The Importance of Chronotype in Shift Work Research

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To my Grandmother

Denise Haan

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1 General Introduction

It has been estimated that every year, as much as 20 million workers in the EU experience work related health problems and an average of 5,720 people die as a consequence of work-related accidents (European Statistical Data Support, 2009). Shift work was thereby shown to be a major risk factor. Yet, increasing demands in global economy and around the clock provision of medical and safety services have rendered shift work an integral and indispensable constituent of modern society. As much as 22% of the working population in the EU work shifts (International Labour Office Geneva, 2004). For the majority, shift work is not a choice but a professional requirement.

Despite the last decades' vast interest into questions related to shift work, we still know very little about the causal pathways leading to health problems in shift workers. This is largely due to past research not properly taking into account the functioning of the inner circadian clock and its influences on shift workers' ability to cope with the demands of working shifts. The current project explores shift workers' sleep and wake behaviour in the field, with a particular emphasis on chronotype-specific differences and how these predict tolerance to shift work, in terms of sleep, well-being, and physical health. Before presenting the different studies, theoretical background and relevant issues within the fields of chronobiology and shift work research will be introduced.

1.1 The Circadian Clock

Evolution has equipped living organisms not only with adaptations to spatial and social niches but also to temporal ones. The physiology of microbes, plants and animals, including humans, has adapted to the 24-hour rotation of the earth. Among the most conspicuous temporal adaptations is the timing of activity and rest. Being at the right place at the right time of day enables better access to valuable resources (e.g. food, mates) and protection from predators. Such an adaptation would be greatly facilitated by an endogenous programme – a circadian clock. An internal circadian clock provides organisms with the amazing evolutionary benefit to anticipate events. Anticipation allows organisms to prepare for environmental changes, such as for example growing fur or storing food before temperature actually decreases. Anticipation also allows for better competition to limited resources, by being one jump ahead of the other. For any organism that is prey of another, it is of vital importance to "know" when a predator is most likely to be around. One would expect natural selection to have favoured individuals with more precise mechanisms of anticipation, whereby long-term evolutionary pressures made individuals increasingly better at anticipating external events (for a review on temporal adaptations, see Roenneberg & Foster, 1997).

1.1.1 An Historical Overview of Circadian Research

The periodic changes in biological functions have long been believed to underlie simple responses to changes in environmental stimuli, such as cyclical changes in lightness and darkness. This view was challenged when in 1729, a French geophysicist --Jean-Jacques de Mairan, published his now well-known *Observation Botanique*. In this article, de Mairan describes a bizarre observation that he made when placing a mimosa plant into a cupboard over a few days. Although the mimosa was obviously devoid of external cycles of light and darkness, it continued to fold and unfold its leaflets in the same rhythmical manner as it did before, when it was standing next to the window. Moreover, the mimosa opened its leaflets a few hours ahead of sunrise, as if it "knew" when a new day was about to begin. De Mairan concluded that the plant's rhythmical functioning must be self-sustained. Beyond that and certainly ahead of his time, de Mairan extended his observation to humans with disordered sleep, encouraging further studies to explore this issue.

It wasn't until 1938, centuries later, that Nathanial Kleitman (now known as the father of sleep research) and his graduate student, Bruce Richardson, took up residence 36 meters underground in a cave in Kentucky, USA, to investigate their own rhythms of sleep and physiology. During their thirty-three day stay, Kleitman and Richardson lived on a 28-hour body temperature cycle, consisting of nine hours of sleep and regular routines of eating, reading, writing and walking. Jean-Jacques de Mairan was right -- when deprived of external signals, the circadian clock continues to oscillate. The persistence of rhythms in the absence of a dark-light cycle or other exogenous time signals clearly indicates the existence of an internal timekeeping mechanism. Self-sustainability is one of the essential features defining the circadian clock today.

Figure 1.1. Nathaniel Kleitman and Bruce Richardson, during their one month stay in a cave in Kentucky in 1938. *Source:* New York Times (http://image.guim.co.uk/Guardian/society/gallery/2007/dec/03/exhibition.art/Kleitman_d-6690.jpg)

More systematic and controlled experiments were followed-up in the 1960's by Aschoff and colleagues in Munich and later in Andechs, Germany. For days, weeks, and even months, people were asked to reside in soundproof and lightproof rooms --deprived of any cues that might indicate the time of day but with the freedom to eat and sleep according to their preferences. In the absence of environmental time cues, the circadian rhythms were *free running,* -- revealing the true period length *tau (τ)* of the endogenous rhythm. Participants with free-running circadian rhythms longer than 24 hours became increasingly late, as they delayed their phase positioning relative to the external phase of the light dark-cycle. In contrast, participants with endogenous rhythms shorter than 24 hours, advanced in their phase relationship to external time. Depending on the extent of deviation from 24 hours (ranges between 23.5 and 25 hours have been observed), it took up to several weeks until the internal clock synchronized back to its original phase positioning. The circadian period also varied according to the nature of the constant condition, such as constant darkness or constant lightness (Aschoff, 1951), indicating that there is no exact free-running period (Roenneberg, Daan, & Merrow, 2003). Around the same time, Colin

Pittendrigh analyzed circadian rhythms in fruit flies and discovered a second essential property of the circadian clock – temperature compensation. Unlike most biochemical reactions, the circadian clock maintains the same period over a range of environmental temperatures (Pittendrigh, 1960).

Today, we know that circadian (from the Latin *circa diem* –about a day) rhythms exhibit even in single cells (Schweiger, Hartwig, & Schweiger, 1986). Circadian oscillations can be found in hormone secretion (e.g. cortisol, melatonin, prolactin, insulin), blood pressure, heart rate, blood volume and flow, heart muscle function, kidney function, urine formation, immune system, blood cell functions, intestinal tract, oesophagus, lung, liver, pancreas, spleen, thymus, as well as rhythms of behaviour (sleep-wakefulness) and cognition (Koopman, Minors, & Waterhouse, 1989; Martin, 1988; Van Cauter et al., 1981; Van Cauter & Refetoff, 1985; Zanello, Jackson, & Holick, 2000). Free-running clocks are distributed around a species-specific mean (Dijk & Lockley, 2002; Klerman, 2001; Klerman et al., 1998; Pittendrigh & Daan, 1976; Wever, 1979), averaging 24.18 ± 0.27 hours in humans (Czeisler et al., 1999). The seeming imprecision in free-running rhythms has been suggested to be an important feature of *rhythmicity* (Pittendrigh, 1960). Reducing the occurrence of drifts, a continuous adjustment to the light-dark cycle results in greater precision of expressed rhythms.

1.1.2 Suprachiasmatic Nucleus (SCN)

All circadian rhythms are determined by the *suprachiasmatic nucleus* (SCN), a cluster of approximately 20,000 neurons (the size of a grain of rice) located in the anterior part of the hypothalamus (Antle & Silver, 2005; Reppert & Weaver, 2001),directly above the optic chiasm. Via its rhythmic outputs, the SCN orchestrates each circadian cellular clock throughout the body's organs and tissues, so as to adjust physiology to Earth's rotation. The electrical potential frequency of neurons of the SCN fluctuates with an approximate 24 hour periodicity, even in complete darkness and when isolated from other areas of the brain (Gillette, 1986; Green & Gillette, 1982; Groos & Hendriks, 1982; Inouye & Kawamura, 1979; Meijer & Rietveld, 1989; Reppert & Uhl, 1987; Rusak & Bina, 1990; Schwartz & Gainer, 1977; Shibata & Moore, 1988; Uhl & Reppert, 1986; Welsh, Logothetis, Meister, & Reppert, 1995). These rhythms are generated by endogenous translation-transcription feedback cycles within each cell, regulated by clock genes (e.g. period 1, 2 and 3 / chryptochrome 1 and 2; clock and bmal1). Animal studies have shown circadian rhythm abolishment after SCN destruction and restoration of circadian rhythms after implantation of fetal SCN cells (Bargiello, Jackson, & Young, 1984; DeCoursey & Buggy, 1989; Drucker-Colin, Aguilar-Roblero, Garcia-Hernandez, Fernandez-Cancino, & Bermudez Rattoni, 1984; Silver, Gladstone, Kahn, Gibson, & Bittman, 1987; Ralph, Foster, Davis, & Menaker, 1990; Ralph & Menaker, 1988).

In real-life conditions, the circadian clock is always exposed to external time cues, called *zeitgeber*, to which the clock synchronizes its rhythms. Light is the most important zeitgeber for most organisms, including humans (Roenneberg & Foster, 1997). Daily changes in lighting quality at dawn or dusk are very stable, providing a reliable source to draw on for information on external time. The importance of light as a zeitgeber is reflected in the anatomical structure of the SCN, which is functionally linked to the visual system through a bundle of cells that project from the optic nerve to the hypothalamus (Moore & Eichler, 1972). In mammals, light as a zeitgeber is detected by means of specialized photo-receptive ganglial cells that make up about 1% of all ganglial cells in the retina (Foster & Hankins, 2002). These photosensitive ganglion cells produce melanopsin, a retinylidene protein (Provencio, Rollag, & Castrucci, 2002; Sekaran, Foster, Lucas, & Hankins, 2003).

Photosensitive, melanopsin-containing ganglion cells have been dubbed *intrinsically photosensitive Retinal Ganglion Cells* (ipRGC), because they respond to light even when synaptic communication in the retina is blocked and when physically isolated from other retinal cells (Berson, Dunn, & Takao, 2002). In humans, the sensitivity of this light reception peaks in the short wavelengths range of the light spectrum (420 to 480 nm) (Brainard et al., 2001; Brainard et al., 2008; Thapan, Arendt, & Skene, 2001). It has been suggested that melanopsin-containing ganglion cells detect the spectral composition of light at dawn (Foster & Wulff, 2005) or changes in spectral composition during the transition from day to night (Roenneberg & Foster, 1997). For a comprehensive review of the characteristics of these receptors, see Foster and Hankins (2007).

Light signals are transduced from melanopsin-containing ganglion cells to the SCN via a direct connection to the ventrolateral SCN --the retinohypothalamic tract. Transmitted light signals in turn activate the c-fos gene of neurons of the ventrolateral SCN (Kornhauser, Nelson, Mayo, & Takahashi, 1990; Rea, 1989; Rusak, 1989; Rusak, Robertson, Wisden, & Hunt, 1990), to then relay this information throughout the SCN via gamma-aminobutyric acid (GABA), which in turn synchronizes the circa-daily-rhythm produced by SCN neurons to exactly 24 hours (Liu & Reppert, 2000). As the central pacemaker, the SCN sends information to other hypothalamic nuclei and to the pineal gland to modulate varying body functions (e.g. body temperature, cortisol, melatonin) by means of signals via the nerve tract and bloodstream. Animal studies have shown that each cell and organ tissue contains a circadian clock that is synchronized to the SCN (Balsalobre, 2002; Buijs & Kalsbeek, 2001; Storch et al., 2002).

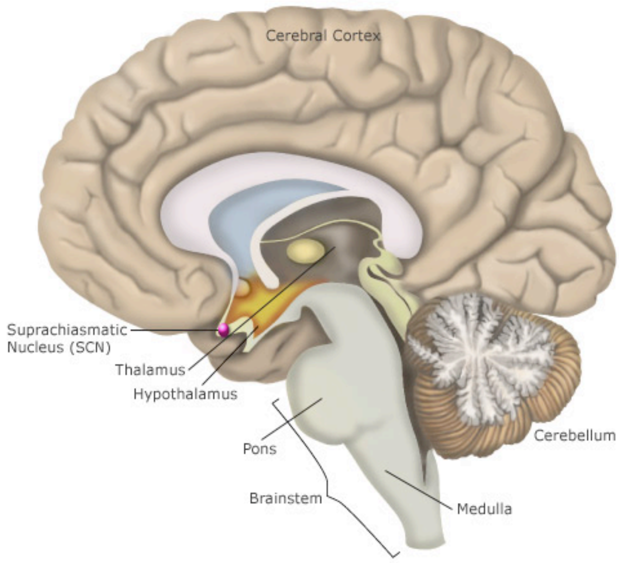

Figure 1.2. Localization of the suprachiasmatic nucleus (SCN) in the human brain. *Source*: Harvard Medical School Division of Sleep Medicine (http://healthysleep.med.harvard.edu/image/200).

1.1.3 The Sleep-Wake Cycle

Being the most overt of human circadian rhythms, the sleep-wake cycle has been one of the first rhythms to be studied in humans. When synchronized to the 24-hour day, the timing of sleep bears a characteristic relationship to the light/dark cycle. In general, humans retire to sleep after onset of darkness, when the body temperature is falling, and wake following sunrise, when the body temperature is rising. When waking, most people experience a transitional state of sleepiness before achieving maximal alertness. This state has been called *sleep inertia* (Lubin, Hord, Tracy, & Johnson, 1976) and can last from minutes to hours (Ferrara, De Gennaro, & Bertini, 2000; Jewett, Wyatt, Ritz-De Cecco, Khalsa, Dijk, & Czeisler, 1999), during which performance is strongly impaired. Conversely, there are times within the 24-hour day, where sleep is difficult to initiate. This *forbidden zone for sleep*, also called the *wake maintenance zone* (Lavie, 1986; Wyatt et al., 1999) has been suggested to occur on average between 19:00 and 21:00 o'clock in humans (Lavie, 1986; Strogatz, Kronauer, & Czeisler, 1987).

In daily life, however, social obligations like work schedules heavily impact the timing of sleep and activity. One way to investigate potential influences from the social clock is to differentiate between the timing of sleep and wakefulness on workdays and free days, as has been assessed by the Munich ChronoType Questionnaire (Roenneberg et al., 2004; Zavada, Gordijn, Beersma, Daan, & Roenneberg, 2005). Roenneberg and colleagues found significant differences between mid-sleep on work (MSW) and free days (MSF). Compared to the distribution of MSW, the distribution of MSF shows a much higher variance and a delay of approximately two hours. The weekly shift between mid-sleep on workdays and free days has been termed *social jetlag* (Wittman, Dinich, Merrow, & Roenneberg, 2006). As such, social jetlag reveals a quantifiable measure of the degree to which the circadian timing of sleep and wake behaviour is displaced by the social clock (degree to which an individual lives against his/her circadian time). In contrast to trans-meridian jetlag, social jetlag is a chronic state of misalignment between the social and the circadian clock and is said to concern the majority of the working population in industrialized societies. Social jetlag has been used as a predictor of cigarette and alcohol consumption and is believed to play an important role in predicting health. A computational model to predict social jetlag in various contexts of work displacement is currently being developed by Roenneberg. First results of this promising model have been discussed in the doctoral dissertation by Kantermann (2008).

In addition to being regulated by the circadian clock, the sleep-wake cycle is also modulated by the homeostatic process. The homeostatic process characterizes an increase in the drive for sleep as an exponential saturating function of wakefulness, recovering only through sleep. When deprived of sleep, people generally find sleep impossible to resist, frequently experiencing brief episodes of involuntary sleep, called micro-sleep (Dinges, 1989; Mitler, Carskadon, Czeisler, Dement, Dinges, & Graeber, 1988). Once sleep has been initiated, the drive for sleep falls rapidly until it levels off, so as to gradually approach an asymptote (see Figure 1.3.). The *two-process model of sleep regulation* predicts the timing and propensity of sleep as a function of a complex interplay between these two integrative processes (Borbély, 1982). While the homeostatic process (S) promotes a wake-dependent increase in the drive for sleep, the circadian process (C) generates a drive for wakefulness during the day. The three-process model of sleep regulation (Akerstedt & Folkard, 1995, 1997; Akerstedt, Folkard, & Portin, 2004; Akerstedt, Kecklund, & Gillberg, 2007; Folkard & Akerstedt, 1992), adds on to this model by including a third factor --SC, the combined effect of the homeostatic (S) and circadian (C) regulation, which is used as a predictor of sleepiness and alertness (see Figure 1.3). This model has been successfully applied in predicting risk of injury and accidents at work.

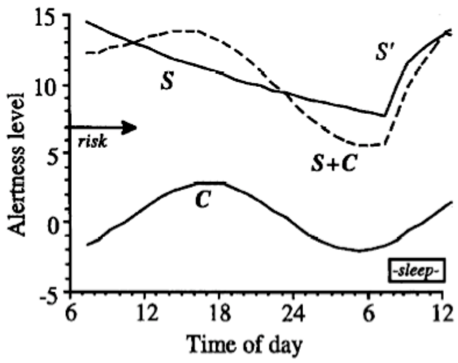

Figure 1.3. The three-process model of sleep regulation when sleep is delayed to 8:00 o'clock. The model includes an homeostatic process (S), a circadian process (C) and the combined effect of both (S+C). *Source*: Akerstedt (1995).

The interaction between the homeostatic and circadian processes ensures a consolidated period of sleep and wakefulness (Dijk & Czeisler, 1994). In the evening, the increased drive for sleep coincides with the circadian decrease in wakefulness, opening the *sleep gate* to promote sleep. The homeostatic drive for sleep is strongest close to the minimum of the endogenous core body temperature rhythm (Dijk, Duffy, & Czeisler, 1992; Johnson et al., 1992). *Sleep latency*, the time that people take to fall asleep, can be used as a measure of sleep propensity as a function of both processes. While the propensity for sleep increases with time awake, circadian alertness interferes with sleep initiation, increasing sleep latency. Studies have shown that sleep latency is shortest in the middle of the night and during the middle of the afternoon (Carskadon & Dement, 1987; Richardson, Carskadon, Orav, & Dement, 1982). In the morning, the circadian wakefulness rises at the time of low homeostatic sleep pressure, promoting wake-up. Wake times correlate with rising body temperature, regardless of when sleep was initiated. Prior to rising body temperature at the circadian nadir, the circadian phase seems to be protective against sleep termination (Czeisler, Richardson, Zimmerman, Moore-Ede, & Weitzman, 1981). Stable sleep-wake cycles can only be maintained when the phase relationship between the timing of the circadian clock opposes the homeostatic deterioration in alertness, such as pertained in the *opponent-process model* (Dijk & Czeisler, 1994).

1.1.4 Entrainment

The process by which the circadian clock synchronizes to a zeitgeber is called *entrainmen*t, the clock's third defining feature. When analyzing the functioning of the clock, one has to distinguish the effects of the circadian clock from the effects of masking, which are mere responses to external stimuli. To see whether a rhythm is masked, organisms are commonly released to constant conditions. Entrainment differentiates itself from mere synchronization in that it is responsive to environmental stimuli—it is a process governed by the internal attributes of the clock (e.g. period) as well as external conditions (Roenneberg, Daan, & Merrow, 2003). The rate and extent to which the clock synchronizes to daylight depends on

1.) the period of the zeitgeber, 2.) the period of the circadian clock in constant conditions (*tau*), 3.) the proportion of zeitgeber stimuli (e.g. light and darkness), 4.) the strength or amplitude of the zeitgeber, 5.) and the system's sensitivity and responsiveness to a zeitgeber.

The first systematic experiments on entrainment were conducted by Pittendrigh, in the 1960's. His findings set the foundation for current views on entrainment. By exposing organisms held in constant darkness to short pulses of light at varying times throughout the day, Pittendrigh analyzed the differential effects of light exposure within the 24-hour day. He noted that entrainment was phase-dependent --the responses of the clock varied in strength and direction over the course of the cycle. Subsequent numerous experiments have found the same effects in humans (Beersma & Daan, 1993). A clock's phase can be defined by any reference point to the phase of a zeitgeber, whereby peaks or onsets are generally used as markers for the internal phase of a cycle and dawn and dusk as external reference points. The phase relationship between internal and external phase is termed the *phase of entrainment* (Roenneberg, Daan, et al., 2003). The phase angle between internal and external phase depends on the individual free-running period (Aschoff, 1979; Roenneberg & Merrow, 2000) and consequently this influences the timing of entrainment to a zeitgeber.

When light pulses are delivered during portions of the internal cycle that normally occur during the day (subjective day), light has little or no effect on the phase positioning of the rhythm. However, exposure to bright light in the early subjective night induces a phase delay, whereas exposure to bright light in the late subjective night provokes a phase advance. Czeisler et al. (1989) found that the greatest phase shift occurs when exposed to bright light three hours before usual awakening. Entrainment to external time cues is feasible only within a certain *range of entrainment*. According to a study from Harvard, the circadian clock in humans can be entrained to a 23.5-hour cycle and a 24.65-hour cycle (Scheer, Wright, Kronauer, & Czeisler, 2007).

The process of entrainment can be visually illustrated with the *phase response curve* (PRC), in the form of a graph depicting observed phase shifts as a function of the oscillator's phase and strength (see Figure 1.4.). The closer a zeitgeber signal is to an oscillator's peak (e.g. temperature maximum) or minimum (temperature minimum), the stronger the resulting phase shift. When light input covers both sides of the PRC (when it covers the internal phase before as well as after the temperature minimum), the phase shifts towards the longest of both light portions (Eastman, 1992). The phase of entrainment is also influenced by the intensity and length of the zeitgeber signal. A weak zeitgeber signal thereby leads to a smaller shift in phase than a stronger signal and a long zeitgeber signal to a stronger shift than a short one. Depending on when light pulses are administered, the clock's velocity also changes. Light at dawn accelerates the clock and light at dusk decelerates the clock (Daan & Beersma, 1984). The PRC and the required zeitgeber strength vary from species to species (e.g. nocturnal versus diurnal).

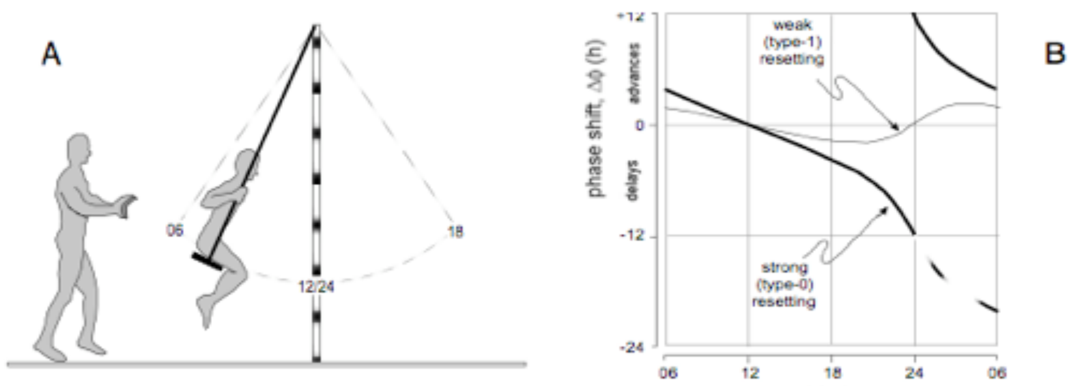

Figure 1.4. To explain the PRC, it has commonly been compared to the functioning of a swing (A). The position of a swing at a given time point will vary depending on the position it had when it was pushed and the strength of the push. The resulting phase shifts can be summarized in the phase response curve (B). *Source:* Roenneberg, Daan et al. (2003).

Recently, this traditional view of entrainment has been challenged by Roenneberg, Hut, Daan, and Merrow (2010). Criticizing the PRC's inability to integrate different approaches to entrainment mechanisms (such as the parametric and non parametric approaches, see Roenneberg, Daan et al., 2003), its inherent circularity in argumentation (explaining the mechanisms underlying phase shifting by means of observed phase shifting), and problems of generalizing entrainment across contexts (e.g. species, nature of light stimuli), Roenneberg et al. propose an alternative approach to entrainment based on the *circadian response characteristic* (CRC), being able to predict entrainment under all conditions, in all species. The CRC is characterized by its shape and asymmetry (see Figure 1.5.) and is based on the assumption that the internal cycle length gets compressed when exposed to light around subjective dawn and expanded when exposed to light around subjective dusk, irrespective of the form of the daily light profile (e.g. single pulse versus 24h light dark cycle). As such entrainment is a self-regulating process, whereby the clock adopts a specific phase relationship to a zeitgeber in order to adjust its cycle length to that of the zeitgeber.

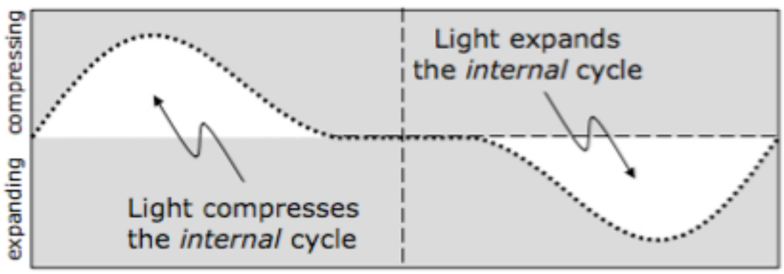

Figure 1.5. Illustration of the circadian response characteristic (CRC). The internal cycle length is compressed by exposure to light in the subjective morning (phase advance) and is expanded by exposure to light in the subjective evening (phase delay). *Source*: Roenneberg et al. (2010).

1.1.5 Zeitgeber

The effect of daylight on the human circadian system had long been underrated. Until the 1980’s it was held that humans, a highly social species, were primarily synchronized to social cues (Aschoff, Hoffmann, Pohl, & Wever, 1975). Studies on blind people, however, have largely disconfirmed the role of the social clock as a primary zeitgeber, as it has been shown that blind people, as well as bilaterally enucleated subjects, display free-running rhythms despite daily exposure to social cues (Klerman et al., 1998; Lewy & Newsome, 1983; Lockley et al., 1997; Sack & Lewy, 1993; Sack, Lewy, Blood, Keith, & Nakagawa, 1992; Skene, Lockley, & Arendt, 1999). A clever large-scale epidemiological study by Roenneberg, Kumar and Merrow (2007) pieced apart the effects of daylight from potential effects of the social clock, by looking at the timing of sleep and wake behaviour in the German population. While social time is the same across Germany, the sleep and wake behaviour of its residents varies systematically from East to West, with changes in the timing of sleep closely matching the longitudinal differences in the timing of sunrise.

Despite more recent findings that reveal the influences of daylight on the circadian system in determining sleep and wake behavior, the social clock is held to be an important zeitgeber in human entrainment. It has been suggested that synchronization to social cues is an indirect consequence of synchronization to activity rhythms (Mistlberger & Skene, 2005). A number of experiments have shown that simply exposing rats to a running wheel can change the phase of the internal clock (Mrosovsky, 1988; Turek, 1989). This suggests that the circadian clock and the sleep-wake cycle are linked by means of a feedback loop mechanism, whereby the circadian clock not only affects the timing of sleep and wakefulness but is itself also affected by the rest-activity rhythms generated by the sleep-wake cycle (Mistlberger & Skene, 2005). In humans, however, activity has been argued to have little effect on the circadian clock (Beersma & Hiddinga, 1998).

There is also strong evidence that melatonin can synchronize the internal clock (for a detailed review, see Mistlberger & Skene, 2005). Daily melatonin administration in blind people has been shown to synchronize free–running rhythms (Sack, Lewy, Blood, Stevenson, & Keith, 1991). Other potential zeitgeber are temperature (Underwood & Calaban, 1987), food intake, and benzodiaepines (hypnotic drugs) (Ralph & Menaker, 1986; Turek & Losee-Olson, 1986), especially when light stimulation is restricted (Foster & Kreitzman, 2004). Peripheral and central clocks have been shown to react at different degrees to varying zeitgebers. While the SCN entrains primarily to light, the liver clock entrains more easily to food schedules. Yet, it is important to note that non-photic time cues are essentially a consequence of cyclical changes in light and darkness, as an effect of Earth's rotation around the sun. As such, daylight characterizes the main and primary zeitgeber evolution has acted on.

It has been suggested that indoor working conditions and urban lifestyle cause strain on the circadian clock. Indoor lighting levels, generally below 400 lux, are extremely low when compared to outdoor lighting intensities, which reach about 10 000 lux on a cloudy day. Decreased zeitgeber strength reduces entrainment to the zeitgeber, leading to a larger variance in the adopted phase relationship (chronotype). As most humans have an internal cycle length exceeding 24-hours, the mean phase of entrainment becomes increasingly delayed with decreasing zeitgeber strength. A study by Roenneberg, Wirz-Justice et al. (2003) has shown that this effect demonstrates itself in human sleep-wake behaviour. The authors found that mid-sleep on free days correlates significantly with reported amount of time spend outdoors, whereby people who reported at least 30 hours of weekly daylight exposure, displayed an almost two hour advance in phase compared to those who only reported 10 hours of weekly daylight exposure. In a German population-wide study, Roenneberg, Kumar et al. (2007) also revealed a decreased entrainment to sun time as a function of living in large cities (population size extending 300,000), as well as a progressively delayed phase with increasing population size. Modern 24-hour city life and increased exposure to artificial lighting in large cities are thereby held to gradually uncouple the circadian clock from the natural light-dark cycle.

Yet, under stringent conditions, also a very weak zeitgeber, such as dim indoor lighting (e.g. 180 lux), can entrain the circadian clock (Boivin & Czeisler, 1998; Martin & Eastman, 1998). This has been shown to occur after long-term exposure to a weakened zeitgeber, whereby entrainment becomes increasingly sensitive as a function of continued exposure. The necessary light intensity required to achieve a certain degree of entrainment thereby depends on the *prior photic history* (Herber et al., 2002). As such, it has been suggested that given the right prior desensitization, even as dim a light as candlelight could, theoretically, entrain the circadian clock (Mistlberger und Skene, 2004).

1.1.6 Chronotype

Individual differences in the adopted phase relationship to a zeitgeber are referred to as chronotype. When the clock's cycle length is longer than that of the zeitgeber ($\tau > T$), the clock needs to adopt a later phase relationship to the external zeitgeber (to get light exposure during the expanding half of the CRC), whereas clocks with a cycle length shorter than that of the zeitgeber ($\tau < T$) need to adopt an earlier phase relationship (to get light exposure during the compression half of the CRC) in order to entrain to the zeitgeber. Chronotype has a slightly positively skewed bell-shaped distribution (Roenneberg et al., 2003), which varies along with zeitgeber strength (the weaker the zeitgeber strength, the larger the variance). As such, few individuals are extreme early (colloquially known as larks) or late (owls) types, with the majority lying in between these two extremes.

Classic markers of the circadian phase are body temperature and melatonin. Body temperature oscillates throughout the 24-hour day, with an amplitude of 0.2-0.5 degrees Celsius that peaks at 37.5°C in the evening hours and has its low at 36.5°C in the morning hours. As a phase marker, body temperature is easily masked by numerous influences, such as physical activity, sleep, and meals. Melatonin is generally considered a more stable and reliable marker for the circadian phase as it has been shown to be less easily affected by influences from activity and meals and to better correlate with sleep times (Benloucif et al., 2005; Griefahn, 2002). Melatonin is secreted at night and is produced by the pineal gland under the direct control of the SCN. It begins to be released approximately two hours prior to sleep begin, peaks about two to three hours after and then gradually declines until awakening (Sack, Blood, & Lewy, 1992). Melatonin is also called the hormone of darkness as its production is inhibited by light. Consequently melatonin should only be collected under dim light conditions. The onset of melatonin secretion in dim light, *dim-light melatonin onset* (DLMO), provides a reliable marker of internal phase (Lewy, Cutler, & Sack, 1999).

As phase markers, both temperature and melatonin require stringent protocols of assessment. These are generally achieved by means of the *constant routine protocol*, where room temperature, humidity and lighting are kept constant across the study period. To control for potential effects of activity, sleep, and food intake, participants are normally required to bed-rest and are kept awake under a constant energy supply (e.g. 100 caloric meals provided every 1 h) (for a detailed review, see Duffy & Dijk, 2002). The assessment itself is quite time-consuming, costly, and rather uncomfortable for participants. Temperature is generally assessed by means of rectal temperature, which needs to be monitored continuously. Melatonin was classically assessed by means of blood samples but modern technology has progressed so that melatonin levels can be retrieved through urine and saliva samples, requiring repeated assessments (e.g. every 30 minutes). Due to these difficulties, many studies have preferred to revert to questionnaire-based assessments of circadian phase, the most commonly being the Morningness-Eveningness Questionnaire (MEQ) by Horne and Østberg (1976). Yet, the use of the MEQ as a measure of circadian phase has been criticized (Roenneberg, Wirz-Justice et al, 2003; Zavada et al., 2005). Based primarily on preferences for morning and evening orientation of activity, the MEQ assesses behavioural aspirations rather than actual behavioural patterns subject to circadian variation.

