schedules phase shifting the clock is adverse.

Caffeine intake is a common countermeasure against acute sleepiness and can therefore reduce injury risks. Caffeine blocks adenosine receptors and suppresses sleep pressure build-up by accumulating adenosine in the basal forebrain. Since caffeine does not positively affect sleep reduction or circadian misalignment, it only antagonizes acute sleepiness, but not pathogenesis.

1.6.3.4 Other Countermeasures

Generally, forwards-rotation (delaying shift schedule) is associated with high levels of shift work tolerance (Barton et al., 1993). Surprisingly, 12-hour shifts were found to improve several parameters, such as sleep, wellbeing and alertness compared to 8-hour shifts (Lowden et al., 1998; Smith et al., 1998). Physical fitness, healthy diet and weight loss positively affected shift workers’ health state. Cardiorespiratory fitness increased and triglycerides, fasting
glucose or blood pressure improved, indicating a diminished risk to develop associated diseases (Neil et al., 2014).

1.6.4 Reactions of Societies

In 2007, the International Academy for Research on Cancer (IARC), a subsection of the World Health Organization, categorized shift work involving circadian disruption as probably cancerogenic (2A) (Straif et al., 2007). This classification was based on evidence in animal models, but insufficient evidence in humans. Epidemiological investigations mainly focused on nurses and female flight personal. The committee annotated that both groups are in addition to shift work also expired to occupational risks, such as chemicals and radiation respectively. In order to close the lacking evidence in humans other occupations, different forms of cancer and also male shift workers should be considered to rule out potential recalling biases. Also a more standardized definition of shift work in epidemiological studies is needed (Stevens et al., 2011). Since Juda and colleagues showed that not only night shifts entail circadian disruption (also morning shifts are disruptive for the majority of chronotypes), it is regrettable that the IARC solely focused on night shift as the only shift ‘containing circadian disruption’.

In 2009, Denmark became the first country financially compensating women, who developed breast cancer after working at least one night shift per week for more than 20 years. The height of compensation is case-dependent and paid by the insurance company of the employer. This decision was discussed as being impetuous because of the missing evidence in humans (Lancet-Editorial Comment, 2009).
1.7 Scope of Research

In the following, two studies are presented, both analysing major aspects of circadian clocks in real life settings: the first study focuses on sleep in shift workers, which is highly controlled by the circadian clock, as described previously. The focus of the second study lies on entrainment by light, which is an important aspect of circadian research, here examined in office workers.

1.7.1 First Study: How Chronotype Influences Nap Behaviour in Shift Workers

Sleep loss is associated with tremendous impairments (e.g. cognitive and emotional) and severe health risks (e.g. cardiovascular diseases, diabetes or gastrointestinal illnesses, see chapter 1.6.2.1). Napping is a powerful countermeasure against sleep deprivation and potentially improves the risk of developing sleep loss-related illnesses and impairments. Sleep curtailment is very common in shift workers, suffering from short sleep durations (on average two hours shorter on morning and night shifts) due to working times and sleep at the wrong internal time of day (Torsvall et al., 1989). Analysing sleep durations with regards to chronotype revealed differences; early chronotypes sleep longer and more in their sleep window on morning, but display a high social jetlag and short sleep episodes on night shifts compared to late chronotypes (Juda et al., 2013a). This chronotype-dependent sleep deprivation potentially entails an increased need for compensatory naps. The first study analyses nap behaviour (nap duration and frequency as well as the percentage of nappers) of rotational shift workers under consideration of type of shift and chronotype.

Nap timing was analysed on a local as well as on individuals’ internal time scale. Furthermore, the percentage of nap taking participants was analysed in regard to main sleep duration. Adding main sleep and nap duration, the 24-hour sleep duration was investigated on different shifts for early, intermediate and late chronotypes. For the first time, the causality of napping an main sleep was
investigated. The effects of the previous main sleep on nap behaviour and the influence of a nap on the subsequent main sleep were analysed systematically.

This study comprises participants from four different shift systems. By this, possible shift system or work environmental effects can be ruled out, *e.g.* increased need of taking a nap because of challenging speed of rotation or physically demanding work tasks. Since nap behaviour is highly individual and also possibly depending on social, physical or time factors, nap behaviour was analysed in respect of these influential factors. Additionally, chronotype and age are highly related: increasing age is associated with earlier chronotypes, older people are known to struggle more with the demands of shift work and, with increasing age, people tend to nap more often. Therefore napping was also analysed in regard to participants’ age.

Shift workers’ nap behaviour could follow different patterns. It was assumed firstly, since different main sleep lengths for chronotypes are known (early types sleeping shortest after night and late types before morning shifts [Juda et al., 2013a]), also the need for a nap in terms of duration, frequency and timing could follow this chronotype-dependency. Secondly, early chronotypes are meant to have a fast homeostatic build-up of sleep pressure, potentially only earlier chronotypes take a nap. Thirdly, due to different nap strategies – in order to compensate sleep need, participants either nap longer, more frequently or show a high delta power during their nap episode – it was hypothesized that no clear nap pattern can be revealed.

The aim of this study was to investigate, if besides many influential factors, such as age, main sleep duration, speed of rotation or nap strategies, chronotype has a significant impact on napping behaviour in shift workers.

### 1.7.2 Second Study: Light Entrainment in Real Life

Entrainment is the major challenge of the biological clock. Since the invention of artificial light, ‘modern’ daily life progressively moved inside buildings and away from the natural light-dark cycle. By switching artificial light sources on and off,
we create our own light-dark cycle, which has little to do with natural light in terms of duration, timing, intensity and spectrum. Since moving away from sunlight in comparatively ‘dark’ buildings, zeitgeber strength (light intensity difference between internal day and night) is very small. The lack of time cues impairs the ability to adapt to the natural light-dark cycle. The second study investigates light levels office workers experience during work- and free days. Light intensities, overall light levels as well as separated for different lux-levels, were compared between forenoon and afternoon on a local time and internal time scale. By separating light exposure into forenoon and afternoon, timing of light exposure was considered, based on the assumption of the model CiRC (Roenneberg et al., 2010a). The analyses were conducted separately for light levels experienced throughout the 24-hour day, during photoperiod (daylight is potentially available) as well as during scotoperiod (artificial light is the only available light source) and findings were compared with each other. Besides general illumination levels, also light intensity-categories were investigated. Since the theory CiRC postulates that light exposure differences between internal fore- and afternoon influences chronotype, it was tested whether the difference could significantly predict participants’ chronotype. In order to explore whether potentially differences in light exposure influences phase and amplitude of accordance between activity- and light-profiles, a vector analysis was conducted, based on a method developed by Rea and colleagues (Rea et al., 2008). From this method conclusions can be drawn with regards to participants’ circadian entrainment.

To rule out potential age-effects or a proceeded yellowing of the eye lens, this study included adults not exceeding the age of 40 years. It is not fully understood, if light perception changes with age; several studies showed age-dependent effects (Duffy et al., 2007), whereas others did not (Benloucif et al., 2006; Gimenez et al., 2014; Najjar et al., 2014). Thus, an age-related change was shown in elderly people between internal period length and sleep timing (Duffy et al., 2002a).
Analyses of light patterns in humans were based on the following hypothesis. Firstly, from subjective ratings of the duration of daylight, it was shown that on average later chronotypes experience less daylight than early chronotypes. The first hypothesis was that late chronotypes are less entrained to a given light-dark cycle due to insufficient *zeitgeber* signals (Roenneberg et al., 2007c). Secondly, it was hypothesized that late chronotypes experience more light during a later time of the internal day, which synchronizes them to a later phase and, on the contrary that early types get more light during the internal forenoon, which makes them so early in their phase of entrainment.

The aim of the second study was to investigate chronotype-differences in light exposure between work- and free days as well as with respect to 24-hour light patterns, timing and light intensities.
2 How Chronotype Influences Nap Behaviour in Shift Workers

2.1 Abstract

Objectives. In this study the impact of internal time (chronotype) on napping behaviour in shift workers was investigated.

Methods. Napping behaviour (duration, frequency and timing) was analysed in 118 employees working forwards-rotating shift schedules (transition times: 6a.m., 2p.m., 10p.m.). For chronotype assessment the MCTQ^Shift was used, sleep parameters were derived from daily sleep logs. Repeated measures and univariate ANCOVAs, mixed models, correlations and t-tests were used to explore nap behaviour based on employees’ internal time. A multiple regression analysis was conducted in order to investigate napping and main sleep causality.

Results. Chronotype influenced napping behaviour: early chronotypes napped predominantly, most frequently and longest on night shifts, late types on morning shifts and intermediate chronotypes on both morning and night shifts (p<0.01). The percentage of napping shift workers was associated with the duration of the main sleep episode, which is in turn chronotype-dependent. Napping in shift workers did not only show a clear chronotype-dependent pattern, chronotype*type of shift could even significantly predict nap duration and timing, whereas social jetlag* type of shift predicted nap frequency (p<0.05). Sleep offset significantly influenced nap duration on morning shifts (p<0.01), on the contrary nap timing showed an impact on sleep begin of the subsequent main sleep on evening (p<0.01) and night shifts (p<0.001).

Conclusions. Napping behaviour in shift workers depended on both chronotype and type of shift. This study displayed that not only night shifts, but also morning shifts imply an increased need for compensatory sleep. Furthermore, the study results emphasized the importance of considering employees’ internal time when studying napping as potential prevention measure against adverse shift work effects on sleep, health and cognition.
2.2 Introduction

Despite shift work being a growing pillar of our industrialized economy, it is associated with several health risks, such as sleep-disturbances, cardio-vascular-diseases, diabetes and even several forms of cancer (Carter et al., 2014; Hansen et al., 2012; Menegaux et al., 2013; Monk et al., 2013; Scheer et al., 2009). Commonly seen in shift workers is both chronic sleep deprivation as well as misedimed sleep at the ‘wrong’ internal time of day, leading to circadian disruption (a state of misalignment between physiological functions and behaviour). Circadian disruption as well as chronic or acute sleep deprivation are suggested to play a central role in the pathogeneses of shift work-associated diseases (Roenneberg et al., 2012; Wittmann et al., 2006). Even if the underlying mechanisms still have to be elucidated, studies show disrupted circadian regulation of the transcriptome after misedimed or curtailed sleep (Archer et al., 2014; Moller-Levet et al., 2013) as well as enhanced levels of immune and oxidative stress, which are in turn risk factors for e.g. cardiovascular diseases (Faraut et al., 2013; Faraut et al., 2012). Changes in metabolism were found after circadian disruption or sleep reduction. Alteration of glucose tolerance and insulin sensitivity, which are risk factors for the development of obesity and diabetes, were described as well as changes in secretion of endocrines, such as melatonin, cortisol, oestrogen, leptin and ghrelin, which in turn regulate a cascade of physiological pathways (Faraut et al., 2013; Knutson et al., 2007; Mullington et al., 2009).

The circadian clock regulates the activation of most genes, thereby controlling metabolism, as well as timing of sleep and activity (Bass, 2012; Czeisler et al., 2007). The central pacemaker, the suprachiasmatic nucleus (SCN), is a small brain region, located directly above the optic chiasm. It entrains to a given light-dark cycle via retinal ganglion cells, melanopsin-comprising photoreceptors showing highest sensitivity in blue wave lengths spectrum (Berson et al., 2002; Brainard et al., 2001; Freedman et al., 1999; Thapan et al., 2001). The SCN actively synchronizes to the perceived light information and produces stable days of approximately 24-hour period length. By controlling other brain regions and therefore hormone secretion, body temperature, sleep
and wakefulness, the SCN synchronizes all peripheral intracellular clocks (Karasek et al., 2006; Zawilska et al., 2009). How the biological clock embeds to a given light-dark cycle can differ up to twelve hours from earliest to latest within a population, resulting into different ‘chronotypes’ (Roenneberg, 2012). The level of misalignment between one’s biologically regulated and actual sleep timing on workdays is rather socially influenced and can for example be captured by the measure of social jetlag (Wittmann et al., 2006).

2.2.1 Investigating the Effects of Naps in the Laboratory and in the Field

Early morning or nightly working times, direction of shift schedule’s rotation and the number of consecutive shifts result in a highly individual chronotype-dependent amount of circadian disruption (i.e. social jetlag) and sleep deprivation (Åkerstedt, 1998b; Folkard et al., 1993; Juda et al., 2013a; Matsumoto et al., 1987). Napping is suggested to compensate for sleep loss and is a common coping strategy in shift workers (Rosa, 1993). Since sleep deprivation is a risk factor for diverse shift work-related illnesses, reducing sleep loss by taking a nap could imply positive health effects. Faraut and colleagues found that after a full night of sleep deprivation and an ensuing eight hour recovery sleep, an additional 30-minute nap reduced elevated leucocytes counts to baseline levels and was comparable to the control group with ten hours recovery sleep (Faraut et al., 2011). In another study, elevated levels of noradrenaline after a night of restricted sleep, were reduced after an afternoon nap (Faraut et al., 2015). From these findings, a positive impact of napping on the physiological stress response can be concluded. In night shift working nurses, odds ratio of self-reported hypertension was elevated as compared to day workers. Napping was found to decrease the odds ratio for hypertension in comparison to non-nappers (Rothenberg et al., 2014). The findings stress the positive effect of napping on the control of blood pressure.

Beside sleep-compensation, immediate effects of napping after sleep deprivation are subject of many studies (Dhand et al., 2006; Hayashi et al., 1999; Hayashi et al., 2005). Subjectively and objectively measured levels of alertness
and performance improved after taking a nap. In general, previous research mainly focuses on night shift-related napping, e.g. nap during night shifts or after night sleep restriction (Carskadon et al., 2001; Davy et al., 2013; Gillberg et al., 1996; Sallinen et al., 1998; Smith et al., 2007; Takeyama et al., 2005). It was shown that in case a nap was taken during the night shift, the positive effects persisted throughout the night. For instance, sleep loss-related immune alterations improve, whereas subjective sleepiness and PVT\(^9\) lapses decrease after taking a nap (Faraut et al., 2011; Faraut et al., 2012; Lumley et al., 1986; Signal et al., 2009; Vgontzas et al., 2007). Highest levels of alertness were found after four hours subsequent to a 60-minute nap. Daytime sleep quality ensuing a nightly nap was subjectively slightly impaired, whereas objective measurements did not show differences in daytime sleep, such as sleep duration (Davy et al., 2013; Sallinen et al., 1998).

Naps shorter than ten minutes have minimal effects. A 30-minute nap is most beneficial as countermeasure against acute sleepiness, without increasing levels of sleep inertia. Enhanced arousal thresholds are maintained throughout the rest of the day and even emotional state improved (Dhand et al., 2006; Gillberg et al., 1996). A 30-minute nap is long enough to compensate acute sleep deprivation, but on the other hand not long enough to fall into deep sleep stages, from which it is difficult to awake and elevate levels of sleep inertia (Ikeda et al., 2010). Although longer naps generally enhance alertness, naps of longer than 45 minutes ensue long durations of sleep inertia. This is problematic if immediately after awakening full cognitive capacity is needed (Dhand et al., 2006).

Nap and non-nap days were found to display differences in several subjective parameters, with nap days showing elevated levels of sleepiness and reduced sleep quality during the main sleep episode (Rosa, 1993). Yet, only little is known, about the effects of a too short main sleep episode on a succeeding nap and/ or its effects on the ensuing main sleep phase. This was mostly analysed in elderly and not in shift workers (Monk et al., 2001; Pilcher et al., 2001; Tamaki et al., 1999). An evening nap increased sleep latency of the following main sleep

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\(^9\) Psychomotor vigilance task: objective measure of reaction times needed for a response to a stimulus, indicating attention levels, alertness or sleepiness.
(Werth et al., 1996). In case a nap comprised long durations of sleep stage N1, the subsequent main sleep show less N1 sleep as compared to a night without prior nap (Feinberg et al., 1992).

2.2.2 Research Aims

In shift work- or nap research employees’ internal time (chronotype) is seldom considered (Åkerstedt et al., 1985; Matsumoto et al., 1987). Given the role of circadian phase in sleep timing, duration and disruption, especially obvious in shift workers, chronotype is potentially a key factor when analysing nap patterns. This study had the attempt to systematically investigate nap behaviour of shift workers in regard to employees’ internal time.

As sleep duration and social jetlag in shift workers are chronotype-dependent (night shifts are most encumbering for early chronotypes and morning shifts for late types (Juda et al., 2013a)), the need for compensatory naps in terms of duration and frequency was expected to show chronotype-differences (hypothesis 1). Generally, intermediate chronotypes’ sleep durations are longer on both morning and night shifts, as compared to early types on night and later chronotypes on morning shifts (Juda et al., 2013a). Thus, the need for compensatory naps on morning and night shifts was expected to be reduced in intermediate chronotypes, as compared to the most encumbered group (hypothesis 2). Sleep timing can be predicted by the two-process model proposed by Borbély (Borbély et al., 1999), with a homeostatic component building up sleep propensity with increasing time awake (process S) and a circadian component (process C), describing the role of the circadian system on sleep timing (Borbély et al., 1999; Ruggiero et al., 2013; Taillard et al., 2003). Nap timing of shift workers was expected to depend on either process (hypothesis 3). Finally, if napping compensates at least partially for shift-related sleep loss, the duration of all sleep episodes (i.e. including naps) will be similar between chronotypes, even if the duration of the main sleep episode differs by chronotype and shift day (hypothesis 4).
Based on these findings, this study furthermore attempted to model nap behaviour in shift workers and to identify significant predictors. In terms of predicting nap behaviour, sleep duration and quality were expected to influence napping in shift workers. Since the prevailing shift schedule immensely dominates free time in shift workers, also the schedule and speed of rotations were thought to influence nap timing (hypothesis 5).

Furthermore, the study aimed to describe the interdependence between naps and previous as well as subsequent main sleep episodes. It was assumed that naps showed a dependency with a curtailed previous main sleep episode, but also interferes with the succeeding main sleep episode. It was hypothesized that a long and late nap influences sleep onset of the following main sleep episode (hypothesis 6).

2.3 Methods

2.3.1 Participants and Shift Schedules

The total sample comprised 118 shift workers (see Tab. 1 for demographic details), of which 102 employees completed the questionnaire for chronotype-assessment (MCTQshif). Participants worked in one of four forwards-rotating shift schedules. Schedules differed in speed of rotation and thus comprised different numbers of consecutive shift or free days. In all four schedules a full rotation covered four weeks, as shown in Fig. 6. Transition times were 6a.m. on morning, 2p.m. on evening and 10p.m. on night shifts. Employees’ work tasks comprised supervision, manipulation and maintenance of heavy machinery, with varying physical demands. Participation was voluntary and annulable at any time without stating reasons. The local ethics committee approved the study design. Participants gave written informed consent and were instructed about study participation. Participants were not financially remunerated, but feedback was offered in terms of individuals’ chronotype and parameters of sleep log data.
2.3.2 Instruments

2.3.2.1 Munich ChronoType Questionnaire for Shift Workers (MCTQ$^{\text{Shift}}$)

For assessing chronotype, the Munich ChronoType Questionnaire for shift workers (MCTQ$^{\text{Shift}}$) was used (Juda et al., 2013b). This questionnaire asks for sleep and wake behaviour separately for morning, evening and night shifts as well as related free days. The questionnaire assesses usual bed and wake-up times of the previous four weeks. The questionnaire furthermore enquires transition times of the different shifts as well as demographic details, such as participants’ sex, age, weight, height, social status and number of children. Participants completed the MCTQ$^{\text{Shift}}$ at the beginning of the data collection. As proposed by Juda and colleagues for shift schedules not comprising free days after evening shifts, chronotype (MSF$_{\text{sc}}^E$) was converted from sleep debt-corrected mid-sleep on free days after night shifts (MSF$_{\text{sc}}^N$) (Juda et al., 2013b). Sleep correction was necessary in order to account for potential catch-up sleep, due to a sleep deficit accumulated during the preceding workweek. The German version of the MCTQ$^{\text{Shift}}$, which was used in this study, can be found in the appendix in chapter 9.1.
2.3.2.2 Sleep Logs

Participants filled out daily sleep logs for at least two weeks, but ideally for a full rotation period (more that 81% of all participants completed the four week period). In order to facilitate completion, which was especially necessary on night shifts, exact dates and weekdays were provided. For assessing daily sleep behaviour, participants indicated immediately after awakening bed time and sleep latency of the previous day, as well as wake-up time, alarm clock usage and get-up time of the present day. Therefrom variables were calculated, as sleep duration, -onset, -offset, -latency and -inertia. Participants also specified whether the present day was a workday (morning, evening or night shift) or a free day. Additionally, participants reported sleep quality of the main sleep episode as well as subjective wellbeing (both on an ordinal scale ranging from 0 'very bad' to 10 'very good'). In case participants took a nap, they were requested to fill in exact times of the beginning and the end of the nap. A German template of a sleep log for shift workers is attached in the appendix 9.3.

2.3.3 Data Processing

Sleep logs were excluded entirely from data analyses if entries covered less than two weeks. In some cases sleep and work times contradicted (e.g. nightly sleep times although participants had to work night shifts or late wake up times on morning shift days) complete sleep log was discarded. Individual entries were excluded if participants were sick or entered unusual bed or awakening times with a co-occurring usage of an alarm clock. Free days were coded according to previous shift, as free day after morning, evening or night shift and analysed separately. All sleep times were assigned to the particular shift schedule, as exemplary shown in Fig. 7. Sleep before morning shifts was assigned to morning shift sleep and after night shifts as night shift sleep. Sleep before, between and after evening shifts was coded as evening shift sleep, due to evening shifts influencing time of awakening or time of going to bed in very late and early chronotypes respectively. In case a day comprised two naps, only nap occurrence was considered, but nap duration or timing were not included. Napping during working hours was extremely rare (n=2) and was therefore discarded. In order
to examine shift-specific after-effects on free day napping behaviour, only the first two free days were included.

Fig. 7. Sleep coding in regard to type of shift. Sleep was assigned to each type of shift differently. Morning shift sleep episode (grey boxes) occurred before, night shift sleep (black boxes) after the night shift. Evening shifts were surrounded by evening shift sleep episodes (striped boxes). Free day sleep (white boxes) were totally unaffected by working times.

