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Katharina Novacic, Claudia Pischke, Charlotte von Gall

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Research Article

Katharina Novacic, Claudia Pischke, Charlotte von Gall*

Body mass index is associated with subjective workload and REM sleep timing in young healthy adults

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Abstract: Sleep is essential for the homeostasis of various brain and body functions. Timing, duration, and composition of sleep are controlled by internal oscillators. In modern society, sleep timing is largely dictated by environmental factors. There is increasing evidence that a severe mismatch between internal sleep needs and external demands leads to circadian misalignment, which is detrimental to physical and mental health. The aim of the present study was to examine relationships between the amount and timing of sleep/sleep stages on weekdays, body mass index (BMI), and psychosocial stress due to perceived workload in a relatively homogeneous cohort of young and lean healthy adults. We used longitudinal real-life Fitbit (Inspire) sleep data in combination with a questionnaire among first-year medical students ($n = 59$) and conducted correlation-based network analysis. BMI was within the normal weight range in the sample. A stronger temporal alignment between rapid eye movement (REM) sleep and total sleep and a higher individual variability of sleep timing was associated with higher BMI, which was associated with lower subjective workload. Our data suggest an interaction between sleep timing, in general, and REM sleep timing, in particular, with metabolic homeostasis and resilience to psychosocial stress.

Keywords: sleep, sleep stages, Fitbit, wearable, circadian misalignment, BMI, depression, social jet lag, psychological stress

* **Corresponding author: Charlotte von Gall**, Institute for Anatomy II, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, NRW, Germany, e-mail: charlotte.vongall@med.uni-duesseldorf.de

Katharina Novacic: Institute for Anatomy II, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, NRW, Germany, e-mail: katharina.novacic@med.uni-duesseldorf.de

Claudia Pischke: Institute of Medical Sociology, Centre for Health and Society, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, NRW, Germany, e-mail: claudia.pischke@hhu.de

1 Introduction

Sleep is a vital restorative body function that is particularly essential for the functioning of the brain, immune system, musculoskeletal system, and endocrine system [1]. While sleeping, the body is in a predominantly anabolic state, which contributes significantly to the homeostasis of vital body functions [1]. Important hormones are released during sleep, including growth hormone, which not only promotes anabolic metabolism but also mental and emotional well-being [2]. Sleep occurs in repeating cycles in which rapid eye movement (REM) and various non-REM sleep stages alternate. REM sleep appears to particularly contribute to sleep quality, cognitive performance, and mood [3,4]. Internal oscillators consist of complex neural networks, control the timing, duration, and composition of sleep [5,6]. Individuals differ not only in their preferred sleep duration but also in their preferred bedtime which is controlled by the circadian clock [7]. The individual chronotype can be defined by the midpoint of sleep on work-free days [7].

However, in modern society, the morning alarm clock largely determines both the duration and the midpoint of sleep on workdays, resulting in suboptimal sleep duration and poor sleep quality [8]. Especially in late chronotypes, early schedules lead to circadian misalignment due to an advance shift in the midpoint of sleep which is called “social jet lag,” (SjL) and is associated with sleep loss [9]. Shift work leads to a particularly high variability in sleep timing and duration and thus to a strong circadian misalignment [10].

There is increasing evidence that poor sleep as a result of circadian misalignment and sleep loss contribute to the so-called “diseases of civilization,” such as chronic stress, obesity, metabolic disorders, cardiovascular diseases, and immune dysfunction [10]. Various data show an association between very short sleep duration (less than 6 h per day) and higher body mass index (BMI) in the obesity range [11–14] especially in women [12,14]. On the other hand, higher BMI in the obesity range seems to be

associated with poor sleep quality [13,15,16] indicating a reciprocal relationship between poor sleep and obesity. In addition, overweight and obese individuals also show greater variability in self-reported sleep duration [17], indicating lower rhythm robustness. On the other hand, there is a complex relationship between sleep and mental and physical health and substance use disorders [18]. In older adults, metabolites are associated with sleep architecture and brain function and possibly also with circadian dysregulation [19]. However, there is hardly any research on the connection between BMI, sleep, psychological stress, and substance use in young individuals in the normal weight range.