Questions in regards to the timing of actual sleep and wake behaviour are ideally suited for a quantification of phase by means of a questionnaire, as sleep-wake behaviour is readily observable and quite easy to report. A study by Martin and Eastman in 2002 has shown a very good correlation: r (26) = .89 between DLMO and self-reported timing of sleep in participants free to choose their own sleep schedules. DLMO predicted the timing of sleep within one hour of the DLMO for 92% of the subjects and in no case did the difference exceed 1.5 hours. The correlation between the DLMO and the MEQ score was comparatively weak: r (26) = - 0.48. The Munich ChronoType Questionaire (MCTQ) (Roenneberg et al., 2004; Roenneberg et al., 2005; Roenneberg, Wirz-Justice et al., 2003) is ideally suited for a quick and inexpensive assessment of the timing of sleep and wake behaviour on work and free days. More detailed information on the MCTQ will be provided in projects one and two, as well as in the General Methods.

1.1.7 Internal De-Synchronization

When scheduled to a 20-hour or 28-hour cycle, the sleep-wake cycle becomes uncoupled from the endogenous circadian period (e.g. temperature and melatonin), in that both oscillate at different cycle lengths. As such, sleep times are scheduled at different circadian phases over the course of time. This phenomenon, called *internal de-synchronization*, is purposefully achieved in forced de-synchrony protocols to disentangle circadian and homeostatic effects on daily rhythms (Dijk & Czeisler, 1995; Hiddinga, Beersma, & Van den Hoofdakker, 1997). When desynchronized, the endogenous circadian period of temperature, melatonin, and cortisol run free (averaging 24.18 hours), as seen in isolation experiments. Internal de-synchronization can also occur when faced with a shift in zeitgeber phase, such as when crossing time zones. Circadian adjustment to an abrupt zeitgeber phase shift is rather slow (one hour per day) (Folkard, Minors, & Waterhouse, 1991) so that the phase shifting of the clock lags behind that of the zeitgeber. Also, not all clocks adjust at the same rate, causing a temporary internal de-synchronization between different body clocks (Scheving, 1976). While the SCN adjusts rather rapidly to new time zones (Yamazaki et al., 2000), peripheral oscillators of internal organs take much longer to adjust (Hastings, Reddy, & Maywood, 2003). This can lead to acute symptoms of fatigue and disordered sleep, known as jetlag. Circadian misalignment and internal de-synchronization are also held to underlie the negative health effects of shift work.

1.2 Adverse Effects of Shift Work

The adverse effects of shift work have been lumped together under the generic term *shift lag*, in which the most frequent complaints are disturbances in sleep and fatigue. Shift workers also have a higher risk for psychological distress as their participation in the community is often heavily compromised.

1.2.1 Disturbed Sleep

As much as 60 to 85% of rotating workers report sleep problems (Carskadon & Dement, 1981; Czeisler et al., 1986; Czeisler et al., 1990; Harma, Tenkanen, Sjoblom, Alikoski, & Heinsalmi, 1998). Shift workers commonly experience difficulties in falling asleep as well as in maintaining sleep. Sleep is often interrupted by spontaneous awakenings, or involuntary termination due to an inability to continue sleep or a need to wake-up early for a morning shift (Akerstedt, 1983; Akerstedt, 2003). These disruptions in sleep lead to an overall reduction in the quantity and quality of sleep. Overall, shift workers get significantly less sleep than day workers (Wilkinson, 1992) and rate significantly lower on sleep quality (Fido & Ghali, 2008, Zverrev & Misiri, 2009).

Yet the sleep problems experienced by shift workers vary according to the schedule they work on. Most studies investigating sleep in shift workers have focused on the night shift, where sleep is being postponed to daytime hours. Daytime sleep is significantly shorter than night sleep (Colligan & Tepas, 1986; Foret & Benoit, 1978; Foret, 1972; Khaleque, 1999; Pilcher, Lambert, & Huffcutt, 2000; Pires et al., 2009; Tilley, Wilkinson, Warren, Watson, & Drud, 1982; Torsvall, Akerstedt, Gillander, & Knutsson, 1989) and does not recover over successive night shifts (Foret & Benoit, 1978). By means of electroencephalography (EEG), studies have shown that sleep following a night shift is reduced by two to four hours (sleep times between four and six hours), showing sleep efficiencies below 80% (Akerstedt & Kecklund, 1991; Akerstedt et al., 2007; Burch, Yost, Johnson, & Allen, 2005; Park, Matsumoto, Seo, Cho, & Noh, 2000; Pires et al., 2009;

Tilley et al., 1982; Torsvall et al., 1989; Yoon, Jeong, Kwon, Kang, & Song, 2002). Daytime sleep involves a substantial loss in rapid eye movement (REM) and stage 2 sleep but not in slow wave sleep (SWS). Night workers often also complain about environmental disturbances that interrupt day sleep, such as excessive heat, daylight, or noise due to traffic, telephone calls or family life (Angus, Heslegrave, & Myles, 1985; Colligan & Tepas, 1986; Khaleque, 1999). Caillot (1959) has shown that sleep disturbances significantly worsen with an increase in the number of children in the household and with a decrease in the number of rooms in the home.

While the night shift is generally considered the most problematic shift for sleep (Colligan & Tepas, 1986; Khaleque, 1999), it has been argued that sleep patterns are even more disturbed on the morning shift (Folkard & Barton, 1993). EEG recorded sleep prior to morning shifts also shows a two to four hour reduction in length and just like daytime sleep, involves a reduction in REM and stage 2 sleep (Akerstedt, 1995b; Akerstedt, 2003). Contrary to day sleep, sleep prior to morning shifts also shows a reduction in SWS, whereby the mere expectation of short sleep seems to trigger this (Kecklund, Akerstedt, & Lowden, 1997). In turn, disturbed sleep is believed to be a major reason underlying the excessive sleepiness experienced by many shift workers (Akerstedt, 1998; Akerstedt et al., 2004).

1.2.2 Fatigue

As much as 80 to 90% of shift workers report that they regularly experience sleepiness on the night shift, of which 10 to 20% admit having experienced involuntary sleep during work hours (Akerstedt, 1995a). In two-night shift studies, sleepiness attained alarmingly high levels on the Perceived Sleepiness Questionnaire, covering 40 minutes of *heavy eye-*

lids (fight against sleep) of which 8 minutes attained the highest possible level of sleepiness, -- *difficulties keeping ones eyes open* (Gillberg, Kecklund, & Akerstedt, 1994). Data from the Karolinska Sleepiness Scale has shown that sleepiness increases over the night shift (Akerstedt, 1995b) and accumulates over successive night shifts (Fröberg et al., 1975, Carskadon et al., 1981), requiring two full nights of sleep to recover (Akerstedt et al., 2000). High levels of subjective sleepiness have also been observed during morning shifts (Akerstedt, 1998; Akerstedt & Kecklund, 1991; Akerstedt, Kecklund, & Knutsson, 1991; Kecklund & Akerstedt, 1993; Kecklund, Akerstedt, Lowden, & von Hedenberg, 1994), with increasing levels of sleepiness as the shift advances (Kecklund & Akerstedt, 1995). Simulated shift work studies using EEG and electrooculographic (EOG) measures while awake, have shown a substantial increase in sleepiness at the end of the night as well as in the middle of the afternoon (Kecklund & Akerstedt, 1993; Sallinen et al., 2004). The high subjective sleepiness scores of shift workers have been shown to pertain on free days (Akerstedt, 1995b).

Sleepiness and fatigue have been associated with distortions in perceptual skills, reasoning abilities, judgment and decision-making capabilities, dichotic temporal order judgment, impairments in memory and learning, increased errors, poor vigilance and attention, and reduced reaction times (Babkoff, Zukerman, Fostick, & Ben-Artzi, 2005; Lal & Craig, 2001; Rogers, Hwang, & Scott, 2004; Van Dongen & Dinges, 2003). The relatively few studies that have investigated shift worker performance in the field have found a decrease in the speed (Browne, 1949; Wojtczak-Jaroszowa & Pawlowska-Skyba, 1967) and accuracy (Bjerner & Swensson, 1953) of task performance in the night shift, as well as a deterioration in attention and vigilance (Hildebrandt, Rohmert, & Rutenfranz, 1974; Prokop & Prokop, 1955). A study on 12 rotating shift workers also showed that reaction time was lowest on the night shift for both simple and complex tasks (Tilley et al., 1982). Also, there was evidence of increased deterioration in response to sleep deprivation. The effects of sleep deprivation on performance can exceed levels acceptable for alcohol intoxication (Dawson & Reid, 1997; Fletcher, Roach, Lamond, & Dawson, 2000).

Sleep deprivation, sleepiness, and fatigue are considered major risk factors of work injury and accidents (Berger & Hobbs, 2006; de Pinho et al., 2006; Folkard & Lombardi, 2004; Folkard & Tucker, 2003; Hakkanen & Summala, 2000; Pandi-Perumal et al., 2006; Roth & Ancoli-Israel, 1999), estimated to cost the US 50 billion US Dollars per year (Leger, 1994). Many studies report an increased rate of accidents at night, in the early morning hours during the night shift (Dinges, 1995; Folkard, 1997; Folkard & Akerstedt, 2004; Folkard & Lombardi, 2004; Hamelin, 1987; Hanecke, Tiedemann, Nachreiner, & Grzech-Sukalo, 1998; Harris, 1977; Hertz, 1988; Knauth, 1998; Langlois, Smolensky, Hsi, & Weir, 1985; Ribak et al., 1983; Smith, Folkard, & Poole, 1994; Thyge Corfitsen, 1986; Wojtczak-Jaroszowa & Jarosz, 1987). Many major catastrophes, such as Chernobyl, Three Mile Island, the grounding of the Exxon Valdez, Bhopal, and the Estonia Ferry have happened in the early morning hours. However, some studies have not found an increase in rate of accidents during night shifts (Fischer, 1986; Novak, Smolensky, Fairchild, & Reves, 1990) whereas others report a greater severity rather than occurrence of injuries (Andlauer, 1967; Colquhoun, Costa, & Folkard, 1996; Ong, Phoon, Iskandar, & Chia, 1987).

1.2.3 Psychological Distress

Shift work has been associated with increased depression, anxiety, stress, and neuroticism (Firth-Cozens & Moss, 1998; Gordon, Cleary, Parker, & Czeisler, 1986; Healy, Minors, & Waterhouse, 1993; Kaliterna, Prizmic, & Zganec, 2004; Nachreiner, 1998; Poissonnet & Veron, 2000). A longitudinal study by Healy et al. (1993) compared the mood of 45 nurses before and after three months of night work and found marked changes in perceived criticism from others, sense of purpose and control, and psychosomatic complaints.

Working atypical hours also directly interferes with shift workers' involvement in family life. A study by Tasto and Colligan (1975) found that night workers had the highest schedule inconsistencies with their spouses and also the highest reports of dissatisfaction by spouses. Shift workers often have to work or sleep when the family is gathering for meals or free-time activities and subsequently miss out on crucial aspects of family unity and child-raising issues. Not surprisingly, many shift workers report feelings of social isolation, higher conflicts in the family, and higher divorce rates (Baker, 1980; Khaleque, 1984; Whitehead, Thomas, & Slapper, 1992). The majority of shift workers also report time constraints in social and leisure activities, describing an overall smaller circle of friends and reduced participation in community activities (Baker, 1980).

Compared to day workers, shift workers also have an increased consumption of tobacco, alcohol, and caffeine (Boggild & Knutsson, 1999; Knutsson, 2004). Psychological, social and lifestyle factors in turn are strong contributors to tolerance to shift work (Costa, 2003; Lal & Craig, 2002; Ruggiero, 2003; Samaha, Lal, Samaha, & Wyndham, 2007; Smith et al., 2005; Tamagawa, Lobb, & Booth, 2007), potentially exacerbating the negative health consequences of shift work.

1.2.4 Physical Health Problems

Shift work also is a well-recognized risk factor for physical health problems. The major health problems in shift workers include digestive, cardio-vascular, metabolic, and reproductive problems, as well as an increased risk for cancer.

1.2.4.1 Digestive problems

Many shift workers complain of digestive problems (Aanonsen, 1959; Angersbach et al., 1980; Fido & Ghali, 2008; Knutsson, 2003; Moore-Ede & Richardson, 1985; Rutenfranz, Colquhoun, Knauth, & Ghata, 1977). Common complaints are dyspepsia (nausea, regurgitation, vomiting, heart burn, bloating, and stomach pain), gastric discomfort, and bowel problems (Segawa et al., 1987). Angersbach and colleagues (1980) showed that differences in gastro-intestinal problems between shift- and day-workers were noticable on average after five years of shift work employment. Pubic ulcers are often the source of these complaints (Harrington, 1978; Thiis-Evensen, 1953, 1958). Shift workers that work night shifts have been shown to have a higher incidence of digestive disturbance than shift workers that do not work night shifts (see Costa, 1996), suggesting that the night shift specifically increases the risk for digestive disturbance. When compared to day and shift workers without night shifts, shift workers with night shifts also have a 2-5 time higher incidence of developing pubic ulcers (see Costa, 1996).

Although the majority of studies have found a higher incidence of digestive problems (including pubic ulcers) in shift workers, it is important to note that a number of studies did not find such an effect (see Costa, 1996). Differences in findings have been attributed to inconsistencies in methodology and shift worker samples examined (Costa, 1996) as well as out-dated diagnostic technologies. The increased focus on other medical conditions (notably cardio-vascular problems), have resulted in a complete absence of studies that have investigated digestive disorders in shift workers within the last 20 years.

1.2.4.2 Cardio-vascular problems

A number of studies have shown an association between shift work and increased incidence of cardio-vascular disorders (for a detailed review see Knutsson, 2003; Knutsson & Boggild, 2000). Shift workers have been found to have elevated levels of systolic and diastolic blood pressure, hypertension (Morikawa et al., 1999; Ohira et al., 2000; Oishi et al., 2005; Prunier-Poulmaire, Gadbois, & Volkoff, 1998), and flattened heart rate (Ishii, Dakeishi, Sasaki, Iwata, & Murata, 2005; Ishii, Iwata, Dakeishi, & Murata, 2004). A large Danish study on 1,293,888, male hospital visits revealed that shift workers had a significantly higher hospitalization ratio due to ischemic heart disease than day workers (Tuchsen, 1993). After adjustment of lifestyle factors, blood pressure and serum lipid levels, Tenkanen et al. (1997) also found a higher relative risk for coronary heart disease in shift workers compared to day workers in a prospective cohort study involving 1806 industrial workers in Finland. The risk of having a myocardial infarction between the ages of 45 and 65 is also higher in shift workers than in day workers (Alfredsson, Spetz, & Theorell, 1985; Kawachi et al., 1995; Knutsson, 1995), and shift workers have a higher morbidity ratio due to ischemic heart disease (Alfredsson et al., 1985; Fujino et al., 2006).

A dose response relationship has been found between years of shift work employment and coronary heart disease in a large-scale prospective four year long follow-up study in 79,109 nurses (Kawachi et al., 1995), and a smaller scale 15 year long follow-up study (Knutsson, Akerstedt, Jonsson, & Orth-Gomer, 1986), with the likelihood of developing heart disease increasing to 151% after six years and to 300% after 15 years of shift work. Workers whose schedule involved night shifts have a higher morbidity ratio of myocardial infarction, compared to those whose schedules are free of night shifts (Alfredsson et al., 1985). A study by Fujino et al (2006), however, found that an increased risk of death due to ischemic heart disease only applied to rotating shift workers, finding no association with ischemic heart disease in permanent night workers. This suggests that the rotation between night and day work may play a central role in the link between shift work and cardio-vascular disease.

1.2.4.3 Metabolic problems

There is considerable evidence that shift work is associated with metabolic abnormalities, further exacerbating the risk for coronary heart disease (Fujino et al., 2006; Tenkanen, Sjoblom, Kalimo, Alikoski, & Harma, 1997). In a recent population-based prospective study, De Bacquer and colleagues (2009) investigated the incidence of developing metabolic syndrome in 1529 employees over the course of six years. They found an increased incidence of metabolic syndrome (odds ratio of 1.77) in rotating shift workers compared to day workers, with the risk of developing metabolic syndrome gradually increasing over the six-year study period (De Bacquer, Van Risseghem, Clays, Kittel., Backer, & Braeckman, 2009). A cross–sectional study on 659 shift workers and 665 day workers by Karlsson and colleagues found a significantly higher incidence of lipid disturbances in shift workers-- high triglyceride levels, low levels of HDL-cholesterol-- with symptoms clustering together more often in shift workers than in day workers (Karlsson, Knutsson, Lindahl, & Alfredsson, 2003). Metabolic disturbances appear to be particularly affected by night work. Theorell and Akerstedt (1976) found increased levels of cholesterol, glucose, uric acid and potassium during the first week after a night shift and Nakamura and colleagues (1997) found increased cholesterol levels, only in shift workers with schedules that involved night work.

Some studies have found an increased risk of developing obesity in shift workers, particularly in night workers (Boggild & Knutsson, 1999; Di Lorenzo et al., 2003; Fujino et al., 2006; Niedhammer, Lert, & Marne, 1996; Suwazono et al., 2006; van Amelsvoort, Schouten, Maan, Swenne, & Kok, 2000), whereas other studies could not find such an association (see (Boggild & Knutsson, 1999) or could only find it in certain age groups

(Karlsson, Knutsson, & Lindahl, 2001). Research also suggests that shift workers are at higher risk for developing diabetes, with the prevalence increasing with length of shift work employment (Kawachi et al., 1995; Morikawa et al., 2005; Suwazono et al., 2006). The prevalence of endocrine and metabolic diseases is twice as high in shift workers than in day workers (Koller, Kundi, & Cervinka, 1978; Mikuni, Ohoshi, Hayashi, & Miyamura, 1983), and insulin resistance markers, such as hypertension, hyperglycemia, hypertriglyceridemia, and hypo-HDL-cholesterolemia, are more common in male shift workers below the age of 50 than in day workers (Nagaya, Yoshida, Takahashi, & Kawai, 2002).

1.2.4.4 Reproductive problems

A number of large-scale studies on live births have found a link between maternal shift work employment and irregular menstruation, low birth weight, preterm birth, and miscarriage (Armstrong, Nolin, & McDonald, 1989; Axelsson & Rylander, 1989; Mamelle, Laumon, & Lazar, 1984; Uehata & Sasakawa, 1982; Xu, Ding, Li, & Christiani, 1994). The increased incidence of reproductive complications in shift workers remained when known confounding factors, such as weight lifting, maternal age at pregnancy, order of birth, stress, occupational exposure to dust/gas/fumes, were controlled for (Xu et al., 1994). In a large-scale study in China involving 845 women, the adjusted odd ratio for preterm birth and low birth weight was 2.0 and 2.1 respectively (Xu et al., 1994). In a review paper of epidemiological studies on female reproductive health in shift workers, Nurminen highlights methodological problems such as disagreement between definitions of shift work, concluding "Although the evidence is not ample and remains ambiguous, it is prudent to consider shift work as a potential risk to reproduction" (Nurminen, 1998, p. 33). Similarly, Schlünssen and colleagues question observed associations between shift work and negative pregnancy outcomes in their review of 22 epidemiological studies, although they recognized some overlapping epidemiological evidence that supports a relationship between permanent night work and late abortion and stillbirth (Schlünssen, Viskum, Omland, & Bonde, 2007). Shift work has also been associated with increased reports of sexual problems (Fido & Ghali, 2008; Rutenfranz et al., 1977), in particular permanent night work (Rutenfranz et al., 1977).

1.2.4.5 Cancer

A set of studies have reported an association between night work and an increased risk of breast cancer (Hansen, 2001a, 2001b; Megdal, Kroenke, Laden, Pukkala, & Schernhammer, 2005; Navara & Nelson, 2007; Schernhammer, Kroenke, Laden, & Hankinson, 2006; Schernhammer et al., 2001; Schernhammer & Schulmeister, 2004), with women between the ages of 30 and 54 most susceptible (Hansen, 2001a). The association between breast cancer and night work is observed in a variety of occupational groups, including nurses, flight attendants, and radio operators, and holds when important confounds such as age, social class, and number of children are controlled for. Increased incidences of other types of cancer in shift workers have also been identified, such as endometrial cancer (Viswanathan, Hankinson, & Schernhammer, 2007), colorectal cancer (Schernhammer et al., 2003), and prostate cancer (Kubo et al., 2006). In 2007, the World Health Organization's International Agency for Research on Cancer listed shift work as a probable carcinogen (IARC Press release No. 180). It has been proposed that light at night (LAN) underlies the carcinogenic effects of shift work as a result of melatonin suppression (for a detailed review on this theory, see a review by Navara & Nelson, 2007). Kantermann and Roenneberg have criticized the causal chain of arguments in the LAN-theory, concluding that there is little evidence that LAN specifically increases the risk of cancer (Kantermann & Roenneberg, 2009).

1.3 Why Is Shift Work Problematic?

Shift workers rarely adjust to the demands of working at atypical hours. This is because they are still exposed to daylight on their free time and are thus continually entrained to a diurnal orientation of their endogenous clock.

1.3.1 Circadian Misalignment

When the timing of sleep is displaced, such as in shift work, the normal temporal relationship between the sleep-wake cycle and the endogenous pacemaker is perturbed. As physiology does not align with the inversed sleep-wake schedule, day sleep following a night shift, takes place during the period of maximum alertness, where sleep is difficult to maintain. This misalignment is believed to be the primary cause underlying shift workers' sleep problems. Accordingly, the International Classification of Sleep Disorder (ICSD-2) has identified disordered sleep due to shift work as one of six types of distinct circadian rhythm sleep disorders (CRSD). The essential feature of CRSD is described as "a persistent and recurrent pattern of sleep disturbance due primarily to alterations in the circadian timekeeping system or a misalignment between the endogenous circadian rhythms and the exogenous factors that affect the timing or duration of sleep" (American Academy of Sleep Medicine, 2005).

Studies have shown that the duration and quality of sleep depends on the degree of misalignment between the sleep-wake cycle and the circadian clock, with shorter sleep episodes as a function of decreasing alignment (Akerstedt et al., 2007; Dumont, Benhaberou-Brun, & Paquet, 2001; Hennig, Kieferdorf, Moritz, Huwe, & Netter, 1998; Koller et al., 1994; Quera-Salva et al., 1997; Roden, Koller, Pirich, Vierhapper, & Waldhauser, 1993; Strogatz, Kronauer, & Czeisler, 1986). Experimental displacement of sleep has shown that sleep maintenance becomes increasingly difficult as sleep onset is postponed to early morning hours (Akerstedt & Gillberg, 1981). A shortening in sleep length can also be observed when having to wake-up very early in the morning, such as demanded on morning shifts. In order to get sufficient sleep on morning shifts, workers would have to go to sleep during the wake maintenance zone, where sleep is difficult to initiate. The earlier the need to rise, the more sleep is lost due to the difficulty to initiate sleep early enough in the evening in order to compensate for the need to get-up early (Akerstedt, 2003; Ingre, Kecklund, Akerstedt, Söderström, & Kecklund, 2008; Kecklund et al., 1997).

Such a misalignment does not only impair shift workers' sleep but also their waking state (Dijk et al., 1992; Jewett & Kronauer, 1999). During morning and night shifts, work has to be accomplished at the circadian nadir of alertness --explaining the high sleepiness and fatigue commonly experienced by shift workers. Experiments using scheduled bright light exposure have shown improved subjective fatigue, performance, and mood as a function of circadian alignment (e.g. melatonin, cortisol and temperature) to the sleep-wake cycle (Baehr, Fogg, & Eastman, 1999; Campbell et al., 1995; Czeisler et al., 1990; Eastman, Boulos et al., 1995; Eastman, Hoese, Youngstedt, & Liu, 1995; Eastman, Liu, & Fogg, 1995; Eastman, Stewart, Mahoney, Liu, & Fogg, 1994; Martin & Eastman, 1998).

The night shift also imposes stress on the homeostatic process, as the time lapsed since waking is considerably longer than on evening and morning shifts. The effect of prior time awake is less established in shift work but has been clearly demonstrated in constant routine experiments (Dijk et al., 1992). This particularly applies to the first night shift

(Akerstedt, 2003), where time awake at shift end extends to 20-22 hours in comparison to only nine hours in day workers. The generally reduced sleep obtained prior to night shifts further increases sleepiness, with sleepiness scores accumulating over successive night shifts. A week of 4.5 hours of daily sleep has been shown to yield sleepiness scores comparable to total sleep deprivation (Carskadon & Dement, 1981).

1.3.1.1 Implications to health

A misalignment between the sleep-wake cycle and the endogenous clock causes physiological activation and hormone secretion at atypical times during the sleep-wake cycle, potentially disturbing the proper functioning of various bodily functions. The increased health problems of shift workers could also be a direct consequence of an internal misalignment between different physiological and hormonal rhythms. The digestive complaints of shift workers for example have been explained on the basis of irregular food intake as well as eating at inappropriate circadian times, during which the alimentary tract is not set to digest food properly (Folkard, Minors, & Waterhouse, 1985; Olson, 1984). Also melatonin and cortisol continue to fluctuate in a diurnal fashion, even after a series of consecutive inversed sleep-wake cycles, with cortisol peaking in the early morning hours and melatonin at night (Boivin & James, 2005; James, Walker, & Boivin, 2004; Sack, Blood et al., 1992; Weibel & Brandenberger, 1998). This causes a misalignment in the dose relationship between different hormones as well as a potential alteration in the normal dosage of secretion. Cortisol for example, has been shown to fluctuate with a higher amplitude in night workers than in day workers (James et al., 2004). Reinberg and colleagues found a positive association between the degree of internal de-synchronization between several circadian rhythms (e.g. body temperature, heart rate, hand grip) and disturbed sleep, fatigue at work and negative mood (Reinberg et al., 1984; Reinberg & Ashkenazi, 2008; Reinberg et al., 1988).

Other studies, however, have failed to find this and some even suggest the opposite. A study by Roden and colleagues (1993) for example, found a greater degree of satisfaction in night workers whose circadian rhythms did not align with the inversed sleep-wake cycle but kept fluctuating on a diurnal phase. Similarly, Costa and colleagues found a positive association between digestive problems and degree of phase shifting in night workers (Costa, Lievore, Casaletti, Gaffuri, & Folkard, 1989). As such, the negative effects of circadian adjustment to shift work on health may be a consequence of social jetlag, due to the demands of shifting between work and free days or between the different shifts (e.g. between morning, evening, and night shifts).

This would suggest that circadian adjustment to shift work has opposing effects on health --although being favourable for sleep (while working on night and morning shifts), circadian alignment to displaced sleep often involves large phase shifts, which may potentially negatively affect health. Consequently, some have proposed a compromised entrainment, in which circadian rhythms are only partially entrained to the displaced sleep-wake cycle (Burgess, Sharkey, & Eastman, 2002; Eastman & Martin, 1999; Smith, Fogg, & Eastman, 2009). For partial entrainment to night work, workers are instructed to adopt as late a sleep schedule as possible on their days off, while circadian adjustment to workdays would be produced by means of scheduled bright light exposure. A compromised circadian phase position to night work has been shown to lead to increased mood, fatigue, and performance in permanent night workers (Smith et al., 2009).

1.3.2 Circadian Adjustment to Shift Work

Some degree of circadian adjustment to shift work may occur. Both simulated and field shift work studies have demonstrated that properly scheduled exposure to bright light can phase shift the circadian clock, so as to successfully entrain to a schedule of night work and day sleep (Bjorvatn, Kecklund, & Akerstedt, 1999; Boivin & James, 2002; Burgess et al., 2002; Czeisler et al., 1986; Czeisler et al., 1990; Dawson & Campbell, 1991). Yet, it seems of utmost importance to time the exposure to bright light correctly. The strength of the effect of light and its direction of phase shifting depends on the timing of exposure relative to an individual's phase response curve. Light exposure before the temperature nadir induces a phase delay, whereas exposure after the nadir induces a phase advance (Czeisler & Dijk, 1995; Dijk & Czeisler, 1995). This makes the use of bright light in shift work settings quite complex to apply.

Most problematic, however, are the impracticalities involved in controlling for proper light scheduling outside of the workplace. The light exposure many night workers receive on their way home for example, has been suggested to be a major cause in preventing circadian adjustment to night shift (Czeisler & Dijk, 1995; Eastman et al., 1994). Daylight in the morning during the commute home after the night shift coincides with the phase-advance portion of the light phase response curve, inhibiting circadian rhythms from phase delaying. Wearing dark goggles during the commute home as well as ensuring a darkened environment for sleep, has been shown to improve circadian alignment to night work (Eastman et al., 1994). A continuous entrainment to night work implies that shift workers need to remain on a reversed light-dark cycle on their days off.

Complicating the matter further is the fact that most industries make use of rotating shift schedules. Adjustment to rotating schedules would require a constant re-adjustment to different schedules by means of intermittent, moving patterns of bright light exposure.

Since most industries make use of a combination of different shift schedules, bright light exposure would have to be tuned to the individual needs of each worker --a rather impractical solution to this problem. Moreover, in the face of rapidly rotating work schedules, circadian phase shifting is too slow to allow for proper circadian adjustment. Under optimal bright light conditions, circadian rhythms take three to four days to adjust to an inversed sleep-wake cycle (Czeisler et al., 1990; Dawson & Campbell, 1991; Dawson, Encel, & Lushington, 1995). When the weekend arrives, the obtained adjustment to night work shifts back to its original diurnal orientation. As most industries today, make use of bright light at the workplace, one should expect shift workers' circadian rhythms to be at least partially affected by this.

Also, it remains open for investigation as to whether and if so, to which degree, the sleep-wake cycle itself affects the circadian clock. Animal studies have shown that scheduled timing of activity can affect the period and phase of circadian rhythms, suggesting that shift work too should phase shift the circadian clock in the direction of the displacement of activity. Two studies by Burgess and Eastman have shown phase shifting effects on melatonin rhythms as a result of imposed late bedtimes and early awakenings, respectively (Burgess & Eastman, 2004, 2006). Displacements in sleep schedules could therefore have at least partial phase shifting effects.

The few studies that have investigated circadian adjustment to shift work in the field have fueled considerable debate, as the results are inconsistent and often heavily masked (Folkard, 2008; Harma, Waterhouse, Minors, & Knauth, 1994). In his literature review on the circadian adjustment of melatonin in permanent night workers, Folkard (2008) defined two criteria for a complete adjustment to night work: a.) low or baseline melatonin levels during the night shift and b.) a peak in melatonin secretion two to three hours after onset of day-sleep. Without the use of external interventions (e.g. bright light), a substantial amount of night workers showed melatonin profiles indistinguishable from those of day workers but almost a quarter (21.1%) of night workers showed a substantial adjustment to night work, in that they fulfilled one of both criteria. Only a small minority of night workers (< 3%) showed complete circadian adjustment to night work.

1.3.3 Individual Differences in Circadian Alignment to Shift Work

Age has been suggested to be an important predictor of shift workers' abilities to adjust to night work. Older shift workers show greater circadian misalignment, rhythm disturbances and sleep problems compared to younger shift workers (Brugere, Barrit, Butat, Cosset, & Volkoff, 1997; Harma, 1996; Koller, 1983). There are also known changes in the functioning of the circadian clock with age, including disruptions in the sleep-wake regulation (see Juda, Münch, Wirz-Justice, Merrow, & Roenneberg, 2006 for a detailed review). These changes in circadian rhythms may, at least in part, contribute to the decreased tolerance to shift work with age. Individual differences in sleep flexibility have also been suggested to influence circadian adjustment to shift work. Some people are more flexible while others are more rigid in their ability to sleep at unusual times. People with flexible sleep patterns can better compensate for sleep disruption (Akerstedt & Folkard, 1996; Knauth et al., 1980; Kogi, 1996; Tepas & Carvalhais, 1990) and are more likely to cope with shift work (Costa et al., 1989; Folkard, Iskra-Golec and Pokorski, 1990; Monk, & Lobban, 1979; Monk & Folkard, 1985). A three-year follow-up study by Kaliterna and colleagues (1995) found that rigidity in sleep consistently predicted poor health in shift workers (Kaliterna, Vidacek, Prizmic, & Radosevic-Vidacek, 1995).

Most importantly, individual differences in the adopted phase relationship to a zeitgeber, the chronotype, should play a decisive role in determining the degree of circadian alignment to an enforced sleep-wake schedule. A preference for eveningness is considered to be one of the main predictors for increased tolerance to shift work (Foster & Kreitzman, 2004; Østberg, 1973). By means of the MEQ, studies have shown that people scoring high on eveningness have greater adaptability to changes in the sleep-wake cycle (for a review see Harma, 1993) and show better overall sleep quality (Khaleque, 1999). People scoring high on morningness have rigid sleep behaviour and express difficulties in extending their sleep in the morning after late bedtime (Duffy, Dijk, Hall, & Czeisler, 1999; Duffy, Viswanathan, & Davis, 1999; Vidacek, Kaliterna, Radosevic-Vidacek, & Folkard, 1988), accumulating a considerable sleep deficit during nightshift periods (Folkard & Monk, 1981). All in all, people with a preference for morningness suffer more from shift work (Hildebrandt & Stratmann, 1979) and a relatively high percentage withdraw from shift work due to medical symptoms (Bohle & Tilley, 1989; Costa et al., 1989; Hauke, Kittler, & Moog, 1979). However, the above studies have not taken into account the actual sleep patterns of different chronotypes on the different shifts and free days.

