Aus dem Institut für Medizinische Psychologie

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Vorstand: Prof. Dr. Martha Merrow

Thank God It's Friday:

Weekends, sleep, internal clocks and adolescents with depression.

Dissertation

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Für meinen Vater Bernd und meine Großmutter Irmgard.

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1 Introduction

A strange thing happens every night: we put on comfy clothes, lie down on an especially for this purpose designed furniture called “bed”, lose consciousness for a few hours, before we get up again and start another day. Though we repeat this pattern day by day, only little is known about the true reason of why we sleep. As Stanford sleep researcher William Dement, who spent 50 years of his life researching sleep, puts it: “As far as I know, the only reason we need to sleep that is really, really solid is because we get sleepy.” (Max, 2010). However, what we *can* do up to this day is to characterize sleep in a variety of dimensions, pinpoint important factors influencing sleep as well as describing consequences of insufficient sleep. Here, we focus on three of those dimensions that are especially important for the two studies of this thesis: Sleep duration, sleep timing and sleep quality.

Sleep duration

Sleep duration differs significantly from person to person. Some rare people can regularly make it with 4 hours, while others need 10 hours per night or more to feel rested and function properly during the day. Additionally, the average sleep duration changes with age, newborns and babies needing up to 17 hours and elderly people needing less then 7 hours (Hirshkowitz et al., 2015). Epidemiological studies could link sleep duration with a variety of health-related conditions such as cognitive functioning (Kronholm et al., 2009; Xu et al., 2011), cardiovascular events (Ikehara et al., 2009; Vgontzas, Liao, Bixler, Chrousos, & Vela-Bueno, 2009) and even mortality (Mesas, López-García, León-Muñoz, Guallar-Castillón, & Rodríguez-Artalejo, 2010). A meta-analysis with seven prospective studies showed that depression in adults was also significantly associated with both short and long sleep duration (Zhai, Zhang, & Zhang, 2015). Another study found that adolescents with acute depression slept significantly less compared to controls (Murray, Murphy, Palermo, & Clarke, 2012).

However, almost none of the studies researching sleep duration and its consequences do account for the fact that sleep duration differs significantly between workdays and work-free days, with the majority of the population sleeping shorter on workdays and compensating for their sleep debt by oversleeping on work-free days (Roenneberg et al., 2015). Additionally, the definition of how many hours define "short" or "long" sleep differs substantially from study to study.

Sleep timing

Sleep timing can refer to a variety of variables: the timing when people fall asleep, the timing when sleep ends as well as the *midpoint of sleep* (i.e., if someone goes to bed at midnight and wakes up at 8 am in the morning, their midpoint of sleep is 4 am). The latter is – in contrast to sleep start and sleep end – (more or less) independent of sleep duration. If it is assessed on work-free days (and corrected for oversleeping on weekends), the midpoint of sleep can be used as a proxy for chronotype (Roenneberg et al., 2015). Chronotype refers to the so-called *phase of entrainment* and gives an approximation of how the internal clock of an individual is embedded into the external time of the 24-hour light-dark cycle. Chronotype changes with age: the average chronotype delays more and more from childhood up to adolescence, reaching a maximum at 19.5 years in women and 20.9 years in men, before this trend reverses and chronotype advances again (Roenneberg, Kuehnle, Pramstaller, Havel, & Merrow, 2004).

Many studies could link a late chronotype with depression (Keller, Zöschg, Grünewald, Roenneberg, & Schulte-Körne, 2016). However, most of them used the Morningness-Eveningness-Questionnaire (MEQ) as a proxy for chronotype – a questionnaire asking for the timing preferences for different activities rather than real sleep timing (see also Roenneberg, 2015). Two studies using the Munich ChronoType Questionnaire (MCTQ) – and therefore actual sleep timing – also found that the later the chronotype, the more depressive symptoms people experience (Levandovski et al., 2011; Wittmann, Paulus, & Roenneberg, 2010). In addition to chronotype, also social jetlag was found to be associated with depressive symptoms (Levandovski et al., 2011). Social jetlag is defined by the difference between the midpoint of sleep on workdays and the midpoint of sleep between work-free days and is a common marker for the misalignment between the internal time of the body (chronotype) and the external time (Roenneberg et al., 2015).

Up to now it remains unclear whether a later chronotype predisposes for depression or depression goes along with a change in chronotype (or, most probably, if this direction is bi-directional; see Keller, Zöschg, Grünewald, Roenneberg, & Schulte-Körne, 2016). However, the fact that advancing chronotype with wake- and/or light therapy is being used as a therapeutic target in depressed patients indicates that a late chronotype could – at least in part – be regarded as a factor causing the development of depressive symptoms (Berger et al., 1997; Kragh & Videbech, 2015; Wirz-Justice et al., 2005). In addition, maybe not only chronotype per se, but rather the collision of a late chronotype with external time constraints such as fixed work- or school start times could lead to - or at least influence - depression.

The significant changes of chronotype in adolescents and the still not fully understood relationship between chronotype, social jetlag, sleep duration and depressive symptoms led to our first research question: do adolescents with remitted depression differ from healthy controls in terms of chronotype, social jetlag and general sleep behaviour such as sleep duration? To answer this question, we assessed chronotype and sleep behaviour (separately for workdays and work-free days) both by an objective sleep recording via 6 weeks of actimetry and a pen-and-paper version of the MCTQ in a group of adolescents with remitted depression as well as in healthy controls (study 1).

Sleep quality

The third important dimension of sleep behaviour is sleep quality. However, there is still no clear consensus on what (good) sleep quality actually is. Traditionally, sleep quality is divided in objective and subjective sleep quality, with the first referring to indices (such as number of short awakenings per night, time spent in REM sleep during one sleep episode, or sleep latency) obtained through objective measurements such as polysomnography (in sleep laboratories) and actimetry (in the real world). In contrast, measures for subjective sleep quality can be obtained through interviews and questionnaires. Interestingly, objective and subjective markers of sleep quality often correlate only weakly – or not at all (Jackowska, Ronaldson, Brown, & Steptoe, 2016).

While preparing the materials for study 1, the instructions of the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) caught our eye. The PSQI is the most common measure of sleep quality and asks for *usual* sleep-wake behaviour during the last month. This quite general instruction in addition to the results obtained in study 1 – that adolescents with depression differ from healthy adolescents, but only on work-free days – inspired our second study: Does sleep quality differ between workdays and work-free days – and, additionally, what does *usual* sleep quality actually reflect? Therefore, we modified the original version of the PSQI asking for *usual* sleep quality and created a version for workdays and a version for work-free days. We additionally assessed chronotype and social jetlag with the MCTQ. All participants filled out all three versions of the PSQI in a randomized order followed by the MCTQ.

2 List of publications

1. **Keller, L. K.**, Grünewald, B., Vetter, C., Roenneberg, T., & Schulte-Körne, G. (2017). Not later, but longer: sleep, chronotype and light exposure in adolescents with remitted depression compared to healthy controls. *European Child & Adolescent Psychiatry, 26,* 1233–1244. doi: 10.1007/s00787-017-0977-z

2. Pilz, L. K.*, **Keller, L. K.***, Lenssen, D., & Roenneberg, T. (2018). Time to rethink sleep quality: PSQI scores reflect sleep quality on workdays. *Sleep*, 1-8, doi: 10.1093/sleep/zsy029

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3 Abstract

This thesis explores the profound differences between sleep on workdays versus sleep on work-free days and the impact of circadian factors such as chronotype and social jetlag. All of these factors play an important role in adolescents with depression (study 1) as well as in the measurement of sleep quality in the general population (study 2).

In ***study 1***, we analysed sleep behaviour of children and adolescents with remitted depression compared to healthy controls using a one-month recording of locomotor activity as well as subjective data on sleep quality and depressive symptoms. Adolescents with remitted depression slept 45 minutes longer on work-free days compared to healthy adolescents, but did not differ in terms of sleep behaviour on workdays, chronotype or social jetlag.

In ***study 2***, we assessed sleep quality in the general population separately for workdays and work-free days, using a modified form of an established sleep quality questionnaire (PSQI). Our results show that the original version of the PSQI, asking for *general sleep behaviour*, mainly depicts sleep on workdays, which is strongly influenced by work schedules. In addition, we could show that a later chronotype was associated with a higher difference in sleep quality on workdays versus work-free days, with this association being mediated by the amount of social jetlag.

Both studies show the - in sleep research often neglected - impact of the differences in sleep behaviour between workdays and work-free days. Additionally, our second study showed the important contribution of circadian

factors on this difference. We believe that incorporating this knowledge is crucial for a better understanding and finally improvement of sleep behaviour in humans.

Study 1: Not later, but longer: sleep, chronotype and light exposure in adolescents with remitted depression compared to healthy controls

The relationship between sleep and adolescent depression is much discussed, but still not fully understood. One important sleep variable is self-selected sleep timing, which is also referred to as chronotype. Chronotype is mostly regulated by the circadian clock that synchronises the internal time of the body with the external light dark cycle. A late chronotype as well as a misalignment between internal time and external time such as social jetlag has been shown to be associated with depressive symptoms in adults.

In this study, we investigated whether adolescents with remitted depression differ from healthy controls in terms of chronotype, social jetlag and other sleep-related variables. For this purpose, we assessed chronotype and social jetlag with the Munich ChronoType Questionnaire (MCTQ), subjective sleep quality with the Pittsburgh Sleep Quality Index (PSQI) and used continuous wrist-actimetry over 31 consecutive days to determine objective sleep timing. Given the potentially mediating effect of light on chronotype and depressive symptoms, we measured light exposure with a light sensor on the actimeter.

In our sample, adolescents with remitted depression showed similar chronotypes and similar amounts of social jetlag compared to controls.

However, patients with remitted depression slept significantly longer on work-free days and reported a worse subjective sleep quality than controls. Additionally, light exposure in remitted patients was significantly higher, but this finding was mediated by living in a rural environment. These findings indicate that chronotype might be modified during remission, which should be further investigated in longitudinal studies.

Study 2: Time to rethink sleep quality: PSQI scores reflect sleep quality on workdays

The Pittsburgh Sleep Quality Index (PSQI) is the most common measure of sleep quality. Its questions refer to "usual" sleep habits during the last month. Considering how different sleep-wake behaviour can be between work- and work-free days, we hypothesized that sleep quality should show similar differences.

We investigated these potential differences in a cross-sectional online study using the original and two adapted versions of the PSQI that replaced "usual" by explicitly referring to sleep on work- or work-free days. Additionally, we investigated how these scores relate to chronotype and social jetlag assessed by the Munich ChronoType Questionnaire. Participants were recruited online, they had to be older than 18 years, following regular weekly work schedules, and should not be shift workers.

All the questionnaires were filled out online. Repeated-measures analysis of variance was used to compare the three different versions of the PSQI (usual, work, work-free). To find out if PSQI score differences could be predicted by chronotype and/or social jetlag a mediation analysis was carried out.

Workday PSQI scores were similar to the original “usual” scores, 2 points higher than the PSQI score on work-free days and above the cut-off designating poor sleep quality. PSQI components and time variables also differed between workdays and work-free days. Chronotype correlated with the difference between PSQI scores on workdays and on work-free days, an association mediated by social jetlag.

Our results suggest that the original PSQI predominantly reports sleep quality on workdays and that work schedules may affect sleep quality. The mediation of social jetlag on the association of chronotype and PSQI score differences could mean that not chronotype per se, but rather the collision of an individuals´ chronotype with fixed work schedules explains the differences between sleep on workdays and work-free days.

Understanding how sleep quality differs between workdays and work-free days, how this difference can adequately be assessed through directing participants to focus on their sleep specifically on workdays vs. work-free days, and how circadian factors modulate this difference, is crucial to improve sleep quality.

4 Contribution to publications

For study 1, I set up the study design, collected the data and conducted the psychiatric interviews with adolescents and their families in the patient group and control group. I analysed the data and wrote the manuscript. Barbara Grünewald helped with the psychiatric interviews. Till Roenneberg supervised the analysis of actimetry data. Gerd Schulte-Körne, Till Roenneberg and Barbara Grünewald supported the revision of the manuscript.

I came up with the research idea for study 2, planned the study and prepared the materials. Together with Luisa Pilz and David Lenssen, I set up an internet database with the questionnaires. All co-authors helped with data collection by forwarding the link to the online study. Luisa Pilz and I contributed equally to data analysis and writing of the manuscript. Till Roenneberg revised the manuscript.

5 Publication 1: Not later, but longer: sleep, chronotype and light exposure in adolescents with remitted depression compared to healthy controls.