### 2.3.4 Statistical Procedure

Analyses were conducted with SPSS Statistics 21.0 (IBM Corp.). Chronotype was calculated as sleep corrected mid-sleep on free days after evening/night shifts, described previously in chapter 2.3.2.1 (Juda et al., 2013b). By the use of an algorithm proposed by Bühner and colleagues (Bühner et al., 2009) arbitrary cut-off values were determined for categorizing shift workers into early (MSF\textsubscript{sc} \textless 4.1), intermediate (4.1 \textless MSF\textsubscript{sc} \textless 5.1) and late types (MSF\textsubscript{sc} \textgreater 5.1).

\[ m = 1 + 3.32 \times \log (K) \]

\( m = \) number of categories  
\( K = \) number of characteristic attributes.

Repeated measures ANCOVAs were conducted in a 3x3-mixed design (within-subject factor ‘shift’: morning vs. evening vs. night shift, between-subject factor ‘chronotype’: early vs. intermediate vs. late types, covariates ‘age’ and ‘shift schedule’). Bonferroni-corrected t-tests were applied as post-hoc comparisons for significant main effects. In all conducted analyses sphericity was always given, therefore it was not necessary to apply Greenhouse-Geisser corrections. The majority of participants did not nap on all three shifts, resulting in several missing data for nap timing. Since repeated measures ANCOVAs require values
Chapter 2: How Chronotype Influences Nap Behaviour in Shift Workers

for each time point, nap timing had to be analysed by using univariate ANCOVAs with age and shift schedule as covariates. The declared statistical level of significance was always two-tailed and tested against an α-level of 0.05. Significant effects validating the hypotheses are mentioned in the main text, additionally, Tab. 3 and Tab. 4 provide an overview of all effect sizes.

For the purpose of determining predictors for nap duration, frequency and timing, a mixed model analysis was applied for each dependent variable. As fixed factors were tested: chronotype, age, sleep duration, sleep quality, speed of rotation, shift system, type of shift and social jetlag as well as five interaction effects, namely chronotype/age/social jetlag*type of shift and chronotype/age*sleep duration. As dependent variables, nap timing, frequency and duration were investigated. In this analyses nap timing was tested on a local time scale only. The reason for not also including nap on an internal time scale is that adjustment of time designations to internal time already includes chronotype-information. Therefore chronotype cannot be used as predictor for internal nap timing, which would mean a circular reasoning. The model did not comprise repeated or random factors, because they were found to not improve the model. For the structure of the variance matrix ‘identity’ was selected. In order to identify predictors, a backwards-directed, stepwise model selection was applied, a method in which the least non-significant predictor gets excluded, provided that the model improves. Model improvement was identified using the ‘Bayesian information criterion’ (BIC) as model selection criterion.

In order to identify whether a nap is due to a shortened previous main sleep episode or effects main sleep of the subsequent night, stepwise multiple regression analyses were conducted. Shift and sleep associations were altered in this analysis, therefore numbers might differ from other analyses. Two different models were constructed in order to analyse nap and main sleep causality. The design was based on the results of a previous correlation analysis, e.g. no correlation between previous main sleep and nap timing was visible and therefore it was not included in the model. The first model investigated the effect of the previous main sleep episode on nap behaviour. As potential predictors the following variables were tested: ‘sleep quality’, ‘sleep duration’, ‘sleep onset’ and
‘sleep offset’ of the previous main sleep episode as well as subjective ‘wellbeing’ on the nap day. The second model examined the effect of a nap on the subsequent main sleep. In this model ‘nap duration’, ‘nap timing’, ‘sleep duration’ and ‘sleep quality’ of the previous main sleep were tested as potential predictors. Since nap timing differed between a local or internal time scale, analyses were conducted on both time scales. Generally a morning shift nap can be followed by another morning, an evening shift or a free day main sleep episode. The succeeding main sleep after a nap on evening shifts can be an evening, night shift or free day sleep. Whereas the main sleep episode subsequent to night shifts naps can be a night shift or free day sleep.

Time designations given in the sleep logs were used to calculate nap onset, -offset, -duration and mid nap. Main sleep or nap duration was calculated as difference between sleep onset minus sleep offset and nap timing was determined as mid nap (nap onset − \( \frac{\text{nap duration}}{2} \)). Individuals’ variables were averaged separately for each type of shift (morning, evening, night shift or free day after morning, evening or night shift), resulting in one value for morning shift nap behaviour (e.g. nap onset) for each participant. Twenty-four hour sleep duration was calculated by adding nap duration to sleep duration of the main sleep episode. Percentage of nappers was designated to a nominal scale, and distinguishes between a ‘napper’, participant generally taking a nap, and a ‘non-napper’, participant never napping during the period of measurement. In order to investigate nap timing on an internal time scale, the individual chronotype (\( \text{MSF}_5^E \)) was defined as biological midnight and all time designations were adjusted ( internal time = local time − \( \text{MSF}_5^E \)). The variable ‘percentage of nappers’ was calculated as proportion of nappers based on the referring chronotype subsample. ‘Nap frequency’ indicated the amount of naps relative to the total number of respective shift days. All demographic variables were extracted from the MCTQ\( ^{\text{Shift}} \). Body mass index was calculated from participants’ body weight and height (\( \text{BMI} = \frac{\text{weight (kg)}}{\text{height (m)}^2} \)). For all continuous variables, outliers were determined (≥1.5 times interquartile range) and excluded from analyses.
2.4 Results

2.4.1 Sample Description

Participants either napped never, on every, or on various types of shifts (morning, evening or night shifts), resulting in different subsample sizes. In total, 23 participants did not nap, 64 shift workers napped on morning, 23 on evening and 70 participants on night shifts.

From 118 participants, 67% lived in a partnership and 46% had more than one child. Further participants’ characteristics such as chronotype, age, sex and body mass index are shown in Tab. 1, for the whole sample as well as separately for each shift schedule. With the help of univariate ANCOVAs participants’ characteristics were compared between the four shift schedules. Participants in shift system four were significantly older compared to schedule one and three \( \text{F}(3, 107)=8.481, \ p<0.001 \), post-hoc test: S4 vs. S1/S3 \( \ p<.001 \). More females participating in this study worked in schedule two and three as compared to schedule four \( \text{F}(3, 107)=11.692, \ p<0.001 \), post-hoc test: S4 vs. S2/S3 \( \ p<.001 \). No differences emerged between shift schedule groups concerning body mass index or chronotype.

Tab. 1. Demographic information of the sample in total and separately for each shift schedule. N=sample size, \( \text{MSF}_{50}^{E} \)=chronotype (sleep corrected mid-sleep on free days after evening shifts), h=hours, yrs.=years, M=mean, SD=standard deviation, R=range, f=females, BMI=body mass index, S1-4=shift system 1-4.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>( \text{MSF}_{50}^{E} ) (h)</th>
<th>Age (yrs.)</th>
<th>Sex (% f)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Total</td>
<td>118</td>
<td>4:26 1:04 2:13-7:25</td>
<td>35.1</td>
<td>9.8</td>
<td>20-57</td>
</tr>
<tr>
<td>S1</td>
<td>11</td>
<td>5:06 1:04 3:28-7:10</td>
<td>28.3</td>
<td>6.2</td>
<td>20-40</td>
</tr>
<tr>
<td>S2</td>
<td>26</td>
<td>4:36 1:08 2:57-7:25</td>
<td>34.5</td>
<td>7.6</td>
<td>24-51</td>
</tr>
<tr>
<td>S3</td>
<td>37</td>
<td>4:29 1:10 2:13-6:16</td>
<td>30.5</td>
<td>8.3</td>
<td>21-47</td>
</tr>
<tr>
<td>S4</td>
<td>44</td>
<td>4:11 0:57 2:35-6:37</td>
<td>39.8</td>
<td>10.4</td>
<td>21-57</td>
</tr>
</tbody>
</table>
2.4.2 Chronotype-related Nap Behaviour and Type of Shift

Regardless of chronotype most participants napped on morning (53%) and night shifts (62%), while only few shift workers napped on evening shifts (19%, p<0.001) Fig. 8A visualizes results and Tab. 2 provides exact numbers of nap taking shift workers in regard to type of shift and chronotype.

Proportion of nappers varied with both type of shift and chronotype (main effect ‘type of shift’: $F_{(2,190)}=3.647$, p<0.05, interaction effect ‘type of shift*chronotype’: $F_{(4,190)}=3.456$, p<0.01; see Tab. 3 for all effect sizes). The majority of early types napped on night shift (70%), from which 31.9% exclusively napped on night shifts and 21% on both extreme shifts. 65% of later chronotypes generally napped on morning shifts. With 27%, the majority of non-napping participants were late chronotypes. Intermediate types napped on morning and night shifts (MS: 63%, NS: 71%; post-hoc comparisons: p<0.006, Bonferroni-corrected, see Fig. 8B). More than 37% of nap taking intermediate types napped on both extreme shifts and even 15% on all three shifts. The group of non-nappers was smallest amongst the intermediate chronotypes compared to the other categories.

Tab. 2. Overview of all shift- and chronotype-specific percentage of nap taking participants. MS/ES/NS=morning/evening/night shift, only MS=percentage of participants napping exclusively on morning shifts, MS+ES=percentage of participants napping exclusively on morning and evening shifts, MS+ES+NS=participants napping on all three types of shift, FDMS/ES/NS=free days after morning/evening/night shifts. Please note that participants could nap on various shifts and therefore are part of several samples at the same time.

<table>
<thead>
<tr>
<th>Workdays</th>
<th>Type of shift</th>
<th>Early type</th>
<th>Intermediate type</th>
<th>Late type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (%)</td>
<td>MS</td>
<td>39.6</td>
<td>63.0</td>
</tr>
<tr>
<td></td>
<td>ES</td>
<td>20.8</td>
<td>21.4</td>
<td>11.5</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>70.2</td>
<td>71.4</td>
<td>36.0</td>
</tr>
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<td>Nap behaviour</td>
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<td>7.4</td>
</tr>
<tr>
<td>(%) on</td>
<td>Only ES</td>
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<td>0</td>
<td>3.8</td>
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</tbody>
</table>
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<table>
<thead>
<tr>
<th>Type of shift</th>
<th>Early type</th>
<th>Intermediate type</th>
<th>Late type</th>
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<td>Only NS</td>
<td>31.9</td>
<td>14.3</td>
<td>4.0</td>
</tr>
<tr>
<td>MS+ES</td>
<td>2.1</td>
<td>3.7</td>
<td>3.8</td>
</tr>
<tr>
<td>MS+NS</td>
<td>21.3</td>
<td>37.0</td>
<td>28.0</td>
</tr>
<tr>
<td>ES+NS</td>
<td>4.3</td>
<td>3.6</td>
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</tr>
<tr>
<td>MS+ES+NS</td>
<td>12.8</td>
<td>14.8</td>
<td>4.0</td>
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**No naps (%)**

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<th>Early type</th>
<th>Intermediate type</th>
<th>Late type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only NS</td>
<td>22.9</td>
<td>17.9</td>
<td>26.9</td>
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</table>

**Free days**

<table>
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<th>Total (%)</th>
<th>FDMS</th>
<th>18.9</th>
<th>32.0</th>
<th>18.2</th>
</tr>
</thead>
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<tr>
<td></td>
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**No naps (%)**

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Likewise, **nap frequency** (a parameter for regularity of napping on a specific shift) was chronotype-dependent. Early chronotypes napped most regularly on night shifts, namely every second night shift and in comparison only every third morning shift on average. Intermediate types showed a high nap frequency on both extreme shifts; every second morning and night shift a nap was taken. Late types napped every 1.8 morning shift and at least every 2.5 night shift comprised a nap (interaction effect ‘type of shift*chronotype’: F(2,188)=5.461, p<0.001, Fig. 8C). Evening shifts displayed least nap frequencies; on average a nap was taken every fourth shift.
**Nap lengths** differed significantly between shifts (main effect 'type of shift': $F_{(2,188)}=7.771$, $p<0.001$), with evening shift naps being in general shorter than morning and night shift naps (*post-hoc* tests: $p<0.006$, Bonferroni-corrected). Age interacted with type of shift, with younger shift workers taking longer naps on morning, but not on night shifts (interaction effect 'type of shift*age': $F_{(4,188)}=3.917$, $p<0.05$). Chronotype also significantly influenced nap duration. Early types napped longest on night shifts (1h 30min) and one hour on morning shifts. Intermediate types had similar nap lengths of 1h 20min on both morning and night shifts. Late types showed longest nap durations (2h 10min) on morning shifts and also napped averagely two hours on night shifts (Fig. 8D, interaction effect 'type of shift*chronotype': $F_{(4,188)}=4.472$, $p<0.01$). In general, late types napped slightly longer as compared to early and intermediate types, albeit this trend did not reach significance.

Tab. 3. Statistical indices of nap behaviour analyses. Repeated measures ANCOVAs were applied with 'type of shift' as within, 'chronotype' as between subject factor as well as 'age' and 'shift schedule' as covariates. *: $p\leq0.05$, **: $p\leq0.01$, ***: $p\leq0.001$, #: $0.05<p<0.1$. ME=main effect, IE=interaction effect, N=sample size.

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### Chapter 2: How Chronotype Influences Nap Behaviour in Shift Workers

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Chapter 2: How Chronotype Influences Nap Behaviour in Shift Workers

On **free days**, only 19 shift workers napped after morning, 7 after evening and 22 after night shifts. Although statistical power was too low (1-\(\beta\)=0.58) with those small sample sizes, nap behaviour showed similar chronotype- and shift-dependent patterns also found on workdays (see Tab. 2 and Fig. 8E-H). Early chronotypes napped mostly on free days after night shifts and from that 45% solely on this type of day. A high number of intermediate types either napped on one or on both free days after the extreme shifts. One third of the intermediate types did not take a nap on free days. Eighteen percent of late chronotypes napped on free days after morning shifts. With 54% most late types did not take a nap on free days.

More participants napped on free days after morning shifts in shift schedule three as compared to schedule four (interaction effect ‘type of shift *shift schedule’: \(F_{(2,114)}=3.841, p<0.05\), **post-hoc** test: \(p<0.002\), Bonferroni-corrected). The main difference between both schedules is a slower speed of rotation in schedule three as compared to schedule four. Generally, early types napped more frequently, but shorter on free days, as compared to the other chronotype-categories, though this trend did not exceed levels of significance. To circumvent sample size, all participants were grouped for subsequent correlation analysis, showing that chronotype was positively associated with nap duration on free days after morning shifts (\(r=0.60, p<0.01, n=19\)), while later types had lower nap frequencies (\(r=-0.51, p<0.05, n=19\)). No associations were observed for free days after evening or night shifts.
Fig. 8. Napping behaviour (percentage of napper, frequency and duration) on work- and free days. Overall analysis of participants taking a nap is shown in panel A and E, whereas in regard to chronotype-categories is provided in panel B and F. Nap frequency (C, G) and duration (D, H) are
given as mean ± standard deviation. Chronotype showed a recurring pattern on workdays: a high percentage of early types napped most frequently and longest on night shifts, late types on morning and intermediate types on morning and night shifts. Note that napping was not restricted to one type of shift, therefore percentages do not sum up to 100. *: p<0.017, **: p<0.006, Bonferroni-corrected, FDMS/ES/NS=free days after morning/evening/night shifts.

2.4.3 Nap Timing

Analysis of nap timing revealed differences in respect of local (clock time) and internal (biological) time scale. On morning shifts, early types napped at 4:20 p.m. local time and more than 60 minutes earlier compared to intermediate chronotypes and late chronotypes (main effect ‘chronotype’: $F_{(2,43)}=3.112$, 0.05<p<0.1, post-hoc test: early type vs. intermediate type 0.05<p<0.1). The majority of early chronotypes displayed a nap timing between 4:00-4:59 p.m., 13% of all napping participants took a nap at that time of day. Most intermediate and late chronotypes took a nap between 5:00-5:59 p.m. with 10% and 13% respectively of all morning shift nappers, see Fig. 9A.

On night shifts, all chronotype-categories napped on average at the same local time of day (between 5:30-6:45 p.m.). The mode for nap timing in early types was between 6:00-6:59 p.m., with more than 15%, napping at that time of day (see Fig. 9B). For most intermediate types, nap timing was between 6:00-7:59 p.m., with 10% in each hourly bin. Late types displayed two modal values at 5:00-5:59 p.m. and 8:00-8:59 p.m., with 5% of all night shift napping participants timing their nap at these times of day.

As mentioned previously, no statistical analyses of evening shift napping was possible, as sample sizes were too small. A table of all effect sizes is given in Tab. 4.
Fig. 9. Timing of nap in hourly bins is shown for morning (A, C) and night shifts (B, D). Nap times are given as mid nap (nap onset–nap duration/2) on a local (A, B) or internal time scale (C, D) separately for early (white bars), intermediate (grey bars) and late chronotypes (black bars).

Adjusting nap timing for chronotype (MSFE as biological midnight) revealed that on morning shifts early and intermediate types napped at the same internal time, around subjective midday (~12:30 p.m.), whereas late chronotypes napped almost 1h 15min earlier than early types at 11:15 a.m. internal time (main effect ‘chronotype’: F(2,44)=7.796, p<0.001, post-hoc test: early type vs. late type and intermediate type vs. late type p<0.01). Early and intermediate chronotypes had a mode at internal noon with 12 and 14% respectively. In contrast, late chronotypes displayed a modal value between 11:00 a.m.-12:59 p.m. internal time with 10% in each category.

On night shifts, late chronotypes napped on average around internal noon (11:40 a.m.) whereas early and intermediate chronotypes approximately three hours later (about 2:30 p.m., main effect ‘chronotype’: F(2,55)=6.862, p<0.01, post-hoc test: early type vs. late type and intermediate type vs. late type p<0.01). Nap timing for most early chronotypes was between 4:00-4:59 p.m. on night shifts.
with 12% as modal value. With 10% most intermediate types took a nap between 2:00-2:59 p.m. and late chronotypes displayed three modal values at the 9:00, 11:00 a.m. and 2 p.m. category with 3% each.

Tab. 4. Statistical indices of nap timing analyses. Univariate ANCOVAs were applied with 'chronotype' as between subject factor as well as 'age' and 'shift schedule' as covariate. *: p≤0.05, **: p≤0.01, ***: p≤0.001, #: 0.05<p<0.1. N=sample size.

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### 2.4.4 Predicting Nap Behaviour

Beyond the impact of age, sleep duration, sleep quality, speed of rotation, shift systems and various interaction effects; chronotype*type of shift was reinforced being the strongest predictor for nap duration (p<0.001) and timing (p<0.001) whereas social jetlag*type of shift (mistimed sleep referring to one's chronotype)
was the strongest one for nap frequency (p<0.05). Since only few participants napped on free days, only nap behaviour on workdays was analysed.

**Nap duration** significantly altered with chronotype on different shift days, meaning that nap duration was predictable by the interaction of chronotype and type of shift. Early chronotypes napped on night shifts on average for 1h 30min (CI\(^1\) 10min to 2h 45min, p<0.05). Late types’ nap duration on morning shifts was around 2h 20min (CI 1h-3h 40min, p<0.001) and on night shifts nap length was about 2h (CI 40min-3h 20min, p<0.001). Intermediate chronotypes napped on both shifts on average 1h 20min on morning and night shifts nap were between 5min and 2h 30min long (CI, p<0.05).

**Fig. 10.** Predictor analysis of nap behaviour. Nap duration was predicted by the interaction of chronotype and type of shift. Nap timing was predicted by sleep quality, shift system and chronotype*type of shift. The interaction of social jetlag and type of shift significantly predicted nap frequency. ET/IT/LT=early/intermediate/late type, MS/ES/NS=morning/evening/night shift, h=hour.

**Nap timing** was predicted by chronotype*type of shift, while sleep quality and shift schedule were marginally significant predictors (0.05<p<0.1). In a slow, but irregular forwards-rotating system (S3) participants napped later (on local time scale) compared to the regular rotating schedule (S4, post-hoc analyses p<0.05). With increasing subjectively rated sleep quality nap timing was in

\(^{10}\) Confidence interval.
tendency delayed by averagely ten minutes (CI 9-21min, 0.05<p<0.1). Early
types napped on average at 4:20p.m. on night shifts (CI 12:30-8:10p.m.,
p<0.001), i.e. about three hours later compared to intermediate types on evening
shifts. Nap timing in late types was around 3:30p.m. on both, morning and night
shifts (CI 11:30a.m.-7:30p.m., p<0.05). Intermediate types napped on average at
4:00p.m. on morning and around 4:50p.m. on night shifts (CI: morning shift
12:00p.m.-7:50p.m. and night shift 1:00p.m.-8:40p.m., p<0.01).

Social jetlag (a measure of circadian misalignment in terms of sleeping
beside the chronotype-dependent sleep window (Wittmann et al., 2006))
predicted nap frequency: On morning shifts, most participants’ sleep timing was
prior to individual sleep windows. Every hour of social jetlag increased nap
frequencies by 7% (CI 4-11%, p<0.001). On night shifts, participants slept after
the internal sleep window, leading to elevated levels of social jetlag. Each hour of
social jetlag increased nap probability by 5% (CI 2-6%, p<0.001) compared to
evening shifts.

2.4.5 Nap and Main Sleep Duration

The percentage of napping participants was associated with the duration of the
main sleep episode: participants with shorter sleep durations commonly napped
and the proportion gradually decreased with increasing sleep duration. Because
too few participants napped on evening shifts (n=23) or free days (n=48), no
analysis was conducted. Predominantly late types displayed short sleep
durations on morning shifts. Only few participants slept less than three hours
before an upcoming morning shift, but all participants with such short sleep
durations displayed a subsequent nap that day. Based on all participants sleeping
between five and six hours before a morning shift, 24 shift workers (or 46%)
also took a subsequent nap. This number was composed of 13% early, 15%
intermediate and 17% late chronotypes (see Fig. 11A).

A similar pattern became apparent on night shifts, although the relation
was not as steep (see Fig. 11B). Shorter main sleep episodes were predominantly
represented by early chronotypes on night shifts. 59% of those sleeping five
hours after a night shift also took a nap. 60% were early chronotypes, 29% intermediate and only 7% were late chronotypes.

Furthermore, the average nap duration correlated with respective sleep durations on morning shifts: the shorter the main sleep, the longer the ensuing nap was (r=-0.36, p<0.01). No similar correlation on night shifts could be found.