1.4 Overview and Research Aims

Existing information on shift workers' sleep and wake behaviour almost exclusively relies on data from simulated shift work experiments under controlled laboratory settings, where the timing of sleep is generally predefined and itself subject to experimental manipulation. To date, we know very little about the sleep and wake behaviour of shift workers in real life contexts. If circadian alignment to the displaced sleep in shift work favours better tolerance, one should expect chronotype to play a central role in predicting tolerance to working a given schedule. Compared to early types, late types should display less misalignment to the sleep-wake cycle of the night shift, and should subsequently have better daytime sleep, less fatigue, and less internal de-synchronization. Early chronotypes, on the other hand, need less phase advance to align to the morning shift and should have greater difficulties adjusting to the night shift. The aim of this doctoral dissertation is to investigate chronotype-specific differences in shift work tolerance in the field, by means of detailed analyses of the actual timing of sleep and wake behaviour on work and free days.

While the few previous studies examining chronotype in shift workers assessed their findings on the basis of individual preferences for morningness/eveningness (Horne & Østberg, 1976; Torsvall & Akerstedt, 1980), this study employs a more direct measure of self-reported actual timing of sleep and wake behaviour through the calculation of mid-sleep on free days (MSF), as assessed by the Munich Chronotype Questionnaire (MCTQ, Roenneberg et al., 2003). This may be particularly relevant for the assessment of chronotype in shift workers, as we don't know how shift work affects sleep preference.

The MCTQ also has the advantage of distinguishing sleep habits on free days from workdays (Roenneberg et al., 2003), and has revealed important information as to the sleep and activity patterns of more than 82,000 people throughout the world to date. As a marker for circadian phase, MSF represents a non-invasive and much less costly alternative to the assessment of melatonin and temperature. Mid-sleep on free days as assessed by the MCTQ (Roenneberg et al., 2003) has shown to be an excellent predictor of circadian phase – correlating highly with daily sleep logs (Kuehnle, 2006), actimetry (Kantermann, Juda, Merrow, & Roenneberg, 2007), rhythms of cortisol, melatonin and temperature, (Havel, 2010; Martin & Eastman, 2002), and the widely used Morningness-Eveningness Questionnaire (Zavada, Gordijn, Beersma, Daan, & Roenneberg, 2005).

Yet, the current algorithms for computing chronotype may not be suited for a shift work population. The degree to which mid-sleep on free days is being affected by shift work has not yet been examined. Therefore, the primary and main goal of **Project One** revolves around establishing an algorithm for chronotype in shift workers. Main variables from the MCTQ will then be tested for external validity in **Project Two**, in a series of four studies, by means of comparison to daily sleep-logs as well as to behavioural and physiological data from actimetry and temperature recordings, and to the Morningnes-Eveningness Questionnaire (MEQ). The goal of the three final studies in **Project Three** is to test the hypothesis that chronotype predicts tolerance to working on the morning, evening, and night shift and that a greater circadian alignment to a given shift is associated with increased health. This will be followed by an **Overall Discussion** of the results and their theoretical and practical implications. For a detailed description of the participants and the materials used, see **General Methods**.

2 General Methods

2.1 Participants

A total of 1298 (492 women, 798 men, and eight of unknown sex) participants (M_{age} = 39.4, age range: 16-63 years) volunteered to take part in the following studies. All participants were employed, either as shift workers or as day workers, in production or administration in manufacturing plants by Volkswagen (automobile and energy production in Wolfsburg), ArcelorMittal (steel manufacturing plant in Luxembourg), Siemens AG (security switch manufacturing plant in Cham and packaging station in Amberg) and OSRAM GmbH (light bulb manufacturing plants in Eichstätt and Augsburg, and head offices in Munich). Participants from another study on daylight savings time, consisting mostly of students, were included for one analysis. All participants were asked demographic questions (see Materials).

Participants were recruited on the basis of their agreement to participate, during employee meetings or invited talks in the factories and offices. The agreement to participate was rewarded by some factories, in the form of a gift voucher worth between 30 to 100 Euros. In the case of a change in work schedule due to study design interventions (such as an increase in the amount of days of night shift work), workers received a financial reward for any extra hours worked, corresponding to their usual hourly wage. In one of the studies, all factory employees received a financial benefit so as to balance out any financial gain received from participating in the study.

Of these, 791 were rotating shift workers, of which 371 (111 women and 260 men, M_{age} = 39.8, age range: 19-57 years) rotated between the morning, evening, and night shifts (three-shift-model) and 420 (141 women, 275 men and four of unknown sex, M_{age} = 39.6, age range: 18-62 years) rotated only between morning and evening shifts (two-shift-model). The remaining 507 participants were non-rotating workers, of which 45 (39 women, five men and one of unknown sex, M_{age} = 44.3, age range: 34-54 years) worked permanent morning shifts, 37 (35 women and two men, M_{age} = 39.9, age range: 31-53 years) permanent evening shifts, 28 (three women and 24 men, M_{age} = 42.8, age range: 27-62 years) permanent night shifts, and 397 (163 women, 232 men and two of unknown sex, M_{age} = 38.3, age range: 16-63 years) typical day work schedules. Table 2.1. presents the timing of shift begin and end for the morning, evening, and night shifts.

Participants had the option to indicate whether they wanted a personalized evaluation of their chronotype, sleep log, and actimetry data, which was confidentially allocated to the participant in a sealed letter.

Table 2.1. *Timing of Shifts*

Shift	Begin	End
Morning Shift	06:00	14:00
Evening Shift	14:00	22:00
Night Shift	22:00	06:00

2.1.1 Ethical Approval

For each study, the ethical committee at the Department of Psychology, Ludwig-Maximilians-Universität in Munich, gave ethical approval. Participants were provided with an informed consent, stating the nature of the participation and the participants' right to withdraw from the study at any time. All questionnaires were coded to allow for anonymous data analysis.

2.2 Materials

The materials used for the current projects included a set of questionnaires, sleep logs for the assessment of daily sleep patterns, Daqtometer® for the assessment of loco-motor activity, and iButtons® for the assessment of distal and proximal body temperature.

2.2.1 Questionnaires

A set of questionnaires was used for the assessment of sleep demographics and chronotype (MCTQ), morningness-eveningness (MEQ), sleep quality (Sleep Questionnaire), subjective well-being (Basler-Befindlichkeitsskala and WHO-5), stress (Perceived Stress Questionnaire), internal locus of control (Multidimensional Health Locus of Control), and health (Physical Health Questionnaire).

2.2.1.1 Demographic and lifestyle information

Participants were asked to provide information regarding their age, gender, weight, height, marital status, number of children and their age, length of shift work employment, and the time required to commute to and from work. Participants were also asked questions in regards to their work schedule and whether they were a smoker or not.

2.2.1.2 Munich Chronotype Questionnaire (MCTQ)

This questionnaire was developed by Roenneberg, Wirz-Justice, and Merrow in 2003, to assess the epidemiology of the human clock by means of sleep demographics. The MCTQ contains simple questions in regards to the timing of sleep and wake habits, such as the bedtime and awakening, sleep latency, and sleep inertia for work and for free days separately. On the basis of these parameters, more parameters can be computed, such as mid-sleep, sleep duration, social jetlag. See project one for a detailed discussion of the variables involved as well as of the specific algorithms used for computing these.

The initially longer version of the MCTQ addressed questions of circadian heritability by including questions in relation to self-perceived circadian typology (ranging from extremely early to extremely late), as well as perceived typology of parents and siblings. The now much shorter version of the MCTQ excludes questions of heritability and questions that showed to be redundant in the longer version through factor-analysis (Kuehnle 2006). Accessible online (www.thewep.org) since 2005, the MCTQ has received much public attention, revealing important information as to the sleep and wake behaviour of more than 82,000 people throughout the world. Variables from the MCTQ have been tested for reliability and external validity by means of repeated assessment and comparison to six weeks of daily sleep logs (Kuehnle, 2006) and rhythms of actimetry (Kantermann et al., 2007). Mid-sleep on free days, the half-way point between sleep onset and sleep end, has proven to be very a reliable and valid predictor for circadian phase, showing high test-test correlation and a high correlation with average MSF obtained by daily sleep logs, melatonin, and cortisol. A previous study by Martin & Eastman (2002) has also shown a high correlation between MSF and DLMO. MSF also correlates highly with the MEQ (Zavada et al., 2005). The MCTQ exists in several languages (English, German, French, Greek, Dutch, Portuguese, Brazilian, Italian, Spanish, Russian and Indian) as well as in a version for schoolchildren. In the current studies, the German version was used. Also, for this project, a shift work version was developed, the $MCTQ^{Shift}$. See project one for details on the development of the $MCTQ^{Shift}$, and project two for information on validity testing.

2.2.1.3 Morningness-Eveningness Questionnaire (MEQ)

This questionnaire was developed in 1976 by Horne und Østberg to assess individual tendency for morning or evening orientation. The MEQ consists of 19 items assessing individual preferences for morning activity versus evening activity. The questionnaire consists of a mixture of scales, some in the form of a 4-choice response scale and others in the form of a continuous rating scale. A sample item is "at what time would you get up if you were entirely free to plan your day?". For the current project, a German version of the questionnaire was used: the D-MEQ by Griefahn, Kuehnemund, Broede, and Mehnert (2001). Where applicable, scores were reversed, as indicated in the manual. Scores are added to obtain an overall MEQ score, with higher scores indicating increased tendency towards morningness. Scores range from 16 to 86 and can be classified into three general types: evening types (scores of 16-41), neutral types (scores of 42-58), and morning types (scores of 59-86). For the current project, an overall mean score per individual was computed. The MEQ and the D-MEQ have been validated by means of subjective circadian phase and physiological data, such as rhythms of temperature, melatonin, and activity and sleep, assessed in constant routines (Gibertini, Graham, & Cook, 1999; Griefahn, 2002; Griefahn et al., 2001; Horne & Østberg, 1976; Kerkhof, 1985). A large-scale study (n = 5000) by Paine and colleagues found that scores of morningness-eveningness held across ethnicity, gender, and socio-economic background (Paine, Gander, & Travier, 2006). For this project, the internal consistency of the questionnaire was good (Cronbach's $\alpha = .90$).

2.2.1.4 Sleep Questionnaire

Sleep quality was assessed by means of the Sleep Questionnaire from the Standard Shift Work Index (SSI) (Barton et al., 1995). The construction of the 11-item questionnaire was based on the sleep section of the Telecom Quality of Life questionnaire by Wallace (Wallace), with further additions. The Sleep Questionnaire assesses sleep habits and the extent to which sleep is disturbed on the morning, evening, and night shift, as well as free days. A sample question is "How well do you normally sleep?". The current project used a German translation of this questionnaire, translated by Knauth (unpublished). Only the questions relating to sleep disturbances were used (items 2.4. to 2.8.). The five items were asked separately for the three shifts and for free days on a five-point Likert scale, ranging from *almost never* to *almost always*, with a score of five indicating high sleep disturbance. Where applicable, scores were reversed, as indicated in the manual. A mean score of health disturbance was computed for each participant, separately for the morning, evening, and night shift, as well as free days, leading to four independent measures of sleep disturbance. For day workers, the same questions were applied in regards to workdays and free days. An overall mean score of sleep quality was computed by averaging all responses. Internal consistency was high (Cronbach's alpha was .77 for the morning shift; .76 for the evening shift; .86 for the night shift; and .85 for free days).

2.2.1.5 Basler Befindlichkeitsskala

The Basler Befindlichkeitsskala (BBS), by Hobi (1985), is a German 16-item semantic differential scale for the clinical assessment of depressed mood. The scale consists of four subscales: vitality (mental and physical vigour), intra-psychic balance (inner mental balance), social extroversion (ability and willingness to form social contacts), and vigilance (ability to direct one's attention), each containing four pairs of opposing adjectives describing differing mood states. A sample item is "secure/insecure". Respondents choose which word of a pair best describes their current state of mood. Responses are measured on a 7-point scale of bipolar terminal labels with one extreme characterizing highly depressed mood and the other highly positive mood. Where applicable, scores were reversed as indicated in the manual. For the current project, a mean score was computed for each participant. Total scores range from 16 to 112, with low scores representing depressed mood. For the current project, a mean score was computed, ranging from 1 to 7. Internal consistency for the morning shift, evening, and night shift was high (Cronbach's α = .93 for the morning shift, .91 for the evening shift, and .94 for the night shift.

2.2.1.6 WHO- Five Well-Being Index (WHO-Five)

The WHO-Five consists of a 5-point-Likert scale assessing positive psychological well-being within the last two weeks. Responses range from *never* to *always*. A sample item is "… I have felt cheerful and in good spirits". The WHO-Five Index was derived in 1998 from a larger rating scale developed by the Psychiatric Research Unit for a WHO project on quality of life in patients suffering from diabetes (WHO 1990). During the first psychometric evaluation, 10 of the original 28 items were selected due to the homogeneity they had shown across various European countries (Bech, Gudex, & Johansen, 1996).

These 10 items were reduced to five items (WHO-Five), so as to include only positively stated questions, covering positive mood (good spirits, relaxation), vitality (being active and waking up fresh and rested), and general interests (being interested in things) (Bech, 1998; 2001). When directly compared to other major scales of well-being, such as the General Health Questionnaire or the Brief Patient Health Questionnaire, the WHO-5 has been shown to perform best in predicting depression (Henkel, Mergl, & Kohnen, 2003). The scale exists in numerous languages. For the current project, the German version was used. The raw score is calculated by totalling the answers from the five items. The raw score ranges from 0 to 25 with high scores representing best possible quality of life. In the current project, an average score was calculated, ranging from 1 to 5. Internal consistency was good (Cronbach's $\alpha = .86$).

2.2.1.7 Perceived Stress Questionnaire

The Perceived Stress Questionnaire (PSQ) was developed by Levenstein and colleagues in 1993 (Levenstein et al., 1993) to assess individual subjective perception of stress and emotional response to stress in a variety of real-life situations. Respondents rate on a 4-point Likert scale, from *almost never* to *usually*, how often an item applied during the last month. The questionnaire consists of 30 items measuring seven factors: harassment, irritability, lack of joy, fatigue, worries, tension, and overload. In 2005, Fliege and colleagues translated the questionnaire to German and reduced it to 20 items based on exploratory and confirmatory analyses, by selecting those items with the highest corrected item-scale correlation. The remaining items fall into four factors-- three relating to stress reactions (worries, tension, joy), and one to perceptions of environmental stressors (demands). The revised German version of the questionnaire proved robust, demonstrating satisfactory reliability values and construct validity, and achieved results comparable to the original English version (Fliege et al., 2005). The German version of the questionnaire has been validated by means of comparison to questionnaires assessing quality of life (WHOQOL) and chronic stress (TICS), and associations to immunological parameters in women suffering from spontaneous abortion (Fliege et al., 2005). For the current studies, the revised German version of the questionnaire was used. A sample item is “you feel mentally exhausted”. Where applicable, responses were reversed and for each individual, an overall score was computed, as indicated in the manual of the questionnaire. Scores range from 0 to 100, with high scores representing high perception of stress and emotional response to stress. For this study, the internal consistency was acceptable (Cronbach’s α = .57).

2.2.1.8 Multidimensional Health Locus of Control Scale (MHLC)

A 20-item German version of the Multidimensional Health Locus of Control Scale (MHLC) developed by Ferring and Filipp in 1995 (Ferring & Filipp, 1995) was used for this project. The scale is based on the MHLC scale developed by Wallston et al. in 1978 (Wallston, Wallston, & DeVellis, 1978) out of the difficulty in predicting health behaviour from generalized expectations. The scale was first developed as a unidimensional measure to assess the degree to which a person believes that his/her health is controlled by internal or external factors and was later extended to a multidimensional scale by including external chance factors, such fate, luck, or chance. The MHLC scale consists of 20 items on a 6-point Likert scale ranging from *strongly agree* to *strongly disagree* with high scores representing high locus of control. A sample item is “Ich kann selbst einiges dazu tun um wieder gesund zu werden”. For the current project, only the subscale relating to internal factors was used. Where applicable, scores were reversed, as indicated in the manual. An average score was computed for each participant on the basis of items from the subscale internal locus of control. The internal consistency for the subscale was good (Cronbach's $\alpha = .82$).

2.2.1.9 Physical Health Questionnaire

Health was measured with the German version of the Physical Health Questionnaire from the Standard Shift Work Index (Knauth, unpublished). Items were selected from existing health measures from the Inventory of Subjective Health, (Dirken, 1967) General Health Questionnaire (Goldberg, 1972) and the Health Survey (Spence, Helmreich, & Pred, 1987). The questionnaire consists of two subscales (consisting of eight items each), asking subjects to rate the frequency of cardiovascular and gastrointestinal disorders, both known to have a high incidence in shift workers. The frequency of symptoms is asked in relation to the past few weeks. Sample items are " How often do you feel tight in your chest?" and "How often do you feel nauseous?". Responses on both subscales are measured on a four-point Likert scale to avoid a tendency towards a central answer. Answers range from *almost never* to *almost always*. Where applicable, scores were reversed, as indicated in the manual. For the current project, an overall health score was computed, by means of an algorithmic mean of the constituent items from both subscales. The internal consistency of both scales was good (Cronbach's alpha was .86 for the digestive scale and .84 for the cardio-vascular scale).

2.2.2 Sleep Logs

A sleep log was composed to assess daily sleep-wake behaviour over a period of six weeks. Participants were asked to fill out the sleep log on a daily basis-- in the morning, immediately after awakening. The following parameters were assessed: timing of bedtime, minutes required to fall asleep, timing of wake-up, timing of get-up, and whether an alarm clock was used or not (*yes*/*no*). Finally, subjects were asked to indicate whether the day in question was a workday or a free day. In case of a work day, subjects were asked to indicate whether the day in question was a morning, evening, or night shift, by crossing out the relevant shift. From these data, sleep onset (SON), sleep offset (SOFF), sleep latency (SLAT), sleep inertia (SIN), mid-sleep (MSW and MSF), and sleep duration (SD) can be computed for workdays and for free days separately, for the morning, evening, and night shift. For day workers, the same sleep logs were applied, except that only two options -- work and fee days, could be crossed out. The sleep logs used included extra items whose evaluation is not discussed in the current project.

2.2.3 Daqtometer®

For the daily assessment of activity and rest, the Daqtometer® by Daqtix GmbR was applied (see Figure 2.1.). The Daqtometer® is a wrist-worn activity and light monitor device (weight: 21 g, dimensions: 40 mm x 44 mm x 12 mm). Light and activity are measured and stored in the internal memory at freely adjustable intervals. For the current project, one-minute intervals were used. Only the activity data was considered. The device is waterproof and can be worn when showering or engaging in sports. Participants who agreed to wear the device, were also given a Daqtometer® protocol. In case of device removal, participants were asked to take note of the timing and date of removal of the device into the protocol.

Daqtometer® set-up and read-out is realized via a USB-infrared interface communication and the Daqtix software application Daqtocontrol.

Figure 2.1. The Daqtometer® is a wrist worn device to measure activity.

2.2.4 iButtons®

For the assessment of distal and proximal body temperature, iButtons® (type DS1922L) by MAXIM were applied (see Figure 2.2.). iButtons® are small computer chips enclosed in a 16 mm thick stainless steel that measure temperature and record the result in a protected memory section. For the current project, data was stored in 10-minute intervals. The iButtons® are attached to the body with breathable, water-resistant medical body tape, two on the shoulder blades and two on the ankles, on the right and left body side. Four iButtons® were used per participant,. For the current study, the iButtons® were worn for three continuous days. Set-up and read-out is realized via a USB-infrared interface communication and MAXIM software application.

Figure 2.2. iButtons® are small chips, the size of a wrist watch battery to assess distal and proximal body temperature

2.2.5 Software for Data Handling and Computation

All data was first entered into Excel 2004 for Mac, where initial data arrangement and computation took place. Statistical analyses were computed by means of SPSS 17 for Mac. Figures were drawn in Excel 2004 and PowerPoint 2004 for Mac. The computation of centre of gravity was established by means of the ChronoOSX 2.0. (Roenneberg, 2010). Estimation of effect size (*g*) and power (β -1) were computed by means of G*Power for Mac (Faul, Erdfelder, Lang, & Buchner, 2007) for t-tests and by means of SPSS for ANOVA.

2.3 Statistical Computations

All statistical tests were checked for violations of assumptions. The assumption of normality of distribution was tested by means of the Kolmogorov Smirnov Test. In case of violation of normality, the Spearman Rho coefficient was used for the computation of correlations instead of the Pearson-Product Moment Coefficient. In regards to analyses of variance, the *F* test is remarkably robust against deviations from normality (see Lindman, 1974, for a summary). Nonetheless, for reasons of precaution, a non-parametric test was computed wherever possible (e.g. Friedman Test as an alternative to a within-subject design ANOVA), in addition to a parametric one when the assumption of normality was violated. In regards to comparisons between two means, Buehner and Ziegler (2009) advise to use the *t*-test despite violation of normality when the sample size is large, which is the case here. For precautionary reasons, however, a non-parametric Mann Whitney Test was computed in addition to an independent t-test when the assumption of normality was violated.

A decision criterion of α = .0.5 (two-tailed, unless indicated otherwise) was applied for single tests, unless the null hypothesis postulated a significant difference, whereas a more stringent decision criterion of α = .2 was applied to reduce the probability of a type II error. When multiple tests were computed, a Bonferroni correction was made through applying a more stringent α.

3 Project One: From the MCTQ to the $MCTQ^{Shift}$

The aim of this project is to develop and evaluate a shift-work adjusted version of the MCTQ, the $MCTQ^{Shift.}$, Developed by Roenneberg and colleagues in 2003, the MCTQ has revealed important information as to the temporal organization of sleep and wake patterns by more than 82,000 people throughout the world. Obtained data from the MCTQ have made great contributions to the understanding of human sleep and wake behaviour, such as the effects of duration of exposure to light, seasonality, longitude, urbanization, and daylight saving time, as well as to the genetic variation of human sleep and wake behaviour (Allebrandt and Roenneberg, 2008; Allebrandt, Teder-Laving, Akyol, Muller-Myhsok, et al., 2010; Kantermann et al., 2007; Roenneberg et al., 2003; 2004; 2007a; 2007b). Still, the current MCTQ leaves no room for answering questions according to a shifting work schedule, and algorithms for chronotype are based on findings obtained by day workers.

3.1 Key Parameters of the MCTQ for Day Workers

The MCTQ consists of two sets of items, one for workdays (6 items) and one for free days (7 items). See Figure 3.1. for an illustration of the MCTQ as well as its constitutive items. Each set consists of five items asking the specific timing of sleep/wake behaviour (e.g. I go to bed at … o'clock). There is one extra item on free days, consisting of a text field in which participants can leave an open comment in regards to having no possibility to freely choose their sleep times (e.g. because of pets or young children). Some parameters are directly obtained from answers provided on the MCTQ. On the basis of these parameters, further parameters can be computed (see Figure 3.2.).

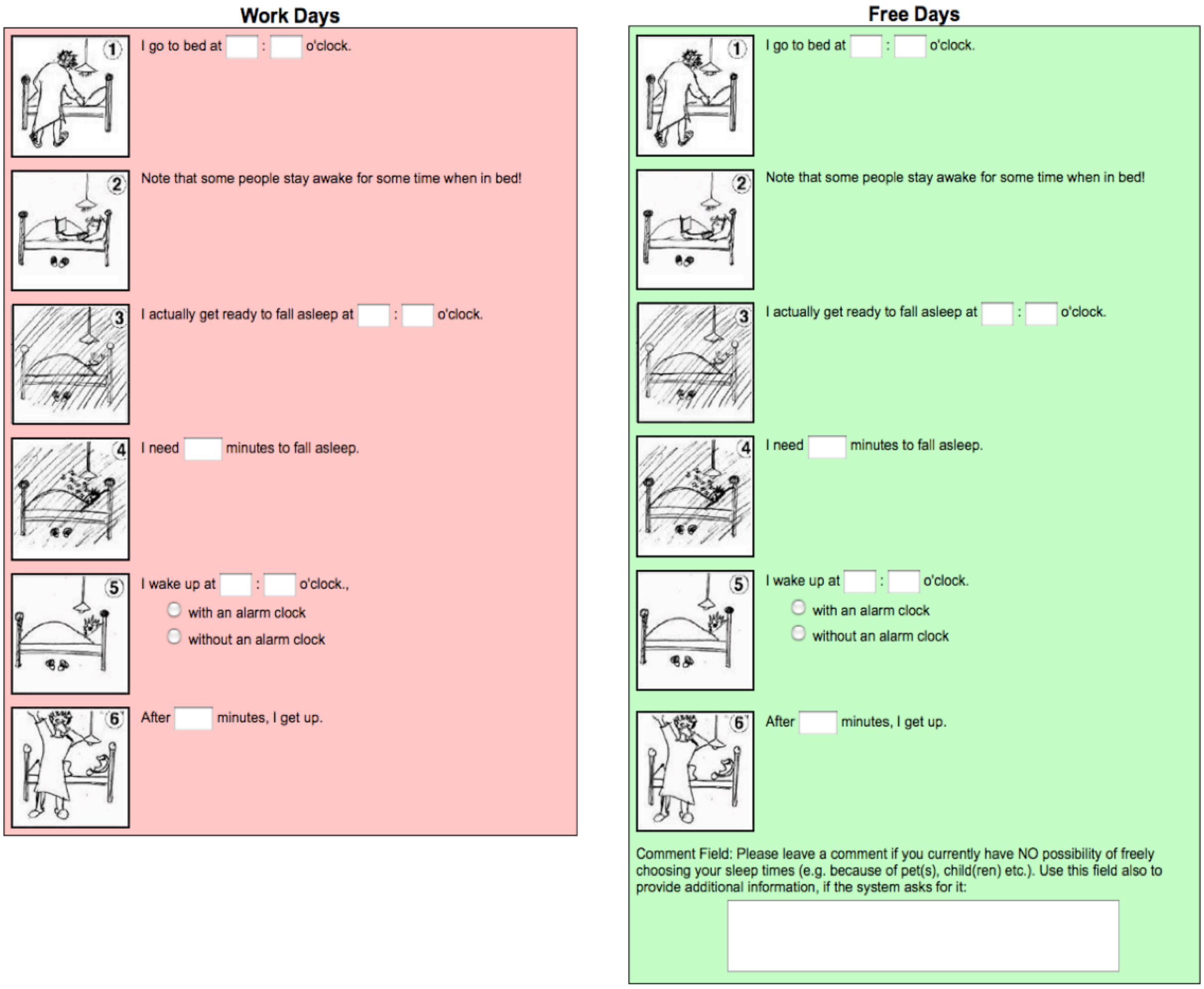

Figure 3.1. Illustration of the online MCTQ for day workers. Questions in regards to sleep behaviour are asked separately for work (red) and for free days (green). *Source*: www.thewep.org

MCTQ Parameters

Obtained Parameters

Item	Variable Name	Derivate	Derivate Work Days/Free Days
3	Bed Time	BT	BT_w / BT_f
4	Sleep Latency	SLAT	SLAT_w / SLAT_f
5	Sleep Offset	SOFF	SOFF_w / SOFF_f
5 (supplement)	Use of Alarm clock	A	A_w / A_f
6	Sleep Inertia	SIN	SIN_w / SIN_f

Computed Parameters

Variable Name	Derivate	Derivate Work Days/ Free Days	Algorithm
Sleep Onset	SON	SON_w / SON_f	BT + SLAT
Sleep Duration	SD	SD_w / SD_f	SOFF - SON
Mid-Sleep	MS	MSW/ MSF	SON + SD/2

Figure 3.2. Some parameters can be directly obtained from individual items of the MCTQ, whereas other parameters need to be computed. Each parameter exists in two forms, once for workdays and once for free days.

The MCTQ's distinction between work and free days has revealed important differences between the two. Table 3.1. shows the mean and standard deviation of the main variables from the MCTQ. Compared to workdays, sleep on free days is shifted to later hours, with an overall greater variability. Where SON_f is delayed by one hour, wake-up (SOFF_f) is delayed by almost two hours, causing an approximate 45-minute increase in sleep duration on free days. The longer sleep duration on free days suggests that many people catch-up on lost sleep accumulated over the workweek (Roenneberg et al., 2003). The reduced variance in the timing of sleep on workdays reflects the influence of external constraints on sleep phase. On average, sleep is longer on free days than on workdays. Average sleep duration (ØSD) is computed by weighting the relative amount of workdays (xw) and free days (xf): ØSD=

(SD_w*xw + SD_f*xf)/(xw+xf). The mean sleep duration for day workers is 7.57 (*SD* = 0.95) hours.

Table 3.1. *MCTQ Parameters in Day Workers*

	Sleep Onset (*M* ± *SD*)	Sleep Offset (*M* ± *SD*)	Sleep Latency (*M* ± *SD*)	Sleep Inertia (*M* ± *SD*)	Mid-Sleep (*M* ± *SD*)	Sleep Duration (*M* ± *SD*)	Alarm %
Work days	-0.31 ± 1.25	6.89 ± 1.22	17.7 ± 16.9	15.8 ± 18.5	3.29 ± 1.12	7.20 ± 1.12	73%
Free days	0.73 ± 1.53	8:94 ± 1.84	14.3 ± 14.4	26.9 ± 33.2	4.83 ± 1.54	8.21 ± 1.42	14%

Note: Mean and standard deviation of main variables from the MCTQ from the large MCTQ databank of entries by 82,686 people.

3.2 Assessment of Chronotype

Inter-individual differences in sleep timing give insight into the human-specific distribution of sleep phase under real life, entrained conditions. For the quantification of chronotype, a single phase marker needs to be assigned, whereby mid-sleep on free days (MSF) has shown to be a stable (high test-re-test reliability) and accurate predictor of chronotype, correlating highly with entries into daily sleep logs, and rhythms of melatonin and cortisol (Kuehnle, 2006; Havel, 2010). MSF has a positively skewed bell-shaped distribution (Roenneberg et al., 2003, 2007a; see Figure 3.4.). As such, few individuals are extreme early or late types, with the majority lying in between these two extremes. Without social obligations, the average chronotype (14.6% of the population when ½ hour bins are used), sleeps between 00:09 und 8:18 o'clock, while 35.02% of the population sleep earlier and 50.38% later, of which 8.2% choose to voluntarily fall asleep as late as 3:00 o'clock or later. The difference in entrained phase between extreme early and late chronotypes can be as much as nine hours.

The timing of mid-sleep on free days is independent of individual sleep need (Roenneberg, 2003, 2007). Yet when work and free days are analyzed separately, one can clearly see a correlation between MSF and sleep duration: the later the MSF, the shorter the sleep duration on workdays and the longer the sleep duration on free days (see Figure 3.3.). The need to rise early for work causes sleep to be prematurely terminated (alarm clock), whereas high circadian alertness in the early evening prevents sleep to be initiated early enough to compensate for the sleep loss. This is held to cause an accumulation of sleep debt over the workweek, which is being compensated for on free days (Roenneberg et al., 2003, 2007). Some extremely late types thereby spend most of their free time recovering from sleep loss.

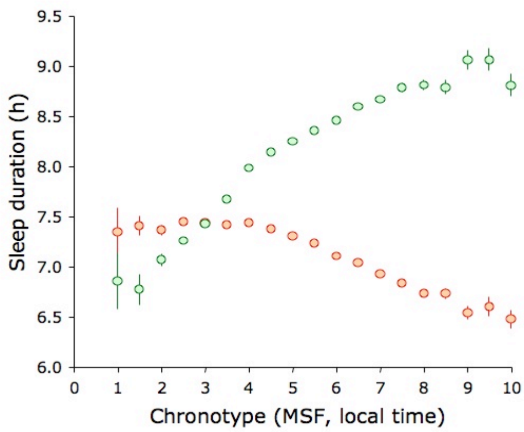

Figure 3.3. While early types accumulate sleep loss on free days, late types do so on workdays, which they compensate for on free days. From the large MCTQ databank (n ≈ 75,000 at the time of analysis). *Source*: Roenneberg and Merrow (2007).

To control for these effects on MSF, a sleep correction has been applied (MSFsc), through which MSF is advanced to earlier times in case of extra sleep on free days due to accumulation of sleep debt over the workweek (Roenneberg et al., 2007). Recently, this algorithm has been modified (MSFscn) by Roenneberg and Juda (see Figure 3.5., unpublished). MSF can further be corrected for intervening influences by age and sex

(MSFsasc) (Roenneberg et al. 2003, 2004). Since the distribution of MSF is positively skewed, most individuals need to be corrected for sleep debt, causing an advance in average MSFsc compared to MSF.