Not later, but longer: Sleep, chronotype and light exposure in adolescents with remitted depression compared to healthy controls

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Abstract

The relationship between sleep and adolescent depression is much discussed, but still not fully understood. One important sleep variable is self-selected sleep timing, which is also referred to as chronotype. Chronotype is mostly regulated by the circadian clock that synchronises the internal time of the body with the external light dark cycle. A late chronotype as well as a misalignment between internal time and external time such as social jetlag have been shown to be associated with depressive symptoms in adults.

In this study, we investigated whether adolescents with remitted depression differ from healthy controls in terms of chronotype, social jetlag and other sleep-related variables. For this purpose, we assessed chronotype and social jetlag with the Munich ChronoType Questionnaire (MCTQ), subjective sleep quality with the Pittsburgh Sleep Quality Index (PSQI), and used continuous wrist-actimetry over 31 consecutive days to determine objective sleep timing. Given the potentially mediating effect of light on chronotype and depressive symptoms, we measured light exposure with a light sensor on the actimeter.

In our sample, adolescents with remitted depression showed similar chronotypes and similar amounts of social jetlag compared to controls. However, patients with remitted depression slept significantly longer on work-free days and reported a worse subjective sleep quality than controls. Additionally, light exposure in remitted patients was significantly higher, but this finding was mediated by living in a rural environment. These findings indicate that chronotype might be modified during remission, which should be further investigated in longitudinal studies.

Key Words

Chronotype, Adolescent depression, MCTQ, sleep, light exposure, wrist actigraphy

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Introduction

The most prominent recurring patterns in humans are wake and sleep. Being awake is mainly associated with daylight, and sleep normally occurs during the night. There are, however, substantial inter-individual differences in self-selected sleep timing – giving rise to different so-called chronotypes [1]. Their distribution in a population is almost normal and spans from extremely early to extremely late chronotypes (also called "larks" and "owls"). Early chronotypes wake up naturally early in the morning and fall asleep early in the evening, whereas late chronotypes fall asleep late in the evening and wake up late in the morning [1]. Chronotype is largely regulated by the circadian clock that synchronizes the internal time of the body with the external light-dark-cycle [2].

An *acute* misalignment between internal (biological) and external (social) time occurs after transmeridian flights and leads to jetlag with symptoms like fatigue, insomnia, headache or digestive problems. A *chronic* misalignment between internal and external time affects for example shift-workers, and is associated with an increased risk for cardiovascular and metabolic diseases, cancer and psychiatric disorders [3–7]. However, such chronic misalignment also occurs in the majority of the population. Many people have to follow fixed work/school schedules that interfere with their chronotype. For example, an early start of work suits early chronotypes, but forces late chronotypes to get up way before their biological wake-up time. Along with late bed times (determined by their internal clock), this leads in late chronotypes to the accumulation of a sleep debt on workdays, which has to be compensated for on work-free days. If the collision of an extremely late (or extremely early) chronotype with external, social time creates a severe strain, it has been called delayed (or advanced) sleep phase syndrome [8]. One way to quantify the chronic misalignment between internal and external time is the absolute difference in sleep timing (not to confuse with sleep duration) between workdays and work-free days and has been referred to as *social jetlag* [9].

A large-scale study with more than 64,000 participants showed that 69% of the population are affected by at least one hour of social jetlag [10]. Social jetlag is associated with a variety of health conditions, from depressive symptoms to metabolic syndromes as well as an increased consumption of nicotine, caffeine and alcohol [9–12]. These results are especially relevant for late chronotypes, since they show the highest amount of social jetlag in the population [9].

Chronotype depends on age and light exposure [13, 14]. Exposure to low light levels during the day (and elevated light levels during the night) generally leads to a later chronotype [15]. Because chronotype is set by light and darkness (*i.e.* sun time) and not by local time, mean chronotype delays by 4 minutes per longitude from east to west [13] and adapts to the changing photoperiods over the course of the year [16]. From childhood to early adulthood, the average chronotype in the population shifts to a later chronotype, with a maximum at around 20 years of age. This trend is then reversed as people become older. Thus, in cross-sectional as well as longitudinal studies, adolescents are found to be the latest chronotypes [17–19].

Most studies suggesting a relationship between chronotype and depression [20, 21] define chronotype as an amalgamated daily preference for different activities (e.g. physical or intellectual work, food intake, sleeping) reflected by a score derived from the Morningness-Eveningness-Questionnaire (MEQ, [22], and other questionnaires based on the MEQ). Low scores on the MEQ indicate Eveningness (which is sometimes referred to as “late chronotype”), high scores indicate Morningness (sometimes referred to as “early chronotype”). Other studies define chronotype as actual self-selected sleep timing (assessed by the Munich ChronoType Questionnaire [23]) as a marker for actual phase of entrainment (i.e., the difference between a given time in a circadian rhythm such as the midpoint of sleep and the time of the external zeitgeber such as mid-dark, see [24] for further explanation). Although chronotype derived from the MCTQ correlates highly with MEQ scores [25], one should keep in mind the different definitions mentioned above (for an in-depth discussion see also [24, 26]). In this paper, we always specify if we refer to MEQ-Scores (i.e., Morningness/Eveningness) or MCTQ-chronotype (i.e., self-selected sleep timing).

Large-scale questionnaire-based studies in the general population showed that Eveningness (assessed by the MEQ) is associated with more depressive symptoms than Morningness [20, 21], and that chronotype (assessed by the MCTQ) also correlates with depressive symptoms [11, 27]. Consistently, adult patients with depressive disorders are more likely to be evening-types (assessed by the MEQ) compared to healthy controls [28–31], and with increased Eveningness, adult patients show a higher severity of depressive symptoms [29, 32, 33]. Questionnaire-based studies in children (≥10 years) and adolescents also found a correlation between Eveningness (assessed by the MEQ) and depressive symptoms [34–38], as well as a correlation between chronotype (assessed with the MCTQ) and depressive symptoms [39]

To our knowledge, only Fares et al. [40] examined and found a relationship between Eveningness (MEQ) and depression in a sample that included clinically depressed adolescents (range: 12 up to 30 years of age). Consistently, phase-advance of the circadian clock (i.e. the chronotype becoming earlier) has been proposed to be associated with symptom improvement under bright light therapy in adult (seasonal) depression [41].

Besides late chronotype and Eveningness, other sleep-related factors are associated with depression. Acutely depressed adolescents show a reduced objective sleep duration [42], reduced subjective sleep latency [43] and (subjectively) complain about more sleep disturbances (mainly insomnia and hypersomnia) and reduced sleep quality (see review by Gregory and Sadeh [44]). According to a meta-analysis by Lovato and Gradisar [45], sleep disturbances predict the onset of a depressive disorder. However, most of these results are based on subjective assessments, and almost none of these studies examined the relationship between sleep, chronotype and depression with long-term monitoring of objective sleep-wake behaviour (*i.e.*, with actimetry).

Thus, while previous studies point to a link between chronotype and onset as well as acute phase of depression, nothing is known to date about what happens to chronotype (and associated sleep variables) when a depressive disorder goes into remission.

We therefore explored chronotype, social jetlag and other sleep variables in a sample of adolescent patients with remitted depression.

For this purpose, we used the MCTQ as a self-report of sleep-wake behaviour. Additionally, we explored whether adolescents in remission from depression show significant differences in objectively measured sleep parameters (e.g., sleep onset, sleep offset and sleep duration), assessed by continuous wrist-actimetry over 31 consecutive days. We also investigated possible differences in subjective sleep latency, subjective sleep quality and stimulant consumption (caffeine, alcohol, nicotine). Last, given the potentially mediating effect of light on chronotype and depressive symptoms, we examined light exposure within both healthy controls and remitted patients.

Methods

Participants

Participants (both patients and controls; age: 12-19 years) were recruited from an on-going, large-scale genetics study on childhood depression in the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University of Munich in a two step-exclusion process. In the first step, we prescreened potential participants as well as their parents via phone for the most important exclusion criteria (substance abuse, psychotic disorders, anorexia nervosa, psycho-stimulant, anti-psychotic or sleep medication, no regular school/vocational training attendance). In the second step, we invited all eligible subjects and their parents to an extensive diagnostic interview for psychiatric disorders at our hospital to check if they meet inclusion criteria. Participants were included in the patient group if they had a previous diagnosis of an unipolar major depressive disorder according to DSM-IV-TR criteria [46] based on a structured diagnostic interview for mental disorders in children and adolescents [47], but were currently in remission. We defined remission as not fulfilling diagnostic criteria for a major depressive disorder at the time of interview. They were excluded if they met criteria for a current depressive disorder or for a current or previous diagnosis of any psychiatric or neurological disorder other than depression. Participants were included in the control group if they did not meet criteria for a current or previous episode of any psychiatric or neurological disorder.

24 patients and 21 controls were initially included in the study. In the final analysis, we excluded participants who (i) did not comply with the study protocol (1 patient, 2 controls), (ii) had a technical failure of wrist actimetry (2 patients), and patients who experienced a depressive relapse (n=2). Our final sample consisted of 19 adolescent patients with a history of depressive disorders, currently remitted, and 19 healthy adolescent controls (see Table 1 for sample characteristics). On average, patients were first diagnosed with a depressive episode 3.2 years (± 1.5) prior to the study, at age 12.8 (± 2.3). Seven patients were on antidepressant medication during the study period (3 citalopram, 2 fluoxetine, 1 mirtazapine, 1 escitalopram). All of them had been on a stable dose-regimen for at least six weeks prior to inclusion into the study and none of them changed medication and/or dosage during the study period.

The study was approved by the ethics committee of the Medical Faculty of the Ludwig Maximilian University Munich and was conducted in accordance with the Declaration of Helsinki. All participants and their parents gave written informed consent.

Procedure

Included patients and controls filled out questionnaires on depressive symptoms, subjective sleep quality, sleep timing, and stimulant consumption (see descriptions of materials below). Between June 15th and July 15th 2012, participants wore an actimeter for the continuous objective assessment of locomotor activity and light exposure. Participants were instructed to (i) log all times when they had to take the actimeter off, and (ii) to avoid covering the light sensor with their sleeves. Participants received a weekly telephone call from the study team which assessed (i) compliance with the actimeter, (ii) whether they had had a depressive relapse, and (iii) whether – for each day in the previous week – they had gone to school or not, and whether they had used an alarm clock.

Materials

Psychiatric interview

We administered the German structured diagnostic interview for mental disorders in children and adolescents "Kinder-DIPS" [47] to ensure that patients and controls fulfilled the inclusion criteria. The "Kinder-DIPS" shows a high inter-rater reliability ($\varkappa$=0.88-0.95) [48]. Two psychologists and a psychiatrist conducted the interviews. All of them received a specific training by one of the authors of the "Kinder-DIPS" that included ratings of transcripts and a supervised interview.

Depressive symptoms

The Beck-Depression Inventory (BDI-II) is a 21-item self-report that covers affective as well as cognitive, behavioural and somatic symptoms of depression. Each item has four potential answers, which are scored from 0 to 3 and summed up to a total score [49]. The German version shows high internal consistency, reliability and validity [50, 51].

To assess depressive symptoms from parents' view, we asked them to fill out the DISYPS-II FBB-DES (diagnostic system for mental disorders in children and adolescents, external parent rating form for depressive disorders) [52]. This rating scale is based on German ICD-10 and DSM-IV criteria and also shows good psychometric properties [52].

Cigarettes, alcohol and caffeine

We also collected information on self-reported cigarette smoking, as well as the average consumption of alcoholic and caffeine containing beverages, per day, week and month. Based on this information, we computed the number of cigarettes and caffeinated beverages per day, as well as the weekly intake of alcoholic beverages, as described in Wittmann et al. [9].

Sleep quality

The Pittsburgh Sleep Quality Index (PSQI) consists of 19 items and is a self-report on subjective sleep quality over the last four weeks. Its items form seven component scores (ranging from 0 to 3) that are added up to a sum score - with higher scores representing worse sleep quality [53]. The German version shows a high test-retest reliability as well as a high criterion validity with sleep log data [54].

Chronotype and social jetlag

The Munich Chronotype Questionnaire (MCTQ) assesses self-reported sleep-wake behaviour. It asks at what time people go to bed and are ready to sleep, how long it takes them to fall asleep (sleep latency), at what time they awake and get up and if their sleep is restricted by an alarm clock. Sleep-wake behaviour is generally queried for workdays and work-free days separately, in our case, for schooldays and weekends. Chronotype is defined as the midpoint (time of day) between sleep onset and sleep offset on work-free days, corrected for oversleeping if individuals sleep longer on work-free days than on work days (formula for mid-sleep on work-free days, MSF: sleep onset on work-free days + sleep duration on work-free days / 2; sleep corrected mid-sleep on work-free days, MSFsc: MSF – (sleep duration on work-free days – average sleep duration throughout the week) / 2; for further explanation, see [55]).