2.4.6 24-hour Sleep Duration

As already shown in previous analyses, chronotype influences sleep duration. Also in this study a chronotype-dependent difference was found in main sleep durations. On morning shifts, early chronotypes slept on average 5h 16min, in comparison late chronotypes slept 4h 40min before an upcoming morning shift. Thus, later chronotypes slept about forty minutes less compared to early types (marginally significant 0.05<p<0.1, see Fig. 11C and D). The reverse pattern was visible on night shifts. Here early chronotypes displayed shortest main sleep durations with 4h 53min on average, in comparison late chronotypes displayed averagely six hours sleep durations. Thus, early types slept approximately one hour less than late types on night shifts (marginally significant 0.05<p<0.1). Intermediate chronotypes’ sleep duration was in-between.

Chronotype furthermore influenced total sleep duration (i.e. adding nap and main sleep resulting in 24-hour sleep durations; interaction effect ‘sleep duration*chronotype’: F(2,32)=6.430, p<0.01). Adding up main sleep and nap durations over 24 hours revealed similar total sleep lengths between chronotype-categories on morning shifts, although a slight tendency for longer 24-hour sleep durations in later chronotypes (early types: 6h 13min, late types: 6h 47min). Twenty-four hour sleep duration of intermediate chronotypes was between early and late types on morning and night shifts. On night shifts, the difference of the 24-hour sleep duration between early and late chronotypes even enlarged. With an average 24-hour sleep duration of 6h 20min, early chronotypes slept in total ~1h 30min less on night shifts than late chronotypes (p<0.05).
Fig. 11. Interaction of main sleep duration and nap behaviour on morning (left panels) and on night shifts (right panels). Percentages of nappers relative to sleep duration (hourly bins) are shown on morning (panel A) and night shifts (B). Short sleep durations increased the percentage of nap takers. Stacked columns visualize the chronotype-distribution within each category. Chronotype- and shift-dependent differences in sleep and 24-hour sleep duration on morning (C) and night shifts (D) are shown as means and standard deviations. Main sleep was shortest on morning shifts in late chronotypes and on night shifts in early types. Participants had on average equally long 24-hour sleep durations on morning, whereas diverging 24-hour sleep durations on night shifts. h=hours, *: p<0.05, (*): 0.05<p<0.1.

### 2.4.7 Causality of Nap and Main Sleep

Multiple regression analyses were conducted in order to gather information about the causality of nap and main sleep; whether the previous main sleep affects napping (model A) or the nap affects sleep begin of the following sleep episode (model B). Analyses on local and internal time scale showed only minor differences.
When analysing time designation on a **local time scale**, sleep duration of the previous sleep episode significantly influenced nap duration on morning shifts (model A). Every hour prolonged main sleep duration reduced subsequent nap duration by 25 minutes \((p<0.001, \text{ see Fig. 12A})\). Nap duration on evening and night shifts was not influenced by previous sleep episode. The time of sleep onset on free days after night shift significantly influenced subsequent nap duration by 9 minutes per hour \((p<0.05)\).

Sleep duration of the previous night affected sleep onset of the subsequent main sleep episode on morning shifts. Early sleep begins were associated with long previous sleep durations. Sleep duration could explain 42% of the variance seen in sleep onset of the ensuing night \((p<0.001)\). After evening and night shifts, the timing of nap affected sleep onset of the ensuing sleep episode. The later the nap was taken, the later the sleep onset of the following night. Every hour of later nap timing delayed sleep onset of the subsequent sleep episode by 35 minutes after evening \((p<0.01)\) and 42 minutes after night shift days \((p<0.01, \text{ see Fig. 12B and C})\). Nap timing clarified more than 20% of the variance in sleep onset of the following sleep episode.

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**Fig. 12.** Causality of nap and main sleep episodes. On morning shifts (panel A) previous main sleep episode influenced nap duration. Nap timing affected sleep onset of the subsequent shift, on evening and night shifts (panel B and C).
Same analyses were conducted for sleep designations on an **internal time scale**. Internal sleep offset as well as sleep duration of the previous main sleep significantly predicted nap duration on morning shifts. Time of awakening influenced nap duration stronger than main sleep duration, which is indicated by a higher beta-weight. Every hour delayed time of awakening reduced nap duration by 22 minutes (p<0.01). With increasing ratings of participants’ subjective wellbeing, nap duration was reduced (p<0.05). The model clarified 40% of the variance in nap duration.

Sleep duration of the previous main sleep episode as well as nap duration showed a significant impact on sleep begin of the succeeding main sleep episode. Sleep duration was the strongest predictor, long durations were related to early sleep begin of the following night by 45 minutes per hour (p<0.001). Nap timing influenced sleep onset of the subsequent main sleep episode after evening and night shifts. Later timed naps delayed sleep onset by 47 minutes after evening (p<0.001) and 29 minutes after night shifts (p<0.001). Also sleep quality of the previous main sleep influenced sleep onset of the following night (p<0.05). Nap timing had a stronger impact on sleep begin as compared to sleep quality, but both variables explained 44% of the variance in sleep onset.

Tab. 5. Investigation of the causality of nap and previous as well as subsequent main sleep episodes. Analyses were conducted for local time and internal time separately. Collinearity was controlled by variance inflation factors. Model A=multiple regression analyses investigating the impact of the previous main sleep on nap duration. Model B=multiple regression analyse examining the effect of napping on sleep begin of the subsequent sleep episode. MSE1=main sleep episode prior to nap, MSE2=main sleep episode ensuing the nap, \( R^2=\) explained variation of the model, corrected value, \( b=\) regression coefficient, \( \beta=\) standardized coefficient, VIF=variance inflation factor, \( N=\) sample size, ..=no result.

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<th>Independent variable</th>
<th>( R^2 )</th>
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2.5 Discussion

In this study nap behaviour in shift workers was investigated in regard to employee's internal time. Firstly, nap behaviour was descriptively analysed, in terms of when, how long and how many participants took a nap. Based on these results, napping was modelled and predicted in shift workers.

Early chronotypes napped predominantly, most frequently and longest on night shifts; likewise did later chronotypes on morning and intermediate types mainly on both extreme shifts. Shorter sleep durations were associated with higher percentages of napping shift workers. Whereas sleep durations differed between chronotypes, adding up nap durations to a 24-hour sleep duration, total sleep lengths showed equal durations on morning shifts, but remained different on night shifts. Thus, by taking a nap, late chronotypes could compensate sleep deprivation on morning shifts, whereas early types failed to fully compensate sleep loss on night shifts. Nap timings showed chronotype-differences when
analysed on an internal time scale: early and intermediate types napped around, whereas late types more than one hour before internal noon on morning shifts. On night shifts, late types napped around internal noon, while early and intermediate types about three hours later. Beyond the clear chronotype-specific nap pattern, nap timing and duration was even predicted by the interaction of chronotype and type of shift (morning, evening or night shift), while the interaction between social jetlag and the type of shift was the strongest predictor for nap frequency. It was shown for the first time that chronotype and circadian misalignment significantly influenced nap behaviour in shift workers. Wake up time of prior sleep episode influenced nap duration negatively on morning shifts, whereas the internal timing of an evening and night shift nap significantly influenced sleep begin of the following main sleep episode. This provides first information concerning the causality of a nap that previous main sleep affects nap duration, whereas nap timing influences sleep of the ensuing main sleep.

The results found in this study clearly showed that not only night shifts, also early awakening before morning shifts and with that reduced sleep lengths, were shown here to entail an increased need for compensatory naps for a majority of the participants (namely for intermediate and late chronotypes). A comparable number of participants napped on morning as compared to night shifts.

Most frequent and longest naps were taken on the most strenuous shift, which are night shifts for early chronotypes and morning shifts for late types. This result is in line with the first hypothesis that chronotype- and shift-related strain entailed a chronotype-dependent need for sleep compensation. In addition to that, the length of main sleep episode was related to the percentage of nap taking participants. Short main sleep increased the probability of taking a nap and with longer durations the probability successively decreased. This association was clear on morning and still persisted, even if not as steep on night shifts. The results underline the general sleep compensatory function of napping after a night of sleep loss.
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Given that intermediate types generally show longer sleep durations and less social jetlag in shift workers (Juda et al., 2013a), a reduced need for sleep compensation and therefore a reduced likelihood to take a nap was hypothesized for intermediate chronotypes. Results disproved hypothesis 2; napping behaviour was not diminished, but rather comparable to early chronotypes on night or late types on morning shifts. Since more than 50% of intermediate types napped on both morning and night shifts, it can be concluded that intermediate types suffer from early awakenings before morning shifts as well as from nightly working hours. Given that an increased need for sleep compensation by taking a nap is most likely a result from preceding sleep deprivation or circadian disruption, which is in turn a potential key factor in the pathogeneses of shift work-associated health risks, further research should bestow more consideration upon intermediate types suffering even from two-out-of-three shifts.

Shift workers showed generally long nap duration, ranging from one through two hours. Åkerstedt and his colleague Torsvall found similar nap lengths in shift workers (Åkerstedt et al., 1985) Yet, there were not such long nap durations seen in morning shift nappers (which most likely coincide with late chronotypes in this study). Late chronotypes displayed in tendency longer nap durations as compared to early and intermediate types. However, a study designed by Lumley and others found no improvement between an hourly and a two-hour nap in terms of sleepiness levels, measured with the sleep patency test (Lumley et al., 1986). Thus, the length of a nap is potentially not a sufficient indicator for estimating how beneficial the nap was.

Nap behaviour did not only show a chronotype-dependent pattern, but even could be predicted by chronotype, which strengthens the immense influence of chronotype on nap behaviour. Besides many other variables, such as age, sleep duration, sleep quality, speed of rotation, shift systems and various interaction, circadian misalignment and individuals’ internal time in interaction with different shift days were the strongest predictors for napping in shift workers. The interaction of chronotype and type of shift (morning, evening and night shift) significantly predicted nap duration and nap timing. Nap durations of
early types on night shifts, intermediate types and late types on morning and night shifts were significantly longer as compared to intermediate types on evening shifts. Late types generally napped comparatively early on both morning and night shifts and early types rather late on night shifts. As did early types, also intermediate types napped generally late on night shifts as compared to morning shifts. Besides chronotype, also sleep quality predicted nap timing: in tendency, worse sleep quality ratings were associated with earlier timed naps. Since sleep quality is one of the big questions still to be answered, there is plenty of room for speculations. The interaction of the amount of social jetlag and type of shift (the concept of social jetlag provides information to what extend someone lives and sleeps against the individual biological rhythm) predicted nap frequency. With increasing social jetlag the number of naps increased on night and morning shifts. Sleeping beside ones sleep window increased nap frequency by 5-7%. It was shown here for the first time that beyond the impact of chronotype and sleep duration, also circadian misalignment significantly increased the need for compensatory naps.

Even though main sleep durations were shorter in late types on morning shifts, by taking a nap they fully compensated sleep deprivation, which became apparent in equally long 24-hour sleep durations between chronotypes. There was a numerical tendency that on average 24-hour sleep lengths were even longer in late types on morning shifts. Due to long nap durations also on night shifts, late chronotypes displayed 24-hour sleep durations of averagely eight hours, which is comparable to normal day workers (Juda, 2010). There is evidence for a higher plasticity in later chronotypes being more flexible in sleep-wake habits (Ishihara et al., 1987; Park et al., 1998). This can explain generally longer nap durations and the ability to compensate sleep loss on morning shifts by taking a nap. A less flexible sleep pattern in early types could be responsible for insufficient sleep compensation on night shifts, visible in short 24-hour sleep durations. Therefore hypothesis 4, saying that since napping compensates sleep deprivation, 24-hour sleep durations would be similar between chronotype-categories, was proven to be only partly true. A diminished flexibility in shifting sleep timing - which is essential after night shifts - could explain shortened main
sleep and possibly impede extended compensatory naps. The tendency of shorter, but more frequent, napping on free days also points towards a more stringent sleep behaviour in early types.

Generally, a clearer relationship between sleep duration, chronotype and nap behaviour on morning shifts became apparent as compared to night shifts. Åkerstedt and Torsvell described similar results, showing a steep relationship between main sleep duration and napping participants on morning shifts, whereas a similar, but not as stringent pattern on night shift days (Åkerstedt et al., 1985). From these findings, it can be assumed that morning shift naps result from a preceding sleep deprivation (and is therefore directly correlated to sleep duration), whereas naps on night shifts might be due to rather anticipated sleep loss (thus not instantly correlated with previous main sleep parameters). The findings concerning nap timing (which will be described in the following) and the causality of napping and main sleep episodes strengthen this hypothesis. Analysing the effect of a nap on the following main sleep, most studies looked at the effect of a nap in elderly participants but not in employees or even shift workers (Campbell et al., 2005; Dautovich et al., 2008; Pilcher et al., 2001; Tamaki et al., 1999). The conducted analyses here considered both, the effect of the previous main sleep on naps as well as the effect of a nap on the ensuing sleep. Hypothesis 6 (postulating that short mains sleep affected nap behaviour and in turn napping affected ensuing main sleep episode) was tested with convincing results on different types of shift. On morning shifts, length of previous main sleep as well as internal time of awakening influenced nap duration, which indicates a direct link and further suggests that morning naps are taken due to prior sleep loss. Later timed naps, as seen on night shifts, influenced ensuing main sleep episode. On night shifts, nap timing affected subsequent sleep begin and was not influenced by previous sleep. In elderly Hays and colleagues found similar effects of a nap on subsequent sleep, although nap timing was not considered (Hays et al., 1996). These results again speak in favour of a more anticipated sleep need on night shift days and its function to reduce sleep pressure. Interestingly naps delayed sleep onset of the subsequent main sleep even after more than eight hours work.
In this study only the effect of a nap on the following main sleep begin, but not on ‘sleep duration’ was examined. A previously conducted correlation analyses, which was done in order to design regression models, revealed that not nap behaviour, but rather the previous sleep lengths influenced succeeding sleep duration on morning and night shifts. Interestingly a positive correlation was found between the two main sleep episodes (MS: r=0.36, p<0.001, n=58 and NS: r=0.61, p<0.001, n=54), meaning that longer sleep durations before a nap were associated with longer main sleep lengths after the nap. Furthermore, sleep duration of the previous main sleep on morning shifts negatively influenced sleep onset of the subsequent sleep episode (long sleep durations leading to an early sleep onset). A possible conclusion for this finding is that general differences in participants’ sleep lengths became apparent, more precisely speaking of long and short sleepers. Long main sleep durations prior to a nap were associated with long main sleep episode after the nap, as seen in long sleepers. In addition, long sleep durations entailed early sleep onsets of the following night, which might be in order to get enough sleep. On the contrary, short sleep durations prior to a nap correlated with short sleep durations of the subsequent sleep episode, typical for short sleepers.

From previous studies it is known that especially late types have to curtail their sleep immensely ahead of time before a morning shift, which results in a REM-sleep loss (Åkerstedt, 1998b; Åkerstedt et al., 1991b). It was found in this study that late types took a nap prior to internal noon on morning shifts. Therefore it can be hypothesized that ‘internally early’ timed nap in late types could possibly compensate for the (REM-) sleep deprivation on morning shift days. Indeed, previous studies found that early timed naps comprise long durations of REM-sleep, which were even unaffected of prior wakefulness (Dinges, 1986). It can be assumed that the nap timing in late types on morning shifts is driven by process S, given that sleep pressure was not fully reduced by the previous main sleep. Also the results concerning nap causality strengthen this assumption. On the contrary, early and intermediate chronotypes on morning shifts and late types on night shifts took a nap around subjective noon. It can be assumed that this nap timing is rather process C-driven, because of the
timing coinciding with an increased sleep propensity at internal noon provided by process C (Bes et al., 2009; Carskadon et al., 1992; Dijk et al., 1995). Although no EEG-data was recorded, the findings most likely affirm hypothesis 3 that nap timing can be explained by process S or C.

On night shifts, early and intermediate types napped comparatively late on night shift days. Besides the association of nap timing and subsequent main sleep, also these findings speak in favour of a rather strategic reason for a late nap before a night shift. A possible conclusion would be that early chronotypes internally napped later in order to reduce build-up of sleep pressure before the upcoming night shift. Previous study results support this hypothesis, describing that late timed naps comprise long slow wave sleep episodes (Maron et al., 1964; Torsvall et al., 1989) and can therefore function as pre-sleep (Feinberg et al., 1992; Werth et al., 1996) and possibly reduce sleep pressure built up by process S.

The reasons for taking a nap are diverse, ranging from acute tiredness, anticipated sleep loss, sleep stage-compensation, to physical or mental exhaustion. Besides homeostatic sleep pressure and circadian sleep timing, also other components influences nap timing, such as working times, social duties or even health state (Silva Costa et al., 2013). Results found in this study suggest that sleep timing was either driven by process S or C. This strengthens the extraordinary control of biology on sleep timing, even in such dominating environments as seen in shift workers.

Besides chronotype, also age influenced nap behaviour: younger shift workers napped longer on morning shifts. Possibly a higher sleep need or social factors in younger participants could explain the findings (e.g. having no children, living alone, being single or in looser partnerships). Although subsamples of shift schedules were very heterogeneous in terms of participants’ age and sex, there was no difference in chronotype between groups. There was only one significant difference in nap behaviour between shift schedules. In a slowly rotating shift schedule (S3), an elevated amount of people napped on free
days after morning shifts as compared to a fast rotating schedule (S4). Please note that shift schedule four does not originally comprise free days after morning shifts and are therefore days of vacation. It is worth mentioning, given small sample sizes on free days, this could also be due to a sample bias. Diverging workloads or levels of physical effenness could also explain differences observed between shift schedules. As shift schedules influence sleep-wake behaviour (Åkerstedt, 1998a; Flo et al., 2013), it can be concluded that a higher number of consecutive shifts leads to an accumulated sleep loss and increases the need for compensatory naps on work- and free days. An assumption is that higher speed of rotation seems to be beneficial in terms of decreasing the need for sleep compensation. Also the predictor analyses found a significant effect of the shift schedule on nap timing. The findings only partly support hypothesis 5, postulating that shift schedules would influence nap timing, and need further examination. Too little is known about the meaning of an early or late nap. As mentioned previously, naps at different times of day comprise different sleep stages and can therefore function as sleep compensation (early naps) or as pre-sleep (late naps). The impact of a slow or fast, regular or irregular shift schedule on nap timing is still open for speculations.

2.5.1 Limitations

Several limitations are noteworthy in this study. Sleep log entries were self-reported and thus depended on the diligence of participants filling in correct sleep/nap times. Sleep logs asked for differentiation between going to bed, trying to fall asleep and sleep latency for main sleep duration, but not for naps. It is not possible to infer from time designations of naps, if this was the time of lying down or actual sleep onset. Sleep logs also lacked sleep quality ratings for naps, usage of an alarm clock as well as subjective feeling of recuperation after the nap. As participation was voluntary and without financial benefits, there may have been a selection bias. However, the same fact also increases the probability that participants filled-out their sleep logs correctly, as they were most likely highly motivated.
Job requirements, physical strain and workload may have varied between the four different production settings, causing different levels of physical efficiency. To account for these potential differences, the covariate ‘shift schedule’ was included. Other factors that may have influenced the participants’ need to take a nap were not enquired (e.g. physical exhaustion, headache or fatigue) or on the contrary prevent from taking a nap (e.g. caffeine intake). A further limitation is that nap behaviour on evening shifts was used as reference category for predicting nap behaviour, albeit only few participants napped on evening shifts.

The timing of naps is generally limited by working hours and the duration of free time. Especially on evening shift, which was used as reference category, the opportunity to take a nap is limited by working times, leaving only early morning or late evening hours for taking a nap.

Although one can attribute sleep compensatory effects to napping, it is not known how equivalent a nap is as compared to main sleep (Tilley et al., 1982). Sleep deprivation is not only a question of duration, also certain sleep stage has to be compensated during napping (Tune, 1969). Although this study did not comprise EEG-recordings, the timing of naps in this study supports the hypothesis that not only durations also the sleep stages are compensated, e.g. potential REM-sleep deprivation on morning shift entails early timed naps, when REM-sleep propensity is generally enhanced.

### 2.5.2 Strengths

A big strength of this study is that nap behaviour was analysed with respect to employees’ internal time in a real shift work setting, without any behavioural restrictions. Employees’ chronotype was assessed with the MCTQ\textsuperscript{Shift}, which provides information about phase angle of entrainment and therefore allow analyses on an internal time scale. Furthermore, the MCTQ\textsuperscript{Shift} is the first questionnaire for chronotype assessment especially adapted for shift workers. With 118 participants and a general measurement period of four weeks, number of cases is considerably high.
Chapter 2: How Chronotype Influences Nap Behaviour in Shift Workers

The major strength is that this study comprises four different shift schedules, which differ in regard to shift and free day sequences and number consecutive shifts, therefore speed of rotation. The chronotype-dependent nap pattern found in this study is stable throughout different shift schedules and is therefore not an artefact resulting from schedule peculiarities or work tasks. For the first time nap behaviour was shown to be predicted by chronotype and social jetlag. Present research is lacking the cause-effect relationship of taking a nap. In this study it was investigated for the first time, whether a nap was taken due to sleep loss in the previous night or whether a nap affects subsequent main sleep. Both were true for different shifts, implying different sleep strategies in shift workers on different shift days. It was a sleep compensatory nap on morning shifts and more a pre-sleep on night shifts. Also the findings concerning nap timing are in line with this assumption. The findings provide important information with regards to influential factors on nap behaviour in shift workers and smooth the way for further research.