Wrist-worn wearables are able to record sleep parameters over long periods of time under real-life conditions, although they still have lower accuracy than polysomnography [20]. In the ChronoSleep study, we used real-life longitudinal Fitbit sleep data in combination with a questionnaire in a small and relatively homogeneous sample of young, healthy adults, first-year medical students. In a previous study, we could show that shorter sleep duration on workdays was associated with a higher subjective workload and higher subjective impact of a high workload on sleep, which, in turn, were associated with higher levels of anxiety and depression [21]. In addition, we identified promising digital markers for objective sleep quality such as REM sleep proportion and consolidation which are associated with the intraindividual phase relationship between total sleep and REM sleep (ICC50REM) [22]. In the present study, we aim to investigate whether there are associations between BMI as a marker for metabolic state and ICC50REM as a marker for internal circadian synchronization in a cohort of lean, healthy young adults. In addition, we aim to investigate whether psychological stress, sleep times, and lifestyle factors, such as physical activity and substance use, interact with these markers.

2 Materials and methods

2.1 Ethics, study design, and sample

This study was performed as part of the ChronoSleep study in agreement with the Declaration of Helsinki ethic requirements and approved by the Research Ethic Committee of the Medical faculty (File number of approval: 2019-3786). The data collection period was between 25 June 2021 and 19 May 2022. Informed consent was obtained after the nature and possible consequences of the study were explained. Exclusion criteria were (1) age below 18 years, (2) shift work, (3) work on weekends, (4) chronic diseases including sleep disorders, and (5) chronic medication

including sleep medication. Part of the data used for this study came from the same dataset of medical students in their first year as described earlier [21,23,24].

Briefly, volunteers received a pseudonym and were equipped with a Fitbit Inspire multisensory (motion and heart rate) sleep tracking device and asked to wear it for 90 days, as continuously as possible, especially at nights. The proprietary Fitbit algorithms detect sleep stages based on heart rate and activity patterns. This software processed the sleep phases (total sleep, light sleep, deep sleep, and REM sleep) obtained through Fitbit data [25]. The Fitbit sleep data collection period includes 64 weekdays, defined as workdays and 26 weekend days, defined as work-free days. The sleep data separated workdays and days off, as there were significant differences in sleep quality [26]. After the data collection period, the volunteers were asked to actively participate in the study by completing an online questionnaire and then authorizing the transfer of sleep data from the Fitbit to the study server. All items in the questionnaire were mandatory and could only be answered once. Of the 90 participants who met the inclusion criteria, 31 were excluded because they did not authorize the data transfer or because of missing sleep data for more than 35 days. This resulted in a final sample size of $n = 59$. In this sample, an average of 82.4 (± 9.7) days of sleep data were recorded. The data collection period between 25 June 2021 and 19 May 2022 fell within the COVID-19 pandemic. During this time, most restaurants, bars, and nightclubs were closed due to the pandemic, so evening gatherings that affect bedtime were largely reduced. In addition, face-to-face teaching before 11a.m. was greatly reduced and more self-study lessons were offered, which gave students more flexibility in their daily schedule. However, from the questionnaire, we know that all subjects used an alarm clock on weekdays, while only 15 subjects used an alarm clock on their days off.

Institutional review board statement: This study was approved by the Research Ethic Committee of the Medical faculty, file number of approval: 2019-3786.

Informed consent: Informed consent was obtained from all subjects involved in the study.

2.2 Data derived from the online questionnaire

The online questionnaire included: (1) items for variables such as age, biological sex, as well as weight and height which were used for the calculation of the (BMI = weight in

kilograms/divided by height in squared meters); (2) subjective workload as a marker for psychosocial stress [21]; and (3) items on sport activities and substance use (for details and scoring refer Table 3).