The MCTQ-based variable for chronotype (MSF_{sc}) correlates with objective sleep timing, the time when people are most active during a 24h day (i.e. the peak of locomotor activity, see next section for details) and dim-light melatonin onset [56–59]. The absolute difference between mid-sleep on workdays and mid-sleep on work-free days is used to quantify social jetlag [9, 10].

Actimetry to assess objective sleep timing, sleep duration and light exposure

Participants wore an actimeter (Daqtometer 2.4 by Daqtix GmbH, Oetzen, Germany) on their preferred wrist for 31 consecutive days. The device records locomotor activity and light exposure. Both were sampled every second, stored in intervals of 10 seconds, and binned in 10 min epochs for analyses. All days were categorized in workdays (i.e. days when participants went to school) or work-free days (i.e. weekend days when participants could sleep in and were not woken by an alarm clock or their parents). From these time series, we extracted sleep timing (sleep begin/end and mid-sleep in local time) and sleep duration using the sleep detection algorithm reported in Roenneberg et al. [55]. Additionally, we calculated MSF_{sc} from objective sleep timing / actimetry in analogue to the MCTQ data.

In order to determine when people were most active during a 24h day, we fitted a 1-harmonic cosine curve to the data [60] and derived the activities' center of gravity (CoG_{act}; *i.e.* the highest point of the cosine curve which reflects the timing of highest activity). We applied the same procedure to the light data to determine when people received the highest light exposure during the day (center of gravity for light, CoG_{light}, i.e. the highest point of the cosine curve see Roenneberg et al. [55] for further details). Furthermore, light data from the actimeters were averaged over 24 h (midnight to midnight) to calculate mean light exposure on workdays and work-free days.

Data Analysis

Actimetry data was analysed using ChronoSapiens 8 [55]. Statistical analysis was performed using SPSS Statistics 22 (IBM SPSS), Microsoft Excel 2011 for Macintosh, as well as GraphPad Prism 6.0 (GraphPad Software Inc.). All variables with the exception of caffeine- and alcohol-consumption, sleep quality (controls), time spent in over 1000 lux on workdays (controls), sleep onset/offset/duration on workdays (patients) were normally distributed, as tested with the Kolmogorov-Smirnov test. We therefore also performed additional non-parametric analyses for those variables, but report parametric test results unless the results of the two tests were inconsistent. We used chi-square tests to determine differences between sex and smoker distributions between groups. All other group differences were determined with either t-tests or analysis of variance (ANOVA). Repeated-measures ANOVA on sleep timing, sleep latency and light exposure was set up with group as between-subjects factor (patients *versus* healthy controls) and type of day as within-subject factor (workdays *versus* work-free days). T-tests served as post-hoc tests. Significant results are reported on a 5% alpha level (marked with asterisk) and trends toward significance on a 10% alpha level (marked with dagger).

In exploratory analyses, we carried out a mediation analysis according to Preacher and Hayes [61] to determine whether population size (based on the participants' postal code) mediated differences in light exposure between patients and controls.

Results

Depressive symptoms

Table 1 shows the characteristics of both groups. Although subjects in the patient group did not meet DSM IV-TR criteria of a major depressive disorder [46] at present, they showed significantly more self-reported (BDI-II) and parent-reported (DISYPS FBB-DES) depressive symptoms than controls. Patients also reported a worse sleep quality (PSQI) than controls. Groups did not differ in regards of consumption of caffeinated or alcoholic beverages and the proportion of smokers. None of the variables displayed in table 1 differed between patients taking antidepressant medication and patients without medication (data not shown).

<<<<<<< *please add Table 1 here* >>>>>>>

Chronotype and social jetlag

Chronotype (MSF_{sc} from MCTQ) did not differ between patients and controls (see Table 2). Also, MSF_{sc} from objective sleep timing / actimetry as well as COG_{act} (activities' center of gravity, *i.e.* timing of highest activity) on work-free days did not differ between patients and controls. Depressive symptoms (BDI-II) did correlate significantly with chronotype, but only in the control group (the later the chronotype the more depressive symptoms) and not in the patient group. This correlation could not be found with MSF_{sc} from objective sleep timing / actimetry as well as with COG_{act} (*i.e.* time point of highest activity) on work-free days. Chronotype (MSF_{sc} from MCTQ) showed a high correlation with MSF_{sc} from objective sleep timing / actimetry (r=0.57, p<0.001) as well as with CoG_{act} on work-free days (r=0.61, p<0.0001). The absolute differences between subjective and objective reports did not differ between patients and controls (for MSF_{sc} from MCTQ with MSF_{sc} from objective sleep timing: controls 00:28h ± 00:43h, patients 00:26h ± 00:53h, *t*(36)=0.12, p=0.908; for MSF_{sc} from MCTQ with COG_{act} on work-free days: controls 11:59h ± 01:13h, patients 12:16h ± 00:57, *t*(36)=0.80, p=0.427; please note that COG_{act} is a marker of highest activity throughout the 24h day, i.e. the mean difference to MSF_{sc} should be approximately 12 hours).

Age did not correlate with chronotype, in neither patients nor controls (*r*=0.31, *p*=0.195; *r*=-0.21, *p*=0.384). Average light exposure on workdays (24h period) was only associated with chronotype in patients (*i.e.* the more light, the later the chronotype; *r*=0.46, *p*=0.047), but not in controls (*r*=0.08, *p*=0.737), whereas on work-free days it did not show associations in neither patients nor controls (*r*=0.18, *p*=0.456; *r*=-0.16, *p*=0.512). The timing of CoG_{light} was also not associated with chronotype, in neither patients nor controls (workdays: *r*=-0.05, *p*=0.850 *versus* *r*=0.04, *p*=0.868; work-free days: *r*=0.32, *p*=0.180 *versus* *r*=0.20, *p*=0.419).

Patients and controls showed comparable levels of social jetlag (from MCTQ; 2:36 ±1:06h *versus* 2:22 ± 0:42h; *t*(36)=0.77, p=0.449), and social jetlag was also not associated with depressive symptoms (BDI-II) in neither group (controls: *r*=0.35, *p*=0.142; patients: *r*=-0.06, *p*=0.815).

Neither social jetlag nor any of the variables reported in table 2 differed between patients with and without antidepressant medication (data not shown).

<<<<<<< *please add Table 2 here* >>>>>>>

Sleep timing, sleep duration and sleep latency

Table 3 shows the descriptive statistics for objective sleep timing and sleep duration (actimetry), as well as subjective sleep latency (MCTQ). Overall, sleep was earlier and shorter on workdays than on work-free days (Table 3). Only on work-free days, patients slept about 40 min longer than controls (*t*(36)=2.13, p=0.009), making the difference in sleep duration between work- and work-free days higher in the patient group (*t*(36)=2.46, p=0.019, see also Table 4). Timing of sleep did not differ between groups. Sleep latency was longer on workdays compared to work-free days and was similar across groups (Table 4). None of the variables reported in table 3 differed between patients with and patients without antidepressant medication (data not shown).

<<<<<<< *please add Table 3 here* >>>>>>>

<<<<<<< *please add Table 4 here* >>>>>>>

Light exposure

Patients were exposed to higher light levels and spent more time in bright light than controls (see Table 5 and 6). The patients' high light levels indicated more exposure to outdoor light, and – in support of this – significantly more patients lived in a more rural environment (X^2=7.13, *p*=0.008). A mediation analysis supported this hypothesis: Light exposure (*i.e.* time spent in light > 1000 lux on workdays; as dependent variable) was predictable by group (patients *versus* controls; as independent variable; β=0.39, *p*=0.017) and by the respective borough's population size (as a proxy for a more urban or rural environment; as mediator; β=-0.40, *p*=0.012). Group also predicted population size (β=-0.43, *p*=0.007). When population size and group were entered into the regression model, population size showed a trend towards significance in predicting light exposure (β=-0.29, *p*=0.089) whereas group did not predict light exposure (β=0.26, *p*=0.126), see figure 1. The Sobel test showed a significant mediation effect (*Z*=2.89, *p*=0.004).

The timing of the highest light exposure during the 24h-day ($\text{CoG}_{\text{light}}$) was later on work-free days than on workdays, but revealed no significant effect of group.

Timing of highest light exposure on workdays was later for patients taking antidepressant medication compared to patients without medication (02:46 pm ± 0:26h *versus* 01:36 pm ± 0:56h, $t(17)=3.09$, $p=0.007$), but no other variable reported in table 5 differed across those two groups.

<<<<<<< *please add Table 5 here* >>>>>>>

<<<<<<< *please add Table 6 here* >>>>>>>

<<<<<<< *please add Figure 1 here* >>>>>>>

Fig. 1 Higher light exposure in patients is mediated through population size as a proxy for an urban/rural environment

Discussion

Here, we explore the relationships between chronotype, social jetlag, objective sleep behaviour and light exposure in a group of adolescents with remitted major depressive disorders and a control group. We found no differences in chronotype and social jetlag between patients and controls, but remitted patients slept significantly longer on work-free days and reported significantly worse subjective sleep quality. We observed higher levels of 24-h-light-exposure in patients, and this association was mediated by living in a more rural environment. In both groups, sleep timing was significantly earlier, sleep duration significantly shorter and sleep latency significantly longer on workdays than on work-free days.

<<<<<<< please add Figure 2 here >>>>>>>

Fig. 2 Possible scenarios on the course of chronotype in depressive disorders

Chronotype

To integrate our findings into the limited data on the association between chronotype and depression, figure 2 shows five possible scenarios how chronotype may change before, during and after depression. Epidemiological studies in both children/adolescents [34, 35, 37–39, 62] and in adults [11, 21, 63] have shown that later chronotypes report more depressive symptoms (Fig. 2, A and B), which is in line with the observations in our control group. This association has led to the assumption that being a late chronotype might be a risk factor for depression [32]: Due to the misalignment between internal biological time and external social time (*e.g.*, work times; Roenneberg et al., 2015), late chronotypes accumulate more social jetlag and sleep deprivation [27]. The latter has been shown to activate the neuroendocrine stress system and reduces the ability to cope with emotional challenges [65], which could contribute to the development of a major depressive disorder [66, 67].

Scenario A proposes in addition, in line with our data, that chronotype is comparable between remitted patients and healthy controls. Chronotype should therefore be modifiable, possibly as a result of remission and/or therapy (for example, cognitive behavioural therapy [68] leading to more outdoor activities and thereby changing light exposure). Scenario B posits that individuals continue to exhibit later chronotypes after remission, e.g. due to a genetic association between chronotype and depression (for a detailed review, see [69]).

A late chronotype could also be a consequence of a depressive disorder (Fig 2., C and D) due to behavioural changes. Depressed patients become less active [70, 71], expose themselves to less light [72, 73] and therefore delay their circadian clock [15]. During remission, chronotype could either change (Scenario C) or remain delayed (Scenario D). Finally, scenario E proposes no association between chronotype and depression, and previous studies could be subject to self-assessment bias often found in adolescents with depressive disorders [74, 75].

Our data speaks in favour of scenario A, C and E, as remitted patients did not differ from healthy controls, but longitudinal studies with high sample sizes are warranted to disentangle the association between chronotype before, during and after depression.

Finally, de Souza & Hidalgo [39] suggested that chronotype (as sleep-corrected mid-sleep on work-free days) is an inappropriate marker for the circadian system in adolescents, because parents control sleep timing. However, studies show that parents can control only the bedtime of their children, not the actual timing of sleep onset [76, 77]. Additionally, we asked all participants on weekly phone calls if their parents waked them up, and included only work-free days in the analysis where participants could sleep in.

Sleep timing, sleep duration and sleep quality

We saw differences between remitted patients and controls in sleep-related variables other than chronotype and social jetlag, that is, a longer sleep duration on work-free days and a reduced subjective sleep quality. The fact that former patients sleep longer on work-free days than controls could be a residual symptom of depression. However, Murray et al. [42] found a reduced objective sleep duration in acutely depressed adolescents. Our results give rise to multiple interpretations: as a higher sleep need, or a need for more catch up-sleep that cannot be addressed on workdays due to external sleep constraints, or a reduced activation or motivation as residual comorbidities of a depressive disorder. It could also be a predictor for relapse, as a recent meta-analysis showed an increased likelihood of depression in both people with short sleep duration (less than 5 or 6 hours) as well as long sleep duration (more than 8 or 9 hours; [78]). However, as in our study only the sleep duration on work-free days differed between groups, it emphasizes the importance of assessing sleep on workdays and work-free days separately, which should be addressed in further studies.

A reduced subjective sleep quality is often found during acute depression in children and adolescents [44] as well as in our sample of remitted patients. It seems likely that it represents an residual symptom of depression and may also be a predictor of relapse, as Lovato & Gradisar [45] found that sleep disturbances predicted the onset of a major depressive disorder in adolescents.