2.5.3 Implications

The necessity of developing both shift- and chronotype-dependent behavioural recommendations ‘if’, ‘when’ and ‘how long’ to nap is clear, as shift work is part of our increasing 24/7-society. Many studies impressively demonstrate the negative effects of chronic sleep curtailment on the whole metabolism (increased insulin-resistance, appetite and food intake, but less energy expenditure), on the immune system (elevated levels of interleukin-6 and c-reactive protein), on the organization of the hormone secretion and on the circadian regulation of the transcriptome (Moller-Levet et al., 2013; Mullington et al., 2009; Nedeltcheva et al., 2014; Scheer et al., 2009). Since napping can act as a countermeasure to reduce sleep deprivation, positively influence immune alterations as well as hormone secretion after sleep restriction (Bracci et al., 2013; Faraut et al., 2011; Vgontzas et al., 2007), it might be a promising approach to positively influence these potential risk factors for the development of several shift work-associated diseases.
The presented findings indicate that chronotype and circadian misalignment are important factors for napping (as a coping strategy against sleep deprivation and circadian disruption). These results emphasize the importance of considering individuals’ internal time when 1) examining the effects of shift work across schedules (fast vs. slow rotation) and 2) designing effective countermeasures on individual level in terms of reducing chronotype-specific shift strain (such as shortened main sleep or increased levels of social jetlag), in order to reduce long term effects on employees’ health and cognition.
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3 Light Entrainment in Real Life

3.1 Abstract

Objectives. Since light is the most dominant synchronizer for the biological clock, in this study continuously measured light exposure profiles were analysed in regard to individuals’ internal time (i.e. chronotype) in order to investigate the effect of light on entrainment of circadian clocks in real life.

Methods. For at least one work- and free day 23 office worker wore light measurement devices at eye level, quantifying spectral composition of light exposure. For chronotype-assessment the MCTQ was used. Repeated and one-way ANCOVAs, correlations and t-tests were conducted for analysing light exposure in real life. General light exposure differences between work- and free days were investigated, as well as light exposure and duration under certain light intensities (≤5lx, 5-100lx, 100-250lx, >250lx, horizontally measured) during photo- and scotoperiod considering individuals’ internal time. A multiple regression analysis was conducted in order to predict chronotype by light exposure. With the help of a vector analysis participants’ entrainment was investigated.

Results. Light exposure during wakefulness (analysed consolidated and separated for photo- and scotoperiod) was comparable between chronotypes. Analysing light exposure under consideration of internal time of day revealed chronotype influencing light exposure on work- and free days. Late chronotypes showed highest light exposures before, whereas early chronotypes after internal noon. The reverse pattern was visible during scotoperiod: late types experienced more light after sunset, but early types before sunrise. Despite different timing of light exposure, all chronotypes displayed a tight coherence between rest-activity and light-dark pattern. Not only general light exposure, chronotype furthermore modulated duration spent under certain light intensity before and after internal noon. Light levels on free days were on average 11-fold higher compared to workdays and could significantly predict chronotype.

Conclusions. Chronotypes showed huge differences in light exposure with regards to internal time of day. Study results can be explained with an embedding of circadian clocks to light and darkness in order to expose to light at the right internal time of day and therewith accurately adjust internal period length to the 24-hour cycle.
3.2 Introduction

In humans, as well as in many animals, the daily routine was adapted to the naturally provided course of light and darkness: we stood up with sunrise and went to bed with sunset. T. A. Edison invented, historically seen, artificial light in the recent past. From then on we successively became independent of sunlight and simultaneously moved our lives inside buildings, where we created our own light-dark cycle by switching artificial light on and off at any time of day. Light exposure within our daily life differs widely from naturalistic light conditions, nowadays light levels during photoperiod (light phase of the 24-hour day) are too small whereas too high during scotoperiod (dark phase) as compared to life without artificial light (Martinez-Nicolás et al., 2011). Work places generally show illumination levels of 300-500lx, in comparison at a cloudy winter day 3,500lx and during summer 20,000-100,000lx can be measured.

Light, especially blue spectrum around 480nm wavelength, is the most important synchronizer (also called zeitgeber) for the biological clock (Duffy et al., 1996). Retinal ganglion cells - a recently discovered melanopsin comprising photoreceptor in the eye - receive light information and transduce them via the optical nerve (Berson et al., 2002; Brainard et al., 2001; Freedman et al., 1999; Thapan et al., 2001). Furthermore, it was shown that also rods and cones contribute to circadian entrainment (Zeitzer et al., 1997). A small paired brain region above the optic chiasm, the suprachiasmatic nucleus (SCN), gathers transmitted light information and actively synchronizes to the given light-dark cycle; a process called entrainment (Roenneberg et al., 2007c). The SCN coordinates the release of neurotransmitters (e.g. melatonin, cortisol) as well as activation and inhibition many connected brain regions, thereby controlling physiology as well as behaviour and synchronizes all peripheral clocks (Karasek et al., 2006; Zawilska et al., 2009). Insufficient light exposure during photoperiod or higher light intensities during scotoperiod cause poor synchronization of the biological clock to the 24-hour cycle. The phase of synchronization is therefore highly individual and can span more than twelve hours from earliest to latest chronotypes (Roenneberg, 2012).
3.2.1 Conceptual Approaches and Status Quo in Research

The human biological system is most sensitive to short wavelengths of the blue spectrum (Brainard et al., 2001). One main focus of recent research was to investigate the effect of different light conditions (in terms of mono- or polychromatic light, intensities and duration) on the biological clock (Czeisler et al., 1989; Jewett et al., 1997; Wright et al., 2013). Phase shifting effects of light are often examined under constant dim light conditions. Under these settings, scheduled bright light pulses of low intensities were found to significantly influence circadian systems (Gronfier et al., 2007; Zeitzer et al., 2000).

The most prominent model to explain and even predict phase shifts of the circadian system is the ‘Phase Response Curve’ (PRC), described by Daan and Pittendrigh 1976 (Daan et al., 1976). The amount and direction our circadian system gets shifted by a discrete light pulse, is phase-dependent with respect to light pulse intensity, timing and duration of light exposure (Duffy et al., 2005). According to the PRC light either resets the biological clock (type 0) or causes a phase advance, when received during internal forenoon or a phase delay when exposed during internal afternoon (type 1)(Minors et al., 1991). Some research found a light insensitive ‘dead zone’ during internal midday (Dumont et al., 1997), whereas others disproved the findings (Jewett et al., 1997).

In 2010, Roenneberg and colleagues described entrainment as a integral function of light exposure over the 24h day, resulting into a new theory named ‘Circadian integrated Response Characteristic’ (CiRC) (Roenneberg et al., 2010a). As compared to the PRC, where light stimuli of a specific intensity and duration causes an immediate shift of the circadian phase, the CiRC rather integrates any light exposures throughout the internal day (therefore considering light history) and relate the amount of light experienced within expanding and compressing portions. A greater proportion of the compressing part shortens, whereas higher proportion during expanding part lengthens internal rhythms (Roenneberg et al., 2010a).
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Fig. 13. The ‘Circadian integrated Response Characteristic’ (CiRC). Panel A shows equal proportion sizes, so that light will not impact internal period length. In case more light hits the circadian system before internal noon in the compressing proportion, internal cycle length is compressed (panel B), whereas higher light levels in the proportion during internal afternoon will expand internal cycle length (panel C). Modified from (Roenneberg et al., 2010a).

Based on daily activity and light profiles, Rea and colleagues introduced a novel approach to quantify light induced circadian entrainment from activity and light measurements, called ‘behavioural entrainment’ (Miller et al., 2010; Rea et al., 2008). The synchrony between light and dark exposure and activity and rest behaviour, and therefrom calculated vectors, describe the degree of individuals’ circadian entrainment. This measurement postulates that if activity- and light patterns show a high accordance, participants are well entrained to the 24-hour light-dark cycle. Vector amplitude indicates the extent the two measurements are related; the angle indicates phase relationship. In case light- and activity-pattern show a high accordance, phase angle of the vector will be around zero and vector amplitude will display high values.

Additionally to laboratory research, light profiles in naturalistic conditions have also been of high interest. Since humans spend most of their time inside buildings, light exposure is generally very low. Studies have shown that time under bright light (≥1,000lx) ranges from 90 to only 120 minutes per day (Espiritu et al., 1994; Martinez-Nicolas et al., 2011; Okudaira et al., 1983; Savides et al., 1986) and also depends on season (Hebert et al., 1998). Generally, humans spend more than half of the time awake in light intensities between 1-100lx.
Seldom differences between work- and free days as well as between chronotypes have been considered. Although Okudaira tracked light exposure throughout work- and free days, the difference between the days were not investigated (Okudaira et al., 1983). Heil and Mathis reported light exposure at work and compared that with non-work and daily light exposure of the same day, but did not consider free days (Heil et al., 2002). Though light exposure was intended to be related to internal time, Martinez-Nicolas and his colleagues did not investigate participants’ chronotype or corrected for internal time of day and provide no information with regards to work- and free days (Martinez-Nicolas et al., 2011).

In order to increase daily light exposure, the elevation of colour temperature or light intensities of artificial light as well as increasing the light permeability of buildings are potential countermeasures (Webb, 2006). The effects of light installations with high emission of blue wavelengths on sleep-wake behaviour were tested. In office workers high light exposure during the day was seen to be positively related to nightly sleep quality ratings as well as increased performance and levels of alertness (Hubalek et al., 2010; Viola et al., 2008). Usually, sleep-wake behaviour is tightly coupled to the progression of dawn (Kantermann et al., 2007). In an intervention study, Vetter et al. however reported that high-intensity blue-enriched office light can override the seasonally modulated naturalistic light exposure, so that employees were synchronized to the light-dark cycle at their workplace, rather than following seasonal changes in photoperiod (Vetter et al., 2011). The importance of seasonal adjustment for physiology, e.g. for immune response, is open for debate.

In industrialized countries humans experience less light during the day, but long unnatural amounts of light in the late evening (Savides et al., 1986; Wright et al., 2013). This evening light was shown to suppress melatonin secretion in the laboratory and in real life conditions (Santhi et al., 2011). When exposed only to daylight, sending participants camping, an accurate entrainment of the circadian clock to sunrise and sunset became apparent (Wright et al., 2013). It was shown that with increasing zeitgeber strength, the variance in phase of

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11 In this study output rhythms of the circadian clock were measured, namely melatonin.
entrainment between participants decreased, so that they ended up at similar phases (Wright et al., 2013). This implies that the brought distribution is an artefact of modern societies, with humans spending most of their time inside buildings.

### 3.2.2 Research Aims

The major aim of this study was to investigate chronotype-differences in light exposure, whereupon conclusions can be drawn in terms of the effect of light on the embedding of circadian clocks to the 24-hour light-dark cycle in real life. To do so, light exposure at eye level was recorded in a real life situation. In non-shift working employees, general differences in light exposure between work- and free days were examined.

Since human being of industrialized societies spend most of the time during the workweek inside buildings, it was hypothesized that light levels would be smaller on workdays as compared to free days (hypothesis 1). Given that late chronotypes are thought to be less entrained to the given 24-hour rhythm (Goulet et al., 2007; Roenneberg et al., 2007c), it was expected that late types get less light in general as well as less bright light (>250lx) throughout the day (hypothesis 2). Analysing light exposure in regard to light timing, late types were expected to display a greater proportion of light during expanding part of the CiRC, as well as increased light levels during scotoperiod, which causes late adjustment of late types. Accordingly, reverse coherences for earlier chronotypes were expected (hypothesis 3).

With the help of a multiple regression model it was explored, if the differences in light exposure before and after internal noon can explain the variance in participants’ chronotype. The aim was to explore the impact of light on chronotype. Yet, the analyses were explorative and did not raise the claim to solve the chicken-and-egg problem, if the timing of light exposure influences chronotype or if chronotype determines the timing of light exposure.
Based on the method proposed by Rea and colleagues (Rea et al., 2008), a vector analysis was conducted in order to quantify entrainment coherence of study participants in respect of individuals’ activity and light profiles. It was assumed that early chronotypes show an earlier, whereas late chronotypes a later angle and potentially also lower amplitude of the relation between light-dark and activity-rest patterns (hypothesis 4).

3.3 Methods

3.3.1 Participants

Twenty-three subjects (21-38yrs., 60% females) were recruited for study participation (see Tab. 6 for further demographic details). Prerequisites for attending were enquired in selection interviews. Subjects were included, in case they were between 20 to 40 years old, resident in Munich (Germany), pursue a profession at least 3 days a week, were non-shift workers, had no time zone travel the previous month and did not suffer from cataract, diabetes or neurologically pre-existing illnesses. Participants gave written informed consent and were remunerated for participation. The local ethics committee approved the study design. In order to analyse activity and light patterns in real life, no behavioural restrictions were given for the period of measurement.

3.3.2 Instruments

3.3.2.1 Questionnaires

3.3.2.1.1 Munich ChronoType Questionnaire (MCTQ)

For chronotype-assessment participants completed the German version (see appendix 9.2) of the Munich Chronotype Questionnaire prior to study begin (Roenneberg et al., 2003). Mid-sleep on free days (MSF_{ad}) was calculated as a phase marker of chronotype and corrected for catch-up sleep due to accumulated sleep deprivation during workweek.
3.3.2.1.2  *Pittsburgh Sleep Quality Index (PSQI)*

In order to detect sleep abnormalities, subjective sleep quality was examined by using the German version of the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). In total 18 items asks for habitual sleep timing, sleep latency and duration, intake of hypnagogues and fatigue during the day. The questionnaire is attached in the appendix in chapter 9.5.

PSQI-scores range from 0 (no sleep quality complains) to 21 points (hugely impaired sleep quality). Participants with a PSQI-score of eight were included in this study.

3.3.2.1.3  *Sleep Logs*

Participants reported several sleep behaviour-related parameters into a customized sleep log daily after awakening. Inquired variables were time to bed, time of falling asleep, sleep latency, wake up and stand up times, as well as work start and end times. Furthermore, subjects rated the duration of time spent outside the previous day. Sleep logs hold space for comments or for mentioning exceptional circumstances. A template of a sleep log for office workers can be found in chapter 9.4.

3.3.2.2  *Measurement Devices*

3.3.2.2.1  *Daqtometer®*

Actimeters (Daqtometer®, Daqtix GmbH, Germany; weight: 21g, dimensions: 40mm x 44mm x 12mm) for measuring locomotor activity was either placed on left or right wrist. Locomotor activity was sampled every 10 seconds and saved in 30-second intervals. Participants were asked to always wear the device. Only when swimming, bathing, having a sauna or if injury risk was increased, it was recommended to remove the device, but participants were requested to fill in exact times and dates into a protocol sheet.
Fig. 14. The Daqtoimeter®: Wrist worn device for continuous measurement of locomotor activity.

3.3.2.2.2 *LightWatcher*

For light measurement participants wore a LightWatcher (Object-Tracker, Austria; weight: 12g, dimensions: 50mm x 19mm x 10mm) on the right hand side attached to spectacle frame. The device measures among other variables temperature, acceleration, activity, atmospheric pressure and is equipped with five light channels ranging from ultra-violet (350nm) to infra-red (875nm). In this study data from red (620nm), green (540nm) and blue (465nm) light channels were incorporated. Spectral composition of light was measured and stored every 10 seconds. Participants were asked not to wear sunglasses during the measurement and to ensure the device not being covered by hair or a cap. Participants were instructed to wear the LightWatcher from waking up until going to bed with a minimum of interruptions (*e.g.* showering, bathing, having a sauna or if injury risk was increased). In case participants removed the LightWatcher they were requested to enter date and exact times into a protocol. During sleep, subjects were asked to place the device as close as possible, *e.g.* on a bedside table.

Fig. 15. The LightWatcher: Device for measuring spectral composition of light at the eye level fixed at a spectacle frame.
3.3.3 Data Processing

Participants wore actimetry and light measuring device from Friday, October 19th until Tuesday, October 23rd, 2012. Data from actimetry and light measurement were subsequently binned in 10-minute intervals. Time designations were adjusted to GMT+1. Intervals of not wearing the device (mentioned in the protocol) were excluded, as well as time points >30 minutes without locomotor activity and no coincident sleep mentioned in sleep logs. Sleep times were derived from actimetry data by an algorithm developed by Roenneberg and colleagues (Ronneberg et al., 2015). Participants were excluded who stayed outside Munich, Germany (n=3) or if working part-time (n=1) due to limited comparability of light profiles.

3.3.4 Statistical Procedure

Data was analysed separately for work- and free days on local and internal time scale. Additionally, photo- and scotoperiod (light and dark phase of a 24-hour day, respectively) were considered. Photoperiod in Munich, Germany (48°08’N, 11°31’E) at this time of year was from 7:42a.m.-6:13p.m.

In order to describe light exposure to an internal time scale, individuals’ sleep corrected mid-sleep on free days was defined as biological mid night and all corresponding time designations were adjusted (internal time = local time – MSFsc).

In order to assure comparability with other studies, irradiance measures of the LightWatcher (mW/m²) were converted into illuminance (lux) by the following equation. The equation was defined by the developer of the LightWatcher, who stated that coefficients were determined by minimizing the absolute error between the given polynomial and \( V(\lambda) \) curve.
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\[ \text{lux} \approx c \times (0.34 \times R + 0.99 \times G + 0.07 \times B) \]

c= calibration factor (constant, 0.73)

R= red light channel (620nm)

G= green light channel (540nm)

B= blue light channel (465nm).

All calculations were executed by using SPSS Statistics 21.0 (IBM Corp.). For chronotype comparisons, participants were categorized into tertiles: the earliest third was declared as early chronotypes, the latest third as late chronotypes respectively. Arbitrary cut-off values for chronotype-categorization were early (\(\text{MSF}_{sc}<3.98\)), intermediate (3.98\(\leq\text{MSF}_{sc}<4.5\)) and late chronotypes (\(\text{MSF}_{sc}\geq4.5\)). For all continuous variables, outliers were determined and excluded (\(\geq1.5\) edge length of boxplot). The shape of the daily light exposure pattern was investigated by evaluating goodness of fit towards a Gaussian or the sum of two Gaussian distributions. The Akaike information criterion (AIC) was applied in order to identify the best fitting model: positive values indicated a better fit of data towards the more complex model (sum of two Gaussian distributions), whereas negative values display a better fit in regard to the simpler model (Gaussian distribution).

By using repeated measures ANCOVA activity and light differences on work- and free days were tested (within-subject factor ‘type of day’: workday vs. free day, covariates ‘chronotype’ and ‘age’). Furthermore, light intensity differences before and after (internal and local) noon were investigated on work- and free days by using two-factorial repeated measures ANCOVA (within-subject factor ‘type of day’: workday vs. free day and ‘before/after’: before vs. after (midday, sunrise/sunset), covariates ‘chronotype’ and ‘age’). Greenhouse-Geisser corrections were always applied if necessary. For post-hoc analyses of significant effects Pearson correlations were used. Significance was tested against an \(\alpha\)-level of 0.05.
Besides analysing general amounts of light, also the duration of time participants experienced light of certain intensities was investigated. Therefore averaged light exposure was categorized into four classes: very dim (<1lx), dim (1-100lx), moderate (100-1,000lx) and bright (>1,000lx) light (Hebert et al., 1998). Yet, these thresholds result from vertical (skywards) measurements. Since the device measured light intensities in participants’ gaze, category thresholds were adapted to horizontal measurement\(^{12}\). Adjusted thresholds for were: ≤5lx, 5-100lx, 100-250lx, >250lx (corresponding to ≤20lx, 20-400lx, 400-1,000lx, >1,000lx for vertical measurements respectively). Two-factorial repeated measures ANCOVAs were conducted (within-subject factor ‘type of day’: workday vs. free day, ‘light category’: <5lx vs. 5-100lx vs. 100-250lx vs. >250lx, covariates ‘chronotype’ and ‘age’) in order to analyse differences in duration of time spent within different light intensities between work- and free days during wakefulness. Light exposure differences were investigated concerning photo- and scotoperiod as well as time of day, meaning before and after internal midday. In order to avoid un-interpretable 4-fold interaction effects, calculations for work- and free days were conducted separately (within-subject factor ‘before/after’: before noon vs. after noon and ‘light category’: <5lx vs. 5–100lx vs. 100–250lx vs. >250lx, covariates ‘chronotype’ and ‘age’).

By conducting a multiple regression analysis, the variability in chronotype was tried to explain by light exposure. Summed light levels after internal or external midday were subtracted from summed light exposure before internal midday. This was based on the entrainment concept CiRC, stating that integrated light levels before and after internal noon determine either a compressing or an expanding effect of light exposure.

In regard to individuals’ light profiles, phase and amplitude of the accordance between light- and activity-profiles were analysed based on the methodology developed by Rea and colleagues (Miller et al., 2010; Rea et al., 2008). Light and activity patterns are cross-correlated over the given time span (here five days: three work- and two free days). Subsequently, a sine curve is

\(^{12}\) Horizontal to vertical measured light intensities differ by factor four, based on own measurements.
fitted to correlation coefficients.

Amplitude was derived using ChronoSapiens (Renneberg et al., 2015), higher values indicating an higher extend of accordance between light- and activity-measurements. Phase angle (relation between light and activity patterns) was the shift of the sine wave under consideration of period length. Sine wave frequency was calculated from period length (the time of one full oscillation: frequency=1/period length). The result was a sine wave (one for each individual) with certain amplitude, frequency and phase shift, describing the correlation coefficients of cross-correlation.

\[ y = A \sin(\omega t + \varphi) \]

A=amplitude
\( \omega \)=frequency
\( \varphi \)=phase shift.

Univariate ANCOVA’s (covariates ‘chronotype’ and ‘age’) were conducted in order to identify differences in amplitude, phase or frequency between chronotypes.

3.4 Results

3.4.1 Participants’ Characteristics

The study comprised 23 non-shift working participants. There was no significant difference between female (f) and male (m) participants with regards to chronotype (f: 4:16±1:12h vs. m: 4:10±0:41h, p>0.200 all), age (f: 28.6±3.9yrs. vs. m: 30.6±3.7yrs.), body mass index (f: 23.0±5.9 vs. m: 24.1±3.4) or scores of the Pittsburgh sleep quality index (f: 4.3±1.9 vs. m: 3.9±1.3). 90% worked five days a week and 35% commuting to work afoot, which increases the probability of getting sunlight. No personal information as family status or number of children was ascertained.
Tab. 6. Descriptive information of study sample. N=sample size, MSF_{sc}=chronotype (sleep corrected mid-sleep on free days), h=hours, M=mean, SD=standard deviation, R=range, yrs.=years, m=males, BMI=body mass index, PSQI=Pittsburgh sleep quality index.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>MSF_{sc} (h)</th>
<th>Age (yrs.)</th>
<th>Sex (% m)</th>
<th>BMI</th>
<th>PSQI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>R</td>
<td>M</td>
<td>SD</td>
<td>R</td>
</tr>
<tr>
<td>Workdays</td>
<td>23</td>
<td>4:12</td>
<td>1:0</td>
<td>1:36-6:30</td>
<td>29.4</td>
<td>3.9</td>
</tr>
</tbody>
</table>

### 3.4.2 Light Profiles

#### 3.4.2.1 Averaged 24-hour Light Profiles

Averaged light exposure over internal 24-hour day (beginning from internal midnight) differed between work- and free days. On average, participants got about 631 lx on work- and 699 lx on free days, which is over 11-fold more on free days. Light exposure on workdays was very homogeneous between subjects (see Fig. 16), whereas on free days the amount of light showed huge intra-individual differences. Light exposure on work- and free days was comparable between chronotype-categories.