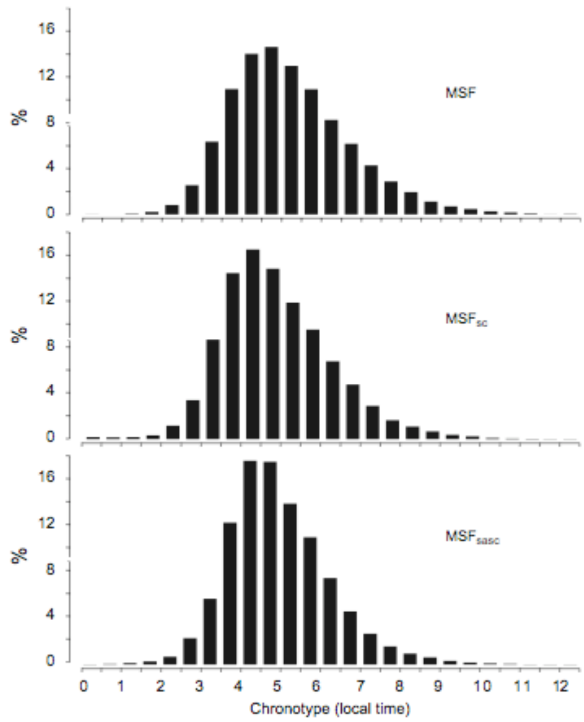

Figure 3.4. Distribution of MSF, MSFsc, and MSFsasc from the large MCTQ databank (*n*=55,000 at the time of publication). The distribution becomes increasingly early and narrow, with increasing corrections made. *Source*: Roenneberg et al., 2007a.

The assessment of chronotype is achieved by means of MSFscn obtained on free days without the use of an alarm clock (A=0). See figure 3.5. for the formula of MSFscn. MSFscn scores (A=0) can be divided into seven chronotype categories: extremely early (≤ 1:59), moderately early (2:00 – 2:59), slightly early (3:00 – 3:59), intermediate (4:00-4:59), slightly late (5:00-5:59), moderately late (6:00-6:59), and extremely late (≥ 7:00). Alternatively, scores can be divided into three chronotype categories: early (≤ 3:59), intermediate (4:00-4:59), and late (≥5:00). Since MSFscn is a continuous variable with arbitrary category limits, we recommend MSFscn to be used as a continuous variable instead of a categorical. Nonetheless, for some statistical analyses, a categorical treatment of MSFscn can sometimes be useful.

New MSF correction for sleep debt MSFscn:

Case 1: SD_f > SD_w -> MSF – ((SD_f – ØSD)/2)

Case 2: SD_f ≤ SD_w -> MSF

Definitions of MCTQ variables:
SD_f = sleep duration free days;
SD_w = sleep duration work days;
SON_f = sleep onset free days;
MSF = mid-sleep free days;
ØSD = average sleep duration

Figure 3.5. To control for sleep debt, MSF was corrected. The initial formula, MSFsc = MSF - (SD_f - ØSD) / 2, was extended to incorporate two clauses to avoid advancing individuals whose sleep was shorter on free days than on workdays.

3.3 Evaluation of the MCTQ^{Shift}

A preliminary shift work-adjusted version of the MCTQ (see Materials below) was the format used to evaluate entries by 371 rotating shift workers. In the first part of this project, main parameters from the MCTQ^{Shift} will be presented and evaluated. Main MCTQ sleep-wake parameters (SON, SOFF, SLAT, SIN, SD, and MS) as well as napping behaviour by rotating shift workers will be presented and compared to the large databank of day workers (n = 82,686). This predominantly descriptive part of the project explores the sensitivity of the MCTQ^{Shift} in capturing circadian effects on the sleep-wake behaviour of shift workers. Circadian influences on shift workers' sleep-wake behaviour should be observable, in terms of inhibitory effects on sleep initiation (on the morning shift) and maintenance (on the night shift), in the face of displaced sleep. Based on other studies (Akerstedt, 1998, Härmä, et al., 1998; Wilkinson, 1992), an overall shortened sleep duration in shift workers is predicted. In order to address specific issues, post-hoc statistical analyses will be computed.

The second aim of this project is to investigate whether current MCTQ algorithms for chronotype can be generalized to a shift work population. The degree to which variables such as MSF are influenced by a previously worked-on schedule, under real life entrained conditions, has not yet been examined. If shift workers do not adjust to changes in work schedule, we would expect the sleep-wake cycle to maintain a diurnal orientation on free days, with MSF remaining constant across the different shifts (morning, evening, and night shifts). On the other hand, if shift workers adjust to working on a given shift, we should expect MSF do be strongly influenced by the previously worked on shift and expect a significant difference between MSF following the morning, evening, and night shift. Observed differences in MSF across shifts provides cues as to the degree of phase shifting due to working on a given schedule. A better understanding of sleep regulation in shift workers will provide a foundation for suggestions as to the required parameters for computing chronotype in shift workers and for necessary sleep corrections. Inter-individual differences in the timing of mid-sleep on free days could, just like in day workers, provide insight into the internal phase of shift workers.

3.4 Methods

3.4.1 Participants

A total of 371 shift workers from the three-shift-model (111 women and 260 men, M_{age} = 39.8, age range: 19-57 years) volunteered to participate in this study. Of these, 176 (107 women and 69 men, M_{age} = 36.4, age range: 19-55 years) worked in normal light conditions and 195 (four women and 191 men, M_{age} = 42.7, age range: 22-57 years) in bright light conditions (Kelvin = 6000). The mean length of shift work employment was 10.2 years. See the General Methods for more information.

3.4.2 Materials

A preliminary shift work-adjusted version of the MCTQ was developed (MCTQ^{Shift}), in which the items from the MCTQ are asked separately for the morning, evening, and night shift, as well as for free days following each of these shifts. An extra question was added to the traditional MCTQ, asking the occurrence and timing of napping (see Figure 3.6.) as napping is held to be an important variant in shift work sleep-wake behaviour (Akerstedt & Torsvall 1985; Knauth et al., 1980, Tepas, 1982, Rosa, 1993). Items in regards to napping were asked for each shift and their respective free days, separately. Also, extra questions were asked in regards to the relative occurrence of morning, evening, and night shifts and their respective free days. See Figure 3.6. for an illustration of the MCTQ^{Shift}. See the Appendix for an overview of the original German version used.

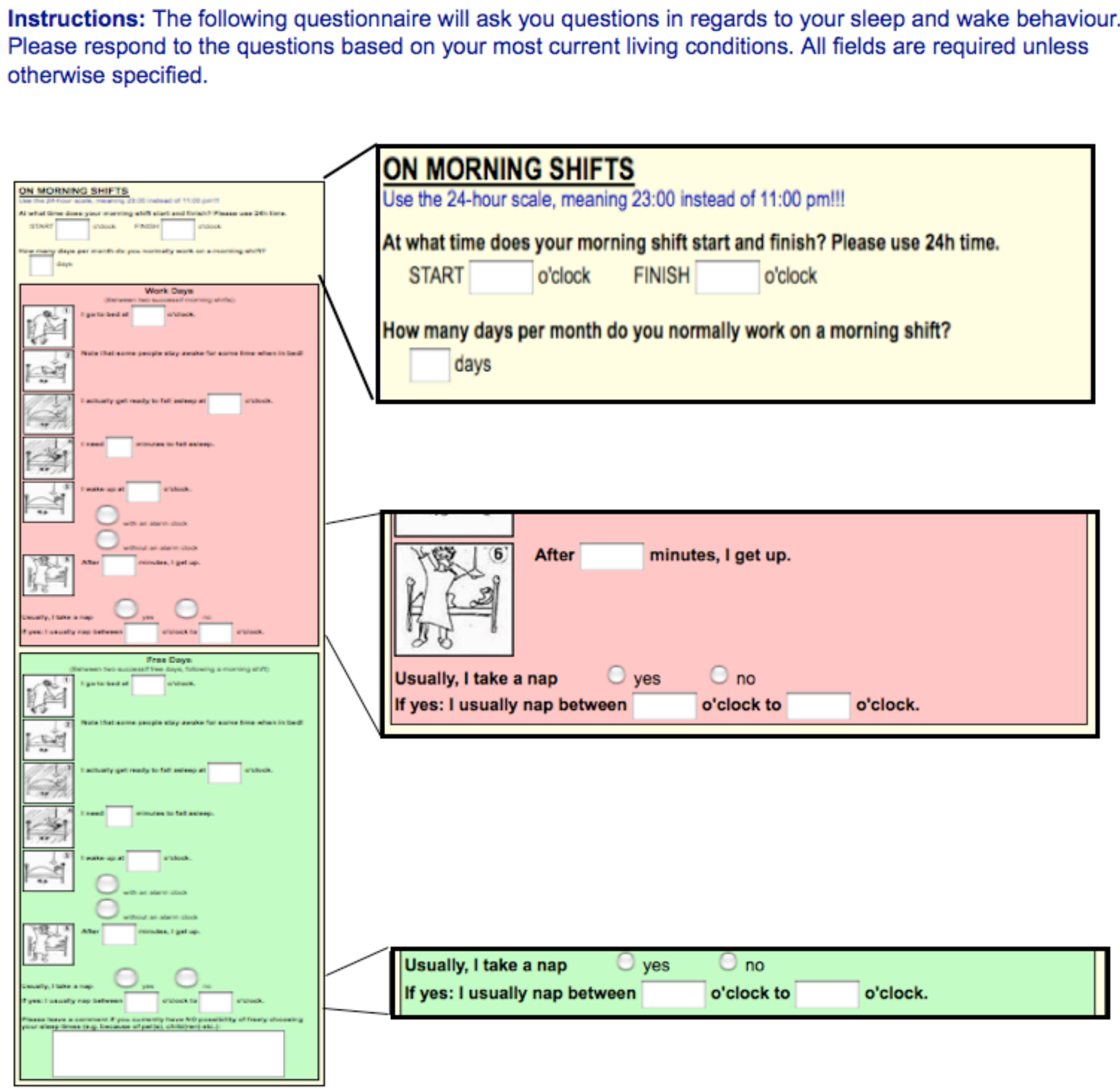

Figure 3.6. Illustration of the MCTQ^{Shift}. For details, see text. *Source*: www.thewep.org.

3.4.3 Procedure

The MCTQ^{Shift} was distributed to the shift workers at their workplace, to be filled out by the participants at their home. The data were collected between March 2006 and October 2008.

3.5 Results

Main variables from the MCTQ^Shift were evaluated and compared to obtained data for the same parameters in day workers (from the large databank, *n* > 82,000)-- first for workdays, and then for free days. This part was purely descriptive, followed by an evaluation of napping and overall sleep duration in shift workers. Finally, possibilities for the assessment of chronotype in shift workers were explored.

3.5.1 Describing the Main MCTQ^Shift Parameters

Main variables from the MCTQ (SON, SOFF, SLAT, SIN, MS, SD, and A) were computed as explained in Figure 3.2. for each shift and their respective free days. Table 3.2. presents the descriptive statistics of the main MCTQ parameters obtained by 371 rotating shift workers.

Table 3.2. *MCTQ^Shift Parameters*

	Sleep Onset (*M* ± *SD*)	Sleep Offset (*M* ± *SD*)	Sleep Latency (*M* ± *SD*)	Sleep Inertia (*M* ± *SD*)	Mid-Sleep (*M* ± *SD*)	Sleep Duration (*M* ± *SD*)	Alarm %
Work Days							
Morning	-1.19 ± 1.15	4.57 ± 0.57	20.2 ± 23.7	06.4 ± 11.3	1.71 ± 0.67	5.77 ± 1.24	86%
Evening	0.89 ± 1.07	8.41 ± 1.33	14.9 ± 17.7	11.7 ± 13.0	4.64 ± 1.01	7.51 ± 1.29	30%
Night	7.55 ± 1.03	13.47 ± 1.53	13.9 ± 19.4	13.8 ± 16.0	10.51 ± 1.03	5.86 ± 1.44	18%
Free Days							
Morning	0.02 ± 1.03	8.13 ± 1.77	15.4 ± 15.6	14.9 ± 23.4	4.07 ± 1.36	8.06 ± 1.56	16%
Evening	0.39 ± 1.48	8.55 ± 1.51	14.5 ± 16.2	11.9 ± 10.9	4.46 ± 1.33	8.13 ± 1.30	18%
Night	1.05 ± 2.46	9.02 ± 2.31	23.1 ± 36.5	13.6 ± 13.4	5.03 ± 2.19	7.92 ± 1.88	18%
n	326	319	330	293	317	314	289

Note: Mean and standard deviation of main parameters from the MCTQ^Shift by 371 rotating workers, grouped separately for the morning, evening, and night shifts, for work and for free days. Use of alarm clock is presented in the form of % of people waking up with an alarm clock. Only individuals with complete data sets (per variable) were considered so that each variable contains the same individuals for all three shifts.

3.5.1.1 Work days

The results showed that sleep on the morning shift is characterized by very early awakening, with little variation compared to free days as well as when compared to day workers. Compared to other shifts, the morning shift showed a high use of alarm clocks (86%), a rather long sleep latency, and relatively short sleep inertia. The almost 4-hour advance in awakening, compared to free days, was matched by an only 1.5-2 hour advance in sleep onset, causing an overall reduction in sleep length by approximately two hours in comparison to free days. Results in regards to sleep on the night shift revealed that sleep is initiated shortly upon return from work, commencing within 1.5 hours after shift end and lasting until the early afternoon. The data showed that sleep is reduced by roughly 2 hours compared to free days, and the majority of shift workers reported not waking-up by means of an alarm clock. Sleep loss on night shifts was comparable to that on morning shifts. Sleep parameters on the evening shift were very similar to those on free days. Compared to free days (on evening shifts), sleep onset on the evening shift was, however, slightly delayed.

3.5.1.2 Free days

Results in regards to free days showed that the sleep-wake cycle maintains a diurnal orientation on free days, with sleep taking place between 0:00 and 9:00 o’clock (see Figure 3.7.A), as observed in day workers. Yet, one could see a 30-minute delay in MSF from the morning to the evening shift and a 60-minute delay from the morning to the night shift. Also, free days following the night shift were characterized by a relatively high variance in SON_f and SOFF_f when compared to other free days, showing great inter-individual differences in sleep phase. Figure 3.7.B shows the frequency distribution of MSF following night shifts. While the majority reported to sleep at night, a small percentage of shift workers reported to maintain an inversed sleep-wake pattern on free days following a night shift. Also, sleep latency was considerably longer on free days following a night shift (note the comparability to sleep latency for workdays on morning shifts).

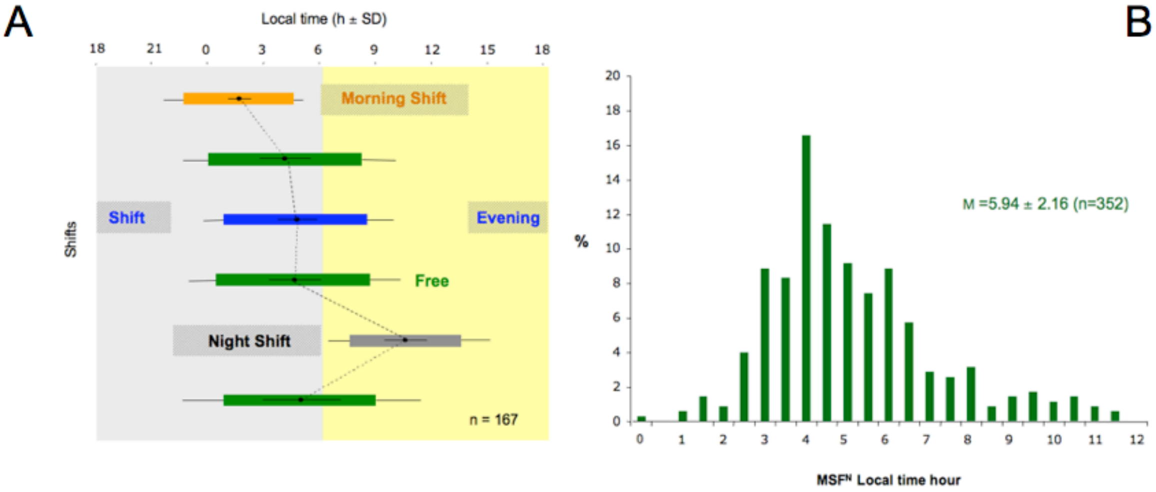

Figure 3.7. A. Progression of sleep phase across the morning, evening, and night shift in 167 rotating shift workers from the manufacturing plant in Cham. Each bar represents the timing of sleep with its corresponding standard deviation. The mid-points reflect the mid-sleep values. The boxes represent the timing of the respective work hours. This graph illustrates the consistency of sleep phase on free days across shift schedules. B. The distribution of MSF^N has a strong positive skew with a double peak, once at 4:00 (as on other free days) and once at 10:00 (as on night shifts).

3.5.1.3 Napping

Napping data was collected from a sub-sample of 132 shift workers (see Table 3.3.). About 1/3 of shift workers reported to regularly nap on morning shifts, and almost 40% reported to regularly nap on night shifts. Both naps lasted an average of 30 minutes. Considerably less shift workers reported to nap on evening shifts and on free days and if they did report to nap, the nap was considerably shorter than on morning and night shifts. Prevalence of napping increased with decreasing length of prior main sleep.

Table 3.3. *Napping in Shift Workers*

Shift	Work Days Napping (%)	Work Days Nap Duration ($M \pm SD$)	Free Days Napping (%)	Free Days Nap Duration ($M \pm SD$)
Morning Shift	31.5%	0.42 ± 0.68	13%	0.13 ± 0.40
Evening Shift	08.0%	0.08 ± 0.37	06%	0.06 ± 0.33
Night Shift	39.5%	0.54 ± 0.86	12%	0.18 ± 0.64

Note: Percentage of rotating workers (n=132) taking naps and mean and standard deviation of duration of naps.

3.5.2 Shift Workers Sleep Less

The results from workdays supported the prediction of reduced sleep duration on morning and night shifts. To see whether this difference was significant inferential statistics were computed. Results from the Kolmogorov-Smirnov test showed a significant deviation for some of the variables involved. As such, a non-parametric test was used in addition to a parametric one. A repeated measure analysis of variance (within-subject design ANOVA) comparing sleep duration in the morning shift (M = 5.77, SD = 1.23), evening shift(M = 7.50, SD = 1.29), night (M = 5.87, SD = 1.44), and free days was computed, whereby only free days following the evening shift were considered (M = 8.13, SD = 1.31). Results showed a significant effect of shift on sleep duration: F (2.63, 848.32) = 372.53, $p \leq .05$, g = 0.54, 1-β = 1 (Huyn-Feldt was used to due violation of sphericity). Results from post-hoc pair-wise comparison showed that sleep duration on free days was significantly longer than sleep duration on the morning and the night shift, as well as on the evening shift. Sleep duration on the evening shift in turn was significantly longer than sleep duration on both morning and night shifts. The latter two did not differ. Results from the Friedman Test confirmed the above findings: χ^2 (3, n = 323) = 559.52, $p \leq .05$, g = 0.54, 1-β = 1.

To investigate differences in average sleep duration between shift workers and day workers, average sleep duration ØSD was computed by means of a weighted average of sleep duration on the morning (SD^M_w), evening (SD^E_w) and night (SD^N_w) shifts as well as on the respective free days (SD^M_f; SD^E_f; SD^N_f). On average, shift workers get a mean of 6.88 hours (SD = 0.94) of sleep, compared to a mean of 7.51 hours (SD = 0.98) in day workers (38 minute difference). On morning shifts, shift workers reported to wake-up on average 2.5 hours before day workers, yet they reported falling asleep only about 45 minutes earlier (note also the similarity in sleep latency), causing an overall reduction in sleep length on morning shifts. A similar reduction in sleep length could be observed on night shifts. When duration of napping was included, ØSD in shift workers increased to a mean of 7.24 hours (SD = 0.96)-- 16 minutes less than ØSD in day workers. To see whether this difference was significant, an independent *t*-test was computed. All assumptions for the independent *t*-test were met (Kolmogorov Smirnov for normality testing and Levene Test for testing homogeneity of variances). Results showed that even when napping in shift workers was considered, the two groups significantly differed in mean ØSD: t (82685) = 3.29, $p \leq .05$, $g = 0.27$, $1\text{-}\beta = .93$.

3.5.3 Assessing Phase of Entrainment in Shift Workers

Overall, the above results showed that sleep on free days maintains a diurnal orientation, suggesting that assessment of chronotype by means of MSF can be generalized to a shift work population. Nevertheless, a small effect of shift schedule on the timing of sleep on free days was observed. In order to investigate this closer, only MSF values from subjects reporting to wake-up without the use of an alarm clock on all free days were considered (n= 175). This constitutes a sample that is less biased by external constraints and therefore a better reflection of the natural sleep cycle of shift workers. After exclusion of those subjects waking-up to an alarm clock, average MSF became delayed by 5-10 minutes. In day workers, removal of alarm clock users did not cause a change in average MSF.

In order to test whether MSF differed significantly between the three shifts, inferential statistics were computed. For all three MSF distributions (MSF^M; MSF^E; and MSF^N), results from the Kolmogorov-Smirnov test showed a significant deviation from normality,. As such, a non-parametric test was computed in addition to a parametric one. A within-subject design ANOVA comparing MSF^M ($M = 4.14$, $SD = 1.38$), MSF^E ($M = 4.57$, $SD = 1.41$) and MSF^N ($M = 4.94$, $SD = 2.13$) showed a significant difference between MSF in the three shifts: F (1.42, 245.68) = 28.94, $p \leq .05$, $g = .14$, $1-\beta = 1$. Post-hoc comparison showed that all three MSF differed significantly from each other. The Friedman test also revealed a significant difference in MSF across the three shifts: χ^2 (2, n = 175) = 70.53, $p \leq .05$.

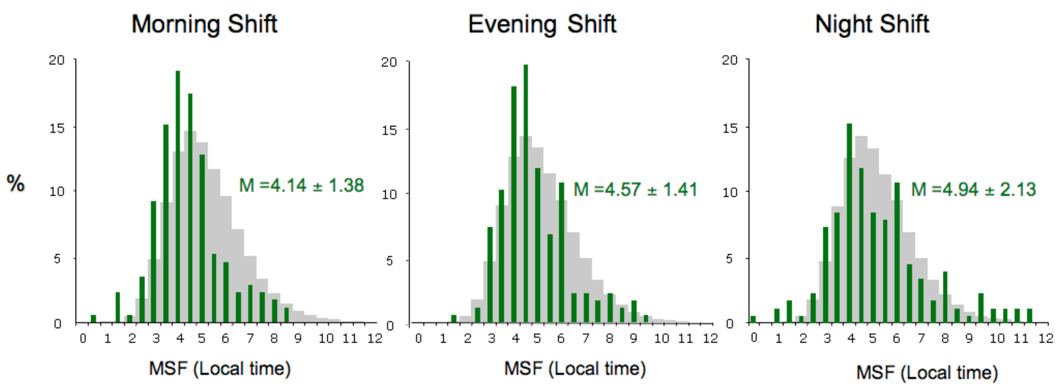

Figure 3.8. Distribution with mean and standard deviation of MSF (without alarm clock) on free days following the morning, evening, and night shifts in 175 rotating shift workers, plotted against the distribution of MSF (without alarm clock) in 70, 058 day workers (grey; M =4.88, SD = 1.51). Individuals with a missing MSF variable were excluded so that all three distributions contain the same n.

The observed shift in MSF could have been a consequence of exposure to bright light at the work place, as some of the manufacturing plants in this study made use of brighter lights (K

= 6000). To investigate this, the same analysis was computed on a selected sample of 103 shift workers known to work under normal light conditions. The results from a within–subject design ANOVA comparing MSF^M (M = 4.34, SD = 1.49), MSF^E (M = 4.83, SD = 1.50) and MSF^N (M = 5.34, SD = 2.30) showed a significant change in MSF across the shift schedules in this sample: F (1.38, 140.98) = 21.94, $p \le .05$, g = .18, 1-β = 1. The Friedman test replicated this finding: χ^2 (2, n = 103) = 49.90, $p \le .05$.

Figure 3.9. reveals the correlations between mid-sleep on workdays and free days for the morning, evening, and night shifts in 169 shift workers reporting to wake up without the use of an alarm clock. Mid-sleep on workdays significantly correlated with free days for all shifts. The correlation between work and free days was highest for the evening shift. Results from the Kolmogorov test showed a significant deviation from normality. As such Spearman Rho correlations were computed.

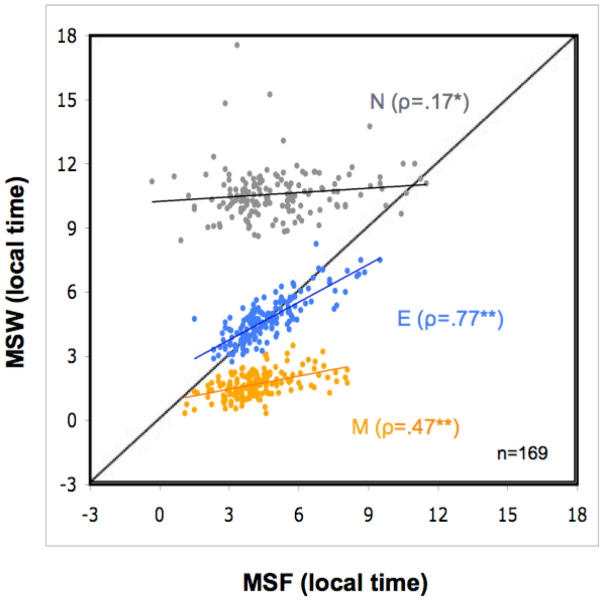

Figure 3.9. The correlations between mid-sleep on work and free days for the morning shift (M), evening shift (E) and night shift (N) in 169 rotating shift workers. The evening shift shows the greatest similarity between work and free days. The values represent Spearman's Rho coefficients. *$p \le .05$; **$p \le .01$.

3.5.4 MSF^{E} Is the Best Choice for Assessing Chronotype in Shift Workers

Although small in its effect, mid-sleep on free days did significantly differ between the three shifts. As the timing of sleep on evening shifts was very similar to that on free days (see Figure 3.9.), mid-sleep on free days following the evening shift (MSF^{E}) represents the best-suited parameter for the quantification of chronotype in rotating shift workers, as it should, if at all, be only minimally affected by the sleep-wake behaviour on evening shifts. The slight delay in sleep onset and the slight reduction in sleep duration on evening shifts, compared to free days, suggest that some shift workers do recover from sleep debt on free days following evening shifts. MSF^{E} should therefore be corrected for sleep debt, in order to control for inter-individual differences in sleep recovery on free days.

MSFscn (sleep corrected mid-sleep on free days) for shift workers was computed as indicated in Figure 3.5., in the same way as for day workers but by means of obtained parameters from the evening shift (MSF^{E}; SD^{E}_w; SD^{E}_f; ØSD^{E}). After exclusion of those subjects waking-up to an alarm clock on free days following an evening shift, MSF^{E} values from 238 rotating shift workers remained. The sleep correction resulted in a mean MSF^{E}scn of 4.23 (SD = 1.47), corresponding to a 20 minute advance compared to MSF^{E} (see Figure 3.10. A). The distribution of MSF^{E}scn is very similar to the distribution of MSFscn in day workers (M = 4.45, SD = 1.40, see Figure 3.10. A.). To test the hypothesis that shift workers do not differ from day workers, an independent t-test was computed, whereby a more stringent decision criterion was set, $\alpha = 0.2$. Results from the Kolmogorov-Smirnov showed a violation of normality in MSF^{E}scn. Results from the t-test showed a significant difference between MSFscn in shift and day workers: t (70294) = 2.51, $p \leq .2$, $g = -.11$, $1-\beta = .80$. Results from the Mann-Whitney test confirmed these results: $z = -2.17$, $p \leq .2$, $g = -.11$, $1 - \beta = .80$.

To explore the possibility that the MSF differences between shift workers and day workers were due to a systematic difference in the local time of sunrise-- the longitude of the study sites (Roenneberg et al., 2007)-- the largest shift work sample was examined for further analysis. This was a sample of 106 shift workers from Cham (12.66 degrees of longitude), with an average MSF^{E}scn of 4.18, (*SD* = 1.57). MSF^{E}scn values of this sample were then transformed to match the average degree of longitude of the large MCTQ database of 82,000 day workers, being 9.18 degrees of longitude (see Figure 3.10. C and D). This transformation was achieved by adding 13.92 minutes to each MSF^{E}scn score. After matching the two samples, the shift worker distribution delayed to an average MSF^{E}scn of 4.41 (*SD* = 1.57). Results from the independent *t*-test showed no difference in MSFscn between shift and day workers: t (105.35) = - .11, p >.2, g = .03, 1-β = .30. Results from the Whitney Mann test confirmed these results: z = - .20, p >.2, g = .03, 1-β = .30. As such, when corrected for sleep debt, the sleep phase of shift workers on free days following the evening shift is comparable to the sleep phase of day workers on free days. Individual differences in MSF^{E}scn can therefore be applied for the assessment of chronotype in rotating shift workers.

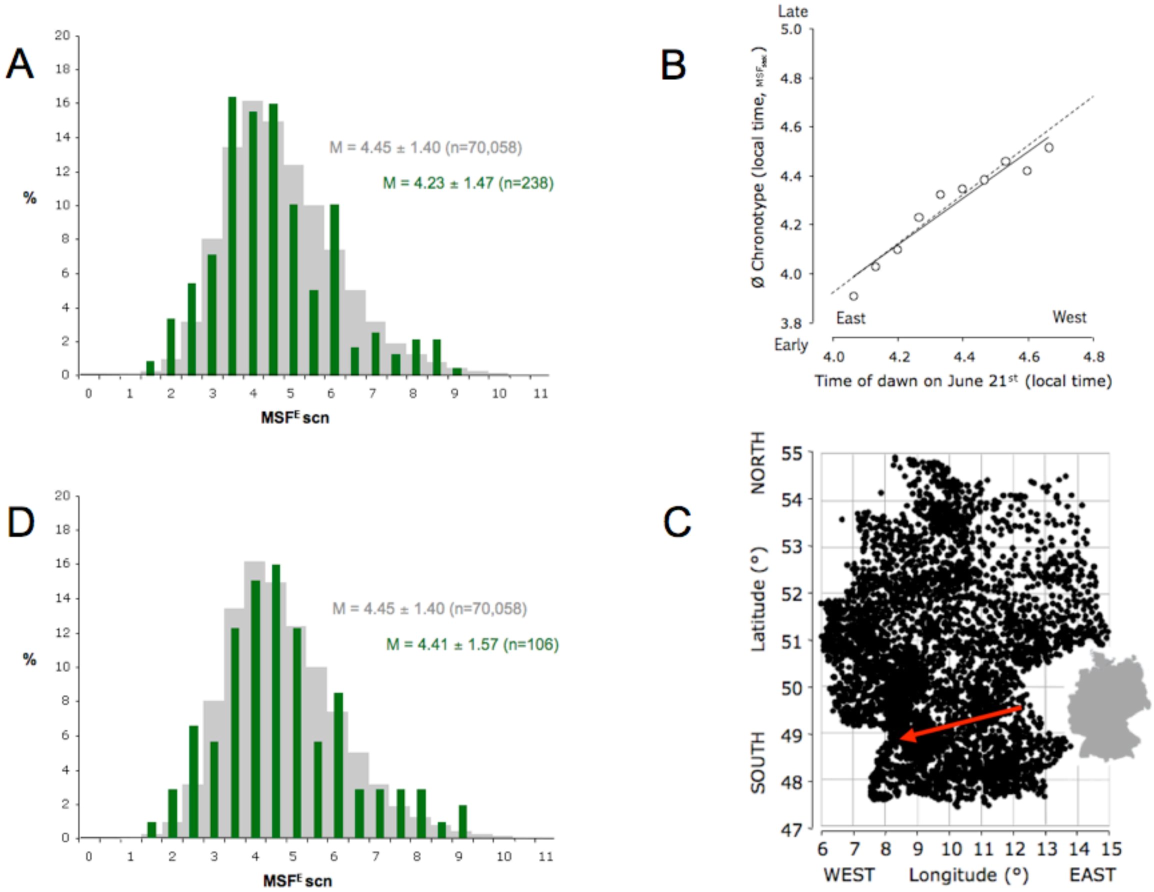

Figure 3.10. A. Frequency distribution of MSF^{E}scn in 238 rotating shift workers (green), plotted against the distribution of MSFscn in 70,058 day workers (grey). B. MSF scores are highly associated to the degree of longitude in people living in areas up to 300,000 inhabitants in Germany. C. In order to match the shift work population from Cham (12.66 degrees of longitude) to the large MCTQ databank of >82,000 day workers, MSF^{E}scn scores were transformed so as to match the average degrees of longitude in day workers (9.18 degrees of longitude). D. After standardizing the degree of longitude, the distribution of MSF^{E}scn is indistinguishable from that of MSFscn in the day worker population (for a statistical analysis, see text). *Source for panel B*: Roenneberg et al. 2007. *Source for panel C*: Kantermann et al. 2007.