Light exposure

Remitted patients showed a higher light exposure than controls, a finding that was mediated by an urban/rural environment, *i.e.*, more patients lived in rural areas and therefore had a higher chance of elevated daylight exposure. These findings are in line with previous research. Carvalho, Hidalgo, & Levandovski [79] report a higher general light exposure in rural populations, and Probst et al. [80] found higher rates of depression in rural compared to urban settings. Irrespective of the environment, Graw, Recker, & Sand [81] showed that patients with (seasonal) affective disorders spent more time outside in bright light in summer as compared to healthy controls. The authors argue that these patients may need a higher light exposure to remain euthymic, which may be true for our sample as well.

Strengths and limitations

Our study shows three major strengths. First, all of our participants and their parents underwent a comprehensive structured diagnostic interview by qualified personnel. Hence, we can be sure that our patient group was homogenous in respect to main diagnosis and featured no psychiatric or somatic comorbidities.

Second, our study validates its results on self-reported sleep timing with a long-term monitoring of objective sleep-wake behaviour and showed no differences between patients and controls in reporting sleep-wake behaviour. Therefore, we ruled out any inaccuracies that could arise due to cognitive biases in the depression group [82].

Third, we collected data simultaneously in all participants during the same period of time in the same year. Hence, we ruled out any seasonal effects on sleep behaviour between groups due to a changing photoperiod [16] that could otherwise have influenced our results. Additionally, we made sure that all participants lived close to the same geographical latitude and longitude. This is especially important, because Haraszti, Ella, Gyöngyösi, Roenneberg, & Káldi (2014) and Roenneberg, Kumar, et al., (2007) showed that chronotype is associated with sun time, which is reflected by longitude within a time zone (in contrast to social time).

Five important limitations should be considered: First, our study has a very small sample size and was only powered to find at least medium sized effects (such as those found for example by Kim, et al., 2010). Therefore, our results have to be interpreted with caution, because our sample size could be too small to detect small effects.

Second, as it is a cross-sectional study, we cannot draw conclusions on cause and effect on the possible association between chronotype and depression.

Third, besides the individual amount of residual depressive symptoms, also the time elapsed since remission might play a role in influencing chronotype after remission. While the residual symptoms are reflected in the BDI-II scores, we lack information about the time since remission and thus cannot rule out a dependency of chronotype on time after remission.

Fourth, 7 out of 19 patients took antidepressant medication during the study period, which could have affected our results: Especially SSRIs are known to interact with the circadian system [84] and suspected to phase-advance patients' circadian clock, but data from studies in human adults are inconsistent [85, 86]. Future studies with larger sample sizes should look at mediating effects of medication, even though in our analysis, there were no differences between medicated and non-medicated patients, with the exception of a slightly later timing of the maximum daylight exposure on workdays.

Fifth, our sample mainly consists of females and thus the application of our results to males may be limited, and previous work suggested that sex influences chronotype [23]. However, the sex distribution in our sample reflects the usual sex distribution of depressed patients in the general population, where depression is up to three times more frequent in female compared to male adolescents [87, 88].

Conclusions

Our study shows no differences in chronotype and social jetlag between adolescents with remitted depression and healthy controls. Possible explanations for this finding are that either (late) chronotype is not associated with the emergence and/or acute phase of depression (scenario E), or that there is an association, and chronotype changes during remission (scenarios A and C). Further studies, especially longitudinal studies, are needed to shed light on the dynamics of sleep wake behaviour and chronotype in adolescent depression. The proposed scenarios should be of value when planning such studies.

!Paragraph deleted as suggested!

Further studies should measure sleep on workdays and work-free days separately and assess if participants are living in an urban or rural environment, as our study showed great differences between different types of days and an influence of the environment on daylight exposure.

Finally, our study shows clearly that sleep quality is still of relevance even after remission of major depression and patients should be asked for it. Parents of adolescents with late chronotypes and/or significant social jetlag should be advised to let their children sleep in on work-free days in order to compensate for a sleep debt.

Conflict of interest

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Table 1. Sample characteristics. Group differences in sex and amount of smokers were tested using chi-square tests, all other variables using t-tests for independent groups. Table shows mean ± standard deviation.

	Patients (n=19)	**Controls (n=19)**	**p**
Age	16.51 ± 1.68	16.06 yrs ± 1.68	0.412
Sex	13 female (68%)	12 female (63%)	0.732
BMI	21.79 ± 4.33	20.73 ± 2.36	0.356
Depressive Symptoms			
- *BDI-II score (Self-report)*	10.47 ± 6.70	3.21 ± 3.10	< ***0.001***
- *DISYPS FBB-DES (Parent-report)*	0.51 ± 0.38	0.15 ± 0.10	< ***0.010***
Sleep quality (PSQI score)	6.58 ± 0.65	4.21 ± 0.53	0.008
Caffeine intake (mg/day)	25.38 ± 48.30	26.04 ± 40.87	0.623
Alcohol intake (g/week)	22.65 ± 30.19	18.05 ± 25.33	0.965
No of Smokers (>1 cigarette per day)	5 (26%)	2 (10%)	0.209

Table 2. Chronotype variables. Group differences were tested using t-tests for independent groups, correlations represent pearson correlation with depressive symptoms (BDI-II score). Table shows mean ± standard deviation.

			Group difference	**Correlation with depressive symptoms (BDI-II)**	
	Patients (n=19)	**Controls (n=19)**	**p**	**Patients**	**Controls**
Chronotype (MSFsc from MCTQ)	04:51 am ± 1:06h	04:49 am ± 0:48h	0.899	0.13	0.62**
MSFsc from objective sleep timing through actimetry	04:24 am ± 0:26h	04:20 am ± 0:25h	0.623	0.15	0.31
COGact on work-free days derived from actimetry	15:49 pm ± 1:06h	15:32 pm ± 0:46h	0.344	0.04	0.34

Table 3. Descriptive statistics objective sleep timing, sleep duration and subjective sleep latency. Table shows mean ± standard deviation.

	Workdays		**Work-free days**	
	Patients	**Controls**	**Patients**	**Controls**
Sleep onset (hh:mm)	11:36 pm ± 01:20h	11:31 pm ± 00:30h	00:56 am ± 01:07h	01:08 am ± 00:52h
Sleep offset (hh:mm)	06:49 am ± 00:49h	06:42 am ± 00:29h	10:05 am ± 01:24h	09:29 am ± 01:06h
Mid-sleep (hh:mm)	03:12 am ± 01:03h	03:06 am ± 00:27h	05:30 am ± 01:10h	05:18 am ± 00:54h
Sleep duration	07:10h ± 00:43h	07:10h ± 00:25h	08:57h ± 01:03h	08:16h ± 00:53h
Sleep latency (min)	29 (22)	24 (26)	25 (20)	16 (13)

Table 4. Group differences in objective sleep timing, sleep duration and subjective sleep latency. Results of the ANOVAs for repeated measures with F-values (df), p-values, and effect sizes η2p including the between-subject factor group (patients *versus* controls) and the within-subject-factor type of day (workday *versus* work-free day).

	Type of day			**Group**			**Group x Type of day**		
	F	**p**	**η^2p**	**F**	**p**	**η^2p**	**F**	**p**	**η^2p**
Sleep onset	126.80 (1, 36)	***<0.001***	***0.78***	0.05 (1,36)	0.832	-	1.24 (1, 36)	0.273	-
Sleep offset	224.20 (1, 36)	***<0.001***	***0.86***	1.92 (1,36)	0.175	-	1.44 (1, 36)	0.238	-
Mid-sleep	222.45 (1, 36)	***<0.001***	***0.86***	0.31 (1, 36)	0.582	-	0.10 (1, 36)	0.753	-
Sleep duration	95.13 (1, 36)	***<0.001***	***0.73***	5.28 (1, 36)	***0.027***	***0.13***	6.06 (1, 36)	***0.019***	***0.14***
Sleep latency	7.57 (1, 36)	***.009***	***0.17***	1.50 (1, 36)	0.228	-	1.67 (1, 36)	0.204	-

Table 5. Descriptive statistics objective light exposure. Light exposure was averaged over 24 hours. Table shows mean ± standard deviation.

	Workdays		**Work-free days**	
	Patients	**Controls**	**Patients**	**Controls**
Average light exposure (lux)	493 ± 206	369 ± 120	440 ± 194	343 ± 191
Time spent in light > 1000 lux (h)	04:54 ± 03:13	02:40 ± 02:09	04:26 ± 02:32	03:07 ± 02:19
$\text{CoG}_{\text{light}}$ (hh:mm)	02:02 pm ± 00:58h	02:14 pm ± 01:02h	03:23 pm ± 01:08h	03:14 pm ± 01:02h

Table 6. Group differences in objective light exposure. Results of the ANOVAs for repeated measures with F-values (df), p-values, and effect sizes η2p including the between-subject factor group (patients *versus* controls) and the within-subject-factor type of day (workday *versus* work-free day).

	Type of day			**Group**			**Group x Type of day**		
	F	**p**	**η^2p**	**F**	**p**	**η^2p**	**F**	**p**	**η^2p**
Average light exposure (lux)	1.99 (1, 36)	0.167	-	4.55 (1, 36)	***0.040***	***0.11***	0.25 (1, 36)	0.622	-
Time spent in light > 1000 lux (h)	0.00 (1, 36)	0.984	-	5.95 (1, 36)	***0.020***	***0.14***	1.15 (1, 36)	0.291	-
CoG$_{light}$ (hh:mm)	21.41 (1, 36)	***<0.001***	***0.37***	0.01 (1, 36)	0.935	-	0.51 (1, 36)	0.479	-

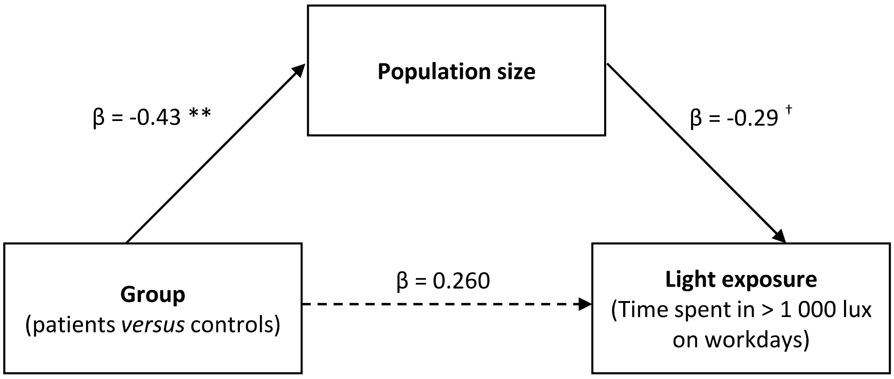
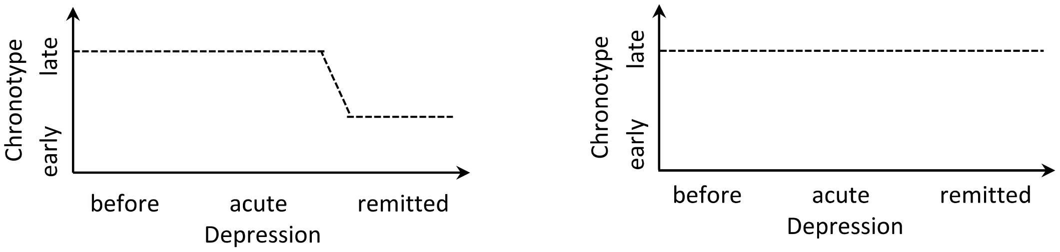
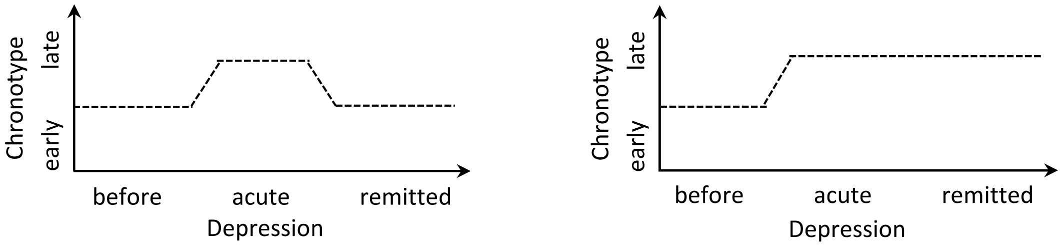


Figure 1



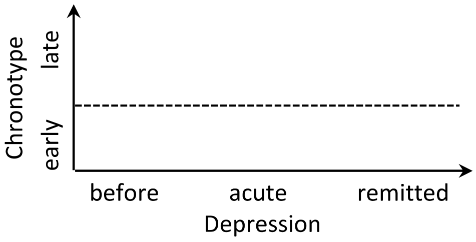
a) Predisposition to depression, modifiable

b) Predisposition to depression, not modifiable



c) Comorbidity, reverts with remission

d) Consequence of depression („scar“)



e) No changes in chronotype

Figure 2

6 Publication 2: Time to rethink sleep quality: PSQI scores reflect sleep quality on workdays.

Time to rethink sleep quality: PSQI scores reflect sleep quality on workdays

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Abstract

The Pittsburgh Sleep Quality Index (PSQI) is the most common measure of sleep quality. Its questions refer to "usual" sleep habits during the last month. Considering how different sleep-wake behavior can be between work- and work-free days, we hypothesized that sleep quality should show similar differences.