![Light exposure graph](image)

Fig. 16. Light exposure averaged over internal 24 hours separately for work (n=19) and free days (n=19). Insets visualize light exposure on workdays (upper inset) and free days (lower inset) separately for chronotype-categories. Whiskers indicate minimum and maximum values, dots single values. Note log-Scale on y-axis. **: p<0.01.
3.4.2.2 Continuous 24-hour Light Profiles

3.4.2.2.1 Fitting Curves to Light Profiles

Light exposure over an internal 24-hour day was hourly binned and compared between chronotype-categories. A comparative nonlinear regression analysis comprising the Gaussian and the sum of two Gaussian distributions was executed in order to identify best fit. The Gaussian distribution describes a uni-modal pattern, whereas the sum of two Gaussian distributions a more bi-modal curve shape. The AIC provided information on the best fitting model: negative values suggest a better fit of the Gaussian distribution, whereas positive values indicate that the sum of two Gaussian distributions fitted better to 24-hour light data.

For early types the Gaussian distribution described 24-hour light exposure on workdays, but the sum of two Gaussian distributions fitted best to light patterns on free days (AIC WD: -6.47, FD: 82.39). The sum of two Gaussian distributions fitted to light patterns for intermediate and late chronotypes on workdays (AIC IT: 6.79, LT: 0.23). For both chronotype-categories the Gaussian distribution described best the shape of light exposure on free days (AIC IT: -10.88, LT: -10.71).

On a local time scale, a Gaussian distribution described 24-hour light pattern on workdays best for all three chronotype-categories (AIC ET: -1.84, IT: -3.69, LT: -10.87). On free days, the sum of two Gaussian distributions described light exposure patterns for early and late chronotypes (AIC ET: 78.29, LT: 0.11), but not for intermediate types (AIC: IT: -8.47, data not shown).
Fig. 17. Light exposure over the course of an internal 24-hour day in hourly bins, averaged for each chronotype-category and separately for workdays (panels A, C, E-G) and free days (panels B, D, H-J n=19). Panel A and B show data on logarithmic scale. Panel C and D show curve fits for all
chronotypes, on a ratio scale. Panel E-J show fitted data separated for early, intermediate and late chronotypes on workdays and panel H-J on free days. Bars indicate standard deviations.

3.4.2.2.2 Light Exposure Onset, Offset and Maximum

Analysing light patterns on local time scale exposed chronotype-differences in terms of light on- and offset. On work- and free days early types experienced light first, followed by intermediate types, whereas late chronotypes experienced light latest of all three chronotype-categories (see Fig. 18). The reverse pattern was visible in the late evening around bedtime on work- and free days. Light levels went down for early types first, late types showed latest light exposure and intermediate chronotypes were in between.

![Graphs showing light exposure over the course of a 24-hour day on a local time scale](image)

Fig. 18. Light exposure over the course of a 24-hour day on a local time scale. Light exposure is binned for each hour, shown separately for chronotype-categories.

Maximal light intensity for all three chronotype-categories lay between 12-12:50p.m. (local time), which coincided with the German lunch break time on workdays as well as solar noon (zenith around 1p.m. for the prevailing photoperiod). On free days, early chronotypes experienced highest light intensities at 14-14:50p.m., whereas intermediate and late chronotypes between 13-13:50p.m.. Furthermore, Fig. 17A and B as well as Fig. 18 show generally high light exposure for early chronotypes after midday on both local and internal time scale.
Light exposure adjusted to internal time showed chronotype-differences. On workdays, early types experienced maximal light intensities around nine to ten hours after internal mid-sleep, intermediate types eight to nine hours and late types seven to eight hours after individuals’ mid point of sleep. On free days, early types showed a light intensity maximum at internal noon, intermediate types nine to ten hours and late types eight to nine hours after internal mid-sleep.

3.4.3 Timing of Light

Throughout the 24-hour day, within photoperiod (from sunrise to sunset) as well as during scotoperiod (during dark phase from sunset to sunrise) all chronotypes experienced equal light levels. Even if total light exposure did not vary for chronotypes, further analyses revealed an altering light exposure concerning chronotype and internal time of day. Later chronotypes got higher light levels during subjective forenoon (totalized light levels from waking up until internal noon), whereas earlier types had higher light exposures during internal afternoon (light levels from internal noon until falling asleep) on work- and free days (interaction effect ‘before/after midday*chronotype’: $F_{(1,12)}=3.689$, $0.05<p<0.1$ and ‘before/after midday*chronotype*type of day’: $F_{(1,12)}=3.976$, $0.05<p<0.1$).

Light exposures before internal midday during photoperiod and wakefulness on work- and free days were in tendency modulated by chronotype (interaction effect ‘type of day*chronotype’: $F_{(1,11)}=3.763$, $0.05<p<0.1$). Late chronotypes got higher values of light during internal forenoon, whereas earlier types experienced brighter light levels after internal noon within photoperiod (see Fig. 19C and D, interaction effect ‘before/after midday*chronotype’: $F_{(1,11)}=4.859$, $p\leq0.05$ and ‘before/after midday*chronotype*type of day’: $F_{(1,11)}=4.559$, $0.05<p<0.1$).
Fig. 19. Influence of chronotype on light exposure. The amount of experienced light depended on both chronotype and internal time of day. Analysing overall light exposure showed a rather inhomogeneous pattern on work- and free days. Separating between photo- and scotoperiod revealed a more stringent pattern of light exposure (panel C and D). Later chronotypes got more light before internal midday and less during internal afternoon. Earlier types experienced most light during internal afternoon. During scotoperiod early chronotypes had higher light levels before sunrise (especially on workdays, panel E), whereas late types showed an increasing light exposure after sunset (panel F). Note that values are visualized as percent of maximum, in order to visualize work- and free day light levels on the same scale.
The reverse pattern was visible during scotoperiod. Earlier chronotypes experienced more light before sunrise and later chronotypes more light after sunset (interaction effect 'before sunrise/after sunset*chronotype': $F_{(1,0)}=15.613$, $p<0.01$).

### 3.4.4 Explaining the Variance in Chronotype

The variance seen in participants’ chronotype was tried to be explained with the amount of daily light exposure. The difference of light before and after internal and external midday was calculated by subtracting summed light levels during afternoon from morning light exposure. This was based on the concept CiRC, postulating that the biological system integrates light levels before and after internal noon and ‘compares’ the area under the curve. The algebraic sign determines in which direction light causes a shift, either making the biological clock earlier (when more light was experienced during internal forenoon) or later (in case higher light exposure was during internal afternoon).

Tab. 7. Predicting chronotype by light exposure (difference of internal forenoon and internal afternoon) on workdays, free days, and age. Variance inflation factors were applied in order to check for collinearity, values were within acceptable range. $R^2$=explained variation of the model, corrected value, $b$=regression coefficient, $\beta$=standardized coefficient, VIF=variance inflation factor, $N$=sample size, $_$=no result.

<table>
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<tr>
<th>Predictor analysis</th>
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<tbody>
<tr>
<td><strong>Predicting variable</strong></td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Workdays</td>
</tr>
<tr>
<td>Free days</td>
</tr>
<tr>
<td>Age</td>
</tr>
</tbody>
</table>

A multiple regression analysis was conducted in order to clarify influencing factors for variance in chronotype. Differences in light exposure during internal forenoon and afternoon on free days significantly predicted chronotype ($p<0.05$) and explained 27% of the variance in the dependent variable. Age and workday
light exposure differences had no predictive effect on chronotype. Light exposure on an external time scale could not predict chronotype neither on work- nor on free days.

### 3.4.5 Duration under Certain Light Intensities

Overall, participants spent about 60%, which means approximately six hours, in light levels between 5 and 100lx on workdays during photoperiod. About one-third of time during photoperiod (more than three hours) was spent in light levels of 100 through 250lx. Early types spent numerically longest, about 55min, in light above 250lx, although there was no statistical difference between chronotype-categories. On free days, participants generally spent longer durations under brighter light intensities. Subjects stayed 40% of the time awake during photoperiod in light intensities between 5 and 100lx. All chronotype-categories spent more than three hours under bright light of more than 250lx. Ten to 15% of time on free days subjects received light intensities between 100 and 250lx (see Tab. 8). Compared to photoperiod, during scotoperiod participants experienced light of less than 5lx but no light above 250lx on work- and free days. On free days, early chronotypes spent significantly less time under light intensities from 5 through 100lx (p<0.05).
Tab. 8. Duration (in 10min) spent in each light category during time awake separated into photo- and scotoperiod. M=mean, SD=standard deviation, lx=lux, n.s.=not significant, ET=early type, IT=intermediate type, LT=late type.

<table>
<thead>
<tr>
<th></th>
<th>Workdays</th>
<th>Free days</th>
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<tr>
<td></td>
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<td>5-100lx</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Photoperiod</td>
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<td></td>
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<td>Early types</td>
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<td>0.0</td>
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<tr>
<td>Intermediate</td>
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<td>0.0</td>
</tr>
<tr>
<td>Late types</td>
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<td></td>
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<td>n.s.</td>
</tr>
<tr>
<td>Scotoperiod</td>
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<td></td>
</tr>
<tr>
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<td>Intermediate</td>
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<tr>
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</tr>
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<td>6.0</td>
</tr>
<tr>
<td>Significance</td>
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Tab. 9. Duration (in 10min) spent in each light category during time awake separated into photo- and scotoperiod as well as internal fore- and afternoon. M=mean, SD=standard deviation, lx=lux, n.s.=not significant, ET=early type, IT=intermediate type, LT=late type.

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<td></td>
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<td>SD</td>
</tr>
<tr>
<td>Photoperiod</td>
<td></td>
<td></td>
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<tr>
<td>Workdays</td>
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<td></td>
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<tr>
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<tr>
<td>Intermediate</td>
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<td>0.0</td>
</tr>
<tr>
<td>Late types</td>
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<td>0.0</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
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### Before internal noon

<table>
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### After internal noon

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<td>SD</td>
</tr>
<tr>
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### Scotoperiod

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<td>SD</td>
</tr>
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<tr>
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### Significance

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</tr>
</thead>
</table>

### Notes

- ET<LT, p<0.05
Analysing the amount of time spent in respective light intensities revealed that different chronotypes spent differently long in certain light intensities and relative to internal time of day.

Duration of time spent within one of four light intensity categories during wakefulness varied in tendency between work- and free days (main effect ‘type of day’: $F_{(1,8)}=4.620$, $0.05<p<0.1$). Analysis did not show a chronotype effect, meaning that all chronotypes spent equally long within each category. Chronotypes also spent comparable long timespans in bright light during wakefulness, when analysed separately for light levels over 250lx (horizontally measured, equals 1,000lx vertically measured).

The amount of time spent within each category differed between chronotypes when analysed in regard to time of day. On workdays, duration of light intensities differed in tendency between categories (main effect: ‘light category’: $F_{(3.24)}=2.986$, $0.05<p<0.1$). Most time was spent under 5-100lx, whereas least time was spent under 5lx light intensities when being awake. Chronotype generally modulated differences between duration of light certain intensities regarding internal time of day (internal forenoon vs. afternoon) on free days (interaction effect ‘before/after*light category*chronotype’: $F_{(3.30)}=9.203$, $p<0.01$). The later the chronotype the longer the duration spent in light intensities of more than 250lx and less under 5-100lx (horizontally measured) during internal forenoon, on the contrary less time was spent during internal afternoon in light levels of 250lx, but more in 5-100lx. Durations spent under bright light (>250lx horizontally measured) showed in tendency chronotype-differences before and after internal noon, late chronotypes spent more time in bright light before internal noon, whereas early types after internal noon (interaction effect ‘before/after*chronotype’: $F_{(1,8)}=4.077$, $0.05<p<0.1$).

Furthermore, duration under certain light intensities was analysed during photoperiod and time awake. On workdays, participants spent longer in light intensities before internal noon compared to durations after internal noon (main effect ‘before/after’: $F_{(1,12)}=5.380$, $p<0.05$). During photoperiod chronotype effected the duration of light before and after internal noon on work- and free
days (WD: interaction effect 'before/after*chronotype': F(1,12)=136.751, p<0.001, FD: interaction effect 'before/after*chronotype': F(1,11)=9.725, p<0.01). Only on workdays chronotype marginally interacted with internal time of day and duration spent within each light category (WD: interaction effect 'before/after*light category*chronotype': F(336)=3.866, 0.05<p<0.1). Later chronotypes were associated with an increasing amount of time under dim artificial light (5-100lx) before, but declining duration after internal noon as compared with earlier chronotypes (see Fig. 4A and B).

Chronotype influenced differences in duration under bright light before and after internal midday, as well as marginally between work- and free days (interaction effect 'before/after*chronotype': F(1,14)=4.695, p<0.05, interaction effect 'type of day*before/after*chronotype': F(1,14)=3.294, 0.05<p<0.1).
Fig. 20. Duration spent within light intensity categories during photoperiod on work- and free days. On workdays (panel A and B) later chronotypes spent more time in light intensities between 5-100lx during internal forenoon, but less during internal afternoon (see insets of panel A and B). On free days (panel C and D) later chronotypes spent increasingly more time under bright light (>250lx) and artificial light (5-100lx, 100-250lx) before internal midday. Durations decreased with higher chronotypes on free days after internal midday (see insets of panel C and D). Note, only light intensities during photoperiod and wakefulness are considered. Due to the prerequisite of ANCOVAs demanding values for each time point, sample sizes are reduced.

During scotoperiod no light levels of greater than 250lx at the eye level was perceived. On free days, participant number (n=7) was too small for valid examination of the amount of time spent in different light intensity categories. On workdays, chronotype significantly interacted with durations spent in each light level before and after internal noon (interaction effect 'before/after*chronotype': F(1,9)=5.313, p<0.05). On workdays, late chronotypes
spent less time in light intensities between 5-100lx during internal forenoon, but more during internal afternoon. The same was true for light intensities of 100-250lx.

Fig. 21. Duration spent in light intensity categories during scotoperiod on workdays. Duration of time spent under light intensities of <5lx and 5-100lx decreased with later chronotype before sunrise and increased after sunset (see insets of panel A and B). Note that in this analysis only light intensities during scotoperiod and wakefulness on workdays are considered. Due to the prerequisite of ANCOVAs demanding values for each time point, sample sizes were too small (n=7) to analyse light exposure on free days.

### 3.4.6 Synchronization to the 24-hour Light-Dark Cycle

This method proposed by Rea and colleagues provides information concerning the accordance between light-dark and activity-rest patterns (Rea et al., 2008). This method was originally developed in order to measure circadian entrainment and disruption, in case light-dark and activity-rest patterns show a tight or poor congruency. High accordance between the two profiles is visible in vector amplitude, whereas phase relationship is shown as phase angle of the vector. Phase angles around zero indicate minimal levels of circadian disruption and point towards a stable entrainment to the 24-hour light-dark cycle.
Fig. 22. Polar plot of vector analysis. The length of the vector indicates the amplitude of the degree of accordance, whereas the angle displays phase relationship between light and activity patterns. Panel A shows all participants, panels B-D show data separately for each chronotype-category. Red lines visualize averages of vector angles.

Analysing amplitude and phase of accordance between activity and light measurements disclosed that both, vector magnitude as well as phase angle, were comparable between chronotype-categories (see Tab. 10). Univariate ANCOVAs revealed no significant differences. Vectors gathered around zero line (see Fig. 22A), which indicates a chronotype-stable relation between light-dark and activity-rest patterns. Intermediate chronotypes displayed smaller amplitudes, which indicates a lesser degree of accordance between light-dark and activity-rest patterns. Yet, these differences were not significant.
Tab. 10. Statistical indices of vector analysis. Univariate ANCOVAs were applied for amplitude and phase of accordance between light-dark and activity-rest patterns with ‘chronotype’ and ‘age’ as covariate. N = sample size.

<table>
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<tr>
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<th>P-value</th>
<th>Effect size (partial η²)</th>
<th>N</th>
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3.5 Discussion

In this study light exposure intensity and timing were analysed on work- and free days in order to describe light exposure patterns in real life.

Workday light exposure was 11-fold less compared to averaged light exposure on free days. All chronotypes received comparable light levels over the course of time. Analysing the timing of light exposure revealed different amounts of light before and after internal noon: late chronotypes perceived most light during internal forenoon, whereas early chronotypes during internal afternoon. On workdays, late chronotypes spent increasingly longer in light intensities from 5 to 100 lx (horizontally measured) before internal midday and less after internal noon. On free days, late chronotypes showed increasing durations spent under intensities of more than 250 lx, 100–250 lx and 5–100 lx. During scotoperiod late chronotypes had an increasing amount of light after sunset and spent most time in light intensities between 5 and 100 lx. Reverse patterns were found for early types respectively. The difference in light exposure before and after internal noon on free days significantly predicted chronotype. Despite these differences in timing of light exposure, all chronotypes showed comparable phases and amplitudes of the accordance between activity- and light-patterns.

Overall light exposure varied widely in terms of ‘type of day’, with free days showing a 11-fold higher and comparatively more heterogenic light exposure as compared to workdays. That light exposure on free days was generally higher
Chapter 3: Light Entrainment in Real Life

and also heterogeneous as compared to workdays, verified the first hypothesis. Similar results were also found by Hubalek and colleagues (Hubalek et al., 2010). On workdays, participants spent on average less than 30 minutes in bright light (>250lx) and in comparison 150 minutes on free days. Also other studies found short (60-90 minutes) daily bright light durations, although these studies did not distinguish between work- and free days (Okudaira et al., 1983; Savides et al., 1986). This implies that five days out of seven comprise relatively dark light intensities. It is doubtful that light exposure on workdays is sufficient for accurate entrainment. Though it was found previously that light intensities of 40-75lx (horizontally measured, equals 150-300lx vertically measured) significantly influenced circadian systems (Gronfier et al., 2007; Heil et al., 2002; Waterhouse et al., 1998), this study showed that light exposure on workdays could not significantly predicted participants’ chronotype. Although age and chronotype are generally related (Roenneberg et al., 2004), it was not a significant predictor in this model. This could be due to small sample numbers as well as the small age-range with little variance.

The theory ‘Circadian integrated Response Characteristic’ (CiRC) postulates that light is integrated separately before and after internal noon, and that the phase shifting property of light is determined by the difference between the two. The difference of light exposure between internal fore- and afternoon on free days significantly predicted chronotype, which strengthens the assumptions of the CiRC as entrainment concept. Additionally, results indicate that certain light intensities are needed, as seen on free days. Light exposure on external time scale had no predictive power.

Objectively measured, all chronotypes experienced equal amounts of light on work- and free days. This result is in line with previous findings (Martin et al., 2012; Staples et al., 2009) and falsified hypothesis 2 that late types would get less light during the day. Whereas objective measurements revealed no differences in neither general light exposure nor under bright light, interestingly subjective ratings of the amount of time spent outside showed in tendency a negative correlation, with later chronotypes spending less time outdoors on free days ($r=-0.43$, $0.05<p<0.1$, $n=19$).
Light patterns over a full internal 24-hour day were analysed separately for chronotype-categories. Early chronotypes displayed a uni-modal curve shape of light exposure on workdays and a bi-modal pattern of free days. Light patterns of intermediate and late types were vice versa. This analysis had an explorative character and should be retested with a higher sample number against the background of the CiRC. In addition, light exposure was descriptively examined on a local time scale. All chronotype-categories experienced maximal light levels around solar noon (around 1 o’clock in the prevailing photoperiod) on workdays, which also coincided with the common timing of lunch break. Therefore, a sensitive analysis was conducted in regard to sun time, in order to consider the availability of sunlight. Also this analysis revealed chronotype-differences. Late types experience more sun after solar noon on free days (but similar light levels compared to the other chronotype-categories before solar midday on free days). In comparison, late chronotypes were less exposed to light during solar morning on workdays. Therefore it can be concluded that it is not the lunch break on workdays causing internal differences in light exposure. It is rather a general difference in timing of light exposure.

In order to analyse timing of light exposure, the fundamental concept of the CiRC, integrating and relating light exposure before and after internal noon (Roenneberg et al., 2010a), was transferred to the here conducted analyses. At first, light exposure was analysed during internal forenoon and afternoon during time awake, regardless of photo- and scotoperiod. Here chronotype-dependent light pattern was not so stringent. This strengthens the importance of considering photo- and scotoperiod, namely if light was experienced during light phase or dark phase of the day, when analysing light patterns.

Light exposure with regards to time of day revealed chronotype-dependent differences. During photoperiod later chronotypes showed increasing light exposure before internal midday, whereas decreasing light levels after internal noon. Thus, later chronotypes were associated with an increasing proportion of light during internal forenoon. Early chronotypes perceived less light during internal morning, but an ascending amount of light during internal afternoon. These light patterns were conversely as previously expected in hypothesis 3.
Previous research found similar results as described in this study, in terms of timing of light exposure: morning/evening types experienced higher light levels later/earlier in the biological day (Emens et al., 2009; Goulet et al., 2007; Staples et al., 2009). On workdays, subjects spent most of the time in light intensities 5-100lx, which matches general workplace lighting of 50-125lx (again horizontally measured) (Heil et al., 2002). An increasing duration was spent in 5-100lx light levels before and a decreasing duration after internal noon in late chronotypes.