3.5.4.1 What about shift workers without evening shifts?

For the assessment of chronotype in shift workers without evening shifts, different algorithms will need to be applied. Based on the data obtained by rotating shift workers from the three-shift-model, expected MSF^{E}scn values can be deduced for shift workers without evening shifts. Figure 3.11. presents the correlations between MSF^{E}scn and MSF following the morning shift (MSF^M), and between MSF^{E}scn and MSF following the night shift (MSF^N) in shift workers from the three-shift-model that reported waking-up without the use of an alarm clock on all free days. For the latter correlation, standardized residuals greater than 3 were removed to exclude values from the second peak obtained by individuals with an inversed sleep cycle. A total of 169 shift workers remained, on the basis of which equations of a straight line were computed by means of the obtained slope and intercept. MSF^M and MSF^N can be corrected to a perfect fit with MSF^Escn by dividing MSF through the respective slope and intercept (see Figure 3.11.). The observed values of the slope and intercept can then be applied for the computation of expected MSF^Escn values in shift workers who do not work evening shifts (e.g. permanent morning and night workers). In the case of a shift rotation between the morning and the night shift, MSF^M appears to be a better choice, as free days appear to be less influenced by morning shifts than night shifts (see Figure 3.7. B). Expected MSF^Escn values can be obtained by means of the following equations:

For Permanent Morning Workers: MSF^M/ (0.7741- 0.6032)

For Permanent Night Workers: MSF^N/ (1.0565 – 0.2984)

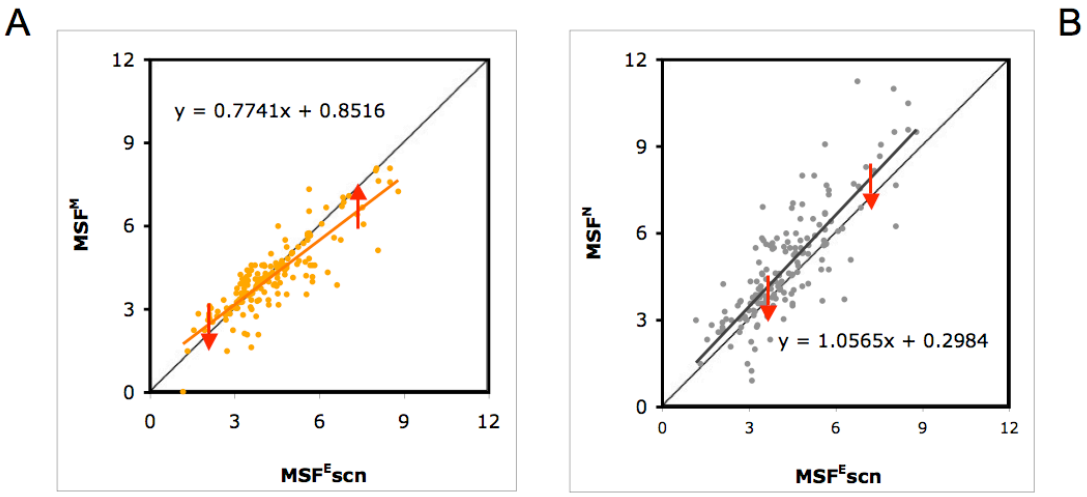

Figure 3.11. Correlations between MSF^Escn and A. MSF following the morning shift (MSF^M) and B. MSF following the night shift (MSF^N) in 169 rotating shift workers from the three-shift-model, with “best fit” straight line, governed by the equation (y=mx+b), containing the slope (m) and intercept (b) of the association between variables. MSF^M and MSF^N are adjusted to a perfect fit with MSFscn, by means of the method of least square MSF^M / m-b for the morning shift and MSF^N /m-b for the night shift.

3.6 Discussion

The MCTQ^{Shift} provides detailed information as to the sleep and wake behaviour of shift workers on the morning, evening, and night shifts as well as possibilities for assessing chronotype in shift workers.

3.6.1 MCTQ^{Shift} Assessment of Sleep-Wake Behaviour

The current data support findings by Akerstedt (2003), showing a displacement and reduction in sleep on morning and night shifts and a slight delay in the timing of sleep on evening shifts. The morning shift is characterized by early awakening with very little variation, revealing high external constraints on sleep behaviour on morning shifts. This is also reflected in the high use of alarm clocks on the morning shift (85%), implying that early awakening is very difficult to initiate. The reduced sleep on the morning shift suggests that sleep is difficult to initiate early enough, to compensate for sleep loss. Accordingly, sleep latency on morning shifts is rather long, suggesting a low drive for sleep at the time of seep initiation. In order to get eight hours of sleep on the morning shift, workers would need to go to sleep at 20:00, a timing that coincides with the wake maintenance zone in day workers (where sleep is difficult to take place). Compared to the evening and night shifts, sleep inertia on morning shifts is also relatively short, possibly resulting from a desire to set the alarm clock for as late as possible to allow for longer sleep.

The two-hour reduction in sleep on the night shift compared to free days, suggests that the delay in sleep is prematurely terminated. The majority of shift workers do not wake-up by means of an alarm clock on night shifts, suggesting that the short sleep on night shifts is spontaneously terminated. The timing of sleep on the evening shift is very similar to that on free days and confirms previous findings by Akerstedt (2003), reporting bedtimes between 23:00-1:00 o'clock and wake times around 8:00 o'clock. Since work only begins at 14:00 o'clock, shift workers can sleep in and fulfil their need for sleep. Accordingly, less than one third of shift workers make use of an alarm clock on evening shifts and sleep inertia is comparable to free days. Sleep duration extends to 7.5 hours on evening shifts, indicating little constraints on sleep. Yet, compared to free days (on evening shifts), sleep onset is slightly delayed, suggesting that the late return from work causes some shift workers to postpone their circadian drive for sleep. This may explain the half-an-hour reduction in sleep length on evening shifts, compared to free days.

Despite immense displacements in the timing of sleep on morning and night shifts, the sleep-wake cycle always returns to a diurnal orientation on free days. Just like in day workers, sleep on free days takes place between 0:00 and 9:00 o'clock and remains stable across the three shifts. Few people wake-up with an alarm clock on free days, reinforcing the notion that the diurnal orientation of sleep takes place without the need for external intervention. This supports the view that shift workers do not adjust to shift work. Sleep inertia, sleep duration, and use of alarm clock on free days are quite similar across the three shifts.

Nonetheless, previously worked on shifts do leave some traces on the sleep-wake behaviour on free days. One can see a 30-60 minute delay in MSF across the three shifts, as a function of the direction of the displaced sleep-wake behaviour on the previously worked shift. This supports the notion of circadian adjustment to displaced sleep by shift work. Also, sleep latency is relatively high on free days following night work, suggesting inhibitory effects on nighttime sleep by night work. Note that there is a relatively large variance in most variables on free days following the night shift, indicating high inter-individual differences in the degree to which the night shift effects sleep on free days. It is unlikely that the observed change in MSF results from an entrainment to light in the workplace as shift workers working under normal light show the same effect. An alternative explanation may be that the sleep-wake cycle itself entrains the circadian clock.

In agreement to previous findings (Akerstedt & Torsvall, 1985; 1991; Härma et al., 1989; Knauth et al., 1980; Rosa, 1993; Tepas, 1982), napping is common in shift workers. Supporting findings by other studies (Akerstedt et al., 1985; Rosa, 1993), the prevalence of napping is directly related to the length of prior main sleep, suggesting that shift workers attempt to compensate for sleep loss through napping. The frequency of napping is twice as high on free days following morning and night shifts than on free days following evening shifts, suggesting that sleep is not only caught up on workdays but also on subsequent free days. Yet, even when napping is being considered, shift workers still do get significantly less sleep than day workers. This finding agrees with previous findings reporting shortened sleep in shift workers (Akerstedt, 1998, Härmä, et al., 1998; Wilkinson, 1992).

3.6.2 How to Assess Chronotype in Shift Workers

As the sleep-wake cycle maintains a diurnal orientation on free days, assessment of chronotype by means of inter-individual differences in MSF can be generalized to a shift work population. When corrected for sleep debt, MSF following an evening shift ($MSF^{E}scn$) is the best choice for assessing chronotype in shift workers. For shift workers that do not work evening shifts, expected $MSF^{E}scn$ can be computed on the basis of MSF values obtained by shift workers that work all three shifts. In the case of a work schedule that shifts between the morning and the night, MSF^{M} is the preferred choice, as MSF^{N} is less reliable due to high inter-individual differences. For the sole purpose of assessing chronotype there is no need to use the full-length questionnaire, as the relevant subsection (e.g. evening shift) should suffice. Yet data from both work and free days is necessary for a sleep correction of MSF. As the distribution of $MSF^{E}scn$ in shift workers is comparable to that of MSFsc in day workers, shift workers can be allocated into chronotype categories, according to the same rules as day workers.

3.6.3 Evaluation of the MCTQ^{Shift}

All in all, the MCTQ^{Shift} proves to be well-suited for the assessment of sleep demographics and chronotype in shift workers. By expanding its questions to shift work schedules, the current questionnaire provides detailed information as to the sleep-and-wake behaviour of shift workers on the morning, evening and night shifts, as well as on their respective free days. Data in regards to workdays match previous findings from a variety of studies, while data from free days reveal novel insights into the timing of sleep outside of the work context. The questionnaire has shown to be sensitive to even small effects, such as effects of the previously worked-on shift on the timing of sleep on free days. The extra items on napping are an important contribution to the MCTQ^{Shift}, playing an essential role in evaluating shift work sleep regulation, as many shift workers catch-up on lost sleep through napping.

4 Project Two: Validating the MCTQ^{Shift}

The MCTQ for day workers has been validated for construct validity by means of comparison to daily sleep logs, to physiological data such as daily rhythms of activity, melatonin, and cortisol, as well as to scores from the Morningness-Eveningness Questionnaire (MEQ) by Horne and Østberg.

4.1 Setting the Framework for the Validation Studies

Comparison to daily sleep logs was done in the realm of a doctoral dissertation by Kuehnle (2006), who compared sleep onset and sleep offset (work and free days) obtained from the MCTQ to averages of the same variables obtained by six week-long sleep logs in 672 day workers. Main MCTQ parameters accurately predicted day workers' actual sleep behaviour as assessed by sleep logs (see Table 4.1.).

Table 4.1. *Correlation Coefficients between MCTQ and Sleep Logs in Day Workers*

	r	*n*
SON_w	0.88	590
SOFF_w	0.80	591
SON_w	0.88	625
SON_f	0.87	625

Note: Pearson Product Moment Correlation Coefficients between main parameters from the MCTQ and averages of the same parameters by six week-long sleep logs in day workers. All correlations were significant at $p \leq .0001$. *Source*: Kuehnle (2006).

The MCTQ assessed mid-sleep on free days has been shown to represent a good predictor for internal phase in day workers. A comparison between MCTQ-derived MSFsc (sleep corrected MSF) and average MSF from sleep logs resulted in a high Pearson Product-Moment correlation coefficient: r (625) = 0.91; $p \leq .0001$ (see Figure 4.1.) (Kuehnle, 2006). In day workers, MSF also correlates well with phase of actimetry from daily wrist activity rhythms (CoAct) when averaged across eight weeks: r (50) = 0.56, $p \leq .0001$ (Kantermann et al., 2007).

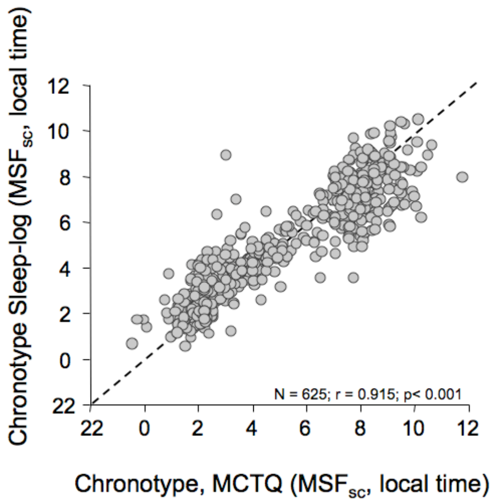

Figure 4.1. Correlation between MSFsc from the MCTQ and average MSF from six week-long sleep logs in 672 day workers. As subjects were retrieved for another study, with the aim of genetic analyses, the sample mostly consisted of extreme chronotypes. *Source*: Kuehnle (2006).

Finally, a study by Zavada, Gordijn, Beersma, Daan, and Roenneberg (2005) has shown that the MCTQ correlates well with the widely used MEQ. Results from 2481 respondents showed that MCTQ-assessed sleep onset, sleep offset, and mid-sleep correlate well with the MEQ score for workdays and even more so for free days (see Table 4.2.). Compared to other MCTQ parameters, MSF showed the highest correlation to the MEQ score (Zavada et al., 2005).

Table 4.2. *Correlation Coefficients between MCTQ and MEQ in Day Workers*

Work Days					Free Days			
Sleep Onset	Mid-sleep	Sleep Offset	Sleep Duration		Sleep Onset	Mid-sleep	Sleep Onset	Sleep Duration
- 0.59	-0.61	-0.48	0.11		-0.64	-0.73	-0.66	-0.16

Note: Pearson Product Moment Correlation Coefficients between main parameters from the MCTQ and the MEQ in 2481 day workers. All correlations were significant at $p \leq .0001$. *Source*: Zavada et al. (2006).

In order to validate the MCTQ^{Shift}, main MCTQ^{Shift} parameters will be tested for construct validity by means of comparison to daily sleep logs. MCTQ^{Shift} derived mid-sleep values (including MSF^{E}scn) will also be compared to actual behavioural assessment of phase of activity and rest by means of actimetry, as well as to the phase of body temperature regulation. Finally, main parameters from the MCTQ^{Shift} will be compared to scores form the Morningness-Eveningness Questionnaire by Horne and Østberg. As all four studies address the same theme (the validity of the MCTQ^{Shift}), the results will be discussed together.

4.2 Day to Day Sleep Logs: Can the Pattern be Captured by the MCTQ^{Shift} ?

In this study, main parameters from the MCTQ^{Shift} will be tested for construct validity by means of comparison to daily sleep logs in order to determine how good the instrument is at actually measuring sleep-wake behaviour in shift workers. Firstly, it will be examined whether main parameters from the sleep logs will yield comparable results to those obtained by the MCTQ^{Shift}. As such, the sleep log data should show a displacement and reduction in sleep on the morning and the night shift, a slight delay in the timing of sleep on the evening shift, and a diurnal orientation of sleep-wake behaviour on free days. The sleep log data should also show a significant change in MSF across the different shifts. To exclude the possibility that changes in MSF across the three shifts arise from a natural variability in the timing of sleep across three weeks, MSF will also be compared across three weeks from sleep log data by day workers as well as by non-rotating night workers.

To validate the $MCTQ^{Shift}$, main parameters (SON_w/f; SOFF_w/f; SLAT_w/f; SIN_w/f; SD_w/f; MSW and MSF) for all three shifts will be correlated to the same parameters assessed by sleep logs. Furthermore, the validity of assessing chronotype by means of $MSF^{E}scn$ (no alarm clock) in shift workers will be examined by means of its correlation to sleep phase, as assessed by MSF from the sleep logs. The criteria for validity will be based on comparisons to the validity of the same data obtained by day workers. A new sample of day workers is selected, consisting of a more representative sample than the one by Kuehnle (2006), where mostly extreme chronotypes were being investigated.

4.2.1 Methods

4.2.1.1 Participants

Fifty-two rotating shift workers from the three-shift model (23 women, 23 men and 6 of unknown sex, M_{age} = 32.5, age range: 21-50); 106 day workers (59 women, 44 men and 3 of unknown sex, M_{age} = 37.5, age range: 18-63); and 22 temporary night workers (10 women and 12 men, M_{age} = 39, age range: 22-50) volunteered to participate in this study. The temporary night workers were rotating shift workers from the three-shift model, employed at a Siemens packaging station in Amberg, who volunteered to work permanent night work for four continuous weeks. The rotating shift workers were employees at an ArcelorMittal steel manufacturing plant in Luxembourg as well as employees at a Siemens security switch manufacturing plant in Cham, Germany. The mean shift work employment was 12.4

years. The day workers were employees at the OSRAM head office in Munich, as well as participants recruited for another study on daylight savings time, consisting mostly of students.

4.2.1.2 Materials

The materials used in this study were daily sleep logs, for the assessment of daily sleep and wake behaviour as well as the MCTQ and the $MCTQ^{Shift}$, depending on whether the participants were day workers or shift workers. Please see General Methods for more detailed information on the materials applied.

4.2.1.3 Procedure

The MCTQ questionnaires and sleep logs were distributed to the shift workers at their workplace, to be filled out by the participants at their home. All participants were thoroughly briefed prior to the start of the study. A one-to-one person training session lasting from 15-20 minutes was undertaken before the study began to ensure that participants were familiar with the sleep log instructions. Participants were asked to return the questionnaire in a sealed envelope to medical personnel at the respective factories. Participants were asked to fill out the sleep logs on a daily basis, in the morning, just after awakening. A locked drop-box was set-up in a central location at the workplace where participants were asked to drop their sleep logs on a weekly basis to promote the continuous filling out of the sleep logs.

The temporary night workers volunteered to work four weeks of continuous night work (each week consisting of five workdays and two free days). The participants filled out daily sleep logs for five continuous weeks, starting one week prior to the first week of night work. The first week of night work was preceded by one week of morning work for one half of the participants, and by one week of evening work by the other half, in order to balance out potential influences by shifts worked previously. The remaining participants worked their usual work schedule. The filling-out of daily sleep logs took place for six continuous weeks.

Data collection by the shift workers took place on two separate occasions: once between February and October 2006 in Luxembourg, and once between June and July 2008 in Cham and Amberg. Data collection for the day workers also took place on two separate occasions in Munich: once between September and October 2006, and once between January and March 2008.

4.2.2 Results

Daily patterns of sleep, as assessed by sleep logs, were first explored and then compared to data obtained by the MCTQ^{Shift}. Next, MSF^{E}scn was correlated to sleep log-assessed sleep phase on free days to examine the validity of MSF^{E}scn as a measure of chronotype.

4.2.2.1 Sleep-wake behaviour from daily sleep logs

Based on the daily sleep log entries by the rotating shift workers, main parameters were computed for each participant, for each day, as indicated in Figure 3.2. (SON_w/f; SOFF_w/f; SLAT_w/f; SIN_w/f; MSW, MSF, and SD_w/f.). These variables were subsequently grouped according to whether the sleep preceded a workday or a free day. For shift workers, the variables were additionally grouped according to the corresponding shift. Sleep prior to the first night shift and prior to the first evening shift was treated as a free day. Sleep following the last night shift was treated as a night shift and sleep following the last evening shift was treated as an evening shift. Figure 4.2. A. displays the daily timing of sleep averaged across all shift workers, on the morning, evening, and night shifts.

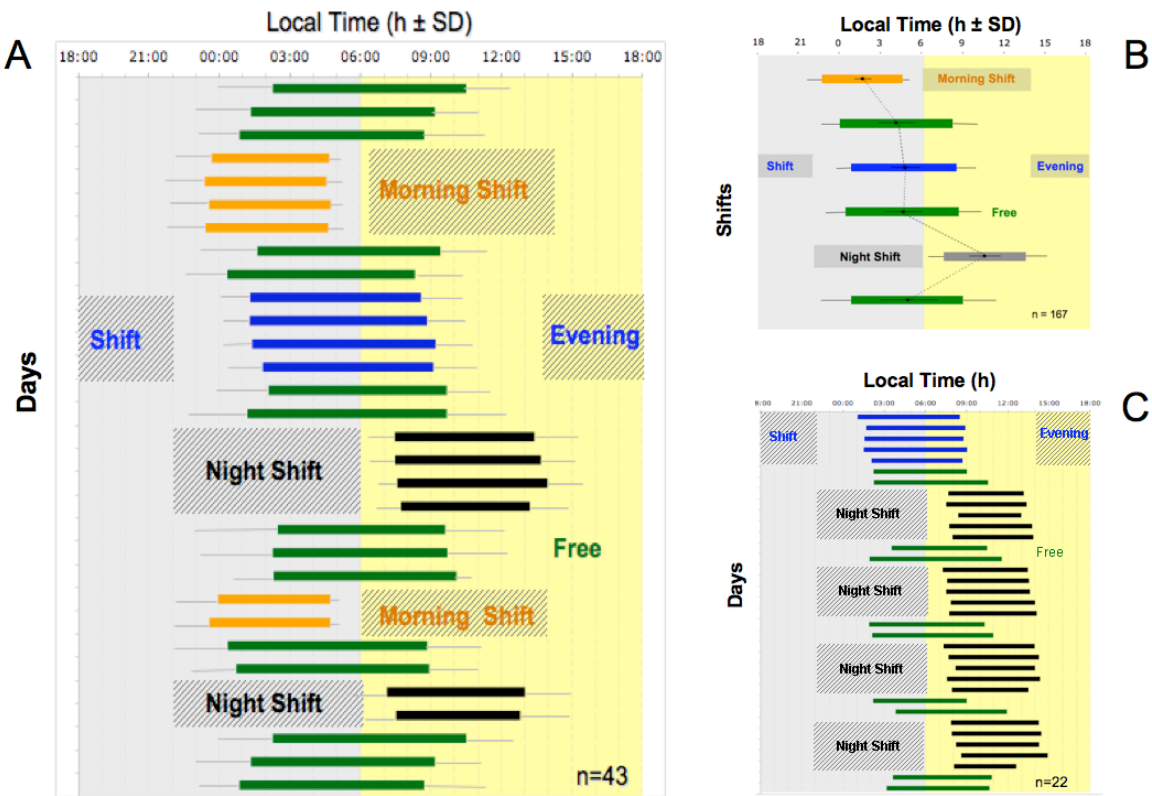

Figure 4.2. A. Daily sleep, averaged across 43 rotating shift workers from the manufacturing plant in Cham, in the morning (yellow), evening (blue), and night (black) shifts and corresponding free days (green) The bars represent the timing of sleep (with SD), the boxes represent the corresponding working hours. The SD on the left of the bar represents the SD for sleep onset and the SD on the right of the bar, the SD for sleep offset. B. MCTQ^{Shift} assessed timing of sleep (bars, with SD and mid-sleep) in the morning (yellow), evening (blue), night (grey) shifts and free days (green) by 167 rotating shift workers (same shift system as sleep logs). C. Daily sleep, averaged across 22 night workers, on the night (black) shifts and corresponding free days (green). The bars represent the timing of sleep; the boxes represent the timing at which work takes place.

Overall, the graph supports the findings obtained from the MCTQ^{Shift}, as discussed in project one (see Figure 4.2. B.). There was a strong displacement and reduction in sleep on the morning and night shift and a slight delay in the timing of sleep on the evening shift. As observed by means of the MCTQ^{Shift}, sleep on the night shift was initiated shortly upon return from work, within 1.5 hours after shift end and lasted until the early afternoon. The small standard deviation observed by the MCTQ^{Shift}-derived sleep offset on morning shifts,could also be observed on the daily sleep logs. Sleep log-assessed timing of sleep on free days also paralleled the findings from the MCTQ^{Shift}. The timing of sleep on free days remained remarkably stable across the different shifts. A statistical comparison between MSF following the morning (M = 4.57, SD = 1.47), evening (M = 5.63, SD = 1.74), and night shifts (M = 5.39, SD = 1.68) by means of a within-subject design ANOVA showed a significant change in MSF between the three shifts: F (2 ; 96) = 20.99, $p \leq .05$, g = .31, 1- β = 1. The Friedman test confirmed this finding: χ^2 (2, n = 49) = 19.39, $p \leq .05$.

In order to see whether the shift in MSF across schedules could simply be attributed to normal variation in the timing of sleep across three weeks, MSF was compared across three weeks in 106 day workers (MSF_1: M = 3.92, SD = 1.29; MSF_2: M = 3.86, SD = 1.43; MSF_3: M = 3.87, SD = 1.51). Results from the Kolmogorov-Smirnov test showed no significant deviation from normality for all three MSF distributions. Results from a within-subject design ANOVA showed no significant difference in MSF for day workers: F (2, 116) = 0.07, p = .93, g = .001, 1- β = .06. This suggests that changes in MSF in rotating shift workers result from influences by previously worked on shift hours. This was supported by sleep log data from 22 shift workers, working four weeks of continuous night work (see Figure 4.2. C.). Results from a within-subject design ANOVA comparing MSF across three subsequent weeks (MSF_1: M = 6.58, SD = 2.63; MSF_2: M = 6.53, SD = 2.20; MSF_3: M = 6.61, SD = 2.30) showed that MSF remained stable over time, even in night workers: F (2, 38) = 0.01, p =.99, g = .001, 1- β = .05. Results from the Kolmogorov-Smirnov test showed no significant deviation from normality for all three MSF distributions.

4.2.2.2 Comparing main parameters from the MCTQ^Shift to sleep logs

In order to compare main parameters obtained from the MCTQ to those obtained from sleep logs, a mean for each variable was computed for each shift and for its corresponding free days. For workdays, the mean was based on an average over four days; for free days, the mean was based on an average over two days. The mixed week was omitted for this data analysis. Please note, that this caused an unequal error rate in averaged scores between workdays and free days, as well as between the sleep log variables and the MCTQ variables. When analyzing the results, this problem should be kept in mind. Table 4.3. presents the correlation coefficients and the Wilcoxon Signed Rank Test statistic for correlations and differences between MCTQ-assessed and sleep log-assessed main variables.

Table 4.3. *Comparison between MCTQ^Shift and Sleep Logs*

	Sleep Onset		Sleep Offset		Sleep Latency		Sleep Inertia		Mid-Sleep		Sleep Duration	
	ρ	*W*	ρ	*W*	ρ	*W*	ρ	*W*	ρ	*W*	ρ	*W*
Work Days												
Morning Shift	.58**	0.8	.74**	0.8	.20	0.5	.49**	6.2**	.62**	0.5	.45**	1.6*
Evening Shift	.67**	2.4**	.66**	1.3*	.60**	0.6	.39*	6.2**	.70**	0.1	.55**	2.4**
Night Shift	.52**	2.3**	.57**	0.4	.40**	1.4*	.59**	6.6**	.56**	0.3	.59**	2.0**
Free Days												
Morning Shift	.35*	0.8	.58**	1.6*	.36*	3.2**	.34*	6.1**	.47**	0.4	.59**	3.0**
Evening Shift	.47**	0.4	.59**	1.3*	.27	0.3	.26	5.7**	.59**	0.2	.54**	1.8*
Night Shift	.53**	2.3**	.66**	1.7*	.65**	1.4*	.37*	6.5**	.64**	0.6	.40**	1.7*

Note: Spearman Rho (ρ) correlation coefficient, one tailed test **p≤.001, *p≤.01 and Wilcoxon Signed Ranks Test (*W*) *p≤.2; **≤.05 (*n*=52). After Bonferroni correction, values with ** remain significant.

Overall, scores form the MCTQ correlated significantly with scores from the sleep logs for all variables, except for SLAT_w on morning shifts and SLAT_f on evening shifts, as well as for SIN_f on evening shifts. Though most variables correlated very well, results from the Wilcoxon Signed Rank Test showed that many variables did differ significantly in their mean rank. Please note however, that mid-sleep values seem to be unaffected by this. Both, MSW and MSF did not differ between the two measurements.

4.2.2.3 Validation of MSF^{E}scn

To test the validity of MSF^{E}scn as a measure of chronotype, MSF^{E}scn from the MCTQ^{Shift} was correlated to the phase of sleep from daily sleep logs, by means of average MSF on the evening shift (MSF^{E} , there were on average two MSF^{E} values per individual). MSF^{E}scn was computed as indicated in Figure 3.5., whereby only individuals who reported not waking up to an alarm clock on free days were considered. A total number of 28 rotating shift workers remained. Results from the Kolmogorov-Smirnov test showed no significant deviation from normality, for both variables. Results from the Pearson Product-Moment Correlation showed that MSF^{E}scn correlated significantly with sleep log assessed MSF^{E}: r (28) = .46, $p \leq .05$ (one-tailed hypothesis).

4.2.2.4 Comparison to day workers

In order to determine the validity of the above findings, the results were compared to correlations between sleep logs and the MCTQ in day workers. Sleep log variables by day workers were computed as explained in Figure 3.2., whereby averages over one week only were used to ensure the comparability between shift workers and day workers. Fifty-two day workers were randomly selected (out of 106) so as to have an equal sample size between day workers and shift workers. The Spearman Rho correlation coefficients and Wilcoxon Signed Rank Test results are presented in Table 4.4. As in shift workers, main parameters from the MCTQ in day workers correlated significantly to main parameters from the sleep logs but scores from the Wilcoxon Signed Rank test did show significant differences between the two measurements for some variables (predominately workdays). Just like for shift workers, MSF did not differ between the two measurements. Overall, the findings by shift workers mirror the findings by day workers.

Table 4.4. *Correlations between MCTQ and Sleep Logs in Day Workers*

	Sleep Onset		Sleep Offset		Sleep Latency		Sleep Inertia		Mid-Sleep		Sleep Duration	
	ρ	*W*	ρ	*W*	ρ	*W*	ρ	*W*	ρ	*W*	ρ	*W*
Work Days	.66**	2.4**	.56**	1.1	.71**	0.7	.38*	6.1**	.69**	1.6*	.29*	1.9*
Free Days	.52**	0.5	.50**	0.2	.66**	0.2	.23	6.0**	.63**	0.4	.32*	0.3

Note: Spearman Rho (ρ) correlation coefficient, one tailed test $**p \leq .004$, $*p \leq .01$. Wilcoxon Signed Ranks Statistic (*W*) $*p \leq .2$; $** \leq .05$ (n=52). After Bonferroni correction, values with **remain significant.

MSFscn in day workers was computed as indicated in Figure 3.5. To allow for better comparison between day workers and shift workers, twenty-eight day-workers were randomly selected out of 80 participants waking up without an alarm clock (to have a comparable *n* to the one of shift workers). MSF from the sleep logs was computed on the basis of one weekend so as to have an equal error rate between the two samples. Results from the Kolmogorov-Smirnov test showed no significant deviation from normality for both variables. In day workers, MSFscn correlates very highly with MSF from sleep logs: $r(28) = .81$, $p \leq .05$ (one-tailed hypothesis).

4.3 Behavioural Phase Markers and their Relationship to the MCTQ^Shift: Actimetry

In this study, MCTQ^Shift-assessed sleep phase by means of MSW and MSF is tested for construct validity by means of comparison to behavioural data from actimetry. MCTQ^Shift -

obtained mid-sleep values are compared to the phase of activity and rest on the morning, evening, and night shifts, as well as on the respective free days. MSF^{E}scn will be correlated to the phase of actimetry on free days following the evening shift to test the validity of MSF^{E}scn as a measure for chronotype. The criteria for validity will be based on comparisons to the correlation between MSFscn and phase of actimetry on free days in day workers.

4.3.1 Methods

4.3.1.1 Participants

A total of 39 shift workers (25 women and 14 men, M_{age} = 31.7 years, age range: 21-50) from the three-shift-model and 70 day workers (41 women and 29 men, M_{age} = 31.7 years, age range: 21-50) volunteered to participate in this study. The shift workers were employees at a Siemens security switch manufacturing plant in Cham, Germany. The mean shift work employment was 10.1 years. The day workers were employees of the OSRAM head office in Munich, as well as participants recruited for a study on daylight savings time, consisting mostly of students. Participants were recruited by means of flyers as well as talks given at scheduled meetings. Participants from the DST study were recruited mostly through personal contact and word of mouth.

4.3.1.2 Materials

The materials used in this study were daqtometer®, for the assessment of 24 hour actimetry rhythms, the MCTQ for day workers and the MCTQ^{Shift} for shift workers, daily sleep logs so as to allocate the actimetry data to corresponding work and free days, and a daqtometer protocol. Please see General Methods.

4.3.1.3 Procedure

The Daqtometer® were distributed to the participants at the workplace to be worn for six continuous weeks (night and day), together with the six-week long sleep logs and the MCTQ/MCTQ^{Shift}. All participants were thoroughly briefed before the study began. A one-to-one person training session lasting roughly 15-20 minutes was conducted before agreement of participation to ensure that participants were familiar with the Daqtometer® and the sleep logs. The participants worked their usual work schedule. Data collection by the shift workers took place between June and July 2008 in Cham. Data collection for the day workers took place at two separate time points in Munich, one between September and October 2006 and one between January and March 2008.