We investigated these potential differences in a cross-sectional online study using the original and two adapted versions of the PSQI that replaced "usual" by explicitly referring to sleep on work- or work-free days. Additionally, we investigated how these scores relate to chronotype and social jetlag assessed by the Munich ChronoType Questionnaire. Participants were recruited online, they had to be older than 18 years, following regular weekly work schedules, and should not be shift workers.

All the questionnaires were filled out online. Repeated-measures analysis of variance was used to compare the three different versions of the PSQI (usual, work, work-free). To find out if PSQI score differences could be predicted by chronotype and/or social jetlag a mediation analysis was carried out.

Workday PSQI scores were similar to the original "usual" scores, 2 points higher than the PSQI score on work-free days and above the cut-off designating poor sleep quality. PSQI components and time variables also differed between workdays and work-free days. Chronotype correlated with the difference between PSQI scores on workdays and on work-free days, an association mediated by social jetlag.

Our results suggest that the original PSQI predominantly reports sleep quality on workdays and that work schedules may affect sleep quality. The mediation of social jetlag on the association of chronotype and PSQI score differences could mean that not chronotype per se, but rather the collision of an individuals´ chronotype with fixed work schedules explains the differences between sleep on workdays and work-free days.

Understanding how sleep quality differs between workdays and work-free days, how this difference can adequately be assessed through directing participants to focus on their sleep specifically on workdays vs. work-free days, and how circadian factors modulate this difference, is crucial to improve sleep quality.

Key Words

PSQI, sleep, sleep quality, sleep timing, work-free days, workdays, MCTQ, social jetlag, chronotype.

Statement of Significance

About one-third of all studies on sleep quality use the PSQI – a questionnaire asking for “usual” sleep - as a primary tool for assessing subjective sleep quality. Here, we compared two modified versions, one for workdays and one for work-free days, with the original PSQI. Our results show that the original PSQI reflects mainly sleep quality on workdays, and that participants sleep significantly better on work-free days. Additionally, circadian factors influence the differences in PSQI scores from workdays to work-free days.

Understanding how sleep quality differs between workdays and work-free days, and how circadian factors modulate this difference, is crucial to adequately assess and, finally, improve sleep quality.

Introduction

The Pittsburgh Sleep Quality Index (PSQI) was developed in 1989 to provide a reliable and standardized measure discriminating ‘good’ from ‘poor’ sleepers with the help of a simple index. The PSQI was also designed to evaluate a range of sleep disturbances that affect sleep quality. It assesses different aspects of sleep quality representing the past month[1] and is currently the most common measure of sleep quality[1,2]. Since 2007, the number of published studies that mention "Pittsburgh Sleep Quality Index" represents more than a quarter of the number of studies mentioning "sleep quality", reaching a noteworthy 34.5 % in the last year (as assessed in Pubmed, on April 12, 2017).

While the PSQI correlates significantly with sleep log data and subjective measures like symptoms of insomnia, depression and anxiety[3–5], its comparisons with objective sleep parameters obtained by polysomnography or wrist actimetry yield heterogeneous results: Spira et al (2012) found only moderate correlations between the PSQI score and actimetric parameters (longer napping, more time spent awake after sleep onset)[6] and Grutsch et al (2011) found that in a patient group lower sleep quality correlates with lower general activity as well as with more time spent asleep (actimetry) – but only in outpatients and not in inpatients[8]; finally, several other studies found no correlations between PSQI scores and objective measures from actimetry and polysomnography (*i.e.*, sleep latency, sleep efficiency, wake after sleep onset, time spent asleep, time spent in REM sleep)[3,4,9].

This inconsistency may reflect the fact that the PSQI addresses *usual* sleep summarized over the course of a month and not a specific night as measured by the objective instruments. Participants might base their responses about usual sleep on either what they do most frequently (*i.e.*, workdays) or on a “weighted average”. Results obtained with the Munich ChronoType Questionnaire (MCTQ) have shown that sleep duration and timing vary substantially between workdays and work-free days[10,11]. One reason is that more than 80% of the population in western countries use an alarm clock on workdays, whereas sleep timing on work-free days (*i.e.,* chronotype) is mainly influenced by the biological clock[12,13]. This characteristic so-called chronotype is normally distributed and spans from extremely early sleep times to extremely late sleep times[10]. Late chronotypes suffer from early work start times and have to get up way before their internal clock wakes them up. This discrepancy between internal time (defined by chronotype) and external time (defined by work schedules) was coined social jetlag[13,14] and is associated with a variety of health risks and diseases (smoking and alcohol consumption[14]; obesity[13]depressive symptoms[15] metabolic disorders[16,17].

Here, we investigated whether PSQI scores differ between workdays and work-free days, and what the original PSQI (asking for *usual* sleep habits) actually represents. Additionally, we explored if the original and the day-specific PSQI scores depend on chronotype and/or social jetlag. For this purpose, in a cross-sectional study, participants filled out three online versions of the PSQI: the original version (asking for *usual* sleep-behavior; $PSQI_{u,}$) and two adapted day-specific versions (asking for sleep-behavior on workdays, $PSQI_{w}$; and work-free days, $PSQI_{f}$) as well as the Munich ChronoType Questionnaire (MCTQ). We hypothesize that “usual” sleep quality reflects sleep quality on workdays, and that sleep quality on workdays is worse compared to sleep quality on work-free days. We also hypothesize that a higher difference in sleep quality between workdays and work-free days is associated with a later chronotype and a higher social jetlag.

Methods

Participants

Between June 11 and July 30, 2015, 341 participants took part in our multi-lingual study (questionnaires were available online in English, German and Portuguese). 147 participants filled out the English version, 125 the Portuguese version, and 69 the German version. Participants were between 18 and 74 years old (mean 35 ± 12 years); 236 were female, 105 male. Average height was 1.69 ± 0.09m, average weight was 67 ± 17kg and average number of workdays per week was 3.8 ± 2.3 days. Tables 1 and 2 show how relevant variables varied according to age, sex and language.

The study was approved by the ethics committee of the Medical Faculty of the Ludwig Maximilian University Munich and was conducted in accordance with the Declaration of Helsinki. All participants provided their informed consent by clicking a statement before proceeding to the survey data collection.

Please add Table 1 here

Table 1. Descriptive statistics and comparisons of PSQI general scores ($PSQI_u$, $PSQI_w$ and $PSQI_f$: mean, standard deviation in brackets) by sex, age and language groups. Results from t-tests or ANOVA followed by Tukey post hoc tests. Out of n = 341, n = 338 were analysed, n = 3 were excluded due to invalid/incomplete datasets.

Please add Table 2 here

Table 2. Descriptive statistics and comparisons of PSQI differences ($PSQI_{diff}$, difference between the score on workdays and work-free days), chronotype (MSF_{sc}) and social jetlag (mean, standard deviation in brackets) by sex, age and language groups. Results from t-tests or ANOVA followed by Tukey post hoc tests. Out of n = 341, n = 264 were analysed for $PSQI_{diff}$, chronotype and social jetlag, n = 76 used alarm clocks on work-free days, i.e. chronotype could not be calculated, n = 1 was excluded as an outlier: more than 3 IQR above Q3 for social jetlag.

Procedure

We used non-representative snowball sampling and recruited participants through social media, e-mails to personal contacts, and posts on discussion boards and mailing lists. Inclusion criteria were being at least 18 years old, following a regular weekly work schedule and not being a shift worker. When accessing the webpage, subjects were informed about the study terms, including confidentiality and data handling policies, as well as ways to contact the research team if they had any further questions. After accepting the study terms, participants were directed to the questionnaires. At first, all participants filled out the original version of the Pittsburgh Sleep Quality Index asking for usual sleep behavior ($PSQI_u$), followed by the two modified versions for workdays ($PSQI_w$) or work-free days ($PSQI_f$) in a randomized order, and finally the Munich Chronotype Questionnaire (MCTQ). All questionnaires had to be completed in one session. On average, participants needed 29 minutes to fill out all questionnaires. Only fully completed questionnaires were saved to the online database.

Materials

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) was developed by Buysse et al (1989)[1]. It is a self-report on subjective sleep quality over the last four weeks with 18 questions. The first four questions enquire about times (bed time, number of minutes it took the participant to fall asleep, get up time, and hours of sleep per night).

The next ten questions ask how often the participant had trouble sleeping because of different reasons (e.g. woke up in the middle of the night, need to go to the bathroom, cough, bad dreams). Each of these questions must be answered on a 4-point scale ranging from “never” to “three times or more a week”. Additional questions include a subjective rating of the participants sleep quality (4-point scale from “very good” to “very bad”), the use of sleep medication as well as trouble staying awake during the day (4-point scale ranging from “never” to “three times or more a week”). The final question asks if it has been a problem for the participant to keep up enough enthusiasm for getting things done (4-point scale ranging from “no problem at all” to “a very big problem”).

The 18 items of the PSQI form seven component score ranging from 0 to 3 (sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, sleep medication, daytime dysfunction) that can be summed up to a general score. Higher scores represent worse sleep quality[1]. The psychometric properties of the English version[1], as well as the German[5] and the Portuguese version[18] are good.

In our study, we used the original PSQI that states "The following questions relate to your usual sleep habits during the past month only". We added two modified versions, one for workdays, stating "The following questions relate to your sleep habits on *workdays* during the past month only", and one for work-free days, stating "The following questions relate to your sleep habits on *work-free days* during the past month only". In the modified versions, we added the term "workdays" (or "work-free days", respectively) to every single question. The words "workdays" and "work-free days" were highlighted in the questionnaires, and attention was drawn, in the instructions, to the fact that there were versions for each one of them.

Munich ChronoType Questionnaire

The English, German and Portuguese core versions of the Munich ChronoType Questionnaire (MCTQ) for non-shift-workers were used to assess sleep-wake behaviour on workdays and work-free days (see https://www.thewep.org/documentations/mctq). The MCTQ asks, separately for workdays and work-free days, at what time people go to bed and are ready to sleep, how long it takes them to fall asleep, at what time they wake up and get up and if they use an alarm clock.

The MCTQ was designed to assess chronotype based on phase of entrainment (relationship between internal and external day). Chronotype is not a score, but a local time (MSF_{sc}: midpoint between sleep onset and sleep offset on work-free days, corrected for oversleep if individuals sleep longer on work-free days than on workdays, see Roenneberg et al., 2015 for exact calculations). Additionally, variables like sleep duration and social jetlag (absolute difference between mid-sleep on work and work-free days) can be derived from the MCTQ[12,14].

Chronotype calculations were considered only if the participant reported not to use an alarm clock on work-free days.

Sample size calculation

Roenneberg et al[11] compared sleep parameters on workdays and work-free days, and the smallest significant effect size was 0.27. To achieve a statistical power of 1-β=.95 with an α<.05 and an effect size of at least 0.2 we needed to recruit 327 subjects to compare workdays and work-free days.

Data Analysis

Statistical analysis was performed using SPSS Statistics 23 (IBM SPSS), Excel 2011 for Macintosh, as well as Prism 6. To confirm data validity, we only included data following a 24h time format. 341 participants completed the questionnaires, 3 were excluded due to invalid/incomplete datasets on one of the PSQIs. All variables followed a normal distribution determined by visual inspection of histograms. We used repeated-measures analysis of variance (ANOVA) with the three different versions of the PSQI (usual, work, work-free) as within-subject factor. If the assumption of sphericity (Mauchly's test) was violated the Greenhouse-Geisser correction was applied. Bonferroni tests were used as post-hoc tests. We used paired sample t-tests to analyse the differences between MCTQ timing variables between workdays and work-free days. Linear regressions were used to determine whether there were associations between PSQI scores, chronotype and social jetlag. To find out if PSQI score differences could be predicted by chronotype and/or social jetlag we carried out a mediation analysis as described by Preacher and Hayes (2004). Additionally, we calculated a "time-free" PSQI score (i.e. the sum of *component 1: sleep quality*, *component 5: sleep disturbances*, *component 6: sleep medication* and *component 7: daytime dysfunction*) to make sure that potential relations between chronotype, social jetlag and PSQI scores were not only due to the fact that PSQI scores also include variables that are derived from information about sleep timing and sleep duration (i.e. *component 2: sleep latency, component 3: sleep duration, component 4: sleep efficiency*). We then calculated an additional mediation model with the "time-free" PSQI score. In multiple regressions, tolerance tests were used as indicators of co-linearity. 76 of 341 participants reported alarm clock usage on work-free days, therefore chronotype could not be calculated. We excluded one extreme outlier (social jetlag 3x the interquartile range higher than 75th percentile). Participants who used alarm clocks on work-free days did not differ from the whole sample in terms of age and sex.