Light during scotoperiod showed a reverse pattern as compared to photoperiod. Late chronotypes displayed increasing light exposure after sunset, whereas early types before sunrise. On workdays, earlier types experienced more light before sunrise. Additionally, correlations found positive associations between chronotype and get up times and work begin (get up: WD: r=0.75, p<0.001, n=19; FD: r=0.59, p<0.01, n=19; work onset: r=0.50, p<0.05, n=18), suggesting that increasing light levels before sunrise emerge from early awakening in earlier chronotypes, therefore getting artificial light in early morning hours before sunrise. Late chronotypes spent an increasing amount of time after sunset in light intensities between 5 and 100lx. These intensities match with typical domestic lighting installations, late types are longer exposed to due to later bed times. A significant correlation of chronotype and time to bed supported this conclusion, with late types having later bedtimes (WD: r=0.66, p<0.01, n=19). It could be discussed that this long period of artificial light is contra productive in terms of accurate entrainment. Studies have shown that even these rather low light intensities are able to phase shift circadian clocks under constant conditions (Duffy et al., 2005) and therefore also potentially influencing entrained circadian systems. On free days, only few participants were already awake before sunrise, so that a valid statistical investigation of light exposure before sunrise and after sunset was not possible.

Experiments under constant bright or dim light conditions show an internal free-running period length of either longer or shorter than the external cycle of 24 hours. But more important than the period length in constant conditions is the internal period length under entrained conditions, when the clock is stably entrained with a specific phase angle of entrainment between
internal and external period (Roenneberg et al., 2010b). A daily task of the circadian systems is to entrain to the sun-given 24-hour external cycle length. Steady-state entrainment depends on the difference between internal period length and the 24-hour light-dark cycle, the zeitgeber strength and the individual responsiveness towards the zeitgeber (Daan et al., 1976). Light is the most important synchronizer for this active entrainment process (Duffy et al., 1996), but, as described earlier, the effect of light depends on internal time of day. Subjects with shorter period lengths (τ<24 hours) have to expand their internal period in order to adjust to the 24-hour external light-dark cycle. Light experienced during internal afternoon will phase delay or expand the circadian rhythm. Subjects with longer periods than 24 hours (τ>24 hours) have to compress their internal period length, which can be achieved by high light levels during internal forenoon, phase advancing or compressing the internal period length.

Participants with internal period lengths of longer than 24 hours have to compress their period length (τ) in order to adjust to the 24-hour external cycle. Following the concept of CiRC (Roenneberg et al., 2010a), the proportion of light exposure before internal noon has to be greater than after internal noon. The circadian system embeds itself to light and darkness in the way that internal forenoon covers most part of photoperiod and that internal afternoon lies in darkness. This can be achieved by a lately timed internal noon, seen in late chronotypes. Hence, based on the findings in this study (that late chronotypes experience most light during internal forenoon) it can be concluded that the circadian system positions itself the way that it receives most light before internal noon in order to compress internal cycle length. This is only possible if the phase angle of external and internal noon is wide, as in late chronotypes. A study from Duffy and colleagues support this hypothesis, describing the relation of eveningness and longer circadian period lengths (τ>24 hours) (Duffy et al., 2001). In case of cycle lengths shorter than 24 hours, it would be reverse. Here the circadian system needs bright light intensities during expanding proportions (internal afternoon). Thus, internal afternoon has to cover most part of the light phase of day, leading to an early timed noon. On the other hand, the circadian
system hides the compressing part in scotoperiod before sunrise. An early timed internal noon accompanies an early midnight, which is used as phase marker for chronotype (MSF_{sc}). It can be concluded that clocks embed to the 24-hour light-dark cycle that the effect of light and darkness at the right ‘internal’ time of day promotes sufficient adjustment of too long or short internal period lengths to the external 24-hour light-dark cycle.

If light and darkness hits the system at the internal right time of day, the entrained internal period length will be approximately 24 hours. In order to test, whether study participants were similarly entrained, a vector analysis was conducted. Although timing of light depended on chronotype, with late types showing high light exposure before internal noon (in the compressing part) and early types after internal noon (in the expanding part) participants displayed comparable amplitudes as well as phase of accordance between activity and light measurements, which indicates a stable entrainment to the 24-hour light-dark cycle. This refutes hypothesis 4, saying that chronotypes differ in phase and amplitude concerning vector analysis.

Another possible explanation for the described chronotype-dependent timing of light exposure would be a diverging sensitivity towards light exposure between chronotypes. Potentially late types are less sensitive to light during internal forenoon, thus higher light intensities are necessary during internal morning to cause an effect. On the contrary, early chronotypes would have a decreased light sensitivity during subjective afternoon, which would entail an increased demand for bright light after internal midday.

### 3.5.1 Limitations

The study comprised only 23 participants, with only one workday and free day. Weather conditions also influence light exposure and outdoor behaviour. On warm and sunny days humans generally spend more time outdoors under bright light as compared to cold and cloudy days (Guillemette et al., 1998; Hebert et al., 1998; Thorne et al., 2009). LightWatchers were attached either to participants’ spectacle frame or at a plain glass spectacle frame. Potentially, the unfamiliar
wearing of the glasses could have influenced participants’ outdoor behaviour. Furthermore, lenses of spectacles slightly scatter short wavelengths, so that the measured intensity of especially blue wavelengths could alter from actual perceived light. Because of the blue light filtering properties, participants were asked not to wear sunglasses during the measurement. Mid-sleep on free days (MSFsc) was assessed as phase marker, but had no further circadian regulated variables such as core body temperature or dim light melatonin onset (DLMO). Chronotype- and age-distributions of incorporated participants were not very broad. It would have been beneficial, if this study comprised a higher number of very early and late chronotypes. Dividing experienced light in ‘before’ and ‘after’ internal noon is a simplistic approach, although based on the theory CiRC.

Based on the findings that late types experience most light during internal forenoon, whereas early types during internal afternoon, it is hypothesized that light exposure at certain times of the internal day is needed for accurate entrainment. Also the finding that the difference in light exposure before and after internal noon on free days could clarify 27% of the variance in chronotype was in line with this assumption. Yet, the results found in this study cannot solve the chicken-and-egg-problem, whether chronotype influences light exposure or whether light exposure influences chronotype. Most likely there is an interdependency of both variables. The findings here are rather exploratory and need further examination.

### 3.5.2 Strengths

Besides the limitations this study comprises several strengths. Unlike most other studies, this study analysed light exposure separately for work- and free days, making a sophisticated comparison between the two different types of day feasible.

In comparison to other studies, chronotype was assessed by using the MCTQ. In comparison to other questionnaires, the phase of entrainment measured by the MCTQ was shown to robustly reflect physiologic rhythms, e.g. gene expression and melatonin secretion (Novakova et al., 2013). Another
advantage of using the MCTQ is, that it provides information about individual’s internal time, so that time designations can be adjusted to participant’s internal time scale.

For analyses of light exposure, it was taken into account that not enough is known about light, passing the eyelids while sleeping (Figueiro et al., 2013; Kantermann et al., 2009). Thus, solely light exposure during time awake was included here. Increasing age has been associated with lens yellowing, potentially affecting input pathways to the circadian clocks. This effect was considered in this study by incorporating solely relatively young participants (age 20-40 yrs.), where lens yellowing would be unlikely.

Most studies measure light with wrist-worn devices and not at eye level (Emens et al., 2009; Goulet et al., 2007; Hebert et al., 1998; Heil et al., 2002; Okudaira et al., 1983; Staples et al., 2009). Devices at wrist measure light intensities skywards with potential 180-degree vertical rotation towards the floor, when turning the hand. This might potentially lead to biased light measurements, which do not reflect actual light intensities perceived by the eyes. In comparison, in this study a device was used, measuring light (intensities as well as spectral composition) in gaze and on eye level. With that it can be assured, that measured data reflects actual received light exposure, compared to wrist worn light measuring devices, where additionally covering of the measuring device by clothes is a common problem.

3.5.3 Implications

As seen previously general light exposure did not show a clear chronotype-depency. When light exposure was analysed separately for photo- and scotoperiod, a clear chronotype-effect became apparent that early chronotypes experienced most light before sunrise and after internal midday, whereas late chronotypes before internal midday and after sunset. In order to find chronotype differences in light exposure, it is important to consider light phase and dark phase of the day.
It was also shown that subjective and objective light perception differed. Subjectively late chronotypes experienced less light, however there was no objective difference in light levels. Although some studies found a good correlation between subjective and objective measurements (Bajaj et al., 2011), it is not recommended to trust subjective ratings.

Living against the biological clock was shown to be associated with several severe diseases (see chapter 1.6.2.2). This phenomenon of circadian misalignment arises, when biological time and social duties contradict. Early working times are most strenuous for very late chronotypes and therefore for the majority within a population. With the help of scheduled light exposure, individual's chronotype can be shifted towards an earlier phase of entrainment. This would diminish discrepancies between internal and local time and the amount someone is living against the biological clock, and potentially minimizing the risk to develop diseases associated with circadian disruption. Study findings stress the importance for late chronotypes to be exposed to high light levels during internal and local forenoon and early types during internal and local afternoon.
Chapter 4: Closing Remarks and Research Prospects

4 Closing Remarks and Research Prospects

This thesis addresses two important features of circadian biology: sleep-wake behaviour and light patterns. Napping and light treatment are beneficial countermeasures against sleep deprivation and circadian disruption. Both are extremely high in shift workers, but also normal office workers suffer from a chronic sleep curtailment and circadian misalignment, especially on workdays. In order to provide recommendations, the first step is to analyse how daily life behaviour is like without any intervention. Though shift-working times are very restrictive, the impact of chronotype on napping behaviour in everyday work was explored. For the first time it was shown that not only sleep duration, also chronotype and even circadian disruption influenced shift workers’ nap behaviour. Furthermore, first hints were provided that main sleep duration influences nap length and that nap timing affects succeeding main sleep. In a second study, light profiles of normal office workers were continuously measured. This study attempted to close the lack in regard to light exposure of our everyday life. Light patterns were analysed separately for work- and free days. Additionally, different effects of light on the circadian system were considered, either compressing or expanding internal period length. Study findings can be explained with the hypothesis that clocks embedded themselves into the 24-hour light-dark cycle that they experienced light at the ‘right’ internal time of day, in order to entrain accurately to the external zeitgeber.

4.1 First Study: How Chronotype Influences Nap Behaviour in Shift Workers

Shift workers’ every day life (e.g. eating, sleeping, wakefulness or even free time) is dictated by the prevailing shift schedule and working times. Previous research found that shift workers suffer from a high amount of circadian misalignment...
and sleep deprivation, which are both associated with type of shift and chronotype (Juda et al., 2013a). Early chronotypes show increased circadian disruption and sleep loss on night shifts, whereas late chronotypes on morning shift days. To overcome these, napping is a common coping strategy. In order to analyse the influence of individuals’ internal time on napping behaviour, sleep-wake behaviour was tracked in 118 shift workers. Participants worked in one out of four different slow and fast forwards-rotating shift schedules and were measured over a full rotation period of four weeks.

Nap behaviour displayed a clear chronotype-dependent pattern: predominantly early chronotypes napped longest and most frequent on night shifts, late chronotypes on morning and intermediate chronotypes even on both extreme shifts. Short main sleep durations increased the probability of taking a nap. This strengthens the sleep compensatory function of napping. By adding the nap duration to the main sleep duration, analyses of 24-hour sleep duration were possible. Late chronotypes, who showed short main sleep durations on morning shifts, displayed equally long 24-hour sleep durations compared to early types, whereas on night shift days, early chronotypes showed shorter main sleep as well as 24-hour sleep episodes. Nap timing was analysed on a local and internal time scale. Late types’ nap timing was early on morning shifts, on the contrary, early and intermediate types timed their nap lately on night shift days. Nap behaviour did not only show a clear chronotype-dependent pattern, individuals’ internal time could even predict nap duration and timing. Additionally, living against the biological clock, measured as social jetlag, significantly increased nap frequency. For the first time, causality of nap and main sleep was described. On morning shifts, the previous sleep episode influenced nap duration, whereas on evening and night shifts nap timing showed an impact on the subsequent main sleep.

Prior to the investigation of participants’ nap behaviour, three hypotheses were postulated. Firstly, previous research found, shift workers’ main sleep duration to be chronotype-dependent (Juda et al., 2013a). The first hypothesis claimed that nap behaviour, in addition to main sleep behaviour, follows a clear chronotype-dependency. Secondly, early chronotypes are meant to more rapidly
build up sleep pressure (Maire et al., 2013; Mongrain et al., 2007). The second hypothesis postulated that, amongst nappers, increased number of early chronotypes or elevated nap durations and frequencies in early chronotypes were expected. Thirdly, sleep deprivation potentially can be compensated by different sleep strategies, either taking frequent naps, having a high delta power during sleep or extremely long nap durations. Thus, the third hypothesis postulated that no nap pattern would be detectable, because of different compensation strategies.

In this study, only the first of the three previously postulated hypotheses concerning general nap patterns of shift workers were proven right. Nap behaviour of shift workers displayed a clear chronotype-dependent pattern, as postulated by the first hypothesis. Åkerstedt and his colleague Torsvall also descriptively analysed napping in shift workers and found similar results as described in this study (Åkerstedt et al., 1985). Yet, they applied the Morningness-Eveningness Questionnaire, which asked for diurnal preference and not for actual phase of entrainment and did not consider participants’ internal time. The second hypothesis postulated that a higher number of earlier chronotypes would nap longer or more frequent. There were no statistical differences in the number of nap takers with regards to chronotype, although there was a numerical trend that most non-nappers were later chronotypes. Increasing age is associated with earlier chronotypes (Duffy et al., 2002a; Roenneberg et al., 2004) and with the tendency to nap more frequently (Dhand et al., 2006). In this study, neither increased napping in early types nor in elderly people became apparent. Most likely participants’ ages were not high enough to exhibit age-related effects on nap behaviour. Different from the sleep strategies described in hypothesis 3, the given results in this study suggested different purposes for taking a nap. Generally, a tight association was shown between main sleep episode and nap on morning shifts: short main sleep durations, as seen on morning shifts, increased nap durations. It can be assumed that morning shift naps are taken due to sleep compensation after acute sleep loss. Terminating sleep early leads to a (REM-) sleep deprivation (Åkerstedt et al., 1991a). Early timed naps, as seen here for late chronotypes on morning shifts,
comprise long durations spent in REM-sleep and therefore potentially compensates for acute REM-sleep loss.

On the contrary, it can be hypothesized that night shift naps are rather taken due to anticipated sleep loss and might have strategic reasons. Late timed naps, as seen in early and intermediate types on night shift days, generally comprise long deep sleep episodes. This deep sleep might reduce sleep pressure and function as pre-sleep. Furthermore, it was shown in this study that late naps on night shifts significantly influenced subsequent sleep begin of main sleep episodes, which also strengthens the assumption of a pre-sleep.

In sleep research, measuring sleep stages provides additional information. Napping of shift workers can be understood more clearly, when sleep stages are considered. With EEG-recordings, one could verify the assumption based on the study findings in terms of different nap strategies and nap timing, namely that early morning shift naps seen in late chronotypes are due to acute (REM-) sleep loss, whereas late naps before night shifts are taken to diminish sleep pressure and function as pre-sleep. On morning shifts, early timed naps in late chronotypes should comprise long periods of REM-sleep. In regard to sleep stages, later timed naps on night shifts (early and intermediate chronotypes) should display long periods spent in deep sleep. This could throw light on the general purpose of napping, which still remains to be elucidated in future research.

In both cases it was concluded that early nap timing after morning shifts and late naps before a night shift, was driven by process S (homeostatic build-up of sleep pressure). Additionally, process C (circadian component) provides sleep windows throughout the 24-hour day, when sleep ability is enhanced (Bes et al., 2009; Bes et al., 1996; Dijk et al., 1994). Participants’ also napped at times, when the circadian component provided a sleep window, more precisely at internal midday. Potentially, a nap driven by process C should differ from process S-driven naps in regard to sleep cycles and stages. Future investigations of nap behaviour are meant to consider sleep stages in order to determine differences concerning nap timing, purpose and if under control of process S or C.
Since napping is meant to be a countermeasure against sleep loss (Rosa, 1993), it was hypothesized that, by taking a nap, sleep deprivation would be minimal and result in equal 24-hour sleep durations between chronotype-categories. This was only true on morning shifts; here late types compensated sleep deprivation by taking a nap. On the contrary, early chronotypes could not compensate shorter main sleep durations on night shifts by taking a nap, so that 24-hour sleep durations were significantly shorter. Late types are known to have the ability to flexibly adapt their sleep-wake behaviour (Ishihara et al., 1987; Park et al., 1998). This could enable late types to nap long enough to fully compensate morning shift-dependent sleep loss. On the other hand, early chronotypes are more rigid in their sleep timing. It can be assumed that a rigid circadian rhythm, as seen in early chronotypes, does not ‘allow’ sleeping long enough to fully compensate sleep deprivation.

Juda and colleagues found moderate levels of circadian misalignment and sleep curtailment in intermediate chronotypes (Juda et al., 2013a). Based on these findings, the hypothesis was derived that general nap behaviour would be reduced in intermediate chronotypes. Different from previous expectations, intermediate chronotypes did not show diminished nap behaviour, but rather similar nap durations and frequencies on both morning and night shifts as extreme chronotypes on their most strenuous shift. Also Åkerstedt and Torsvall showed that participants napping on both morning and night shifts were rather ‘intermediate types’, although chronotype was measured here as diurnal type in regard to morningness and eveningness (Åkerstedt et al., 1985). The findings concerning increased napping in intermediate types on both extreme shifts lead to two exhortations: firstly, to stop disregarding adverse effects of morning shifts and not solely focussing on night shifts, as well as secondly to bestow consideration upon the negative effects of shift work on intermediate chronotypes (and therefore the majority of a population).

This study comprised four different regular and irregular, slow and fast forwards-rotating shift schedules. The prevailing shift schedule affected nap behaviour, in a slow forwards-rotating shift schedule, an increasing number of participants napped on free days after morning shifts. Furthermore, participants
took later naps as compared to a fast speed of rotation. This suggests that also shift schedules show an impact on sleep loss and the subsequent need for sleep compensation. Potentially higher numbers of consecutive shifts lead to accumulated sleep deficits. Thus, fast rotations would be more beneficial in terms of less accumulation of sleep loss. How nap timing is influenced by different shift schedules remains open for further investigations.

It is well known that naps potentially affect succeeding main sleep, although findings are very heterogeneous, with some studies showing no effect of napping on the following sleep, whereas others find an impact (Campbell et al., 2005; Stepanski et al., 2003; Tamaki et al., 1999; Werth et al., 1996). It was shown that time spent within a certain sleep stage during an evening nap, was subtracted from the time of the ensuing main sleep episode (Feinberg et al., 1992). Previous research focussed either on the effect of previous main sleep (curtailment) on napping or the effect of a nap on the following main sleep episode. In this study for the first time the whole chain of causation was considered. It was shown here that the interrelation depended on type of shift and again findings are in line with the hypothesis of different purposes of napping. On morning shift days, previous main sleep episode negatively influenced nap duration. It can be assumed that this nap was taken in order to compensate previous sleep loss. On evening and night shifts, nap timing significantly influenced sleep onset of the following night. This rather suggests, the nap was taken due to anticipated sleep need, which functions as pre-sleep and delays subsequent timing of main sleep.

Although shift work is associated with a broad spectrum of impairments for mental and physical health, it is too idealistic to think that shift work will be disestablished in the near future. Shift work-associated illnesses mostly entail long-term therapy as well as temporary or even permanent unemployability. The financial strain for healthcare systems in general and budgets of health insurance companies is immense. Not enough is known about the positive effects of napping on pathogenesis, but study results are promising, that a simple thing as taking a nap counteracts the development of diseases and therefore can potentially relieve government budgets. Additionally, minimizing the number of
illness-related days of absence is of big interest for employers. Therefore, we are facing a triple-win situation for employees, employers and healthcare system. For companies, the measurability of profits and savings are two of the major criteria for the decision to financially support such research projects. To this day, most industrial companies unfortunately are not willing to invest money if there is no direct measureable output. Research budgets are not sufficient for covering those costs completely. As long as employees are considered as interchangeable goods, employers will not expand (financial) effort and will not risk to spend money in investigating the positive impact of napping on shift workers’ health, without making profit. Yet, future research is urgently needed, aiming at the development of recommendations (with regards to individuals’ internal time), at what time of day, how long and how often a nap is most beneficial for employees’ health state.

4.2 Second Study: Light Entrainment in Real Life

Light is the primary synchronizer for circadian systems to adapt to the 24-hour light-dark cycle. Melanopsin comprising photoreceptors exhibit a sensitivity maximum around 480nm. Light is perceived by these photosensitive retinal ganglion cells and transduced via the optical nerve. The suprachiasmatic nucleus is a small paired brain region, located directly above the optic chiasm. It produces stable oscillations of approximately 24 hours (therefore termed circadian oscillator; circa: approximately, dies: one day), but also actively synchronizes to the 24-hour external light-dark cycle, a process called entrainment. By regulating hormone secretion, the SCN forwards light information, therewith synchronizing all peripheral oscillators to the same phase.

In the second study light exposure of 23 office workers was continuously measured throughout daily routine on work- and free days. The purpose of this study was to investigate light entrainment in real life. Statistical analyses were based on the theory ‘Circadian integrated Response Characteristic’ (CiRC). Light exposure during early morning hours compresses, whereas during late evening
hours extends internal period length. Based on this, light exposure was separated in regard to time of day (experienced during fore- or afternoon) as well as photo- and scotoperiod (light or dark phase of a day).

The investigation of light patterns in office workers was based on previously postulated hypotheses. Subjectively estimated, late chronotypes experience less light throughout a day (Roenneberg et al., 2007c). From these findings, it was assumed that late types are less well entrained to the 24-hour light-dark cycle due to insufficient zeitgeber strength. Secondly, it was hypothesized that late types display elevated levels of light exposure during internal afternoon and evening (due to late bed- and wake-up times), synchronizing them to a later phase. None of the previously postulated hypotheses turned out to be correct.

Light exposure on workdays was 11-fold smaller and very homogenous amongst participants as compared to free days. All chronotype-categories experienced equal amounts of light on work- and free days. Objectively measured, all chronotypes experienced similar light levels and durations under certain intensities. On the contrary, subjectively rated durations of time spent outdoors revealed a chronotype-association, with late types spending less time outside as compared to earlier types. Based on a recently developed light questionnaire, Bajaj and colleagues found a good coherence between subjectively rated and objectively measured light exposure (Bajaj et al., 2011). In respect of the given results found in this study, it cannot be recommended to rely on subjectively rated light exposure. This may result in misleading findings. However, it is not known if this difference between subjective and objective light measurement is due to a simple recall bias or if there is rather a systematic discrepancy in light perception between chronotypes. Interestingly not only in this study here, also previously it was described that late chronotypes subjectively experience less light (Roenneberg et al., 2007c).