4.3.2 Results

The phase of activity was analyzed by means of the centre of gravity method (CoACT) (see Kenagy, 1980), which is independent of the individual shape of the activity profile. Daily values of centre of gravity (ψ_{Act}) were calculated individually for each participant with the ChronoProgramm. Based on entries into the daily sleep logs, the data were then categorized according to whether the given day was a workday or a free day, as well as according to the shift it belonged to. Time spans of removal of the Daqtometer® were excluded. A moving average sine adaptation over subsequent days for each shift without smoothing or filtering resulted in seven ψ_{Act} data points per shift, which were averaged to obtain a mean ψ_{Act} for work and for free days separately. From the entries into the MCTQ^{Shift}, mid-sleep was computed for workdays and for free days, for each shift, as indicated in Figure 3.2. The mixed week was excluded from analysis. Only participants with complete data sets were included. Thirty-three participants remained.

Table 4.5. *Correlation Coefficients between MCTQ^{Shift} and Actimetry*

	Work Days	Free Days
Morning Shift	- .02	.47*
Evening Shift	.62*	.70*
Night Shift	.56*	-.68*

Note: Spearman Rho correlation coefficients (ρ) between mid-sleep from the MCTQ^{Shift} and average centre of gravity from the actimetry data (ψ_{Act}) in 33 rotating shift workers. To correct for Bonferroni, alpha was set at .01. *$p \leq .01$.

Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for some of the variables involved. As such, only non-parametric correlations were computed, by means of Spearman Rho correlations. To correct for Bonferroni, alpha was set at .01 (1-tailed). Table 4.5. presents the correlations between mid-sleep values from the MCTQ^{Shift} and the ψ_{Act} for work and for free days, for each shift. Overall, mid-sleep values from the MCTQ^{Shift} correlated well with the corresponding phase of activity, for all free days and for workdays, except for the morning shift. The reason why phase of activity in the morning shift did not correlate with MSW may be due to the low variance on morning shifts, due to the high constraints on the timing of sleep and activity. The best correlation was obtained for free days following the evening shift.

4.3.2.1 Validation of MSF^{E}scn

The validity of MSF^{E}scn as a measure of chronotype was examined by means of comparison to phase of activity on free days following the evening shift. MSF^{E}scn was computed for each individual as indicated in Figure 3.5., whereby only individuals who reported not waking-up to an alarm clock were considered. Only individuals for whom all data were present were considered. A total number of 26 rotating shift workers remained. Results from the Kolmogorov-Smirnov test showed no significant deviation from normality for all variables involved. Alpha was set at 0.01 to correct for Bonferroni. Results from the Pearson Product-Moment Correlation showed that MSF^{E}scn correlated significantly with ψ_{Act} for free days following the evening shift: r (26) = .48, $p \leq .05$ (one-tailed hypothesis).

4.3.2.2 Comparison to day workers

In order to compare the validity of MSF^{E}scn as a measure of chronotype in shift workers to that of MSFscn in day workers, the same analysis was computed for day workers. Daily values of centre of gravity (CoGs, ψ_{Act}) were calculated for work days and for free days, which were averaged over one workweek. From the entries into the MCTQ, MSFscn was computed as indicated in Figure 3.5. After exclusion of individuals waking up with the use of an alarm clock, 41 day workers remained. Results from the Kolmogorov-Smirnov test showed no significant deviation from normality for both variables involved. In day workers too, MSFscn significantly correlated with Centre of Gravity of activity on free days (Pearson Product-Moment correlation): r (41) = .39, $p \leq .05$ (one-tailed).

4.4 Physiological Phase Markers and their Relationship to the MCTQ^{Shift}: Body Temperature Regulation

This study examines 24-hour fluctuations in skin temperature in 15 rotating shift workers on the morning, evening and night shifts. Temperature will be analyzed by means of the distal-proximal gradient (DPG), an indicator of thermoregulation (see Kräuchi, 2007) and will be correlated to the phase of sleep as assessed by the MCTQ^{Shift}. Based on controlled laboratory observations in day workers, it is predicted that shift workers will also show inter-individual differences in the phase of the temperature cycle and that these will correlate with MCTQ^{Shift}-obtained MSF^{E}scn values. The validity of MSF^{E}scn as a measure of chronotype will be examined by means of comparison to phase of sleep on the evening shift, as this shift is relatively free of external constraints and thereby characterizes a better reflection of the internal phase than the morning or night shift. Specifically, we expect people with high MSF^{E}scn scores (late chronotypes) to display later DPG peaks than people with low MSF^{E}scn scores (early chronotypes).

4.4.1 Methods

4.4.1.1 Participants

A total of 14 (nine women and five men, M_{age} = 31 years, age range: 21-50) rotating shift workers from the three-shift-model volunteered to participate in this study. Participants were employees at a Siemens security switch manufacturing plant in Cham, Germany. The mean shift work employment was 10.8 years.

4.4.1.2 Materials

The instruments used in this study were iButtons® for the assessment of skin temperature and the MCTQ^{Shift} for the assessment of chronotype. Please see General Methods.

4.4.1.3 Procedure

The iButtons® were worn for 72 hours on three separate occasions from the second to the fourth workday: once on the morning shift, once on the evening shift, and once on the night shift. The iButtons® were taped on the shoulder blades (proximal) and ankles (distal) of the shift workers with medical tape 15 minutes before the start of the shift and removed 72 hours later. This was done by the principal investigators or by medical personnel. Participants were asked to wear the iButtons® for the entire duration of the 72 hours, including when showering. The MCTQ^{Shift} was distributed at the workplace to be filled out at home. All participants were thoroughly briefed before the start of the study and informed about their right to withdraw from the study at any time. Data collection took place between June and July 2008.

4.4.2 Results

Distal and proximal temperature values were assessed in 17-minute intervals for 72 hours: on the morning, evening, and night shift respectively (only on workdays). Only the second day (24h - 48h) was considered (being the third working day for each shift), from 0:00 to 23:59 o'clock. Temperature fluctuations were assessed by means of the distal-proximal gradient (DPG), which was computed by subtracting the mean proximal value from the mean distal value for each data point, per individual. The 24-hour progression of the DPG across each shift, per participant is presented below. DPG values ≥ -1 (red line) characterize values associated with reduced sleep onset latency and can thereby be viewed as a predictor of high sleepiness (see Kräuchi, 2007). Figure 4.3. presents the DPG fluctuations for each participant.

A first look at the course of DPG across the three shifts reveals that the DPG values were highly masked: DPG always increased during sleep, independent of the timing of sleep (whether at night or during the day). Nonetheless, the data show valuable results worth taking note of. DPG on the evening and night shifts often increased before sleep onset (see for example, 44, 45, 46, and 68 for the evening shift and 30, 32, 43, 44, 50, and 55 for the night shift). Also, on both evening and night shifts DPG decline often preceded sleep offset (see for example 43, 45, and 46 for the evening shifts and 30, 32, 43, 45, 46, 50, 55, 67, and 69 for the night shift). One can also see that DPG values often exceeded the red line (high sleepiness) during work hours on the night shift but also on the evening shift.

To explore the relationship between sleep phase and temperature phase, the centre of gravity method was applied to the temperature data (see Kenagy, 1980). Values of centre of gravity (ψ_T) for the morning, evening, and night shifts were calculated individually for each participant with the ChronoProgramm. From the entries into the MCTQ^{Shift}, mid-sleep on work days (MSW) for each shift was computed, as indicated in Figure 3.2. Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for some of the variables involved. As such, only non-parametric correlations were computed through using Spearman Rho correlations, whereby ψ_T on a given shift was correlated to MCTQ^{Shift}-assessed MSW for that shift. Alpha was set at .016 to correct for Bonferroni. As we expect a positive correlation between the variables, a one-tailed hypothesis was tested. The results showed that ψ_T did not significantly correlate with MSW on the morning shift: ρ (14) = .26, p = .22 and on the evening shift: ρ (13) = .13, p = .33, but correlated significantly with

MSW on the night shift: ρ (14) = .64, $p \leq .01$. It is important to note here that the sample size was very small. A quite large effect size would be required to detect significance with such a small sample size. Though most of the above correlations were non-significant, they did, however, demonstrate a trend towards an association in the expected direction.

4.4.2.1 Validation of MSF^Escn

MSF^Escn was computed for each individual as indicated in Figure 3.5., whereby only individuals who reported not waking up to an alarm clock were considered. Twelve participants remained. The Spearman Rho correlation between MSF^Escn and ψ_T on the evening shift was also non-significant: ρ (12) = .29, *p* =. 18. Again, this may be due to the small sample size. Note that the coefficient was nonetheless higher than the correlation with MSW^E.

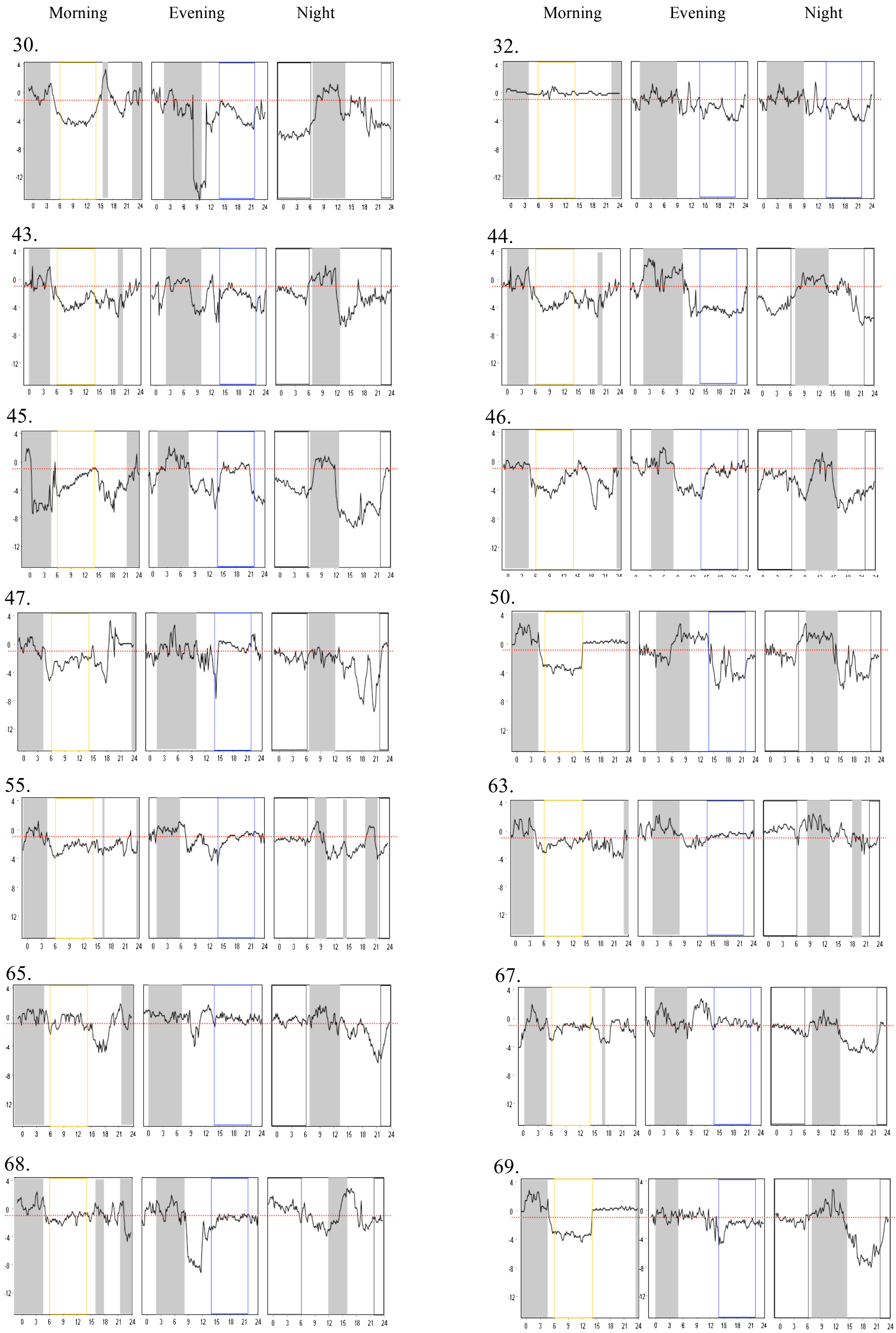

Figure 4.3. Temperature regulation (DPG) throughout the 24-hour day, on the morning, evening, and night shifts. The background specifies the timing of sleep (grey) and the timing of work (coloured boxes). Values above the red line suggest high sleepiness. For more information see text.

4.5 Generalizing MEQ and MCTQ Findings to Shift Workers

In this study, $MCTQ^{Shift}$-assessed parameters are tested for convergent validity by means of comparison to scores from the Morningness-Eveningness Questionnaire by Horne and Østberg. The same MCTQ variables as the ones implemented in the study by Zavada et al. (2006) will be used. These are SON_w/f, SOFF_w/f, MSW and MSF for the morning, evening, and night shifts. Also the MEQ will be correlated to MSF^{E}scn scores. The criteria for validity will be based on comparisons to the validity of the same data obtained by day workers. We should expect to find results comparable to those obtained by day workers in the study by Zavada et al. (2006).

4.5.1 Methods

4.5.1.1 Participants

A total of 75 male shift workers (M_{age}= 44.6, age range: 22-57) volunteered to participate in this study. Participants were recruited with the assistance of VW medical faculty. All shift workers were employees at a VW power plant in Wolfsburg, Germany. The mean length of shift work employment was 20.4 years.

4.5.1.2 Materials

The materials used in this study were the Morningness-Eveningness Questionnaire by Horne and Østberg and the $MCTQ^{Shift}$. Please see General Methods.

4.5.1.3 Procedure

Both questionnaires were distributed at the workplace to be filled out during work hours within a few weeks. This took place between December 2006 and January 2007 at a Volkswagen power plant in Wolfsburg.

4.5.2 Results

Main parameters from the $MCTQ^{Shift}$ were correlated to the MEQ score and compared to findings obtained by day workers. Next, $MSF^{E}scn$ were correlated to the MEQ score, to assess its convergent validity in the assessment of chronotype.

Based on the $MCTQ^{Shift}$ data obtained by 75 rotating workers, sleep onset (SON_w/f), sleep offset (SOFF_w/f), and mid-sleep (MSW/MSF) were computed as explained in Figure 3.2. Total MEQ scores by the same shift workers were computed by adding individual scores from each item. Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for some of the variables involved. As such, only non-parametric correlations were computed by means of Spearman Rho correlations. Alpha was set at 0.002 (one-tailed hypothesis) to correct for Bonferroni. Table 4.6. presents the correlations between MEQ and selected variables from the $MCTQ^{Shift}$. The obtained MEQ score had a mean score of 53.49 (*SD* = 11.67). As expected, MEQ scores correlated highly with $MCTQ^{Shift}$ parameters for free days. Like in day workers, MEQ correlated best with MSF, compared to SON_f and SOFF_f, whereby the highest correlation was obtained for MSF following the evening shift. The MEQ correlated significantly less well with $MCTQ^{Shift}$ parameters on the morning and the night shifts.

Table 4.6. *Correlations between $MCTQ^{Shift}$ and the MEQ*

	Work Days				Free Days		
	Sleep Onset	Sleep Offset	Mid-Sleep		Sleep Onset	Sleep Offset	Mid-Sleep
Morning Shift	-.35**	.00	-.29*		-.52**	-.50**	-.54**
Evening Shift	-.47**	-.63**	-.58**		-.52**	-.68**	-.70**
Night Shift	-.02	-.49**	-.46**		-.49**	-.55**	-.58**

Note: Spearman Rho (ρ) correlations between $MCTQ^{Shift}$ parameters and the MEQ score in 75 rotating shift workers. **p≤ 0.002, * p≤ 0.01 (one-tailed). After Bonferroni correction values with ** remain significant.

4.5.2.1 Validating $MSF^{E}scn$

$MSF^{E}scn$ was computed as indicated in Figure 3.5., whereby only individuals who reported not waking-up to an alarm clock on free days were considered. A total of 29 shift workers remained (many did not answer the question at all and were thereby also excluded), leading to a mean $MSF^{E}scn$ of 3.92 (*SD* = 1.56). Note that $MSF^{E}scn$ correlated even better to the MEQ than MSF^{E}: Spearman Rho Correlation Coefficient ρ (29) = -.77, $p \leq 0.001$ (Pearson-Product-Moment correlation coefficient was: r (29) = -.78, $p \leq .001$).

4.6 Discussion of the Validation Studies

Overall, the above findings indicate that the $MCTQ^{Shift}$ can accurately predict actual timing of sleep in shift workers as assessed by daily sleep logs, even though absolute values may indeed sometimes significantly differ between the two measurements. Still, mid-sleep on free days seems unaffected by the choice of measurement used. When filling out the MCTQ, people seem to compute an algorithmic average of their sleep times that surprisingly fits their actual sleep phase with accuracy, not the specific timing of sleep onset and sleep offset. As such, sleep phase and chronotype can be effectively and accurately determined by means of the $MCTQ^{Shift}$. $MCTQ^{Shift}$ mid-sleep on free days also correlated very well with the phase of actimetry and with the widely used MEQ, whereby critical variables used for the assessment of chronotype in shift workers (MSF^E) correlated best. MSF^Escn, as a measure of chronotype correlated significantly with the phase of sleep from sleep logs, activity, and rest from actimetry, and with the MEQ. The correlation between MSF^E and actimetry and between MSF^E and the MEQ became even more significant when corrected for sleep debt. The MEQ correlates significantly less well with $MCTQ^{Shift}$ parameters on the morning and the night shifts, reflecting the high external constraints on the sleep-wake behaviour during both of these shifts. The obtained correlations were comparable to those observed in day workers.

The temperature data was highly masked by sleep. Yet one can clearly see anticipatory temperature regulation. DPG often increases before sleep onset and often declines before sleep termination. This suggests a causal link between temperature regulation and sleep, with an increase in DPG promoting sleep and a decrease in DPG promoting awakening. DPG values have been associated with a reduction in sleep latency (see Kräuchi, 2007), supporting the above argument. As observed in project one, awakening generally happens without the use of an alarm clock on the evening and night shift, indicating that awakening occurs naturally on these shifts. Most importantly, these anticipatory effects of thermoregulation could also be observed when sleep was highly displaced, such as on night shifts, suggesting that rhythms of body temperature do adjust to displaced sleep.

5 Project Three: Reconsidering Adverse Effects of Shift Work in the Light of Chronotype

It has been widely assumed that circadian adjustment presupposes tolerance to shift work. Chronotype should play a decisive role in determining the degree of circadian alignment to working shifts. Indeed, studies have shown an overall better tolerance to shift work by late types (Duffy, Dijk, Hall, & Czeisler, 1999; Duffy, Viswanathan, & Davis, 1999; Foster & Kreitzman, 2004; Østberg, 1973; Hildebrandt and Stratmann, 1979; Khaleque, 1999; Vidacek, Kaliterna, Radosevic-Vidacek, & Folkard, 1988).

Yet, the relationship between chronotype and tolerance in shift workers should strongly depend on the shift in question. There should be differential constraints by the morning, evening, and night shifts on late and early chronotypes, whose effects may ultimately be balanced out in shift workers that work all three shifts. Compared to late types, early types should display less misalignment to the imposed sleep-wake cycle of the morning shift and should thereby display better tolerance to morning work. Late types on the other hand should have greater alignment to the enforced sleep-wake cycle of the night shift and should thereby display better tolerance to night work compared to early types. On the basis of three studies, this project will explore chronotype-specific tolerance to the demands of working on the morning, evening, and night shifts, whereby tolerance will be investigated in terms of disruption of sleep (study 5.1) and in terms of psychological distress (study 5.2). Lastly, it will be examined whether chronotype differences in tolerance to displaced sleep predict workers' health (study 5.3).

5.1 Chronotype and Sleep in Shift Workers

This study examines shift worker tolerance to working on the morning, evening, and night shift in terms of chronotype differences in sleep parameters. For the first part, chronotype-specific sleep-wake behaviour by means of the $MCTQ^{Shift}$ will be explored. This descriptive part of the study provides fieldwork data in regards to chronotype differences in sleep demographics on the morning, evening, and night shift, as well as on respective free days. Chronotype differences in the timing of sleep are expected on both free and workdays. Specifically, on free days late types are expected to show a delayed sleep phase compared to early types, regardless of the prior work schedule. Regarding workdays, chronotype differences in circadian alignment to working on the morning, evening, and night shifts are expected. Specifically, one should expect late types to have difficulties in advancing sleep onset on the morning shift and early types to have difficulties sleeping in on the evening and night shifts.

In the second part of the study, the association between chronotype and sleep disturbance on the different shifts will be investigated, in terms of social jetlag and duration and quality of sleep. Compared to early types, late types should require less phase shifting of main sleep to adjust to the demands of working on the night shift, but should have considerably larger phase shifting of main sleep to adjust to the demands of working on the morning shift. As such, one should expect early types to display more social jetlag and lower duration and quality of sleep than late types on the night shift. In contrast, late types should show more social jetlag, and lower duration and quality of sleep than early types on the morning shift. Ultimately, the chronotype-specific differences may be balanced out over the three shifts. As such, when averaged across the three shifts, social jetlag, sleep duration, and sleep quality should not correlate with chronotype.

5.1.1 Methods

5.1.1.1 Participants

A total of 371 shift workers from the three-shift-model were assessed for chronotype. After exclusion of those participants waking-up to an alarm clock on free days following the evening shift, a total of 238 shift workers remained (83 women and 155 men; M_{age} = 38.9, age range: 19-56 years). Of these, 115 were early types ($MSF^{E}scn \leq$ 3:59), 63 were intermediate types ($MSF^{E}scn$ from 4:00 to 4:59), and 60 were late types ($MSF^{E}scn \geq$ 5:00). Questions in regards to sleep quality were assessed in a sub-sample of 94 shift workers from the three-shift-model (58 women and 36 men; M_{age} = 36.2, age range: 19-55 years). This sample consisted of 50 early types, 21 intermediate types, and 23 late types.

5.1.1.2 Materials

The materials used in this project were the $MCTQ^{Shift}$ for the assessment of shift worker sleep demographics and chronotype, as well as the Sleep Questionnaire from the Standard Shift Work Index for the assessment of sleep disturbance. Please see General Methods for a detailed discussion of the questionnaires used.

5.1.1.3 Procedure

The set of questionnaires were collected between March 2006 and October 2008. The questionnaires were distributed to the shift workers at their workplace, to be filled out at their home. Each set of questionnaires included an informed consent, stating the nature of the participation and the participants' right to withdraw from the study at any time. Participants had the option to indicate whether they wanted a personalized evaluation of their chronotype, which was confidentially allocated to the participant in a sealed envelope.

5.1.2 Results

First, chronotype-specific sleep and wake behaviour were explored seperately for free days and workdays. Next, associations between chronotype and sleep disruption on the morning, evening, and night shifts were investigated in terms of social jetlag, sleep duration, and sleep quality.

5.1.2.1 Chronotype-specific sleep-wake behaviour

Main variables from the $MCTQ^{Shift}$: sleep onset (SON), sleep offset (SOFF), sleep latency (SLAT), sleep inertia (SIN), mid-sleep (MS), sleep duration (SD), and use of alarm clock (A) were computed for each chronotype separately, as explained in Table 3.2., for the morning, evening, and night shifts, as well as for the respective free days. The descriptive data for free days are presented in Table 5.1. and for workdays in Table 5.2.

5.1.2.2.1. Free days

Compared to early types, late types reported falling asleep and waking up considerably later on all of the free days. The data demonstrates that previous shift work had some effect on the timing of sleep on free days for all three chronotypes. Sleep on free days delayed from the morning to the night shift for all types. This applied to sleep onset, sleep offset, and mid-sleep. Yet, the shift in mid-sleep from the morning to the night shift was noticeably larger for late types (1 hour and 17 minutes) than for early types (35 minutes).

Except for the free days after the night shift, early types showed overall shorter sleep latency than late types, indicating a higher drive for sleep. Compared to other free days, sleep latency was considerably longer on free days following the night shift (as observed in project one). This applied to all three chronotypes. The use of alarm clocks was generally low on free days, for all types (the 0% use of alarm clock on the evening shift is a result of the previous selection criteria for the assessment of chronotype). Chronotype differences in sleep duration, sleep latency, and sleep inertia were non-consistent.

Table 5.1. *MCTQ^{Shift} Parameters on Free Days*

	Sleep Onset ($M \pm SD$)	Sleep Offset ($M \pm SD$)	Sleep Latency ($M \pm SD$)	Sleep Inertia ($M \pm SD$)	Mid-Sleep ($M \pm SD$)	Sleep Duration ($M \pm SD$)	Alarm %
Morning Shift							
Early Types	-0.81 ± 0.80	07.31 ± 1.47	12.7 ± 09.2	15.8 ± 19.4	03.25 ± 0.88	8.11 ± 1.59	04%
Intermediate	0.18 ± 0.94	08.15 ± 1.10	14.9 ± 09.8	17.1 ± 31.7	04.16 ± 0.75	7.96 ± 1.38	10%
Late Types	1.30 ± 1.42	09.77 ± 1.90	17.2 ± 19.2	15.4 ± 10.3	05.52 ± 1.44	8.40 ± 1.67	02%
Evening Shift							
Early Types	-0.70 ± 0.76	07.72 ± 0.99	12.5 ± 08.7	10.9 ± 12.7	03.51 ± 0.59	8.42 ± 1.33	00%
Intermediate	0.71 ± 0.62	08.54 ± 0.76	14.0 ± 08.7	12.0 ± 09.8	04.62 ± 0.37	7.83 ± 1.16	00%
Late types	2.27 ± 1.25	10.50 ± 1.49	18.7 ± 31.9	13.3 ± 08.7	06.36 ± 1.15	8.20 ± 1.34	00%
Night Shift							
Early Types	-0.14 ± 1.99	07.82 ± 1.94	22.3 ± 32.0	15.4 ± 20.3	03.84 ± 1.63	7.96 ± 2.03	06%
Intermediate	1.29 ± 2.20	08.99 ± 1.31	26.5 ± 48.4	12.5 ± 10.6	05.14 ± 1.60	7.70 ± 1.70	09%
Late Types	2.66 ± 2.06	11.00 ± 2.23	22.8 ± 36.6	13.3 ± 11.0	06.80 ± 2.02	8.31 ± 1.78	05%

Note: Mean and standard deviation of main variables from MCTQ^{Shift} parameters on free days by 119 rotating shift workers, grouped separately for early (n=56), intermediate (n=27), and late types (n=36), on the morning, evening, and night shifts. Use of alarm clock is presented in the form of % of people waking-up with the use of an alarm clock. Only individuals with complete data sets were included in the table so that all variables contain the same number of individuals across the three shifts.

5.1.2.2.2. Work days

Table 5.2. *MCTQ^{Shift} Parameters on Work Days*

	Sleep Onset (*M* ± *SD*)	Sleep Offset (*M* ± *SD*)	Sleep Latency (*M* ± *SD*)	Sleep Inertia (*M* ± *SD*)	Mid-Sleep (*M* ± *SD*)	Sleep Duration (*M* ± *SD*)	Alarm %
Morning Shift							
Early Types	-1.61 ± 0.92	4.57 ± 0.70	15.3 ± 12.7	05.9 ± 12.8	01.46 ± 0.55	6.23 ± 1.06	80%
Intermediate	-1.13 ± 0.86	4.63 ± 0.57	19.2 ± 14.7	06.2 ± 06.6	01.78 ± 0.53	5.75 ± 1.04	92%
Late Types	-0.51 ± 1.41	4.63 ± 0.41	25.9 ± 35.4	08.0 ± 08.7	02.09 ± 0.78	5.13 ± 1.44	100%
Evening Shift							
Early Types	0.42 ± 0.74	7.72 ± 1.04	13.5 ± 11.5	11.2 ± 13.4	04.06 ± 0.63	7.32 ± 1.27	16%
Intermediate	1.07 ± 0.78	8.50 ± 0.83	13.8 ± 08.8	14.5 ± 18.7	04.78 ± 0.64	7.42 ± 0.98	17%
Late types	1.59 ± 1.36	9.90 ± 1.11	21.1 ± 19.7	11.8 ± 08.7	05.74 ± 0.92	8.31 ± 1.66	25%
Night Shift							
Early Types	7.57 ± 1.10	13.15 ± 1.46	12.7 ± 19.3	16.1 ± 22.9	10.36 ± 1.10	5.57 ± 1.38	07%
Intermediate	7.58 ± 0.73	13.33 ± 1.42	13.7 ± 16.8	14.0 ± 11.4	10.46 ± 0.79	5.73 ± 1.59	13%
Late Types	7.67 ± 0.96	14.35 ± 1.42	15.8 ± 25.9	14.7 ± 12.1	10.95 ± 1.04	6.63 ± 1.26	19%

Note: Mean and standard deviation of main variables from MCTQ^{Shift} parameters on workdays by 120 rotating shift workers, grouped separately for early (*n*=56), intermediate (*n*=28), and late types (*n*=36), on the morning, evening, and night shifts. Use of alarm clock is presented in the form of % of people waking up with an alarm clock. Only individuals with complete data sets for all variables were considered so that all variables contain the same number of individuals across the three shifts.

The delayed sleep of late types and the advanced sleep of early types also applied to workdays in regards to all three shifts (see mid-sleep values). The chronotypes did not differ in sleep offset on the morning shift nor on sleep onset on the night shift, but differed considerably in sleep onset on the morning shift, with late types falling asleep much later than early types, as well as in sleep offset on the night shift, where late types sleep in much longer. As such, late types get substantially less sleep on the morning shift but get considerably more sleep on the night shift, compared to early types. Significantly more late types than early types reported to wake up to an alarm clock on the morning shift and considerably more late types reported to wake up to an alarm clock on the night shift. Chronotype differences in sleep latency and sleep inertia were less consistent. For all types and overall, sleep latency was highest on the morning shift-- late types take longer to fall asleep, irrespective of the shift. No clear patterns of sleep inertia could be observed, except that for early and late types alike, it was highest on the night shift.

5.1.2.2 Chronotype and sleep disruption

In order to investigate the association between chronotype and impaired sleep on the morning, evening, and night shift, $MSF^{E}scn$ (without alarm clock) as assessed by means of the $MCTQ^{Shift}$, was correlated to social jetlag, sleep duration, and sleep quality, separately for the morning, evening, and night shifts. Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for all of the variables involved. Non-parametric statistics were therefore computed.

5.1.2.2.3. Chronotype and social jetlag

In order to investigate the association between chronotype and social jetlag, social jetlag values for the different shifts were computed by means of absolute differences between $MSF^{E}scn$ and MSW, for the morning shift (SJ^{M}), for the evening shift (SJ^{E}), and for the night shift (SJ^{N}) separately. Also, for each individual, ØSJ was computed on the basis of a weighted average from the absolute differences between $MSF^{E}scn$ and MSW and between $MSF^{E}scn$ and MSF, separately for the morning, evening, and night shifts. Values were weighed on the basis of the relative occurrence of each work and free day. Table 5.3. presents the descriptive data for these variables, averaged for each chronotype category.

Table 5.3. *Chronotype-Specific Social Jetlag*

Chronotype	Morning Shift ($M \pm SD$)	Evening Shift ($M \pm SD$)	Night Shift ($M \pm SD$)	Ø ($M \pm SD$)	*n*
Early Type	1.64 ± 0.72	0.90 ± 0.78	7.23 ± 1.24	2.40 ± 0.50	110
Intermediate	2.64 ± 0.60	0.56 ± 0.50	6.03 ± 0.84	2.29 ± 0.39	61
Late Type	4.16 ± 1.22	0.67 ± 0.59	4.74 ± 1.22	2.44 ± 0.54	58

Note: Only individuals with complete data sets for all variables were considered.

Compared to early types, late types reported considerably more social jetlag on the morning shift but substantially less on the night shift. Results from Spearman Rho correlations showed that $MSF^{E}scn$ correlates significantly with social jetlag, on the morning shift: ρ (232)= .86, $p \leq .01$, on the evening shift: ρ (238)= -.29, $p \leq .01$ and on the night shift: ρ (231)= - .29, $p \leq .01$. Please note that these correlations remained significant when controlled for influences of age through partial correlations, for the morning shift r (222) = .86, $p \leq .01$, evening shift r (222) = - .30, $p \leq .01$, and night shift r (222) = - .75, $p \leq .01$ respectively.