Results

Differences between $PSQI_u$, $PSQI_w$ and $PSQI_f$

Internal consistency

The internal consistency for $PSQI_u$ ($\alpha = 0.62$), $PSQI_w$ ($\alpha = 0.67$) and $PSQI_f$ ($\alpha = 0.68$) was considered acceptable. The largest item-total correlation coefficients were found for *component 1: sleep quality* ($r = 0.56$, $r = 0.56$, $r = 0.61$), the smallest for *component 6: sleep medication* ($r = 0.14$, $r = 0.11$, $r = 0.21$).

General PSQI score

As shown in figure 1 and table 3, $PSQI_u$, $PSQI_w$ and $PSQI_f$ scores differ significantly. Post-hoc comparisons revealed a significant difference between $PSQI_u$ vs. $PSQI_f$ and $PSQI_w$ vs. $PSQI_f$, but not between $PSQI_u$ vs. $PSQI_w$. Neither of the three PSQI general scores differed between participants who used and who did not use an alarm clock on work-free days ($PSQI_u$: $p=0.533$, $PSQI_w$: $p=0.551$, $PSQI_f$: $p=0.312$).

Please add Figure 1 here

*Figure 1. PSQI score differences between "usual", "workdays" and "work-free days". Black dots show means, whiskers show standard deviations. ****=p<0.0001.*

PSQI component scores

PSQI component scores and comparisons between conditions are shown in table 3. Apart from *component 6: sleep medication*, all component scores (that are summed up to the general PSQI score) differ between “usual” and “work-free days” as well as between “workdays” and “work-free days”. Figure 2 displays the differences between PSQI component scores on workdays and work-free days, showing a higher sleep quality, a reduced sleep latency, a longer sleep duration, a higher sleep efficiency, as well as less sleep disturbances and less daytime dysfunction on work-free days compared to workdays.

Please add Table 3 here

Table 3. Descriptive statistics and comparisons of PSQI general score, PSQI components scores and PSQI time variables (mean, standard deviation in brackets). Results from repeated measures ANOVA followed by Bonferroni’s multiple comparisons tests. Out of n = 341, n = 338 were analysed, n = 3 were excluded due to invalid/incomplete datasets.

Please add Figure 2 here

Figure 2. Differences in PSQI component scores between workdays and work-free days. Component scores ranging from 0 to 3. Black dots show mean differences, whiskers show standard deviations. Note, the higher the component scores, the worse the sleep.

PSQI time variables

Table 3 shows that all PSQI variables asking for answers on a time scale (i.e. bedtime, sleep latency, get up time, and sleep duration) differ significantly between “workdays” vs “work-free days” and between “work-free days” vs “usual”, but only get up time differed between “usual” vs “work-free days”. Figure 3 shows that participants go to bed and get up later and sleep longer on work-free days compared to workdays.

Please add Figure 3 here

Figure 3. Differences in PSQI time variables bedtime, get up time and sleep latency between workdays and work-free days. Black dots show mean differences, whiskers show standard deviations.

PSQI score differences, chronotype and social jetlag

Descriptive statistics from the MCTQ can be seen in Table 4. Chronotype predicts PSQI score differences ($PSQI_{diff}$: r = -0.159, p = 0.010; β = 0.140, p = 0.025) in a linear regression model adjusted for age (β = -0.114, p = 0.066) and sex (β = 0.121, p = 0.046). Also social jetlag predicts $PSQI_{diff}$ (r = -0.221, p < 0.0001; β = 0.193, p = <0.0001), adjusted for age (β = -0.106, p = 0.052) and sex (β = 0.098, p = 0.062).

In a mediation model, $PSQI_{diff}$ could be predicted by chronotype (as independent variable, β = 0.159, p = .010) and by social jetlag (as mediator, β = 0.221, p < .0001). Chronotype also predicted social jetlag (β = 0.551, p < .0001). When social jetlag and chronotype were entered into the model, social jetlag predicted $PSQI_{diff}$ (β = 0.315, p < .0001), whereas chronotype did not predict $PSQI_{diff}$ anymore (β = -0.015, p = .833). The Sobel test showed a significant mediation effect (Z = 4.136, p < .0001) of social jetlag on the relationship between chronotype and $PSQI_{diff}$.

A mediation model calculated with PSQI scores excluding all sleep timing related variables (i.e. component 2: sleep latency, component 3: sleep duration, component 4: sleep efficiency) yielded similar results: $PSQI_{diff}$ without time variables could be predicted by chronotype (as independent variable, β = 0.124, p = .044) and by social jetlag (as mediator, β = 0.238, p < .0001). In a regression with both chronotype and social jetlag, only the latter predicted $PSQI_{diff}$ without time variables (β =

0.346, $p < .0001$; chronotype: $\beta = -0.066$, $p = 0.345$). Also for $PSQI_{diff}$ without time-related variables, the Sobel test showed a significant mediation effect ($Z = 4.150$, $p < .0001$) of social jetlag on the relationship between chronotype and $PSQI_{diff}$.

In both models (e.g., with the PSQI score difference between workdays and work-free days and with PSQI scores difference excluding timing-related components 2-4 as dependent variables), tolerance was greater than .10 (0.737) and the variance inflation factor was lower than 10 (1.36), indicating that co-linearity does not account for our results.

Please add Table 4 here

Table 4. Descriptive statistics and comparisons of MCTQ timing variables, chronotype and social jetlag. Results from t-tests. N = 341 were analysed for MCTQ time variables; n = 264 where analysed for chronotype and social jetlag, n=76 used alarm clocks on work-free days, i.e. chronotype could not be calculated, n = 1 was excluded as an outlier: more than 3 IQR above Q3 for social jetlag.

Please add Figure 4 here

Figure 4. The relationship between PSQI Score difference (work-free days minus workdays) and chronotype is mediated by social jetlag.

Discussion

To our knowledge, the PSQI has never before been asked in form of day-specific versions, *i.e.*, separately for workdays and work-free days. Our results show a substantial difference between workdays and work-free days in terms of sleep quality in a general population. $PSQI_w$ was 2 points higher than $PSQI_f$ and above the cut-off for poor sleep quality (>5), suggesting that beyond the impact on sleep timing and duration, the effects of imposed work schedules extend to sleep quality. *Usual* PSQI scores were indistinguishable from workdays' scores, suggesting that the $PSQI_u$ mainly assesses workdays' sleep quality. The difference between $PSQI_w$ and $PSQI_f$ scores was not a direct effect of sleep duration and timing (influencing the total score), as the difference also pertained when analysing the difference in separate components other than sleep duration and timing (*i.e.*, sleep quality, sleep disturbances, daytime dysfunction), suggesting that other aspects are affected as well. We also found that the later the chronotype, the higher the difference between $PSQI_w$ and $PSQI_f$ scores, and that this association was mediated by social jetlag.

In our study, chronotype correlated with the difference between $PSQI_w$ and $PSQI_f$ scores. Previous studies found that chronotype has a significant effect on sleep quality as measured by actigraphic measures. Evening types were reported to have decreased sleep quality and shorter sleep duration when compared to morning and intermediate types during the week, reaching the same levels in the weekend[19]. Alternatively to a direct effect of chronotype on the PSQI differences, we have shown that this relationship is mediated by social jetlag. That means that possibly it is not being a late chronotype per se that explains the association with higher PSQI differences, but rather the collision of a late chronotype with time constraints of the external word, which can be quantified by social jetlag. Late chronotypes often need to adapt to conventional early work schedules, so the later the chronotype, the greater the social jetlag and so the difference between sleep quality on workdays compared to work-free days. Two studies that lead into that direction were conducted in shift-workers - a group of people that is highly affected by social jetlag: the interaction of chronotype and shift modulated sleep disturbances[20] and tailoring work schedules to reduce social jetlag improved sleep quality[21].

One could argue that the relationship between chronotype/social jetlag and PSQI difference was only due to components overlapping, since variables such as sleep duration are used for the calculation of both chronotype/social jetlag and PSQI scores. However, the result of the mediation model was similar after removing the variation in sleep quality due to sleep timing and duration. Additionally, PSQI scores and sleep duration (as measured by sleep logs) were previously reported to overlap only to a small extent in a nonclinical population, and sleep quality components other than duration were suggested to be widely responsible for the association between sleep quality and measures of health and wellbeing[22]; besides, a variety of studies presents evidence on the association between poor sleep and health problems[23,24]. A recent meta-analysis on the relationship between sleep and work suggests that sleep quality has been examined more often than sleep quantity, was only modestly related to it and was significantly associated to more correlates (e.g. trait negative affect, workload, perceived control, depression, fatigue, general strain, and work-family control) and with larger average sizes, especially for variables related to the employees' perceptions or emotions[25].

Other factors related to the work life beyond social jetlag and sleep duration probably contribute to the observed differences between workdays and work-free days. Stress and strain at the workplace have been associated with poor sleep quality[26,27]. Among work stressors related to disturbed sleep are high demands, persistent thoughts about work, low social support at work, and high physical work[28]. All these factors could be working together, as it has been proposed that circadian misalignment could render the organism to an allostatic overload and therefore reduce the ability to cope with stress[29].

Our results should be interpreted with caution, because a conclusion about causality between social jetlag and sleep quality cannot be taken in a cross-sectional study. Co-linearity could have also influenced our results, however, tests for co-linearity indicated it was not large enough to affect the predicted values. It should also be noted that the PSQI cut-off score of 5 has been debated in the literature, and some authors suggested higher thresholds to classify "good" and "poor" sleepers[30,31]. The study design could be subject to recall bias, i.e. participants usually work more days per week than they have work-free days, which might have led to a more accurate representation of sleep on workdays compared to work-free days. Additionally, all three versions of the PSQI were completed in one session which might have influenced our results, i.e. subsequent tests might have been affected by earlier responses and participants might have over- or underestimated the differences between workdays and work-free days. However, our main aim was to assess data on sleep quality regarding the previous month to make it as comparable as possible to the original PSQI. At least we randomized the order of completion of the PSQI for workdays and for work-free days to counterbalance any effects due to sequence.

Since this was an online advertised survey, it was subject to volunteer bias (i.e., people particularly interested in sleep could be more prone to participate and to perceive differences between workdays and work-free days) and the sample was quite heterogeneous (e.g. from different countries and cultural backgrounds), which could compromise internal validity. However, chronotype in our sample followed a normal distribution and was similar compared to the large MCTQ database[12]. Additionally, the online survey allowed us to reach a geographically diverse sample, potentially increasing the study external validity. We did not use any objective measurement, which might be seen as a limitation. However, sleep quality can by definition be considered as a subjective perception, with still no consensus on what good sleep in fact implies[32]. Objective measurements refer to the assessment of behaviours that are considered to be correlates of sleep quality. When comparing the relationship with work-related outcomes of subjective and objective measurements of sleep quality, Litwiller et al (2017) have seen that the latter were used in fewer studies, showed a small non-significant correlation with the subjective measurements and were not as strongly correlated to variables related to perception and emotions[25]. One possible explanation is that the rating of subjective sleep quality is influenced by negative affect, which could confound the impact of its relationship with health outcomes. However, it has also been suggested that objective and subjective measures appraise different aspects of sleep quality and that one cannot function as a surrogate for the other[33,34]. In that case, it would be interesting to see if objective sleep quality measures also differ when comparing workdays and work-free days.

Our study showed that if we aim to assess sleep quality as correctly as possible, we should start by asking separately for workdays and work-free days. To understand the discrepancy between them, we still need to uncover how chronotype and social jetlag as well as other factors contribute to poor sleep quality. Further studies using objective measurements of sleep quality could be a next step to understand how these relationships are intertwined. Additionally, studies in sleep disorders patients investigating how sleep quality differs on workdays when compared to work-free days might help us to understand how these patterns might be clinically relevant. Finally, this understanding might foster purposeful solutions, e.g. the use of chronotype-based work schedules, to improve sleep quality and health.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Figure Captions

Figure 1. PSQI score differences between “usual”, “workdays” and “work-free days”. Black dots show means, whiskers show standard deviations. ****=p<0.0001.