On both work- and free days, late chronotypes experienced most light during internal forenoon, whereas early types during their internal afternoon. On workdays, this was visible for light intensities between 5-100lx (measured in
participants’ gaze). On free days, the chronotype-dependent difference in light exposure was visible for light intensities between 5-100lx, 100-250lx (typical indoor light installations) and also for more than 250lx (daylight intensities). Despite the fact that some studies found minimal light intensities (as seen here on workdays) can serve as primary synchronizer, it was found in this study that light intensities on workdays could not predict chronotype. Only higher light intensities perceived on free days showed a significant impact and clarified variance in participants’ chronotype. Therefore it can be concluded that - as postulated by the CiRC - the difference of light experienced during internal forenoon or afternoon on free days influenced chronotype.

This study showed that 24-hour light profiles differed between chronotypes and type of day. Early chronotypes displayed a uni-modal distribution on workdays and a bi-modal pattern on free days, the opposite was found for intermediate and late chronotypes. This investigation had a rather explorative character. From the given result, one cannot infer to underlying mechanisms or reasons for this difference between chronotype-categories; therefore future examination is needed.

Prior to the analyses it was hypothesized that elevated light levels during internal afternoon and evening causes the late phase of entrainment seen in late chronotypes. In this study, late chronotypes were found to experience high levels of artificial light after sunset and therefore during internal evening. Different from previous expectations, late types displayed elevated light exposure during internal forenoon, when light has generally a compressing effect on the circadian system. On the contrary, early chronotypes experienced most light during their internal afternoon, when light shows an extending effect on internal period lengths. Similar to this study Emens and his colleagues analysed daily light profiles throughout the year within a study sample, comprising many participants and a broad age-range, with regards to internal time of day and found comparable results (Emens et al., 2009). Based on previous studies where the same results were described for different age groups, concerning light exposure on an internal time scale (Goulet et al., 2007; Staples et al., 2009), Emens separated participants into extreme and intermediate chronotypes. In
comparison, a continuous distribution of chronotype was incorporated in this study and light measurements were more precise, since measured at the eye level and not at participants’ wrist. Given that also other studies found chronotype-dependent differences in light exposure, strengthen the results found in this study and can be explained, when put into context of accurate entrainment.

Internal cycle lengths of longer or shorter duration than 24-hours require a day-to-day correction in order to accurately synchronize to the 24-hour day and to prevent free-running. Light is the most important synchronizer for the human circadian clock. Depending on internal time, light has different effects on light entrainable circadian systems: light during internal forenoon compresses, whereas light during internal afternoon expands circadian oscillators. Duffy and colleagues showed that chronotype and internal period length are highly related, with late types showing a longer internal period length. For accurate synchronization it is important to actively expand or compress too short or too long internal period lengths. This is feasible, when oscillators with period lengths longer than 24 hours, experience most light during the compressing part. From the given findings it can be hypothesized that clocks with longer than 24-hour cycle lengths, embed themselves into the 24-hour light-dark cycle that the compressing proportion (during internal forenoon) is moved towards the light phase of the day, in order to perceive maximal light intensities. On the contrary, the expanding proportion, which would have a contrary effect, is hidden in darkness after sunset. Therefore, phase of entrainment is comparably late in those people displaying long internal period lengths, which can be measured with the help of the MCTQ as late chronotypes. On the other hand, short internal period lengths need expanding impact of light in order to entrain accurately to light and darkness. By shifting the internal noon forwards, most light hits the circadian system during the expanding proportion (during internal afternoon), whereas the compressing proportion is hidden in darkness before sunrise. This early embedding due to accurate entrainment of short internal period lengths is measured as early chronotype.
Although timing of light exposure differed between chronotypes, either compressing or expanding the circadian system, all chronotypes showed similar phase and amplitude of accordance between light- and actimetry-patterns, which indicates similar levels of behavioural entrainment (Rea et al., 2008). From this it can be inferred that light at different times of day (late types during internal forenoon and early types during internal afternoon) was necessary for accurate entrainment.

Although the results speak in favour of this hypothesis, this study cannot elucidate the chicken-and-egg-problem in regard to internal period length and the effects of light on chronotype: does chronotype influence the timing of light exposure or does the timing of light exposure determine chronotype? Either computational modelling or replication in the laboratory (with higher sample size, broader chronotype- and age-distributions) is needed to investigate the cause-and-consequence of light and chronotype.

Generally, it became apparent in this study that especially on workdays illumination levels were rather little (with averagely 63lx horizontally measured13). Additionally, it was found that only light exposure on free days could significantly predict participants’ chronotype. Based on that, it can be concluded that human beings of industrialized societies (working predominantly inside buildings) live in ‘biological darkness’ at least five out of seven days each week. Increasing light intensities of indoor lighting systems is one possibility to increase zeitgeber strength, but the consequences are not fully understood yet. Blue-enriched artificial light positively influenced employees’ daytime performance and sleep, but the phase of entrainment were found to adapt to the artificial light-dark cycle and to uncouple from the tight adjustment to sun time, potentially prohibit seasonal adjustment (Kantermann et al., 2007; Vetter et al., 2011; Viola et al., 2008). Instead of simply switching light installations on and off, more complex lighting systems are needed, dynamically adjusting light intensities and spectral composition to time of day and time of year. During dark phase of the 24-hour day (scotoperiod) artificial light should not comprise blue wavelengths, whereas during photoperiod light source should be blue-enriched

13 Corresponding to approximately 250lx vertical measurement.
and simulate spectral composition of daylight. Another promising approach is to increase the light permeability of buildings, especially rooflights were found to be most beneficial in terms of light-flooding rooms. Recently, Austria changed the guidelines architects and light designer rely on, in terms of the proportion between room- and window-sizes. The new guidelines require less window areas, which is a tremendous setback. It is our duty to spread the knowledge in regard to the importance of light for accurate entrainment (which in turn reduces the negative consequences of social jetlag and sleep loss) to decision-making committees, architects, light designers and production companies.

Considering chronotype displayed huge differences when analysing nap behaviour in shift workers or light exposure in office workers. This emphasizes the importance of incorporating chronotype in statistical analyses, because of the huge impact of chronotype on our life.
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Chapter 5: References


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The person who was involved most is you, Christian Schuh. I deeply thank you for your endless patience in terms of listening to my thoughts. Thank you for your love and your everlasting support! You have been my mainstay, without you this would not have been possible!

I am proud to say, my little soul mate that I was accorded the honour of knowing and loving you. Thank you for entering my life, for your warming little paws when crawling into my lap. I always wanted to spend more time with you. I deeply miss you, Lucy Matera!
6.2 To Industry Partners

The greatest thank belongs to all study participants, who did not hesitate to wear actimeters at the wrist, LightWatchers at the spectacular frame (noteworthy not all participants were spectacle wearer) and fill in sleep times every morning for four weeks. Fully equipped participants had to endure side-glances or questions about measuring devices. The two most amusing encounters were first a female participant being asked, if she was one of the Power Rangers (a children’s program about powerful superheroes) by two little boys and second an elderly women at a bakery counter asking, if the wrist worn actimeter was a new generation of an electronic gyve.

My special thanks belongs Dieter Lang (OSRAM GmbH), for ‘enlightening’ me with physical metrics of radio- and photometry, for our good collaboration and our valuable discussions. Thanks to Luzian Wolf (Object-Tracker) for technical support concerning the LightWatcher.

I thank all industry partners where we conducted our studies. Without their permission, support and trust, the first study would not have been possible: ThyssenKrupp electrical steel GmbH (location Bochum, Germany) as well as Siemens AG (location Amberg, Berlin and Cham). I owe gratitude to some people for their extraordinary support. Dirk Sievers and Frank Patschkowski backed us up as employee representatives from the very beginning. Simone Smaga, from the human resource department, supported the idea and the realization of the shift work study. Special thanks belong also to Dr. Jörg Augustin and Jens Roßkothen for their encouragement. On-site we thank Thomas Bendel and Thomas Schulte-Strathaus, Gaby Konetzka and Dirk Stahlschmidt, without you the project would have been different. Thank you for your friendly and caring welcome, for being there when ever needed and beyond.

Thanks to the Friedrich-Baur-Foundation, it was possible to financially remunerate participants of the second study and also purchase further equipment and devices.
7 Deutsche Zusammenfassung


7.1.1 Der Einfluss des Chronotyps auf das Nickerchen-Verhalten bei Schichtarbeitern


Späte Nickerchen enthalten dagegen meist lange Tiefschlafphasen und können damit Schlafdruck minimieren. Es kann geschlussfolgert werden, dass das späte Nickerchen bei frühen und intermediären Typen an Nachtschichtstagen nicht aus dem akuten Schlafdruck, sondern eher auf Grund eines assoziierten Schlafmangels während der Nachtschicht getätigt wurde und damit dem Abbau des Schlafdrucks diente. Auch die Analyse hinsichtlich der Wechselbeziehung zwischen Nickerchen und Hauptschlafphasen unterstreicht die Hypothese der schichtspezifischen Schlafstrategien. An Frühschichten beeinflusste die Schlafdauer der vorherigen Nacht die Nickerchen-Dauer, woraus ebenfalls geschlossen werden kann, dass dieses Nickerchen zur Kompensation vorangegangener Schlafdepravation erfolgte. An Spät- und Nachtschichten hat die vorherige Schlafphase keinen Effekt. Hier beeinflusste die zeitliche Terminierung des Nickerchens den Beginn des nachfolgenden Hauptschlafs, was dafür spricht, dass durch das Nickerchen bereits Schlafdruck abgebaut werden konnte.

Spättypen konnten den Schlafmangel an Frühschichtstagen mittels eines längeren Nickerchens ausgleichen, was an einer vergleichbar langen 24-Stunden-Schlafdauer (Dauer Hauptschlaf+Nickerchen) zu Intermediär- und Frühtypen zu sehen war. Frühtypen gelang es jedoch nicht, die kurze Hauptschlafdauer an Nachtschichten mit einem Nickerchen vollständig auszugleichen; die 24-Stunden-Schlafdauer war kürzer als bei Spättypen. Dies unterstreicht die schon häufiger beschriebene Fähigkeit von Spättypen das Schlafverhalten flexibler anzupassen.

Ein Nickerchen zu halten ist wohl die effektivste Maßnahme gegen Schlafmangel und wirkt sich damit potentiell positiv auf die Entstehung aller mit Schlafmangel assoziierten Krankheiten aus. Studien haben gezeigt, dass durch ein Nickerchen physiologische Parameter, die durch akuten oder chronischen Schlafentzug im pathologischen Grenzbereich lagen, verbessert wurden. Da die Abschaffung von Schichtarbeit aus gesundheitlichen Gründen zu idealistisch ist, sollten Forschungsarbeiten zukünftig anstreben, Chronotyp-basierte Empfehlungen auszusprechen, wann, wie lange und häufig ein Nickerchen
gemacht werden sollte, um Schlafmangel und Krankheitsentstehung optimal entgegenzuwirken.

7.1.2 Entrainment unter natürlichen Bedingungen


In der Studie wurde gezeigt, dass die Lichtexposition an freien Tagen durchschnittlich 11-mal höher und sehr viel heterogener zwischen den Studienteilnehmern war als an Arbeitstagen. Obwohl kein Unterschied in der gemessenen Lichtexposition zwischen Chronotypen vorherrschte, war die

Während der Photoperiode bekamen frühe Chronotypen signifikant mehr Licht zum internen Nachmittag, hingegen zeigten Spättypen eine höhere Lichtexposition zum internen Vormittag. An Arbeitstagen handelte es sich vornehmlich um Lichtintensitäten zwischen 5-100lx (in Blickrichtung gemessen). Diese Chronotyp-Unterschiede hinsichtlich der zeitlichen Terminierung der Lichtexposition waren bei Lichtintensitäten über 250lx (was auf Augenhöhe gemessen Tageslicht entspricht) sowie zwischen 100-250lx und 5-100lx sichtbar (was Innenraumbeleuchtung entspricht). In der Skotoperiode war der umgekehrte Effekt sichtbar, spätere Chronotypen bekamen zunehmend mehr Licht (5-100lx) nach Sonnenuntergang, hingegen Frühtypen vor Sonnenaufgang. Obwohl es große Unterschiede der zeitlichen Terminierung der Lichtexposition zwischen Chronotypen gab, zeigten alle Studienteilnehmer in einer Vektoranalyse hohe Übereinstimmungen zwischen Licht- und Aktivitätsprofilen, was als Maß herangezogen werden kann, wie gut eine Person synchronisiert ist.

Wie bereits von der CiRC postuliere, konnte gezeigt werden, dass die Differenz der integrierten Lichtmenge zum internen Vor- und Nachmittag die Einbettung des circadianen Systems in den 24-Stunden-Tag und damit den individuellen Chronotyp beeinflusst. Aus den Ergebnissen dieser Studie kann abgeleitet werden, dass die Lichtintensitäten an Arbeitstagen zu gering waren, um die innere Uhr an den 24-Stunden-Tag zu synchronisieren, dies war nur durch die höheren Lichtintensitäten an freien Tagen der Fall. Obwohl Laborstudien unter nicht-synchronisierten, konstanten Bedingungen gezeigt haben, dass bereits geringe Lichtmengen circadiane Systeme synchronisieren
können, wurde das in dieser Feldstudie unter synchronisierten Bedingungen nicht bestätigt.


Basierend auf den Ergebnissen dieser Studie wurden erste Hinweise gefunden, warum sich die circadianen Systeme von Menschen innerhalb einer Bevölkerung unterschiedlich in den 24-Stunden-Tag einbettet: damit Licht zur richtigen Zeit das circadiane System trifft, um somit zu kurze oder zu lange innere Periodenlängen über Lichtsynchronisation an den Außentag anzupassen. Obwohl die Teilnehmer zu unterschiedlichen Zeiten Licht bekamen, zeigten alle

# 8 Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>24/7</td>
<td>Around the clock</td>
</tr>
<tr>
<td>A</td>
<td>Amplitude</td>
</tr>
<tr>
<td>AIC</td>
<td>Akaike information criterion</td>
</tr>
<tr>
<td>a.m.</td>
<td>Ante meridiem, before midday</td>
</tr>
<tr>
<td>ANCOVA</td>
<td>Analysis of covariance</td>
</tr>
<tr>
<td>ATP</td>
<td>Adenosine triphosphate</td>
</tr>
<tr>
<td>AVP</td>
<td>Arginine vasopressin</td>
</tr>
<tr>
<td>b</td>
<td>Regression coefficient</td>
</tr>
<tr>
<td>β (beta)</td>
<td>Standardized coefficient</td>
</tr>
<tr>
<td>BIC</td>
<td>Bayesian information criterion</td>
</tr>
<tr>
<td>Bmal1</td>
<td>Brain and muscle ARNT-like protein 1</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>Calcium ion</td>
</tr>
<tr>
<td>cAMP</td>
<td>Cyclic adenosine monophosphate</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CiRC</td>
<td>Circadian integrated response characteristic</td>
</tr>
<tr>
<td>Clock</td>
<td>Circadian locomotor output cycles kaput</td>
</tr>
<tr>
<td>CREB</td>
<td>cAMP response element-binding protein</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>Cry</td>
<td>Cryptochrome</td>
</tr>
<tr>
<td>CSM</td>
<td>Composite scale of morningness</td>
</tr>
<tr>
<td>DLMO</td>
<td>Dim light melatonin onset</td>
</tr>
<tr>
<td>DMH</td>
<td>Dorsomedial hypothalamus</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>Dr.</td>
<td>Doctor</td>
</tr>
<tr>
<td>E</td>
<td>East</td>
</tr>
<tr>
<td>EEG</td>
<td>Electroencephalography</td>
</tr>
<tr>
<td>e.g.</td>
<td>Exempli gratia, for example</td>
</tr>
<tr>
<td>ES</td>
<td>Evening shift</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>ET</td>
<td>Early type</td>
</tr>
<tr>
<td>Et al.</td>
<td>Et alii and others</td>
</tr>
<tr>
<td>f</td>
<td>Females</td>
</tr>
<tr>
<td>FD</td>
<td>Free day</td>
</tr>
<tr>
<td>FDES</td>
<td>Free days after evening shift</td>
</tr>
<tr>
<td>FDMS</td>
<td>Free days after morning shift</td>
</tr>
<tr>
<td>FDNS</td>
<td>Free days after night shift</td>
</tr>
<tr>
<td>FEO</td>
<td>Food entrainable oscillator</td>
</tr>
<tr>
<td>Fig.</td>
<td>Figure</td>
</tr>
<tr>
<td>g</td>
<td>Gram</td>
</tr>
<tr>
<td>GABA</td>
<td>Gamma-aminobutyric acid</td>
</tr>
<tr>
<td>GHG</td>
<td>Greenhouse Geisser correction</td>
</tr>
<tr>
<td>GMT</td>
<td>Greenwich mean time</td>
</tr>
<tr>
<td>h</td>
<td>Hour</td>
</tr>
<tr>
<td>HAT</td>
<td>Histone acetyl transferase</td>
</tr>
<tr>
<td>IARC</td>
<td>International agency for research on cancer</td>
</tr>
<tr>
<td>IBM Corp.</td>
<td>International business machines corporation</td>
</tr>
<tr>
<td>IE</td>
<td>Interaction effect</td>
</tr>
<tr>
<td>i.e.</td>
<td>Id est, that means</td>
</tr>
<tr>
<td>IL</td>
<td>Interleukin</td>
</tr>
<tr>
<td>IT</td>
<td>Intermediate type</td>
</tr>
<tr>
<td>LT</td>
<td>Late type</td>
</tr>
<tr>
<td>lx</td>
<td>Lux</td>
</tr>
<tr>
<td>M</td>
<td>Mean</td>
</tr>
<tr>
<td>m</td>
<td>Males</td>
</tr>
<tr>
<td>m²</td>
<td>Square metre</td>
</tr>
<tr>
<td>MCTQ</td>
<td>Munich ChronoType Questionnaire</td>
</tr>
<tr>
<td>MCTQ&lt;sup&gt;Shift&lt;/sup&gt;</td>
<td>Munich ChronoType Questionnaire for shift workers</td>
</tr>
<tr>
<td>ME</td>
<td>Main effect</td>
</tr>
<tr>
<td>MEQ</td>
<td>Morningness-Eveningness questionnaire</td>
</tr>
<tr>
<td>min</td>
<td>Minute</td>
</tr>
<tr>
<td>mm</td>
<td>Millimetre</td>
</tr>
<tr>
<td>MS</td>
<td>Morning shift</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>MSE1</td>
<td>Main sleep episode prior to nap</td>
</tr>
<tr>
<td>MSE2</td>
<td>Main sleep episode ensuing the nap</td>
</tr>
<tr>
<td>MSF&lt;sub&gt;E&lt;/sub&gt;</td>
<td>Mid-sleep on free days after evening shifts, sleep corrected</td>
</tr>
<tr>
<td>mW</td>
<td>Milliwatt</td>
</tr>
<tr>
<td>N</td>
<td>North</td>
</tr>
<tr>
<td>n</td>
<td>Sample size</td>
</tr>
<tr>
<td>N1</td>
<td>Non-REM sleep stage 1</td>
</tr>
<tr>
<td>NAD(P)H</td>
<td>Nicotinamide adenine dinucleotide (phosphate)</td>
</tr>
<tr>
<td>nm</td>
<td>Nanometre</td>
</tr>
<tr>
<td>Npas2</td>
<td>also known as MOP4, Neuronal PAS domain-containing protein 2</td>
</tr>
<tr>
<td>NS</td>
<td>Night shift</td>
</tr>
<tr>
<td>n.s.</td>
<td>Not significant</td>
</tr>
<tr>
<td>ω (omega)</td>
<td>Frequency</td>
</tr>
<tr>
<td>p</td>
<td>P-value</td>
</tr>
<tr>
<td>Per</td>
<td>Period</td>
</tr>
<tr>
<td>Φ (phi)</td>
<td>Phase shift</td>
</tr>
<tr>
<td>p.m.</td>
<td>Post meridiem, after midday</td>
</tr>
<tr>
<td>PRC</td>
<td>Phase response curve</td>
</tr>
<tr>
<td>pRGC</td>
<td>Photosensitive retinal ganglion cell</td>
</tr>
<tr>
<td>Process S/C/W</td>
<td>Process sleep homeostasis/circadian/alertness</td>
</tr>
<tr>
<td>Prof.</td>
<td>Professor</td>
</tr>
<tr>
<td>Ψ (psi)</td>
<td>Phase angle difference between zeitgeber and oscillator</td>
</tr>
<tr>
<td>PSQI</td>
<td>Pittsburgh Sleep Quality Index</td>
</tr>
<tr>
<td>PVN</td>
<td>Paraventricular nucleus of the hypothalamus</td>
</tr>
<tr>
<td>PVT</td>
<td>Psychomotor vigilance test</td>
</tr>
<tr>
<td>R</td>
<td>Range</td>
</tr>
<tr>
<td>R&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Explained variation of the model, corrected value</td>
</tr>
<tr>
<td>REM</td>
<td>Rapid eye movement</td>
</tr>
<tr>
<td>RIP</td>
<td>Rest in peace</td>
</tr>
<tr>
<td>RNA</td>
<td>Ribonucleic acid</td>
</tr>
<tr>
<td>RORα</td>
<td>RAR-related orphan receptor alpha</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>S1-4</td>
<td>Shift system 1-4</td>
</tr>
<tr>
<td>SCN</td>
<td>Suprachiasmatic nuclei</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>Sin</td>
<td>Sine</td>
</tr>
<tr>
<td>SPSS</td>
<td>Software for statistical analysis</td>
</tr>
<tr>
<td>SPZ (d/v)</td>
<td>Dorsal/ventral subparaventricular zone</td>
</tr>
<tr>
<td>SWD</td>
<td>Shift work disorder</td>
</tr>
<tr>
<td>SWS</td>
<td>Slow wave sleep</td>
</tr>
<tr>
<td>T</td>
<td>Period length of the <em>zeitgeber</em></td>
</tr>
<tr>
<td>Tab.</td>
<td>Table</td>
</tr>
<tr>
<td>τ (tau)</td>
<td>Period length of the oscillator</td>
</tr>
<tr>
<td>TNFα</td>
<td>Tumour necrosis factor alpha</td>
</tr>
<tr>
<td>VIF</td>
<td>Variance inflation factor</td>
</tr>
<tr>
<td>VIP</td>
<td>Vasoactive intestinal peptide</td>
</tr>
<tr>
<td>VLPO</td>
<td>Ventrolateral preoptic nucleus of the hypothalamus</td>
</tr>
<tr>
<td>VRC</td>
<td>Velocity response curve</td>
</tr>
<tr>
<td>vs.</td>
<td>Versus</td>
</tr>
<tr>
<td>WD</td>
<td>Workday</td>
</tr>
<tr>
<td>Yrs.</td>
<td>Years</td>
</tr>
</tbody>
</table>
### 9.1 Munich Chronotype Questionnaire for Shift Workers (MCTQ\textsuperscript{shift})

**Informationen zu Ihrer Person**

1) Alter: ________ Jahre  
2) Geschlecht: weiblich □ männlich □  
3) Größe: ________ cm  
4) Gewicht: ________ kg  
5) Höchster Abschluss:  
   □ Hauptschulabschluss  
   □ Realschulabschluss  
   □ Abitur/Fachabitur  
   □ Sonstiger Abschluss: _____________________________  
6) Sind Sie:  
   □ verheiratet / in Partnerschaft lebend  
   □ getrennt lebend / geschieden  
   □ verwitwet  
   □ allein stehend  
7) Wie viele Kinder leben in Ihrem Haushalt?  
   bis 5 Jahre ________ Kinder  
   6 - 15 Jahre ________ Kinder  
   älter als 15 Jahre ________ Kinder  
8) Arbeiten Sie... Teilzeit □ oder Vollzeit □ ?  
9) Seit wann arbeiten Sie schon im Schichtdienst? ________ Jahre ________ Monate ________ Wochen  
10) Wie gelangen Sie zu Ihrem Arbeitsplatz?  
    □ In einem geschlossenen Fahrzeug (z.B. Auto, Bus, U-Bahn)  
    □ Nicht in einem geschlossenen Fahrzeug (z.B. zu Fuß, mit dem Rad)  
11) Sind Sie  
    □ Instandhalter  
    □ Ersthelfer  
    □ Schichtleiter  
12) Fahren Sie mit einer festen Fahrgemeinschaft zur Arbeit? □ Ja □ Nein  
13) Ich möchte meinen Chronotyp erfahren! □ Ja □ Nein

Hier finden Sie Fragen bezüglich Ihres Schlaf- und Wachverhaltens in dieser Jahreszeit an Arbeitstagen und an freien Tagen. Beantworten Sie bitte ALLE Fragen, auch wenn manche Fragen schwierig zu beantworten scheinen. Spontane Antworten sind meistens die besten Antworten!  