In addition to this, early types showed substantially higher social jetlag on the night shift than on the morning shift. Though for late types too, social jetlag was higher on the night shift than on the morning shift; the difference in social jetlag between these two shifts was minimal when compared to early types. Results from a within-subject design ANOVA, comparing social jetlag on the morning, evening, and night shift, with chronotype as a between-subject factor (early, intermediate, and late), showed a significant interaction between the effect of shift and chronotype: F (3.22, 357.69) = 142.48, $p \leq .05$, $g = .56$, $1\text{-}\beta = 1$ (Huyn-Feldt was used because of violation of sphericity). $MSF^{E}scn$ did not significantly correlate with ØSJ: ρ (221) = -.04, $p = .53$.

5.1.2.2.4. Chronotype and sleep duration

In order to investigate the association between chronotype and sleep loss on the morning, evening, and night shifts, sleep duration for the different shifts was computed as indicated in Figure 3.2. Please see Table 5.4. for the descriptives. Alpha was set at .01 to correct for Bonferroni. Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for some of the variables involved. Spearman Rho correlations show a significant correlation between $MSF^{E}scn$ and sleep duration, on the morning shift: ρ (230) = -.40, $p \leq .01$; evening shift: ρ (238) = .30, $p \leq .01$; and night shift: ρ (231) = .35, $p \leq .01$. Please note that these associations remained significant when controlled for age through partial correlations, for the morning shift: r (220) = - .46, $p \leq .01$, evening shift: r (220) = .20, $p \leq .01$, and night shift: r (220) = .32, $p \leq .01$.

Results from a within-subject design ANOVA, comparing sleep duration on the morning, evening, and night shift, with chronotype as a between-subject factor (early, intermediate, and late categories) showed a significant interaction between the effect of shift and chronotype: F (3.85, 423.83) = 24.76, $p \leq .05$, g = .18, 1-β = 1 (Huyn-Feldt Statistic was used because of violation of sphericity).

Table 5.4. *Chronotype-Specific Sleep Duration*

Chronotype	Morning Shift (*M* ± *SD*)	Evening Shift (*M* ± *SD*)	Night Shift (*M* ± *SD*)	Ø (*M* ± *SD*)	*n*
Early Type	6.23 ± 1.06	7.32 ± 1.27	5.57 ± 1.38	6.96 ± 1.00	107
Intermediate	5.75 ± 1.04	7.42 ± 0.98	5.73 ± 1.59	6.80 ± 0.92	59
Late Type	5.13 ± 1.44	8.32 ± 1.66	6.63 ± 1.26	7.21 ± 1.14	57

Note: Only individuals with complete data sets for all variables were considered.

In order to investigate the association between chronotype and overall sleep duration (ØSD), individual ØSD was computed by means of a weighted average from values of sleep duration on the morning, evening, and night shifts as well as on the respective free days (SD^M_f; SD^E_f; SD^N_f). The values were weighted in regards to the relative amount of occurrence of each variable. Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for all variables. Spearman Rho correlations showed no significant correlation between MSF^Escn and ØSD: ρ (223) = .11, $p = .11$.

5.1.2.2.5. Chronotype and sleep quality

In order to investigate chronotype differences in sleep quality, individual mean scores of responses from the sleep questionnaire were computed for the morning (SQ^M), evening (SQ^E), and night shift (SQ^N), as well as for free days (SQ^F) as a baseline. An overall average score of sleep quality per individual was computed by means of an algorithmic mean between SQ^M, SQ^E, SQ^N, SQ^F. Scores range from 1-5, with a score of 5 representing high sleep disturbance. Table 5.5. presents the mean scores from the sleep questionnaire for the three chronotype categories.

Table 5.5. *Chronotype-Specific Sleep Disturbance*

Chronotype	Morning Shift (*M ± SD*)	Evening Shift (*M ± SD*)	Night Shift (*M ± SD*)	Free (*M ± SD*)	Ø (*M ± SD*)	*n*
Early Type	2.97 ± 0.78	2.41 ± 0.56	3.31 ± 0.98	1.99 ± 0.54	2.47 ± 0.46	50
Intermediate	3.57 ± 0.71	2.34 ± 0.73	2.89 ± 0.81	1.71 ± 0.53	2.39 ± 0.35	21
Late Type	3.50 ± 0.74	2.33 ± 0.53	2.40 ± 0.79	1.96 ± 0.67	2.35 ± 0.44	23

Note: Only individuals with complete data sets for all variables were considered. The scale goes from 1-5, with a score of 5 indicating highest sleep disturbance.

Late types reported considerably higher sleep disturbance on the morning shift, whereas early types showed substantially higher sleep disturbance on the night shift. Also, late types indicated higher sleep disturbance on the morning shift compared to the night shift, whereas the opposite could be observed in early types. Overall, sleep disturbance was higher on workdays than on free days for all chronotypes. On free days, as well as on the evening shift, early and late types showed similar scores of sleep disturbance.

Results from Spearman Rho showed a significant correlation between $MSF^{E}scn$ and sleep quality on the morning shift: ρ (94)= .37, $p \leq .001$ and on the night shift: ρ (94)= -.48, $p \leq .001$; but not on the evening shift: ρ (94)= - .15, $p = .15$. Also, chronotype did not correlate with sleep quality on free days: ρ (95)= -.15, $p = .14$. Please note that the associations remained significant when controlled for age in partial correlations, for the morning shift: r (91) = .40, $p \leq .01$ and for the night shift: r (91) = - .39, $p \leq .01$.

Results from a within-subject design ANOVA that compared sleep quality on the morning, evening, and night shift with chronotype as a between-subject factor (early, intermediate, late), showed a significant interaction between the effect of shift and chronotype: F (3.36, 153.08) = 9.08, $p \leq .05$, $g = .17$, $1 - \beta = 1$. (Huyn-Feldt was used because of violation of sphericity). Overall, sleep quality across all shifts (ØSQ), did not correlate with $MSF^{E}scn$: ρ (94)= - .16, $p = .12$.

5.1.3 Discussion

As predicted, one can see clear chronotype differences in the timing of sleep on free days and workdays, as well as a significant association between chronotype and the degree of sleep disruption on the morning, evening, and night shifts.

5.1.3.1 Chronotype-specific sleep and wake behaviour

In regards to free days, late types fall asleep and wake-up considerably later than early types, regardless of the prior work schedule. The data also suggest some degree of circadian adjustment to shift work. All three chronotypes show a shift in sleep phase on free days as a function of the prior work schedule. Still, the shift in MSF is considerably larger for late types than for early types. This suggests that late chronotypes may be capable of larger phase shifts. Indeed, simulated shift work experiments have shown greater melatonin phase shifting abilities by late types (as assessed by means of the MEQ, Baehr et al., 1999; Eastman et al., 1995). The increased sleep latency on free days following the night shift in respect to all three chronotypes suggests that the inhibitory effects on sleep, on free days following night work (see project one), are independent of the degree of circadian alignment to night work.

Regarding workdays, the data agree with what one would expect from chronotype differences in circadian alignment to working on the morning, evening, and night shift. As predicted, late types show difficulties in advancing sleep onset on the morning shift and early types show difficulties in sleeping in on the evening and night shifts. With the enforced early wake up on the morning shift and the late bedtime on the night shift little room is left for the expression of inter-individual differences in the sleep phase but they do leave noticeable marks on sleep duration. Whereas late types get considerably less sleep on the morning shift, they get considerably more sleep on the night shift when compared to early types. Early types also get more sleep on the morning shift than on the night shift, while the opposite can be observed for late types. The high use of alarm clocks by late types on the morning shift reflects the difficulty in waking up on the morning shift by late types. On the night shift, considerably more late types than early types wake up with alarm clocks. This suggests that late types could sleep longer than they actually do on night shifts (probably due to domestic/social reasons) and shows that for early types, the premature termination of sleep is generally involuntary. Though all types get most sleep on the evening shift, late types still get substantially more sleep than early types. Since chronotype does not correlate with sleep need (Roenneberg et al., 2003), the reduced sleep in early types on the evening shift is likely to reflect constraints on sleep duration by late work hours.

5.1.3.2 Chronotype differences in sleep disruption

Depending on the shift involved, the three chronotypes experience different degrees of constraints on sleep. On the morning shift, late types show significantly higher social jetlag and reduced duration and quality of sleep compared to early types, while the contrary was observed on the night shift. The results in regards to social jetlag confirm hypothesized chronotype differences in alignment to displaced sleep. Early types require less phase shifting of sleep to align to the displaced sleep of the morning shift, whereas late types require less phase shifting of sleep to align to the displaced sleep of the night shift.

Overall, these findings support the assumption of tolerance to shift work being a reflection of the degree of misalignment between the sleep-wake cycle and the circadian clock. The observed associations between chronotype and sleep disruption remain when controlled for age, revealing results inconsistent with claims that the effects of chronotype are caused by intervening influences of age (Akerstedt, 1999; Seo et al., 2000). On free days, as well as on the evening shift, early and late types show similar scores of sleep disturbance, underlining that the observed chronotype differences result from the displaced sleep on the morning and night shifts.

With the exception of one study by Torsvall and Akerstedt (1980), the observed findings disagree with the few studies that have examined chronotype differences in sleep on the morning and night shifts. A study by Seo et al. (2000), as well as a study by Khaleque (1999), did look at differences in sleep duration between morning and late types, as assessed by the Morningness-Eveningness Questionnaire (MEQ). Seo et al. found a shorter sleep duration in late types on both, the morning and the night shift, whereas Khaleque found no differences between morning and late types in seep duration on any of the three shifts, with all three chronotypes showing a drastic reduction in sleep duration on the night shift compared to the morning and evening shifts (which did not differ in sleep duration). Also, opposed to current findings, Khaleque found better sleep quality in late types for all three shifts. The differences in observed findings may very well be due to differences in measurements used. Being a measure of preference instead of actual timing of sleep, the MEQ may be less sensitive in detecting effects of work schedule on sleep duration.

Another element to consider is differences in population, which may help explain the incongruent findings. The study by Seo et al. took place in Japan and the one by Khaleque in India. From the MCTQ data bank of day workers, it is known that mid-sleep on free days is generally earlier in Japan and in India, compared to Western Europeans (likely due to differences in zeitgeber strength and length of exposure). It would be interesting for future research to investigate the impact of geophysical factors, such as climate, on the sleep-wake behaviour in shift workers.

Finally, when averaged across the three shifts, chronotype differences in social jetlag, sleep duration, and quality are balanced out. This shows that ultimately, the three chronotypes experience the same degree of constraints in rotating workers. This may explain why many studies have failed to find chronotype differences in tolerance to shift work (Breithaupt, 1978; Costa et al., 1989; Härmä, 1995; Kaliterna, Vidacek, Prizmic, Radosevic-Vidacek, 1993; Kaliterna, Vidacek et al., 1995; Tamagawa, 2007), as tolerance is generally examined in terms of overall values (e.g. somatic health, psychophysiology, sleep disturbance, fatigue, and mood). Accordingly, a study by Folkard and Hunt (2000) found that early types showed better tolerance among day workers whereas late types showed better tolerance among night workers.

5.2 Chronotype and Psychological Well-being During Work Hours

In this somewhat experimental study, chronotype differences in subjective well-being during work times on the morning, evening, and night shifts will be explored. Based on the obtained results of study 5.1, chronotype differences in well-being on the morning and night shifts are predicted. Specifically, on the morning shift, late types are expected to have lower well-being than early types, whereas on the night shift, early types are expected to have lower well-being than late types. Also, early types are expected to have better well-being on the morning shift than on the night shift. Late types on the other hand are expected to have better well-being on the night shift than on the morning shift. Finally, it is predicted that the association between chronotype and well-being will be balanced out across the three shifts, meaning that chronotype should not correlate with well-being when averaged across the three shifts.

5.2.1 Methods

5.2.1.1 Participants

A total of 75 male rotating shift workers (three-shift-model), employed at a VW power plant, volunteered to participate in this study. The participants were recruited with the assistance of medical staff from VW. All shift workers worked on a rapidly backward rotating shift model. After removing participants who reported waking up with an alarm clock, 54 remained (30 early types, 12 intermediate types, and 12 late types). The mean age of the participants was 45 years (age range: 22–57 years). The average shift work employment was 21 years.

5.2.1.2 Materials

Materials used in this study were the $MCTQ^{Shift}$ for the assessment of chronotype and the Basler Befindlichkeitsskala for the assessment of well-being. Scores (mean) range from 1 to 7, with a high score indicating high well-being and a low score indicating major depression. Please see General Methods for a detailed description of the materials used.

5.2.1.3 Procedure

The participants first filled out the $MCTQ^{Shift}$ at their workplace during paid work time. The study required shift workers to report their current subjective well-being by means of the Basler-Befindlichkeitsskala on three separate occasions: once on the morning shift, once on the evening shift, and once on the night shift. The assessment of well-being always took place on the second working day, three hours after work began. There were 3-5 days between each assessment. The study took place between December 2006 and February 2007.

5.2.2 Results

Mean scores of well-being were computed for each individual, separately for the morning, evening, and night shift in a subsample of 54 shift workers from the three-shift-model. An overall average score of well-being was computed by means of an algorithmic mean between the three shift-specific scores. Table 5.6. presents descriptive statistics for well-being on the three shifts, grouped into three chronotype categories.

Table 5.6. *Chronotype and Well-Being at Work*

Chronotype	Morning Shift (*M* ± *SD*)	Evening Shift (*M* ± *SD*)	Night Shift (*M* ± *SD*)	Ø (*M* ± *SD*)	*n*
Early Type	4.46 ± 1.11	5.09 ± 0.76	4.18 ± 0.98	4.58 ± 0.76	30
Intermediate	4.34 ± 0.91	5.26 ± 0.63	4.13 ± 1.10	4.58 ± 0.73	12
Late Type	4.10 ± 0.81	5.47 ± 1.06	4.83 ± 0.87	4.80 ± 0.74	12

Note: Only individuals with complete data sets for all variables were considered. The scale goes from 1 (high depression) to 7 (high well-being)

Late types reported considerably lower well-being on the morning shift compared to early types whereas early types reported lower well-being on the night shift compared to late types. In order to see whether the observed findings were statistically significant, inferential statistics were computed. Results from the Kolmogorov-Smirnov test showed no significant deviation from normality for all scores involved. Alpha was set at .01 to correct for

Bonferroni. Results from Pearson-Product Moment correlations showed that $MSF^{E}scn$ correlates significantly with well-being on the night shift: r (55) = .35, $p \leq .01$ but not on the morning shift: r (54) = - .10, p = .45 and on the evening shift: r (54) = .29, p = .03. When controlled for age, the correlation between well-being and chronotype on the night shift remained significant: r (52) = .29, $p \leq .05$. Overall well-being did not correlate with $MSF^{E}scn$: r (54) = .22, p = .12.

Also, late types showed better well-being on the night shift than on the morning shift, whereas early types showed better well being on the morning shift than on the night shift. Results from a within-subject design ANOVA, comparing well-being on the morning, evening, and night shifts, with chronotype as a between-subject factor (early, intermediate, and late), and controlling for age, showed a significant interaction between the effects of shift and chronotype: F (4, 100) = 2.50, $p \leq .05$, g = .09, $1 - \beta = .69$, indicating that the well-being of the three chronotypes was differentially affected by the three shifts.

5.2.3 Discussion

Supporting predictions, the findings demonstrate chronotype-specific differences in well-being across the different shifts. When asked to report current subjective well-being on the night shift, early types indicate significantly lower well-being than late types. This association remained when controlled for age, contradicting claims that chronotype differences in tolerance may be due to intervening influences by age (Akerstedt, 1999; Seo et al., 2000). Also, as predicted for early types, well-being improves on the morning shift but for late types it decreases substantially compared to the night shift. The correlation between chronotype and well-being did not hold for the morning shift and for the evening shift, but a tendency in the right direction could be observed.

As chronotype differences on the different shifts have generally been ignored, studies have failed to detect these marked inter-individual differences in well-being. A number of studies however have shown a correlation between chronotype and mood in day workers, with late types showing more depressed mood than early types (Giannotti, Cortesi, Sebastiani, & Ottaviano, 2002; Hasler, Allen, Sbarra, Bootzin, and Bernet, 2010; Hidalgo, Caumo, Posser et al., 2009; Mecacci & Rocchetti, 1998; Randler, 200; Wittman et al., 2006). As typical day work schedule represents more constraints on late types than early types, it has been argued that the decreased well-being in late types results from increased social jetlag in late types (Wittman et al., 2006). The current findings support this claim. Interestingly, a recent study on the effect of sleep deprivation on depressed mood showed a strong effect of circadian preference (Selvi, Gulec, Argargun, Besiroglu, 2007). While morning types showed a significant increase in depression after a night of sleep deprivation, late types showed a significant decrease in depression. As such, shift work may differentially affect the mood of early and late types.

5.3 Attempts to Find Predictors for Health in Workers

This study examines whether observed chronotype differences in tolerance to shift work predict health. To start with, chronotype-specific scores of health problems as well as social jetlag will be explored for rotating shift workers from the three-shift model (with night shift) and the two-shift-model (without night shift), as well as for day workers to establish differences between the populations. Also, chronotype differences in smoking behaviour will be explored. Studies that have shown that smoking is more prevalent in shift workers (Boggild and Knutsson, 1999, Metz, 1960). Wittmann et al. (2006; 2010) have found a strong correlation between cigarette smoking and chronotype in day workers, with late types being much more likely to be smokers than non-smokers. The authors have argued that the heightened prevalence of smoking results from the increased social jetlag in late types due to constraints by early work hours. This may account for the increased smoking in shift workers, as shift workers likely experience high social jetlag.

The second aim of the present study will be to investigate whether the observed tolerance variables in studies 5.1 and 5.2, subject to influences by chronotype, predict the health of workers. From a large databank of 790 workers, significant predictors of health will be investigated. The effect of shift work on health is a complex and dynamic topic of investigation, incorporating both external and internal factors. There are numerous psychological and lifestyle risk factors that can act as confounds, mediators, or modifiers when predicting health in shift workers, such as attitudes to health, coping strategies, perceptions of stress, obesity, age, and sex (Boggild & Knutsson, 1999; Colligan and Tepas, 1986; Di Lorenzo et al., 2003; Fujino et al., 2006; Knutsson et al., 1995; Lal and Craig, 2002; Lazarus & Folkman, 1984; Lazarus and Launier, 1978; Murices and Monteil, 1964; Niedhammer, Lert, & Marne, 1996; Ruggiero 2003; Samaha et al. 2007; Smith et al. 2005; Suwazono et al., 2006; Tamagawa et al. 2007; Tasto, 1976; van Amelsvoort, Schouten, Maan, Swenne, & Kok, 2000). It is predicted that primary tolerance variables--social jetlag, sleep duration, sleep quality, and well-being-- will predict health beyond external factors such as stress, locus of control, age, BMI, sex, and smoking. This databank is well suited for examining such a research question, as it consists of a highly variable sample due to the different work schedules involved.

5.3.1 Methods

5.3.1.1 Participants

A total of 790 workers volunteered to participate in this study. The sample consisted of 164 (102 women, 62 men, M_{age} = 36.7, age range: 19-55 years) rotating shift workers from the three-shift-model, 411 (137 women, 270 men, and four of unknown sex, M_{age} = 39.6, age range: 18-62 years) rotating shift workers from the two-shift-model, 45 permanent morning workers (39 women, five men, and one of unknown sex, M_{age} = 44.3, age range: 34-54 years), 37 permanent evening workers (35 women and two men, M_{age} = 39.9, age range: 31-53 years), 28 permanent night workers (three women, 24 men, and one of unknown sex, M_{age} = 42.8, age range: 27-62 years), and 105 day workers (26 women, 78 men and one of unknown sex, M_{age} = 36.7, age range: 16-60 years). The shift workers were OSRAM and Siemens employees at manufacturing plants in Augsburg, Eichstätt and Cham. The day workers were OSRAM and Siemens employees at the same manufacturing plants as the shift workers.

For the computation of social jetlag, a larger sample was used, consisting of 371 (111 women and 260 men, M_{age} = 39.8, age range: 19-57 years) shift workers from the three-shift-model, 420 (141 women, 275 men and four of unknown sex, M_{age} = 39.6, age range: 18-62 years) from the two-shift-model, and 327 (128 women, 197 men and one of unknown sex, M_{age} = 38.3, age range: 16-63 years) day workers. The shift workers were OSRAM and Siemens employees at manufacturing plants in Augsburg, Eichstätt and Cham. The day workers were OSRAM and Siemens employees at the same manufacturing plants as the shift workers, as well as employees of OSRAM head office in Munich.

5.3.1.2 Materials

The materials used in this project were the MCTQ and $MCTQ^{Shift}$ for the assessment of sleep demographics and chronotype, as well as a set of questionnaires, including the Multidimensional Health Locus of Control Scale, the Perceived Stress Questionnaire, the WHO-5 Well-Being Index, and two questionnaires from the Standard Shift Work Index (SSI) -- the Sleep Questionnaire and the Physical Health Questionnaire. Additionally, demographic questions were assessed, such as age, gender and BMI. Subjects were also asked to indicate whether they were a smoker (yes/no) and if yes, the amount of cigarettes on average smoked per day. Please see General Methods.

5.3.1.3 Procedure

The set of questionnaires were distributed to the shift workers at their workplace, to be filled out by the participants at their home. The set included an informed consent, stating the nature of the participation and the participants' right to withdraw from the study at any time. Participants had the option to indicate whether they wanted a personalized evaluation of their chronotype, which was confidentially allocated to the participant, in a sealed envelope. All questionnaires were given a code number so as perform analyses in an anonymous fashion. The questionnaires were collected between July 2007 and October 2008.

5.3.2 Results

First, shift workers with and without night work were compared to day workers in scores of health, overall social jetlag, and prevalence of smoking to examine differences between these populations. Next, predictors of health were explored to determine the unique contribution of sleep and well being in predicting workers' health.

5.3.2.1 Health, social jetlag and smoking

The participants were grouped into three chronotype categories, as described in project one, whereby only individuals not waking up with an alarm clock on free days were considered. For each individual, a mean health score (digestive and cardio-vascular) was computed as well as a total score of social jetlag by adding the accumulated social jetlag over a period of six weeks, so as to be able to compare workers from different work models. Table 5.7. presents the descriptive data for average social jetlag, health and prevalence of smoking, for three work models (three-shift-model, two-shift-model, and day workers), grouped into chronotype categories (permanent work models were excluded from consideration due to too small sample size). All three samples consisted of a much higher number of early types than intermediate and late types.

Table 5.7. *Health, Smoking, and Social Jetlag in Shift Workers and Day Workers*

	Health Problems ($M \pm SD$)	Smokers (%)	*n*	Average Social Jetlag ($M \pm SD$)	*n*
Three Shift Model					
Early	1.75 ± 0.44	37.3%	49	94.54 ± 28.40	104
Intermediate	1.73 ± 0.42	47.6%	20	90.49 ± 25.70	60
Late	1.85 ± 0.52	87.0%	22	95.97 ± 27.30	56
Two Shift Model					
Early	1.77 ± 0.52	27.4%	104	37.32 ± 15.34	107
Intermediate	1.67 ± 0.49	35.5%	70	48.11 ± 14.84	73
Late	1.59 ± 0.39	60.0%	69	72.44 ± 28.14	71
Day Workers					
Early	1.51 ± 0.41	15.0%	69	29.00 ± 17.44	178
Intermediate	1.47 ± 0.25	25.9%	9	46.86 ± 14.19	58
Late	1.60 ± 0.34	35.9%	10	91.84 ± 36.40	38

Note: Only individuals with complete data sets were included. Scores of health problems range from 1 (low health problems) to 4 (high health problems).

5.3.2.1.1 Health

To compare health between the three work models, a complex analysis of variance (ANCOVA) was computed with health as a dependent variable and shift models and chronotype as between-subject factors. Results showed a significant effect of shift model on health: F (2,430) = 3.62, $p \leq .05$, g = .06, 1-β =1, but no significant effect of chronotype: F (2,430) = 0.27, p = .76, g = .00, 1-β =.09, and no significant interaction between the effects of work model and chronotype: F (4, 430) = 1.33, p =.26 , g = .01, 1-β =.41. Note that the estimation of effect size was very small. Post-hoc pair wise comparisons revealed that day workers differ significantly in health from shift workers working on the three-shift-model (with night shift), but not from shift workers working on the two-shift model. Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for health. Results from the Kruskal-Wallis test confirmed the above finding: χ^2 (2, n = 637) = 19.11, $p \leq .05$, g = .06, 1-β = 1.

5.3.2.1.2 Social jetlag

One can see that all three chronotypes showed considerably more social jetlag on the three-shift model (with night shift) than on the two-shift model (without night shift). When compared to day workers, the three chronotypes revealed very different results. Regarding early types, day workers reported less social jetlag than shift workers from the three-shift model. However, late types showed similar social jetlag regardless of their positions as day workers or shift workers. In day workers, the discrepancy in social jetlag between the three chronotypes was largest. Overall, early types showed greater differences in social jetlag between the different work models compared to late types. Results from a univariate analysis of variance (ANCOVA) with social jetlag as a dependent variable, and both work model and chronotype as independent variables, showed that the three work models differed significantly in social jetlag: F (2, 736) = 210.39, $p \leq .05$, $g = .36$, $1\text{-}\beta = 1$. Post-hoc pair-wise comparison showed that day workers only differed from the three-shift-model, not from the two-shift-model. Also there was a significant interaction between the effect of shift model and chronotype on social jetlag: F (4, 736) = 31.39, $p \leq .05$, $g = .15$, $1\text{-}\beta = 1$. This means that the effect of shift model on the degree of social jetlag is different for the three chronotypes. Results from the Kolmogorov-Smirnov test showed a significant deviation from normality for social jetlag. Results from the Kruskal-Wallis test confirmed the above finding: χ^2 (2, n = 996) = 380.40, $p \leq .05$, $g = .15$, $1\text{-}\beta = 1$. Social jetlag correlated with digestive health: ρ (577) = .09, $p = .04$, but not with cardio-vascular health: ρ (573) = - .02, $p = .70$. When corrected for Bonferroni, the correlation between social jetlag and digestive health became non-significant.

5.3.2.1.3 Smoking

One can see a much higher percentage of smokers in shift workers than in day workers, particularly in the three-shift model (with night shift). This applied to all three chronotypes but in particular to late types. To explore the relationship between chronotype, social jetlag and smoking, a logistical regression was computed with the binary variable “smoker/non-smoker” as a dependent variable and the variables social jetlag and chronotype (MSFscn) as independent variables. Since this is an exploratory analysis, a forward regression was computed in order determine the unique predictive significance of the independent variables. Results showed that smoking behaviour was significantly predicted by chronotype: *Wald* (1) = 20.63, $\beta = .66$, $p \leq .05$, and social jetlag *Wald* (1) = 15.51, $\beta = .03$, $p \leq .05$, independent of each other. Together, the model explains 11% of the observed variance in smoking behaviour. Multi-collinearity was tested by means of tolerance and VIF. Results showed no problems of multi-collinearity based on criteria by Menard (1995) and Myers (1990).

5.3.2.2 Predictors of health

To determine the unique contribution of main study variables in predicting health scores, a multiple regression analysis was performed. At first, a regression analysis was computed whereby all study variables were entered at once (as advised by Field (2000)) so as to establish the importance of the unique predictors and to remove non-significant variables from further analyses. Health was entered as a dependent variable and the main predictors --average work sleep duration, average social jetlag, overall sleep quality, and average well-being-- were entered as predictors. Additionally, sex as well as variables known to predict health were entered into the regression: age, BMI, being a smoker (binary), and average scores of stress and internal locus of control (see General Methods for an explanation of how these scores were obtained). All study variables were tested for multi-collinearity by means of the tolerance and VIF statistic. Results showed no problem of multi-collinearity based on criteria by Menard (1995) and Myers (1990). The initial results showed that both average social jetlag and chronotype were non-significant predictors of health: they were therefore removed from subsequent analyses.

Next, a two-step forced-entry multiple regression was performed with health as a dependent variable to determine the unique contribution of the main study variables. In the first step, variables known to predict health were entered: Age, sex, BMI, stress, smoking, and locus of control. Results showed that variables from step 1 contribute 33% of the variance in health. Overall, women, smokers, and people of older age and higher BMI reported increased health problems. Replicating past research, stress and locus of control also were significant predictors of health. The most important predictor of health was perceived stress, whereby individuals with high stress reported significantly more health problems. People with a low feeling of internal control reported significantly more health problems than individuals with a high locus of control. All entered variables predicted health, independent of each other.

In step 2, main study variables --work sleep duration, sleep quality, and well-being-- were added to the model (see Table 5.8.). Supporting predictions, main study variables significantly added to the model. All main study variables uniquely predicted health independent from each other, as well as from variables known to predict health. Specifically, short sleep duration, high sleep disturbance, and reduced well-being independently predicted decreased health. The addition of the new predictors caused a 6% increase in the amount of variance that can be explained by the model. Altogether, the model explains 39% of the variance in health.

Table 5.8. *Hierarchical Regression Analysis for Variable Predicting Health Problems*

Predictor Variables	β	R^2	R^2 Change
Step 1		.33**	.33**
Stress	.44**		
BMI	.17**		
Sex	.15**		
Locus of Control	-.15**		
Age	.14**		
Smoker	.10*		
Step 2		.39**	.06**
Well-being	-.23**		
Sleep Duration	-.12**		
Sleep Quality	-.08*		

Note: Values and significance levels are given for each variable at the point of entry into the regression equation (n = 790). * $p \leq .05$, ** $p \leq .01$

5.3.3 Discussion

Shift workers with night work have more health problems and a higher prevalence of smoking compared to day workers. As predicted, sleep and well-being significantly predict workers' health.

5.3.3.1 Increased health problems in shift workers

The current results support findings by other studies showing increased health problems in shift workers compared to day workers (Aanonsen 1959; Alfredsson, Spetz, & Theorell, 1981; Carpentier, et al., 1977; Colquhoun, Knauth, & Ghata, 1977; Knutsson et al. in 1986; 1995; Tenkanen et al., 1998; Rutenfranz, Angersbach et al., 1980), whereby only shift workers with night work showed increased health problems, as has also been observed by Nakamura et al. (1997) and Alfredsson et al. (1985).

Also, shift workers with night work showed significantly higher social jetlag when compared to day workers, as well as to shift workers whose schedule did not include night work. Yet, differences in social jetlag between day workers and shift workers with night work could only be observed for early types. Late types showed as high social jetlag amongst day workers than amongst shift workers with night work. Overall social jetlag only correlated marginally with digestive health and no correlation could be observed with cardio-vascular health. The reason for the low association between social jetlag and health may be due to a very small effect size and high inter-individual differences in coping and lifestyle. Also, it may be the case that social jetlag, as a measure of displaced sleep, cannot be totalled in terms of degree of displacement over the course of six weeks but that it should account for the direction of displacement and the amount of shifting between directions. Compared to day workers, shift workers have a much stronger social jetlag on both the morning and the night shifts. However, this effect is balanced out by the low social jetlag on the evening shift, when averaging or totalling social jetlag. It could be that the effect of displaced sleep is more of a categorical nature rather than a continuous effect. Future research should take a closer look at this.

Also, when analyzing the effects of health, shift work research commonly encounters a problem called the *healthy worker effect* --the inherent bias in health data stemming from prior processes of self-selection in the workforce-- whereby sick individuals are more prone to drop-out of employment, rendering the shift work population healthier than day workers (Knutsson, 2003, 2004; Knutsson & Akerstedt, 1992). As such, it may well be that the observed health problems in shift workers are underrepresented.

5.3.3.2 Increased smoking in shift works

Replicating findings by other studies (Boggild and Knutsson, 1999, Metz, 1960), a high prevalence of smoking in shift workers was observed. The prevalence of smokers was more than double in shift workers with night work than in day workers, for both, early and late types. While all chronotypes are more at risk to be a smoker when working night shift than not, late types are particularly prone to be smokers when working night work, reaching a percentage as high as 87% in shift workers with night work. In agreement with Wittman et al. (2006; 2010), social jetlag proved to be an important predictor of smoking behaviour, independent of chronotype. In addition to this, when considering the fact that in late types absolute values of social jetlag are similar between day and shift workers with night work, other stressors involved with working nights seem to play an influential role as well. For example, Knutsson (2004) has suggested that shift workers may use cigarettes as coping means to counteract fatigue. The present results expand on this thought by suggesting that late types are more likely to use cigarette smoking as a coping strategy than early types.

Finally, it is worth noting that all three samples consisted of an unequal distribution of chronotype. There were considerably more early types in all three samples. This disagrees with studies reporting an overrepresentation of late types in the three-shift model (Knutsson and Akerstedt, 1992; Petru, Wittman, Nowak, Birkholz, & Angerer, 2005).