Figure 2. Differences in PSQI component scores between workdays and work-free days. Component scores ranging from 0 to 3. Black dots show mean differences, whiskers show standard deviations. Note, the higher the component scores, the worse the sleep.

Figure 3. Differences in PSQI time variables bedtime, get up time and sleep latency between workdays and work-free days. Black dots show mean differences, whiskers show standard deviations.

Figure 4. The relationship between PSQI Score difference (work-free days minus workdays) and chronotype is mediated by social jetlag.

Table Captions

Table 1. Descriptive statistics and comparisons of PSQI general scores ($PSQI_u$, $PSQI_w$ and $PSQI_f$: mean, standard deviation in brackets) by sex, age and language groups. Results from t-tests or ANOVA followed by Tukey post hoc tests. Out of n = 341, n = 338 were analysed, n = 3 were excluded due to invalid/incomplete datasets.

Table 2. Descriptive statistics and comparisons of PSQI differences ($PSQI_{diff}$, difference between the score on workdays and work-free days), chronotype (MSF_{sc}) and social jetlag (mean, standard deviation in brackets) by sex, age and language groups. Results from t-tests or ANOVA followed by Tukey post hoc tests. Out of n = 341, n = 264 were analysed for $PSQI_{diff}$, chronotype and social jetlag, n = 76 used alarm clocks on work-free days, i.e. chronotype could not be calculated, n = 1 was excluded as an outlier: more than 3 IQR above Q3 for social jetlag.

Table 3. Descriptive statistics and comparisons of PSQI general score, PSQI components scores and PSQI time variables (mean, standard deviation in brackets). Results from repeated measures ANOVA followed by Bonferroni's multiple comparisons tests. Out of n = 341, n = 338 were analysed, n = 3 were excluded due to invalid/incomplete datasets.

Table 4. Descriptive statistics and comparisons of MCTQ timing variables, chronotype and social jetlag. Results from t-tests. N = 341 were analysed for MCTQ time variables; n = 264 where analysed for chronotype and social jetlag, n=76 used alarm clocks on work-free days, i.e. chronotype could not be calculated, n = 1 was excluded as an outlier: more than 3 IQR above Q3 for social jetlag.

Table 1: PSQI general scores

					Comparisons		
	n	PSQIu	PSQIw	PSQIf	PSQIu	PSQIw	PSQIf
Sex							
Male	105	5.00 (2.42)	5.02 (2.77)	3.50 (2.46)	$t_{248.96} = -3.46$	$t_{239.44} = -3.52$	$t_{336} = -2.04$
Female	233	6.08 (3.05)	6.24 (3.34)	4.16 (2.87)	$p < 0.01$	$p < 0.01$	$p < 0.05$
Age							
18 – 30 yr.	158	6.15 (2.87)	6.33 (3.16)	4.03 (2.64)	$F_{(3, 334)} = 2.17$	$F_{(3, 334)} = 2.82$	$F_{(3, 334)} = 1.16$
31 – 40 yr.	88	5.20 (2.66)	5.14 (2.89)	3.61 (2.74)	$p = 0.09$	$p < 0.05$	$p = 0.32$
41 – 50 yr.	39	5.72 (2.67)	6.03 (3.24)	3.77 (2.37)	-	18-30 yrs vs. 31-40 yrs ($p < 0.05$)	-
> 50 yr.	53	5.49 (3.43)	5.57 (3.72)	4.47 (3.36)			
Language							
English	146	5.54 (2.91)	5.68 (3.38)	3.83 (3.00)	$F_{(2, 335)} = 0.97$	$F_{(2, 335)} = 0.71$	$F_{(2, 335)} = 0.32$
German	69	5.68 (2.79)	5.75 (2.84)	3.96 (2.26)	$p = 0.38$	$p = 0.49$	$p = 0.73$
Portuguese	123	6.03 (2.96)	6.14 (3.23)	4.11 (2.74)	-	-	-

Table 1. Descriptive statistics and comparisons of PSQI general scores ($PSQI_u$, $PSQI_w$ and $PSQI_f$; (mean, standard deviation in brackets)) by sex, age and language groups. Results from t-tests or ANOVA followed by Tukey post hoc tests. Out of n=341, n=338 were analysed, n=3 were excluded due to invalid/incomplete datasets.

Table 2: PSQI Score differences, chronotype and social jetlag by sex, age and language

					Comparisons		
	n	PSQIdiff	Chronotype	Social Jetlag	PSQIdiff	MSFsc	SJL
Sex							
Male	88	1.51 (2.22)	4:50 (1:41)	1:23 (1:06)	t_{262}= -1.96	$t_{139.68}$= -1.96	t_{262}= -0.37
Female	176	2.12 (2.12)	4:38 (1:17)	1:26 (1:00)	p = 0.05	p = 0.33	p = 0.71
Age							
18 – 30 yrs.	110	2.34 (2.46)	5:01 (1:31)	1.44 (1:07)	$F_{(3, 260)}$ = 3.38	$F_{(3, 260)}$ = 5.53	$F_{(3, 260)}$ = 8.65
31 – 40 yrs.	74	1.55 (2.19)	4:45 (1:15)	1:21 (0:53)	p < 0.05	p < 0.01	p < 0.001
41 – 50 yrs.	34	2.29 (2.76)	4:21 (1:10)	1:18 (0:58)	18-30 yrs vs. > 50 yrs (p < 0.05)	18-30 yrs vs. > 50 yrs (p < 0.01)	18-30 yrs vs. > 50 yrs, 31-40 yrs vs. > 50 yrs (p < 0.001, p < 0.05)
> 50 yrs.	46	1.22 (2.15)	4:06 (1:30)	0:52 (0:45)			
Language							
English	113	1.81 (2.45)	4:44 (1:35)	1:15 (0:53)	$F_{(2, 261)}$ = 0.22	$F_{(2, 261)}$ = 1.52	$F_{(2, 261)}$ = 4.11
German	48	2.00 (2.31)	4:22 (1:19)	1:23 (1:03)	p = 0.80	p = 0.22	p < 0.05
Portuguese	104	2.00 (2.43)	4:48 (1:18)	1:38 (1:07)	-	-	en vs. pt (p < 0.05)

*Table 2. Descriptive statistics and comparisons of PSQI differences (PSQIdiff, difference between the score on workdays and work-free days), chronotype (MSFsc) and social jetlag (mean, standard deviation in brackets) by sex, age and language groups. Results from t- tests or ANOVA followed by Tukey post hoc tests Out of n=341, n=338 were analysed for PSQIdiff, n=3 were excluded due to invalid/incomplete datasets; n=264 where analysed for chronotype and social jetlag, n=76 used alarm clocks on work-free days, i.e. chronotype could not be calculated, n=1 was excluded as an outlier: +3*IQR for social jetlag.*

Table 3: PSQI general scores, PSQI component scores and PSQI time variables

				ANOVA			Post-hoc comparisons (Bonferroni)		
							usual*work	usual*free	free*work
	Usual	**Workdays**	**Work-free days**	**F (df)**	**p**	**η2p**	**p**	**p**	**p**
PSQI general score	5.75 (2.91)	5.86 (3.22)	3.96 (2.76)	204.7 (1.53, 518.4)	<0.0001	0.38	0.3885	<0.0001	<0.0001
Components									
1 - Sleep quality	1.11 (0.68)	1.21 (0.75)	0.83 (0.71)	94.76 (1.51, 510.3)	<0.0001	0.22	<0.0001	<0.0001	<0.0001
2 - Sleep latency	1.02 (0.93)	0.92 (0.96)	0.64 (0.79)	72.07 (1.66, 558.0)	<0.0001	0.18	0.0002	<0.0001	<0.0001
3 - Sleep duration	0.52 (0.71)	0.64 (0.85)	0.15 (0.50)	92.21 (1.61, 543.6)	<0.0001	0.21	<0.0001	<0.0001	<0.0001
4 - Sleep efficiency	0.38 (0.78)	0.43 (0.81)	0.26 (0.62)	11.52 (1.94,652.7)	<0.0001	0.03	0.6706	0.0021	<0.0001
5 - Sleep disturbances	1.14 (0.45)	1.09 (0.46)	0.98 (0.48)	32.58 (1.77,595.2)	<0.0001	0.09	0.0089	<0.0001	<0.0001
6 - Sleep medication	0.31 (0.82)	0.30 (0.81)	0.24 (0.75)	5.30 (2.69, 570.4)	0.0081	0.02	1.0000	0.0015	0.0937
7 - Daytime dysfunction	1.27 (0.81)	1.28 (0.84)	0.87 (0.77)	97.50 (1.57, 530.2)	<0.0001	0.22	1.0000	<0.0001	<0.0001
Time variables									
Bedtime (hh:mm)	23:43 (01:26)	23:36 (01:17)	00:28 (01:31)	112.9 (1.93, 651.1)	< 0.0001	0.25	0.1850	< 0.0001	< 0.0001
Latency (min)	19.35 (18.28)	19.89 (19.99)	16.52 (16.67)	15.16 (1.49, 501.6)	< 0.0001	0.04	0.6274	0.0002	< 0.0001
Get up (hh:mm)	07:32 (01:45)	07:17 (01:32)	09:17 (01:42)	318.4 (1.87, 630.4)	< 0.0001	0.49	0.0026	< 0.0001	< 0.0001
Sleep Duration (hh:mm)	07:01 (01:07)	06:52 (01:29)	08:11 (01:17)	187.8 (1.60, 538.9)	< 0.0001	0.36	0.0686	< 0.0001	< 0.0001

Table 3. Descriptive statistics and comparisons of PSQI general score, PSQI components scores and PSQI time variables (mean, standard deviation in brackets). Results from repeated measures ANOVA followed by Bonferroni's multiple comparisons tests. Out of n=341, n=338 were analysed, n=3 were excluded due to invalid/incomplete datasets.

Table 4: MCTQ variables

			Comparisons	
	Workdays	**Work-free days**	**t (df)**	**p**
Bedtime (hh:mm)	23:29 (01:14)	00:25 (01:36)	-13.62 (340)	<0.0001
Being ready to sleep (hh:mm)	23:49 (01:15)	00:43 (01:38)	-14.38 (340)	<0.0001
Sleep latency (min)	20 (25)	17 (16)	3.09 (340)	0.002
Sleep onset (hh:mm)	00:09 (01:24)	01:00 (01:42)	-12.75 (340)	<0.0001
Sleep end (hh:mm)	07:14 (01:31)	09:02 (01:47)	-19.20 (340)	<0.0001
Sleep inertia (min)	23 (64)	33 (70)	-3.79 (340)	<0.0001
Getting up (hh:mm)	07:37 (01:51)	09:35 (02:12)	-19.02 (340)	<0.0001
Sleep duration (hh:mm)	07:04 (01:27)	08:02 (01:42)	-9.81 (340)	<0.0001
Total time spent in bed (hh:mm)	08:07 (01:44)	09:09 (02:05)	-9.69 (340)	<0.0001
Chronotype (MSFsc), (hh:mm)	04:43 (01:28)			
Social jetlag (hh:mm)	01:25 (01:05)			

*Table 4. Descriptive statistics and comparisons of MCTQ timing variables, chronotype and social jetlag. Results from t-tests. N=341 were analysed for MCTQ time variables; n=264 where analysed for chronotype and social jetlag, n=76 used alarm clocks on work-free days, i.e. chronotype could not be calculated, n=1 was excluded as an outlier: +3*IQR for social jetlag.*