Anleitung zum Ausfüllen des Munich ChronoType Questionnaire (MCTQ)
**Zeichnung 1:** Der Zeitpunkt zu dem Sie sich am jeweiligen Tag ins Bett gelegt haben.

**Zeichnung 2:** Manche Menschen bleiben noch eine Weile wach, wenn sie im Bett liegen!

**Zeichnung 3:** Die Uhrzeit, zu der Sie die „Entscheidung treffen“ zu schlafen
(z.B. Licht ausschalten und die Augen schließen etc.).

**Zeichnung 4:** Anzahl der Minuten, die Sie im Schnitt zum Einschlafen benötigen.

**Zeichnung 5:** Die Uhrzeit, zu der Sie am entsprechenden Tag aufgewacht sind.

**Zeichnung 6:** Die Uhrzeit, zu der Sie Ihr Bett verlassen haben.

**Wecker:** Sind Sie durch einen Wecker / anderen Störfaktor geweckt worden (JA) oder von selbst aufgewacht (NEIN, auch wenn sie vor dem Wecker aufwachen)?

Bitte achten Sie darauf die Uhrzeiten an Hand der 24-Std. Skala anzugeben (23.00 statt 11.00 Uhr)!!

<table>
<thead>
<tr>
<th>Zwischen zwei Frühschichttagen!</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ich gehe ins Bett um ___________ Uhr.</td>
</tr>
<tr>
<td>Manche Menschen bleiben noch eine Weile wach, wenn sie im Bett liegen!</td>
</tr>
<tr>
<td>Ich bin bereit einzuschlafen um ___________ Uhr.</td>
</tr>
<tr>
<td>Um einzuschlafen, brauche ich ___________ Minuten.</td>
</tr>
<tr>
<td>Ich wache um ___________ Uhr auf.</td>
</tr>
<tr>
<td>□ mit Wecker □ ohne Wecker</td>
</tr>
<tr>
<td>Ich stehe auf nach ___________ Minuten.</td>
</tr>
</tbody>
</table>

Normalerweise mache ich ein Nickerchen □ ja □ nein
Wenn ja, dann von ___________ Uhr bis ___________ Uhr

Bitte geben Sie HIER an, falls Sie in dieser Schichtbedingung KEINE Möglichkeit haben Ihre Schlafzeiten selbst zu bestimmen (z.B. wegen eines Haustieres, Kind(er)...):
Zwischen zwei Spätschichttagen!

Ich gehe ins Bett um ________ Uhr. (Zeichnung 1)

Manche Menschen bleiben noch eine Weile wach, wenn sie im Bett liegen! (Zeichnung 2)

Ich bin bereit einzuschlafen um ________ Uhr. (Zeichnung 3)

Um einzuschlafen, brauche ich ________ Minuten. (Zeichnung 4)

Ich wache um ________ Uhr auf. (Zeichnung 5)

☐ mit Wecker ☐ ohne Wecker

Ich stehe auf nach ________ Minuten. (Zeichnung 6)

Normalerweise mache ich ein Nickerchen ☐ ja ☐ nein
Wenn ja, dann von ________ Uhr bis ________ Uhr

Bitte geben Sie HIER an, falls Sie in dieser Schichtbedingung KEINE Möglichkeit haben Ihre Schlafzeiten selbst zu bestimmen (z.B. wegen eines Haustieres, Kind(er)...):

Zwischen zwei Nachtschichttagen!

Ich gehe ins Bett um ________ Uhr. (Zeichnung 1)

Manche Menschen bleiben noch eine Weile wach, wenn sie im Bett liegen! (Zeichnung 2)

Ich bin bereit einzuschlafen um ________ Uhr. (Zeichnung 3)

Um einzuschlafen, brauche ich ________ Minuten. (Zeichnung 4)

Ich wache um ________ Uhr auf. (Zeichnung 5)

☐ mit Wecker ☐ ohne Wecker

Ich stehe auf nach ________ Minuten. (Zeichnung 6)

Normalerweise mache ich ein Nickerchen ☐ ja ☐ nein
Wenn ja, dann von ________ Uhr bis ________ Uhr

Bitte geben Sie HIER an, falls Sie in dieser Schichtbedingung KEINE Möglichkeit haben Ihre Schlafzeiten selbst zu bestimmen (z.B. wegen eines Haustieres, Kind(er)...):
Zwischen zwei freien Tagen nach einer Nachtschicht!

Ich gehe ins Bett um _______ Uhr.  
(Zeichnung 1)

Manche Menschen bleiben noch eine Weile wach, wenn sie im Bett liegen!  
(Zeichnung 2)

Ich bin bereit einzuschlafen um _______ Uhr.  
(Zeichnung 3)

Um einzuschlafen, brauche ich _______ Minuten.  
(Zeichnung 4)

Ich wache um _______ Uhr auf.  
(Zeichnung 5)

☐ mit Wecker ☐ ohne Wecker

Ich stehe nach _______ Minuten auf.  
(Zeichnung 6)

Normalerweise mache ich ein Nickerchen ☐ ja ☐ nein

Wenn ja, dann von _______ Uhr bis _______ Uhr

Bitte geben Sie HIER an, falls Sie in diesem Fall KEINE Möglichkeit haben Ihre Schlafzeiten selbst zu bestimmen (z.B. wegen eines Haustieres, Kind(er)):

Wie lange pro Tag, halten Sie sich im Durchschnitt im Tageslicht auf (unter freiem Himmel; ohne Dach über dem Kopf)?

An Frühschichttagen _____ Stunden _____ Minuten
An Spätschichttagen _____ Stunden _____ Minuten
An Nachtschichttagen _____ Stunden _____ Minuten
An freien Tagen _____ Stunden _____ Minuten

Im Folgenden finden Sie Fragen zur Ihrer Arbeit, damit wir besser den Zusammenhang zwischen Schichtarbeit und dem Schlaf-Wach-Verhalten verstehen können.

Wie sind Ihre Arbeitszeiten...

...in der Frühschicht: Von _______ bis _______ Uhr
...in der Spätschicht: Von _______ bis _______ Uhr
...in der Nachtschicht: Von _______ bis _______ Uhr

*Nummer _______________

MCTQ shift © 2011 Céline Vetter & Till Roenneberg, LMU München
9.2 Munich ChronoType Questionnaire (MCTQ)

Anleitung:

Informationen zu Ihrer Person

| Datum: | __________ |
| Name: | __________________________ |
| eMail: | __________________________ |
| Alter: | _____ Jahre |
| Geschlecht: | weiblich ☐ männlich ☐ |
| Größe: | _____ cm |
| Gewicht: | _____ kg |
| Land: | __________________________ |
| Wohnort: | __________________________ |
| Postleitzahl: | __________ |

Ich gehe einer regelmäßigen Arbeit nach (schließt Hausfrau oder Hausmann ein):
Ja ☐ ich arbeite an 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ Tagen in der Woche.
Nein ☐

Ist Ihre Antwort „Ja, an 7 Tagen" oder „Nein“ dann überlegen Sie bitte, ob sich Ihre Schlafzeiten nicht dennoch an allgemeinen ,Werktagen‘ und ,Wochenenden‘ unterscheiden und füllen den MCTQ entsprechend aus.
Arbeitsdetails

Ich war innerhalb der letzten 3 Monate als Schichtarbeiter tätig.

Nein  Ja  (bitte weiter bei „Meine Arbeitszeit ist ...“)

Meine übliche Arbeitszeit ...
... beginnt um _______ Uhr.
... endet um _______ Uhr.

Meine Arbeitszeit ist ...
... sehr flexibel  ... ein bißchen flexibel  ... eher nicht flexibel  ... sehr unflexibel

Zu meinem Arbeitsplatz gelange ich ...
... in einem geschlossenen Fahrzeug (z.B. Auto, Bus, U-Bahn).
... nicht in einem geschlossenen Fahrzeug (z.B. zu Fuß, mit dem Rad).
Ich arbeite zu Hause.

Für den Hinweg zum Arbeitsplatz benötige ich täglich ___ Stunden und ___ Minuten.
Für den Rückweg vom Arbeitsplatz benötige ich täglich ___ Stunden und ___ Minuten.

MCTQ

Zeiten bitte anhand der 24 Stunden Skala angeben (z.B. 23.00 statt 11.00 abends)!

Arbeitstage

Zeichnung 1:  Ich gehe ins Bett um _________ Uhr.
Zeichnung 2:  Manche Menschen bleiben noch eine Weile wach, wenn sie im Bett liegen!
Zeichnung 3:Ich bin bereit einzuschlafen um _________ Uhr.
Zeichnung 4:Um einzuschlafen, brauche ich _________ Minuten.
Zeichnung 5:  Ich wache um _________ Uhr auf.
Zeichnung 6:  Ich stehe auf nach _________ Minuten.
Ich benutze einen Wecker an Arbeitstagen:  Ja  Nein
Wenn „Ja“: Ich wache regelmäßig VOR dem Weckerklingeln auf:  Ja  Nein
**Freie Tage**

Zeichnung 1: Ich gehe ins Bett um _______ Uhr.
Zeichnung 2: Manche Menschen bleiben noch eine Weile wach, wenn sie im Bett liegen!
Zeichnung 3: Ich bin bereit einzuschlafen um _______ Uhr.
Zeichnung 4: Um einzuschlafen, brauche ich _______ Minuten.
Zeichnung 5: Ich wache um _______ Uhr auf.
Zeichnung 6: Ich stehe auf nach _______ Minuten.

Meine Aufwachzeit (Zeichnung 5) wird durch einen Wecker bestimmt: Ja ☐ Nein ☐

Aus bestimmten Gründen kann ich meine Schlafzeiten auch an freien Tagen **nicht** selbst bestimmen:
Ja ☐ Wenn „Ja“: Kind(er)/Haustier(e) ☐ Hobbys ☐ Andere ☐, 
zum Beispiel:_______________________________________________________
_________________________________________________________________

**Stimulantien**

Bitte **Durchschnittswerte** angeben!

<table>
<thead>
<tr>
<th>pro ➔ Tag / Woche / Monat</th>
<th>Ich rauche _____ Zigaretten ...</th>
<th>☐ ☐ ☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ich trinke _____ Gläser Bier (0,33l) ...</td>
<td>☐ ☐ ☐</td>
<td></td>
</tr>
<tr>
<td>Ich trinke _____ Gläser Wein (02,l) ...</td>
<td>☐ ☐ ☐</td>
<td></td>
</tr>
<tr>
<td>Ich trinke _____ Gläser Schnaps / Whiskey/ Gin (2cl) usw. ...</td>
<td>☐ ☐ ☐</td>
<td></td>
</tr>
<tr>
<td>Ich trinke _____ Tassen Kaffee ...</td>
<td>☐ ☐ ☐</td>
<td></td>
</tr>
<tr>
<td>Ich trinke _____ Tassen schwarzen Tee ...</td>
<td>☐ ☐ ☐</td>
<td></td>
</tr>
<tr>
<td>Ich trinke _____ Dosen koffeinhaltige Limonaden ...</td>
<td>☐ ☐ ☐</td>
<td></td>
</tr>
<tr>
<td>Ich nehme Schlaf fördernde Medikamente _____ mal ein ...</td>
<td>☐ ☐ ☐</td>
<td></td>
</tr>
</tbody>
</table>

**Aufenthalt im Freien**

Im Durchschnitt halte ich mich so lange draußen bei Tageslicht auf (ohne Dach über dem Kopf):

An Arbeitstagen: _____ Stunden _____ Minuten
An freien Tagen: _____ Stunden _____ Minuten
### Schlafensbuch - Tragen Sie Ihre Daten immer NACH DEM AUFSCHNITT ein!

<table>
<thead>
<tr>
<th>Woche</th>
<th>Tageslicht</th>
<th>Wohlbefinden</th>
<th>Nickerchen (vor - nach)</th>
<th>Zu Bett</th>
<th>&quot;Jetzt schlafen&quot;</th>
<th>&quot;Aufwachen&quot;</th>
<th>Wecker</th>
<th>Schlafqualität</th>
<th>Freizeit</th>
<th>Spätschicht</th>
<th>Nachtschicht</th>
<th>Freier Tag</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mo</td>
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<td>Di</td>
</tr>
</tbody>
</table>

Bemerkungen (z.B. Krankheit, Medikamente, Stress...)}
9.4 Sleep Log for Office Workers

### Schlaftagebuch (bitte immer nach dem Aufstehen ausfüllen!)

<table>
<thead>
<tr>
<th>Datum (gestern)</th>
<th>Beispiel</th>
<th>Tag 1</th>
<th>Tag 2</th>
<th>Tag 3</th>
<th>Tag 4</th>
<th>Tag 5</th>
<th>Tag 6</th>
<th>Tag 7</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Lichtexposition in h</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wohlbefinden(*)</td>
<td>7</td>
</tr>
<tr>
<td>&quot;Zu Bett&quot; Uhrzeit</td>
<td>22:45</td>
</tr>
<tr>
<td>&quot;Jetzt schlafen&quot; Uhrzeit</td>
<td>23:55</td>
</tr>
<tr>
<td>Einschlafdauer in Min.</td>
<td>10</td>
</tr>
</tbody>
</table>

### heute

<table>
<thead>
<tr>
<th>Datum (heute)</th>
<th>Beispiel</th>
<th>Tag 1</th>
<th>Tag 2</th>
<th>Tag 3</th>
<th>Tag 4</th>
<th>Tag 5</th>
<th>Tag 6</th>
<th>Tag 7</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Aufgewacht Uhrzeit</th>
<th>06:50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aufgestanden Uhrzeit</td>
<td>07:05</td>
</tr>
<tr>
<td>Wecker (ja/nein)</td>
<td>ja</td>
</tr>
<tr>
<td>Schlafqualität(*)</td>
<td>8</td>
</tr>
</tbody>
</table>

**(*) Bitte bewerten Sie auf einer Skala von 0-10, 0 = sehr schlecht ... 5 = neutral ... 10 = sehr gut**

<table>
<thead>
<tr>
<th>Uhr abgenommen</th>
<th>14:00-15:15</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>LightWatcher abgenommen</th>
<th>14:00-15:15</th>
</tr>
</thead>
</table>

**Besonderheiten (ggf. separates Blatt nutzen)**

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Links-/Rechtshänder: ____________  Uhr AN: ____________

Uhr linkes/rechtes Handgelenk: ____________

Nummer: ____________
9.5 Pittsburgh Sleep Quality Index (PSQI)

Schlafqualitäts-Fragebogen (PSQI)

Die folgenden Fragen beziehen sich auf Ihre üblichen Schlafgewohnheiten und zwar nur während der letzten vier Wochen. Ihre Antworten sollten möglichst genau sein und sich auf die Mehrzahl der Tage und Nächte während der letzten vier Wochen beziehen. Beantworten Sie bitte alle Fragen.

1. Wann sind Sie während der letzten vier Wochen gewöhnlich abends zu Bett gegangen?
   übliche Uhrzeit:

2. Wie lange hat es während der letzten vier Wochen gewöhnlich gedauert, bis Sie nachts eingeschlafen sind?
   in Minuten:

3. Wann sind Sie während der letzten vier Wochen gewöhnlich morgens aufgestanden?
   übliche Uhrzeit:

4. Wieviele Stunden haben Sie während der letzten vier Wochen pro Nacht tatsächlich geschlafen?
   (Das muß nicht mit der Anzahl der Stunden, die Sie im Bett verbracht haben, übereinstimmen.)
   Effektive Schlafzeit (Stunden) pro Nacht:

Kreuzen Sie bitte für jede der folgenden Fragen die für Sie zutreffende Antwort an. Beantworten Sie bitte alle Fragen.

5. Wie oft haben Sie während der letzten vier Wochen schlecht geschlafen, ...
   a) ... weil Sie nicht innerhalb von 30 Minuten einschlafen konnten?
      ☐ Während der letzten vier Wochen gar nicht
      ☐ Weniger als einmal pro Woche
      ☐ Einmal oder zweimal pro Woche
      ☐ Dreimal oder häufiger pro Woche

   b) ... weil Sie mitten in der Nacht oder früh morgens aufgewacht sind?
      ☐ Während der letzten vier Wochen gar nicht
      ☐ Weniger als einmal pro Woche
      ☐ Einmal oder zweimal pro Woche
      ☐ Dreimal oder häufiger pro Woche

   c) ... weil Sie aufstehen mußten, um zur Toilette zu gehen?
      ☐ Während der letzten vier Wochen gar nicht
      ☐ Weniger als einmal pro Woche
      ☐ Einmal oder zweimal pro Woche
      ☐ Dreimal oder häufiger pro Woche
d) ... weil Sie Beschwerden beim Atmen hatten?
- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

e) ... weil Sie husten mußten oder laut ge-
schnarcht haben?
- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

f) ... weil Ihnen zu kalt war?
- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

g) ... weil Ihnen zu warm war?
- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

h) ... weil Sie schlecht geträumt hatten?
- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

i) ... weil Sie Schmerzen hatten?
- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

j) ... aus anderen Gründen?
Bitte beschreiben:

Und wie oft während des letzten Monats konnten Sie aus diesem Grund schlecht schlafen?
- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

6. Wie würden Sie insgesamt die Qualität Ihres Schlafes während der letzten vier Wochen beurteilen?
- Sehr gut
- Ziemlich gut
- Ziemlich schlecht
- Sehr schlecht
7. Wie oft haben Sie während der letzten vier Wochen Schlafmittel eingenommen (vom Arzt verschriebene oder frei verkäufliche)?

- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

8. Wie oft hatten Sie während der letzten vier Wochen Schwierigkeiten wachzubleiben, etwa beim Autofahren, beim Essen oder bei gesellschaftlichen Anlässen?

- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

9. Hatten Sie während der letzten vier Wochen Probleme, mit genügend Schwung die üblichen Alltagsaufgaben zu erledigen?

- Keine Probleme
- Kaum Probleme
- Etwas Probleme
- Große Probleme

10. Schlafen Sie allein in Ihrem Zimmer?

- Ja
- Ja, aber ein Partner/Mitbewohner schläft in einem anderen Zimmer
- Nein, der Partner schläft im selben Zimmer, aber nicht im selben Bett
- Nein, der Partner schläft im selben Bett

Falls Sie einen Mitbewohner/Partner haben, fragen Sie sie/ihn bitte, ob und wie oft er/sie bei Ihnen folgendes bemerkt hat.

a) Lautes Schnarchen

- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

b) Lange Atempausen während des Schlafes

- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

c) Zucken oder ruckartige Bewegungen der Beine während des Schlafes

- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche
d) Nächtlliche Phasen von Verwirrung oder Desorientierung während des Schlafes

- Während der letzten vier Wochen gar nicht
- Weniger als einmal pro Woche
- Einmal oder zweimal pro Woche
- Dreimal oder häufiger pro Woche

e) Oder andere Formen von Unruhe während des Schlafes

Bitte beschreiben:

Machen Sie bitte noch folgende Angaben zu Ihrer Person:

Alter: _______ Jahre
Geschlecht: ☐ weiblich
☐ männlich
Körpergröße: ............ Gewicht: .............
Beruf:
☐ Rentner(in)
☐ selbständig
☐ Schüler/Student(in)
☐ Angestellte(r)
☐ Arbeiter(in)
☐ arbeitslos/ Hausfrau(mann)