5.3.3.3 Sleep and well-being predict health

Overall, there is no reason to expect chronotype differences in health, except in the context of specific external constraints. In rotating workers, effects on health may have been balanced out by opposing constraints by the morning and night shift but in permanent shift models, chronotype differences in health should be expected. Unfortunately, the sample size of non-rotating shift workers in the current study was too small to accurately analyze this. However, if the observed increased health problems in shift workers underlie a misalignment between the sleep-wake cycle and the endogenous circadian clock, one should expect that parameters known to be influenced by chronotype on the morning, evening, and night shifts, significantly predict health. The present findings support this. Well-being, sleep duration, and sleep quality, shown to be affected by chronotype on the morning, evening, and night shifts (in studies 5.1 and 5.2 of this project), each uniquely predicted health. Moreover, these findings predicted inter-individual differences in health above and beyond variables already known to predict health such as age, sex, BMI, stress, locus of control, and smoking.

Social jetlag, *per se,* did not predict health. This suggests that it may not be the misalignment *per se* but rather the effect such a misalignment has on sleep and well-being that ultimately affects health. This agrees with a study by Drake et al. (2004), showing a three time increase in risk of developing stomach ulcers in night workers who reported less than 5.5 hours of daily sleep compared to night workers reporting more than 6.4 hours of daily sleep. Also numerous studies have shown an association between negative mood and somatic health problems in shift workers (Akerstedt, 1980; Hennig et al., 1998; Parkes, 2002; Tamagawa, 2007).

5.4 Conclusion

The current findings support the notion that a misalignment between the sleep-wake cycle and the endogenous clock disturbs sleep and well-being. As predicted, early types showed better tolerance to the morning shift, whereas late types showed better tolerance to the night shift. On the morning shift, late chronotypes showed significantly higher social jetlag and decreased duration and quality of sleep when compared to early types, and an overall reduced tolerance when compared to the night shift. The reverse was observed for early types. Also, during the night shift, late types feel significantly better than early types. In turn, the combined effects of chronotype on sleep and well-being in the face of constraints by work schedule increase the variability of individuals to cope with shift work. Duration and quality of sleep along with well-being significantly predict health. Overall, the present findings agree with theories pertaining that health problems in shift work stem from a conflict between displaced work hours and the output of the circadian clock (Akerstedt, 2003). However, the current results expand upon this by stressing the importance of mediators (such as duration and quality of sleep and psychological well-being) and how chronotype affects and modulates them.

6 Overall Discussion

The aim of this doctoral dissertation was to explore shift worker sleep and wake behaviour in the field, with a particular emphasis on chronotype-specific differences and how these predict tolerance to shift work. In order to do so, a shift-work version of the MCTQ ($MCTQ^{Shift}$) was first evaluated and validated. The main findings will be thematically summarized below, followed by a discussion of study limitations. The chapter concludes by highlighting the relevance of obtained findings in developing practical recommendations for improving workers' health, well-being, and safety.

6.1 Evaluation and Validation of the $MCTQ^{Shift}$

In comparison to daily sleep logs, the $MCTQ^{Shift}$ proved to be a sensitive and valid instrument for the assessment of shift worker sleep-and-wake behaviour, most importantly for the assessment of sleep phase by means of mid-sleep values. This finding applied to the morning, evening, and night shift, as well as to their respective free days. $MCTQ^{Shift}$-assessed sleep phase also correlated highly with the widely used Morningness-Eveningness Questionnaire (MEQ), as well as with objective behavioural data of activity and rest rhythms as assessed by means of actimetry. The $MCTQ^{Shift}$ thereby fulfils the same test criteria for validity as the MCTQ for day workers (see Kantermann et al., 2007; Kuehnle, 2006; Zavada et al., 2005).

The $MCTQ^{Shift}$ revealed to be an excellent instrument for the assessment of chronotype in shift workers. Like day workers, shift workers can be chronotyped on the basis of their timing of sleep on free days, whereby free days following an evening shift have shown to be the best choice. When corrected for sleep debt, mid-sleep on free days following an evening shift ($MSF^{E}scn$) shows a distribution, mean, and variance indistinguishable from the sleep-corrected mid-sleep on free days (MSFscn) in day workers. As observed in day workers, MSF correlates better to the MEQ than sleep onset and sleep offset on free days, with the highest correlation being obtained for MSF following the evening shift. This correlation becomes even better when corrected for sleep debt. For shift workers that do not work evening shifts, expected $MSF^{E}scn$ scores can be computed on the basis of observed data from shift workers that rotate between all three shifts.

Given the benefits in time efficiency, phase assessment by means of the $MCTQ^{Shift}$ is an excellent alternative to sleep logs and physiological measures. The relative ease of assessing sleep-wake behaviour and chronotype in shift workers by means of the $MCTQ^{Shift}$ makes this questionnaire not only useful for research purposes but also for physicians.

6.2 Sleep and Wake Behaviour in Shift Workers

Supporting laboratory findings (see Akerstedt, 2003; Strogatz, Kronauer, & Czeisler, 1986), the current fieldwork data ($MCTQ^{Shift}$ and daily sleep logs) show a shortening in sleep length on the morning and the night shifts due to difficulties involved in advancing sleep onset on the morning shift and in delaying wake-up on the night shift. These findings support the notion of a misalignment between the sleep-wake cycle and the circadian clock on the morning and night shifts. As physiology does not align with the displaced sleep, the normal temporal relationship between the sleep-wake cycle and the endogenous pacemaker is disturbed, rendering sleep difficult to initiate and to maintain.

Having never been systematically examined before this study, the results from free days shed new light on current knowledge. On free days, the sleep-wake cycle maintains a diurnal orientation and remains remarkably stable across the morning, evening, and night shifts, suggesting an absence of effect by previous displacement of sleep due to shift work. Sleep log data, from 22 shift workers asked to work four continuous weeks of night work, demonstrated that the diurnal orientation and constancy of the sleep-wake cycle on free days applies to non-rotating night workers. The obtained data therefore agree with studies that demonstrate a lack of circadian adjustment to shift work.

Yet, a 30-60 minute shift in the timing of sleep on free days could be observed in rotating shift workers, as a function of the direction of displaced sleep on the previously worked on shift. This suggests that some circadian adjustment to shift work does occur. It is unlikely that the observed effect derives from entrainment to light at the work place, as no difference could be observed between shift workers that work in normal versus bright light environments, unless normal light is as effective in entraining the circadian clock of shift workers as bright light. This however seems unlikely, as numerous laboratory studies have shown strong phase shifting effects in response to manipulations of light intensity and colour spectrum (Dawson et al., 1993; Gonfier et al., 2004; Homma et al., 1987; Kubota et al., 2002; Revel et al., 2005; Wright & Lack, 2001; Wright et al., 2004).

The shift in MSF across the three schedules could be a result of entrainment to the adapted sleep phase on the previously worked-on shift. Ultimately, the timing of sleep and activity decides when eyes are to be open for entrainment by light. In agreement with this, two laboratory studies by Burgess and Eastman have shown that scheduled displacement in bedtime and awakening could phase shift melatonin rhythms (Burgess & Eastman, 2004, 2006). Also, experiments on rodents and humans have shown phase shifting effects by scheduled activity (Buxton et al., 2003; Mrosovsky, 1988; Turek, 1989). This supports the notion of a complex feedback loop mechanism between the circadian clock and the sleep-wake cycle, whereby the circadian clock not only orchestrates but is itself subject to being modified by the sleep-wake cycle (see Mistlberger & Skene, 2005).

6.3 Chronotype-Specific Sleep and Wake Behaviour in Shift Workers

Supporting predictions, notable chronotype differences in shift worker sleep and wake behaviour were found. Regarding free days, late types report going to bed and waking up at later times than early types for all free days. The previously observed shift in the timing of sleep on free days across the different shift schedules could be observed in all three chronotypes, with late types however showing overall greater phase shifting than early types. This supports laboratory findings regarding larger phase shifting abilities in late types (Baehr et al., 1999; Eastman et al., 1995). In regards to workdays, the findings agree with what one would expect from chronotype differences in circadian alignment to working on the morning, evening, and night shifts. Whereas late types have difficulties in advancing their sleep onset on the morning shift, early types have difficulties sleeping in on the evening and night shifts, resulting in a chronotype-specific reduction in sleep length on the different shifts.

6.4 The Role of Chronotype in Helping Shift Workers Sleep and Feel Better

As predicted, chronotype plays a decisive role in predicting tolerance to working on the morning, evening, and night shifts. Chronotype correlates to the degree of misalignment to the displaced sleep, with considerably lower social jetlag in early types on the morning shift and considerably lower social jetlag in late types on the evening and night shifts. This supports findings by Crowley et al. (2003) showing chronotype to be the most important predictor for determining whether a participant’s circadian rhythms would sufficiently delay to align with daytime sleep.

On the morning shift, early types display significantly longer and better quality sleep than late types. On the night and evening shifts, however, late types show significantly longer and better sleep than early types. These findings agree with results from laboratory studies showing a decrease in sleep duration and quality as a function of degree of misalignment between the sleep-wake cycle and the circadian clock (Akerstedt et al., 2007; Dumont et al., 2001; Hennig et al., 1994; Quera-Salva et al., 1997; Roden et al., 1993).

Results from an experiment requiring 54 shift workers to report their current subjective well-being on three separate occasions, once on the morning, once on the evening, and once on the night shift, revealed differential constraints on the mood of late and early chronotypes. While early types feel better on the morning shift than on the night shift, the reverse can be observed for late types. Chronotype differences in well-being were especially pronounced on the night shift, with early types showing significantly lower well-being than late types.

The shift-specific effects were balanced out in shift workers that work all three shifts. The three chronotypes did not differ in overall social jetlag, sleep duration, sleep quality, and well-being, when these were averaged across all shifts. This may explain the often inconsistent findings regarding chronotype as a predictor to shift work tolerance, as studies generally do not differentiate between the different shift schedules (Breithaupt et al., 1978; Costa et al., 1989; Härmä, 1995; Kaliterna, Vidacek, Prizmic, Radosevic-Vidacek, 1993; Kaliterna, Vidacek et al., 1995; Tamagawa et al., 2007). Further, a self-selection has been shown to occur in which early types are more likely to work permanent morning shifts and late types more likely to work permanent night shifts (Paine, Gander, and Travier, 2006; Petru et al., 2005).

6.5 Sleep and Well-Being Predict Better Health

In agreement with other findings (Aanonsen 1959; Alfredsson, Spetz, & Theorell, 1985; Angersbach et al., 1980; Knutsson et al., 1986; Rutenfranz et al., 1977; Tenkanen et al., 1998, 1995), the present results show significantly more health problems (digestive and cardio-vascular symptoms) in shift workers than in day workers. However, only shift workers whose schedule included night work differed significantly in health from day workers. This suggests that night work presents a special risk for health. Also, shift workers with night work show significantly more social jetlag than shift workers without night work, with the latter showing no difference in social jetlag in respect to day workers. These findings support Reinberg's view on the importance of circadian stability (see Reinberg, 2008).

Also, supporting other studies (Boggild & Knutsson, 1999), the current data show a substantial increase in the prevalence of smoking in shift workers, compared to day workers. Though late types are more likely to be smokers, independent of their work schedule, all chronotypes are substantially more likely to be smokers when working night shifts, with late types reaching a percentage as high as 87%. This suggests a heightened risk of smoking as a function of increased demands by work schedules.

The observed influence of chronotype on sleep and well-being in the face of constraints by work schedules increase the variability of individuals to cope with shift work. Results from a diverse sample consisting of rotating and permanent shift workers, as well as day workers, showed that duration of sleep, quality of sleep, and well-being each uniquely predict health-- above and beyond factors known to be associated with health, such as age, sex, BMI, stress, locus of control, and smoking behaviour.

6.6 Study Limitations

Due to the correlational design of the study, no directional relationship can be inferred from the observed results. We cannot conclude with confidence that reduced sleep duration, quality, and well-being cause health problems. Still, there are convincing experimental findings suggesting a direct causal link between sleep, as well as psychological well-being, and health. Experimental studies have shown that sleep deprivation decreases immune functioning through reduced natural killer cell activity, suppressed interleukin -2 production, and increased levels of circulating prointflammatory cytokines (Irwin, Wang, Campomayor, Collado-Hidalgo, & Cole, 2006; Vgontzas et al., 2004) and reduced antibody response to hepatitis A (Lange, Perras, Fehm, & Born, 2003) and influenza immunizations (Spiegel, Sheridan, & Van Cauter, 2002). A recent study by Cohen and colleagues found that poor sleep efficacy and short sleep duration during two weeks preceding viral inoculation of RV-39 in quarantine conditions was associated with an increase in self-reported severity of illness symptoms as well as objectively measured virus-specific antibody concentration (Cohen, Doyle, Alper, Janicki-Deverts, & Turner, 2009). The authors report a substantial risk of developing illness with getting less than seven hours of sleep per night.

Also depressed mood is held to constitute a significant risk factor for the development and progression of some illnesses, such as coronary heart disease, diabetes, cancer, chronic pain, disability, chronic fatigue, and obesity (see Steptoe, 2006). It is also well recognized that depressed mood contributes to the development of various somatic disorders (see Hazen, Soudry, and Cosoli, 2008).

Certainly the strongest evidence for a causal relationship between variables is obtained by means of experimental manipulation. Yet, despite the obvious ethical issues underlying the non-experimental approach to some of the current investigations, it is important to note that experimental studies on shift work tolerance can only examine and reveal short-term consequences. A better grasp into the long-term effects of shift work, such as effects on health, can only be achieved by means of fieldwork studies.

6.7 On the Way to Recommendations

The final aim of shift work research should be one of practical implication. Recommendations for improving the health and safety of workers are pressing. At present, we still know very little about the mechanisms underlying the health problems of shift workers. The current findings highlight the importance of sleep and well-being in promoting the health of workers, and the role of chronotype in affecting these aspects of health.

Though invaluable in their contribution to shift work research, field studies are rare due to their costly and time-consuming nature. The current studies provide first fieldwork insights into the sensitivity and responsiveness of sleep-regulating processes in the face of demands by work schedules. The data reveal that shift workers' sleep and wake behaviour is influenced by circadian patterns, inhibiting the initiation and maintenance of displaced sleep. Through this, chronotype proves to be a central role in predicting the degree to which sleep is displaced and disturbed, as well as in predicting the degree of distress experienced by workers at work. Several interventions have been proposed in facilitating circadian adaptation to shift work. However, the present findings reveal that preventative advice only makes sense in the light of chronotype.

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8 Summary

8.1 English Summary

When the timing of sleep is displaced in shift work, workers can have symptoms similar to jetlag. Although travellers normally adjust to the new time zone within a few days, most shift workers never adjust to the demands of displaced work hours. This is because shift workers are still being exposed to the natural daylight cycle and thereby remain synchronized to a diurnal orientation of their circadian clock. The consequential symptoms include impaired sleep, fatigue, psychological distress, digestive and cardiovascular problems, metabolic abnormalities, reproductive complications, and even a greater risk of developing cancer. Inter-individual differences in the adopted phase relationship to the dark-light cycle chronotype should play a decisive role in determining the degree of circadian alignment to working on the morning, evening, and night shifts. The current project explores shift worker sleep and wake behaviour in the field, with a particular emphasis on chronotype-specific differences and how these predict tolerance to shift work in terms of sleep, well-being, and health.

The Munich ChronoType Questionnaire (MCTQ) has revealed important information as to the temporal organization of sleep and wake patterns of more than 82,000 people throughout the world. Mid-sleep on free days (MSF), the half-way point between sleep onset and sleep end, has been shown to be an excellent predictor of chronotype in day workers, correlating highly with assessed phase from daily sleep logs, actimetry, melatonin and cortisol, as well as with the widely used Morningness-Eveningness Questionnaire by Horne and Østberg. However, items from the current MCTQ are geared towards a day working population and it is not clear whether the assessment of chronotype by means of MSF can be generalized to a shift work population.

At this point, we know very little about the sleep and wake behaviour of shift workers in the field, particularly in regards to free days. Existing knowledge is almost exclusively based on simulated shift work studies, where the timing of sleep is not free but predefined and subject to experimental manipulation. The main goal of **Project One** was to explore the sleep and wake behaviour of rotating shift workers by means of a shift work adjusted version of the MCTQ ($MCTQ^{Shift}$), with the aim of establishing an algorithm for assessing chronotype in shift workers. Main parameters from the $MCTQ^{Shift}$ were subsequently tested for validity in **Project Two**, by means of comparison to daily reports of sleep patterns from sleep logs, to the phase of actimetry and body temperature regulation, and to the MEQ. In **Project Three** it was examined whether circadian alignment to the morning, evening, and night shift, in terms of inter-individual differences in chronotype, predict tolerance to shift work.

Project One: From the MCTQ to the $MCTQ^{Shift}$

Main parameters form the $MCTQ^{Shift}$ were evaluated on the basis of entries by 371 rotating shift workers and compared to the large databank of day workers (n > 82,000). Results support laboratory findings showing a shortening in sleep length as a consequence of difficulties in advancing sleep on the morning shift and in delaying sleep on the night shift. Though many shift workers catch up on lost sleep by napping, shift workers show an overall reduced sleep duration when compared to day workers. These findings imply that sleep in shift workers is regulated by circadian influences, rendering sleep difficult to initiate and to maintain when it is being displaced by external constraints (shift schedules). Accordingly, the sleep-wake cycle of shift workers maintains a diurnal orientation on free days, with sleep taking place between 0:00 and 9:00. This demonstrates that just like day workers, shift workers can be assessed for chronotype on the basis of their timing of sleep on free days.

In addition to this, a 30 to 60-minute delay in the timing of sleep on free days was observed as a function of the direction of the displaced sleep on the previously work schedule, suggesting some degree of circadian adjustment to displaced sleep. This supports the notion of a complex feedback loop mechanism, whereby the circadian clock not only affects the sleep-wake cycle but is itself subject to being affected by the sleep-wake cycle.

As the timing of sleep on free days is only being minimally affected by the evening shift, MSF following the evening shift (MSF^E) is best suited for the assessment of chronotype in shift workers. When corrected for effects of sleep debt (MSF^Escn), MSF following the evening shift yields a distribution indistinguishable from that of the sleep corrected MSF in day workers. For shift workers that do not work evening shifts, expected MSF^Escn can be computed on the basis of MSF values obtained by shift workers that work all three shifts.

Project Two: Validating the $MCTQ^{Shift}$

When cross-referenced with entries into daily sleep logs (for approximately four weeks) by 52 rotating shift workers, the $MCTQ^{Shift}$ was shown to accurately capture shift workers' sleep and wake patterns on work and on free days. Sleep log data also revealed a significant change in MSF across the three shifts, which could not be observed by comparing MSF across three weeks in night workers (n = 22) and day workers (n = 106). $MCTQ^{Shift}$ assessed sleep phase correlated highly with the phase of sleep by daily sleep logs and with behavioural rhythms of actimetry (n = 33). $MSF^{E}scn$ thereby realizes the same criteria for validity as the MCTQ-assessed chronotype in day workers (sleep logs n = 33 and actimetry n = 41). Also, as noted in day workers, mid-sleep on free days in shift workers correlated highly with the MEQ (n = 75).

Results from 24-hour recordings of body temperature regulation in 14 shift workers on the morning, evening, and night shifts, showed a high masking effect of sleep. Yet, changes in temperature regulation often preceded sleep begin and end, suggesting a direct causal link between the thermoregulation and sleep. Moreover, these anticipatory effects of temperature regulation could also be observed when sleep was highly displaced, such as on night shifts, suggesting that rhythms of body temperature regulation do adjust to displaced sleep. The phase of temperature regulation on the morning, evening, and night shift did not significantly correlate with $MCTQ^{Shift}$-assessed sleep phase and with chronotype.

Project Three: Reconsidering Adverse Effects of Shift Work in the Light of Chronotype

As predicted, chronotype correlates with the degree of constraints on sleep experienced on the morning, evening, and night shifts. As a result of such constraints, late types showed significantly higher social jetlag (n= 232, sleep loss n = 230, and sleep disturbance n = 94) than early types on the morning shift. Early types, on the other hand, revealed significantly higher constraints on the night shift (social jetlag n = 231, sleep loss n = 230, and sleep disturbance n = 94) compared to late types on the night shift. Likewise, chronotype correlated with subjective well-being during night work (n = 54), with early types feeling significantly less well than late types. Also, early types reported lower well-being on the night shift than on the morning shift, while the opposite could be observed for late types. However, when averaged across the three shifts, chronotype did no longer associate with the degree of social jetlag and the duration and quality of sleep, indicating that, overall, the three chronotypes experience the same degree of constraints as do rotating workers.

Replicating findings by other studies, current results showed increased health problems (cardiovascular and digestive) and a higher prevalence of smoking in shift workers with night work compared to day workers. Shift workers with night work also displayed higher social jetlag than day workers, underlining the importance of a stable circadian structure. In order to examine whether observed chronotype differences in sleep and well-being on the morning, evening, and night shifts predict health, a multiple regression was computed on the basis of entries by 790 workers (rotating and permanent shift workers, as well as day workers) to test the unique contribution of study variables in predicting the variability in workers' health. Results showed that sleep duration, sleep quality and subjective well-being uniquely predict health-- beyond factors known to predict health, such as age, sex, BMI, stress, locus-of-control, and smoking.

Conclusion

The present findings demonstrate that chronotype, faced with constraints by the social clock, has a significant influence on sleep and well-being and thus the health of shift workers.

8.2 Deutsche Zusammenfassung

Wird die Schlafphase gegenüber der äußeren Nacht verschoben wie es bei Schichtarbeitern der Fall ist, so können Jetlag-ähnliche Symptome auftreten. Während sich Reisende normalerweise innerhalb weniger Tage an die neue Zeitzone anpassen, gelingt es den Schichtarbeitern in der Regel nicht. Dies liegt an der konkurrierenden Lichtexposition, welcher die Schichtarbeiter ausgesetzt sind, da Tageslicht der wichtigste Zeitgeber für die innere Uhr ist. Somit bleibt die innere Uhr der Schichtarbeiter selbst bei einer veränderten Schlaf-Wach-Rhythmik an den äußeren Tag angepasst. Die hieraus folgenden Symptome umfassen Schlafstörungen, Müdigkeit, gastrointestinale und kardiovaskuläre Erkrankungen, Stoffwechelstörungen, Fertilitätsstörungen, so wie ein erhöhtes Krebsrisiko. Die individuellen Unterschiede der Anpassung an den Tag-Nacht-Rhythmus (so genannter Chronotyp) bestimmen wesentlich das Ausmaß der Anpassung an die Früh-, Spät- und Nachtschicht. In der vorliegenden Arbeit wurde das Schlaf-Wach-Verhalten bei Schichtarbeitern unter Feldbedingungen unter besonderer Berücksichtigung der chronotyp-spezifischen Unterschiede untersucht.

Mittels des Munich ChronType Questionnaire (MCTQ) konnten wichtige Erkenntnisse über die zeitliche Organisation des Schlaf-Wachverhaltens bei bisher über 82000 Menschen gewonnen werden. Die Schlafmitte an freien Tagen (*mid-sleep on free days* = MSF), also der zeitliche Mittelpunkt zwischen dem Zeitpunkt des Einschlafens und des Aufwachens, konnte als aussagekräftiger prädiktiver Faktor bei Tagesarbeitern identifiziert werden. MSF zeigte eine hohe Korrelation mit der anhand von Schlaftagebüchern, aktimetrischen und neuroendokrinen Daten (Melatonin und Kortisol

Profile) ermittelten circadianen Phase, sowie mit dem häufig eingesetztem Morningness-Eveningness Questionnaire von Horne und Østberg.

Derzeit kommt der aktuelle MCTQ bei Tagesarbeitern zum Einsatz. Ob sich dieser auf Schichtarbeiter mit wechselnden Arbeitszeiten übertragen lässt, bleibt noch zu erforschen. Bis dato liegen wenige Feldstudien zum Schlaf-Wach-Verhalten der Schichtarbeiter vor. Insbesondere liegen wenige Erkenntnisse zum Schlaf-Wach-Verhalten der Schichtarbeiter an freien Tagen vor. Die bisherigen Erkenntnisse basieren weitgehend auf Simulationsstudien mit fest definierten Schlafprotokollen und Arbeitsschichten. In der vorliegenden Arbeit sollte einerseits das Schlaf-Wach-Verhalten von in rotierenden Schichten Beschäftigten mittels einer modifizierten MCTQ Version ($MCTQ^{Shift}$) untersucht werden, um einen Algorithmus zur Erfassung des Chronotyps zu etablieren (Projekt 1). Darüber hinaus sollen die Grundvariablen des $MCTQ^{Shift}$ anhand verschiedener Methoden der circadianen Phasenerfassung (Schlaftagebücher, Aktimetrie, Körpertemperatur) und anhand des MEQ validiert werden (Projekt 2). Ferner sollte untersucht werden, inwiefern der individuelle Chronotyp eine prädiktive Aussage hinsichtlich der Verträglichkeit der Schichtarbeit ermöglicht (Projekt 3).

Projekt 1: Vom MCTQ zum $MCTQ^{Shift}$

Die Grundvariablen des $MCTQ^{Shift}$ wurden anhand von Angaben von 371 rotierenden Schichtarbeitern evaluiert. Als Kontrollgruppe diente eine große Datenbank von Tagesarbeitern (n>82000). Analog zu den Ergebnissen aus kontrollierten Laborstudien zeigte sich durch die erschwerte Vorverlagerung der Schlafphase während der Frühschicht und deren Verzögerung in der Nachtschicht die Schlaflänge verkürzt. Obwohl einige Schichtarbeiter ihre Schlafschuld durch ein Nickerchen zu kompensieren versuchen, schlafen Schichtarbeiter im Vergleich zu Tagarbeitern im Allgemeinen weniger. Diese Befunde legen nahe, dass der circadian regulierte Schlaf eines Schichtarbeiters durch eine Veränderung der Arbeitszeit gegenüber dem äußeren Tag sowohl bezüglich des Einschlafens als auch bezüglich des Durchschlafens beeinträchtigt wird. Dementsprechend bleibt der Schlaf-Wach-Zyklus der Schichtarbeiter an freien Tagen an den äußeren Tag synchronisiert (Schlaf findet zwischen 0:00 und 9:00 Uhr statt). Dies zeigt, dass der Chronotyp eines Schichtarbeiters genau so wie der des Tagesarbeiters anhand der Schlafphase an freien Tagen erfasst werden kann.

Jedoch zeigte sich eine 30-60-minutige Verzögerung des MSF. Folglich verschiebt sich der MSF in gleiche Richtung wie die vorangegangene schichtabhängige Schlafphase. Das weist möglicherweise auf einen komplexen Rückkopplungsmechanismus hin, wonach die innere Uhr nicht nur den Schlaf-Wach-Zyklus beeinflusst, sondern auch ihrerseits von diesem beeinflusst wird. Da der Zeitpunkt der Schlafphase an freien Tagen lediglich geringfügig von der vorangegangen Spätschicht beeinflusst wird, ist der MSF nach der Spätschicht (*MSF evening shift* = MSF^E) am besten zur Erfassung des Chronotyps geeignet. Wird die Schlafschuld herausgerechnet, so zeigt MSF^E die gleiche Verteilung wie der schlafkorrigierte MSF der Tagesarbeiter. Anhand der vorliegenden MSF Daten bei rotierenden Dreischichtsystemen ist eine Einschätzung des zu erwartenden MSF^E auch bei Schichtsystemen, welche keine Spätschicht beinhalten, möglich.

Projekt 2: Validierung des $MCTQ^{Shift}$

Die Angaben aus Schlaftagebüchern von 52 Schichtarbeitern über einen Datenerhebungszeitraum von circa vier Wochen zeigen, dass der $MCTQ^{Shift}$ treffend das Schlaf-Wach-Verhalten an Arbeitstagen und freien Tagen wiedergibt. Die anhand der

Daten aus Schlaftagebüchern demonstrierte schicht-spezifische Veränderung des MSF konnte bei Dauernachtschichtarbeitern (n = 22) und Tagesarbeitern (n = 106) nicht beobachtet werden. Die mittels des $MCTQ^{Shift}$ erfasste Schlafmitte korrelierte sowohl mit der Schlafphase aus Tagebüchern als auch mit den aktimetrischen Messungen (n = 33). $MSF^{E}scn$ erfüllte dabei die gleichen Validitätskriterien (Schlaftagebücher n = 28 und aktimetrische Messungen n = 26) wie der durch den MCTQ erfasste Chronotyp für Tagesarbeiter (Schlaftagebücher n = 28 und aktimetrischen Messungen Schichtarbeiter n = 41). Analog zu Befunden von Tagesarbeitern, zeigte die Schlafmitte an freien Tagen bei Schichtarbeitern auch eine hohe Korrelation mit dem MEQ (n = 75).

Die Aufzeichnung der Körpertemperaturregulation über 24 Stunden bei 14 Schichtarbeitern während der Früh-, Spät- und Nachtschicht zeigte einen ausgeprägten Maskierungseffekt des Schlafes. Die Veränderungen der Temperaturregulation gehen dem Einschlafen und den Aufwachen voraus und weisen hin auf eine direkte kausale Verbindung zwischen der Temperaturregulation und dem Schlaf. Weiterhin konnten die antizipatorischen Effekte der Temperaturregulation auch bei einer Verschiebung der Schlafphase, wie zum Beispiel bei der Nachtschicht, im Sinne einer Anpassung an verschobene Schlaf-Wach-Rhyhtmik gezeigt werden. Die Phase der Temperaturregulation während der Früh-, Spät- und Nachtschicht zeigte keine signifikante Korrelation mit der mittels MCTQ erfassten Schlafphase oder dem Chronotyp.

Projekt 3: Beurteilung der negativen Auswirkungen von Schichtarbeit unter Berücksichtigung des Chronotyps

Wie postuliert, korreliert das Ausmaß der Schlafstörung in der jeweiligen Schicht mit dem Chronotyp. Bei Spättypen zeigte sich während der Frühschicht eine signifikant höhere Rate an Social Jetlag (n = 232), Verkürzung des Schlafes (n = 230) und Durchschlafstörungen (n = 94). Bei Frühtypen hingegen zeigten sich während der Nachtschicht signifikant höhere Einschränkungen der gleichen Variablen (Social Jetlag n = 231; Verkürzung des Schlafes, n = 231; Durchschlafstörungen n = 94). Analog dazu korrelierte der Chronotyp mir der subjektiven Befindlichkeit während der Nachtschicht (n = 54), wobei die Frühtypen im Vergleich zu Spättypen signifikant schlechtere Befindlichkeit aufweisen. Während Frühtypen sich in der Frühschicht wohler fühlen als in der Nachtschicht, fühlen sich späte Chronotypen in der Nachtschicht wohler als in der Frühschicht. Es fand sich jedoch kein chronotyp-spezifischer Unterschied hinsichtlich des Social Jetlags, der Schlaflänge und der Qualität wenn diese gemittelt wurden über die drei Schichten.

Wie bei anderen Studien bereits dargelegt, zeigte sich bei Schichtarbeitern, deren Schichtsystem die Nachtschicht beinhaltet, im Vergleich zu Tagesarbeitern eine häufigere Prävalenz an gastrointestinalen und kardiovaskulären Erkrankungen sowie eine höhere Prävalenz an Nikotinabusus. Darüber hinaus präsentierten Schichtarbeiter, deren Schichtsystem die Nachtschicht beinhaltet, einen höheren Social Jetlag im Vergleich zu Tagesarbeitern. Dies verdeutlicht die Wichtigkeit einer stabilen circadianen Phase. Um zu untersuchen, in wie fern die ermittelten chronotyp-spezifischen Unterschiede im Schlafverhalten und in der Befindlichkeit während der jeweiligen Schicht die Varianz der Gesundheit der Schichtarbeiter erklären, wurde eine Multiple Regression berechnet (n = 790 Schichtarbeiter und Tagesarbeiter). Somit konnten die einzelnen Beiträge der beobachteten Variablen gesondert berechnet werden. Die Ergebnisse zeigten, dass die Schlafdauer, Schlafqualität und subjektive Befindlichkeit für sich neben den bekannten Faktoren wie Alter, Geschlecht, Stress, interne Kontrollüberzeugung und Rauchen den Gesundheitszustand von Schichtarbeitern gesondert erklären.

Schlussfolgerung

Die Ergebnisse dieser Arbeit verdeutlichen den Zusammenhang zwischen Schlaf und Gesundheit sowie zwischen Befindlichkeit und Gesundheit. Der Chronotyp spielt hierbei eine wesentliche Rolle bezüglich der Beeinträchtigung beider Parameter durch die soziale Uhr.

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10 Curriculum Vitae

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