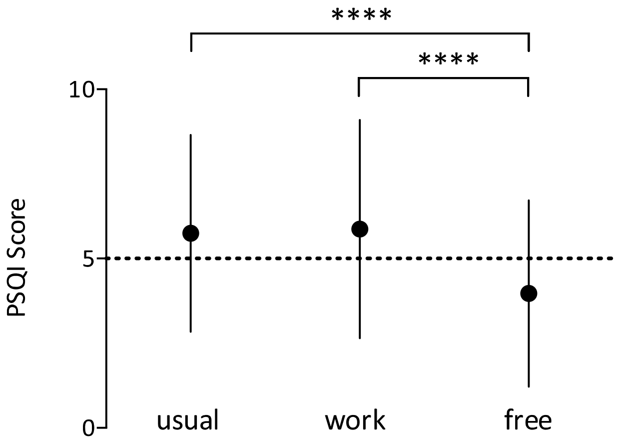

Figure 1

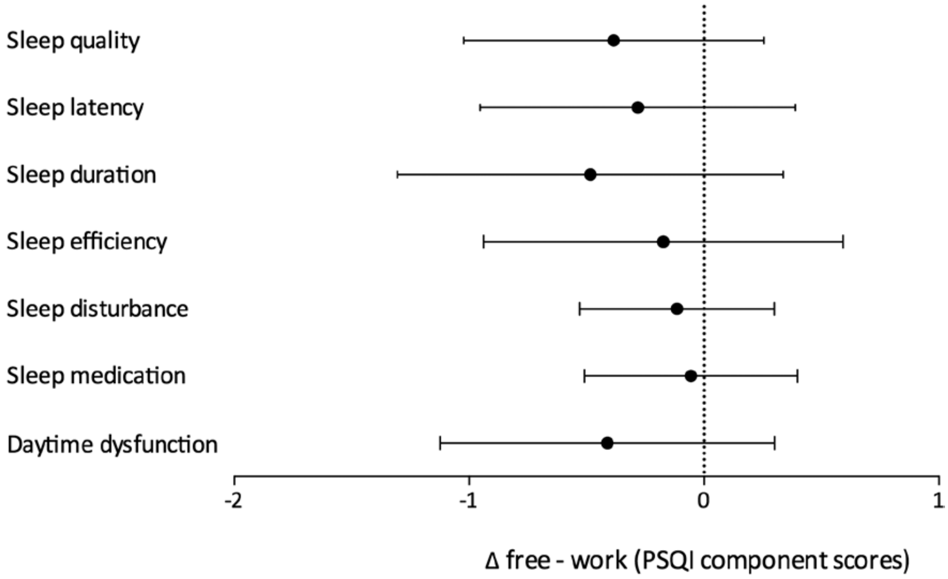

Figure 2

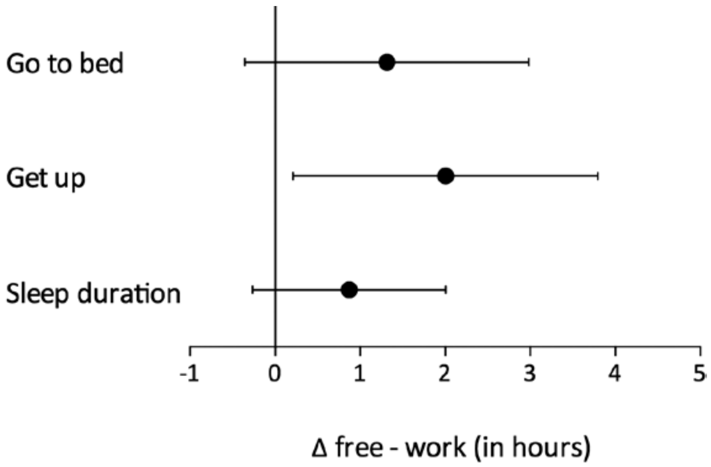

Figure 3

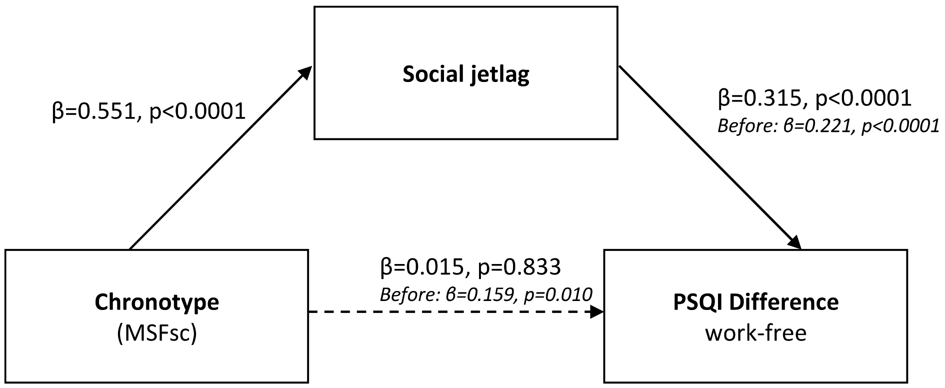

Figure 4

7 Deutsche Zusammenfassung

Die vorliegende Dissertation beschäftigt sich mit den Unterschieden zwischen Schlafverhalten an freien Tagen und Schlafverhalten an Arbeitstagen sowie dem Einfluss der circadianen Faktoren Chronotyp und sozialer Jetlag, die einerseits bei Jugendlichen mit depressiven Erkrankungen (Studie 1) und andererseits bei der Messung von Schlafqualität in der Allgemeinbevölkerung (Studie 2) eine wichtige Rolle spielen.

In ***Studie 1*** wurde das Schlafverhalten von Kindern und Jugendlichen mit remittierter Depression im Vergleich zu gesunden Kontrollprobanden mithilfe einer einmonatigen objektiven Aufzeichnung lokomotorischer Aktivität sowie subjektiver Daten zu Schlafqualität und depressiver Symptomatik analysiert. Es zeigte sich, dass Jugendliche mit remittierter Depression an freien Tagen im Mittel ca. 45 Minuten länger schliefen als gesunde Jugendliche, sich im Hinblick auf ihre Schlafdauer an Schultagen, ihren Chronotyp sowie das Ausmaß ihres sozialen Jetlags nicht voneinander unterschieden.

In ***Studie 2*** wurde Schlafqualität in der Allgemeinbevölkerung mithilfe einer modifizierten Form eines etablierten Fragebogens zur Schlafqualität (PSQI) separat für Arbeits- und freie Tage bestimmt, in Bezug zu „allgemeiner Schlafqualität“ gesetzt und der Einfluss circadianer Faktoren wie Chronotyp und sozialer Jetlag exploriert. Unsere Ergebnisse zeigen, dass die üblicherweise eingesetzte Version des PSQI, die nach „allgemeinem Schlafverhalten“ fragt, hauptsächlich Schlafverhalten unter der Woche abbildet, das stark durch vorgegebene Arbeitszeiten beeinflusst ist. Zudem hing in unserer Studie ein später Chronotyp mit einer höheren Differenz der Schlafqualität an Arbeits- mit freien Tagen zusammen, wobei dieser Zusammenhang durch das Ausmaß sozialen Jetlags vermittelt wurde.

Beide Studien zeigen den in der Schlafforschung häufig vernachlässigten Einfluss von Arbeits- bzw. freien Tagen auf das Schlafverhalten. Zudem bestätigt die zweite Studie den wichtigen Einfluss circadianer Faktoren. Dieses Wissen sollte in weitergehenden Forschungsvorhaben dringend berücksichtigt werden mit dem Ziel, das Schlafverhalten von Menschen besser verstehen und somit langfristig verbessern zu können.

Studie 1: Nicht später, aber länger: Schlaf, Chronotyp und Lichtexposition bei Jugendlichen mit remittierter Depression im Vergleich zu gesunden Kontrollprobanden

Der Zusammenhang zwischen Schlaf und Depressionen bei Jugendlichen ist trotz vieler Forschungsarbeiten noch nicht vollständig verstanden. Ein wichtiger Faktor ist dabei der selbstgewählte Schlafzeitpunkt, der auch als Chronotyp bezeichnet wird. Der Chronotyp wird vor allem durch die innere Uhr reguliert, die die Innenzeit des Körpers mit dem Licht-Dunkel-Wechsel der Außenzeit synchronisiert. Ein später Chronotyp sowie eine mangelnde Passung zwischen Innen- und Außenzeit, wie z.B. sozialer Jetlag, wurde bei Erwachsenen mit depressiven Symptomen in Verbindung gebracht.

In dieser Studie untersuchen wir, ob sich Jugendliche mit remittierter Depression in Bezug auf Chronotyp, sozialen Jetlag und weitere schlafbezogene Variablen von gesunden Kontrollprobanden unterscheiden. Zu diesem Zweck wurden Chronotyp und sozialer Jetlag durch den Munich ChronoType Questionnaire (MCTQ) und subjektive Schlafqualität durch den Pittsburgh Sleep Quality Index (PSQI) erhoben. Zusätzlich trugen alle Probanden einen Monat lang ein Aktimeter zur kontinuierlichen Aufzeichnung lokomotorischer Aktivität, aus der sich objektive Schlafzeiten ableiten lassen. Aufgrund des möglichen Einflusses von Licht auf Chronotyp und depressive Symptome wurde zudem die Lichtexposition durch einen Lichtsensor am Aktimeter gemessen.

In unserer Stichprobe zeigten Jugendliche mit remittierter Depression im Vergleich zu Kontrollprobanden ähnliche Chronotypen und ein ähnliches Ausmaß an sozialem Jetlag. Patienten mit remittierter Depression schliefen jedoch an freien Tagen deutlich länger und berichteten von einer schlechteren subjektiven Schlafqualität als die Kontrollprobanden. Darüber hinaus zeigte sich bei Patienten eine signifikant erhöhte Lichtexposition, wobei dieser Zusammenhang durch das Leben in einer ländlicheren Umgebung vermittelt wurde.

Diese Befunde könnten einen Hinweis dafür liefern, dass sich der Chronotyp nach Remission einer depressiven Störung verändert, was in Langzeitstudien weiter untersucht werden sollte.

Studie 2: Zeit, Schlafqualität neu zu denken: PSQI-Scores messen Schlafqualität an Arbeitstagen

Der Pittsburgh Sleep Quality Index (PSQI) ist der bekannteste Fragebogen zur Messung subjektiver Schlafqualität. Er erfragt die „gewöhnlichen" Schlafgewohnheiten während des letzten Monats. Da sich das Schlafverhalten zwischen Arbeits- und freien Tagen meist stark unterscheidet, stellten wir die Hypothese auf, dass sich ähnliche Unterschiede auch in der subjektiven Schlafqualität zeigen. Diese potentiellen Unterschiede wurden mithilfe einer webbasierten Querschnittstudie untersucht. Alle Teilnehmer füllten die normale sowie zwei angepasste Versionen – die explizit nach Arbeits- bzw. freien Tagen fragen - des PSQI aus. Darüber hinaus untersuchten wir, ob Zusammenhänge zwischen diesen drei Variablen und Chronotyp sowie sozialem Jetlag bestehen, die mit dem Munich ChronoType Questionnaire (MCTQ) erhoben wurden. Alle Teilnehmer wurden online rekrutiert, mussten >18 Jahre alt sein, einer regelmäßigen Arbeit nachgehen und keine Schichtarbeit leisen. Unterschiede zwischen den drei Versionen des PSQI wurden mit Varianzanalysen festgestellt. Eine Regressions- und Mediationsanalyse diente dem Zweck herauszufinden, ob Unterschiede im PSQI-Score durch circadiane Faktoren vorhergesagt werden können.

Der PSQI-Score an Arbeitstagen glich dem „gewöhnlichen“ PSQI-Score, während die Schlafqualität (d.h. der PSQI-Score) an freien Tagen signifikant besser war – und 2 Punkte über dem Cut-Off für schlechte Schlafqualität lag. Die einzelnen Komponenten und Zeitvariablen des PSQI unterschieden sich ebenfalls zwischen Arbeits- und freien Tagen. Der Chronotyp korrelierte mit dem Unterschied zwischen PSQI-Scores an Arbeits- und freien Tagen und wurde durch das Ausmaß an sozialem Jetlag vermittelt.

Unsere Ergebnisse deuten darauf hin, dass der „gewöhnliche“ PSQI-Score überwiegend Schlafqualität an Arbeitstagen abbildet, an denen das Schlafverhalten meist von festen Arbeitszeiten beeinflusst ist. Die Vermittlung von sozialem Jetlag auf den Zusammenhang zwischen PSQI-Score Unterschieden und Chronotyp könnte bedeuten, dass nicht Chronotyp per se, sondern die Kollision individueller Chronotypen mit starren Arbeitszeiten die Unterschiede in der Schlafqualität zwischen Arbeits- und freien Tagen erklärt.

Weitere Studien sollten demnach Schlafqualität differenzierter erfassen und auch circadiane Faktoren stärker beachten, um Schlafqualität umfassender verstehen und letzten Endes verbessern zu können.

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10 Eidesstattliche Versicherung

Keller, Lena Katharina

Name, Vorname

Ich erkläre hiermit an Eides statt, dass ich die vorliegende Dissertation mit dem Thema

Thank God It's Friday:
Weekends, sleep, internal clocks and adolescents with depression.

selbständig verfasst, mich außer der angegebenen keiner weiteren Hilfsmittel bedient und alle Erkenntnisse, die aus dem Schrifttum ganz oder annähernd übernommen sind, als solche kenntlich gemacht und nach ihrer Herkunft unter Bezeichnung der Fundstelle
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Ich erkläre des Weiteren, dass die hier vorgelegte Dissertation nicht in gleicher oder in ähnlicher Form bei einer anderen Stelle zur Erlangung eines akademischen Grades eingereicht wurde.

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