2.3 Data derived from the longitudinal Fitbit sleep stage recordings

Based on the longitudinal Fitbit sleep stage recordings, the following variables were calculated for workdays using a customized Python (version 3.10) application [23,24,27]:

- I. The midpoint of sleep in clock time (MS) (in hours, digital format).
- II. The standard deviation of the midpoint of sleep (MS_std). A measure of intraindividual variability in sleep time.
- III. The intraindividual phase relationship between total sleep and REM sleep (ICC50REM). For this, bivariate correlations between the midpoint of sleep (in clock time) and the time at which 50% of deep or REM sleep (in clock time) was reached were computed for Spearman's rank coefficients with a confidence interval of 95% for each subject. Higher ICC50REM indicate stronger temporal alignment between REM sleep and total sleep [24].

2.4 Statistics

Statistical analyses were performed using Prism 7.01 (Graph Pad). A confidence interval of 95% was used consistently. *P*-values <0.5 were considered statistically significant. Gaussian distribution was analyzed using D'Agostino–Pearson normality test. Correlations between variables were calculated using Spearman test. If variables were normally distributed, linear regression was performed. Visualization of correlation coefficients and network analysis were performed using R-Studio.

3 Results

3.1 Characteristics of the sample

The characteristics of the sample regarding items on sex, age, and BMI are shown in Table 1. The high proportion of females (73%) reflects the distribution of biological sex among first-year medical students. The BMI was normally distributed and mostly within the normal range, only few

Table 1: Sample characteristics

Variable	Mean ± std	Total (%)
Sex		
Female		43 (73%)
Male		16 (27%)
Age (years)	21.18 ± 2.36	
18–20		31 (53%)
21–23		16 (27%)
24–26		9 (15%)
27–29		2 (3%)
BMI (kg/m ²)	22.03 ± 2.78	
16.3–18.4 (underweight)		5 (8%)
18.5–24.9 (normal)		48 (81%)
25.9–29.0 (overweight)		6 (10%)
30.0–34.9 (obesity, first class)		0
35.0–39.9 (obesity, second class)		0
>40 (extreme obesity, third class)		0

Table 2: Subjective workload based on the item in the questionnaire “How high would you rate your workload in general?” Modified after von Gall et al. [21]

Variable	Score	Mean ± std	Total (%)
Subjective workload		2.6 ± 0.62	
Low	1		1 (2%)
Medium	2		24 (41%)
High	3		31 (52%)
Very high	4		3 (5%)

Table 3: Sports and substance consumption, assessed by questionnaire

Variable	Score	Total (%)
Sports at least 30 min at a time		
Never or occasionally	0	10 (17%)
Once or twice a week	1	21 (36%)
Several times a week	2	25 (42%)
Daily	3	3 (5%)
Several times a day	4	0
Caffeine consumption		
Never or occasionally	0	19 (32%)
Once or twice a week	1	5 (8%)
Several times a week	2	9 (15%)
Daily	3	12 (20%)
Several times a day	4	14 (24%)
Alcohol consumption		
Never or occasionally	0	42 (71%)
Once or twice a week	1	15 (25%)
Several times a week	2	2 (3%)
Daily	3	0
Several times a day	4	0
Nicotine consumption		
No	0	55 (93%)
Yes	1	4 (7%)

Table 4: Sleep duration and midpoint of sleep on workdays and SJL (all in decimal format) assessed by longitudinal Fitbit sleep recordings

Variable	Mean ± std
Sleep duration (h)	
Mean (SD)	7.92 ± 0.69
Intraindividual variability (SD_std)	1.25 ± 0.35
Midpoint of sleep in clock time	
Mean (MS)	4.06 ± 0.76
Intraindividual variability (MS_std)	1.1 ± 0.07
SJL (min)	55.51 ± 3.9

Table 5: REM sleep proportion and phase relationship between REM sleep and total sleep on workdays assessed by longitudinal Fitbit sleep stage recordings

Variable	Mean ± std
REM sleep percent	21.2 ± 21220.53
Phase relationship between REM sleep and total sleep (ICC50REM)	0.64 ± 0.02

subjects were slightly under- or overweight. None of the subjects were obese.

The distribution of subjective workload is shown in Table 2. Most of the students report a medium to high workload. The characteristics of the sample regarding sports and substance use are shown in Table 3.

The midpoint of sleep on workdays (MS) was 4.06 ± 0.76 and the intraindividual variability of MS (MS_std) was 1.1 ± 0.07 . The sleep duration on workdays (SD) was 7.88 ± 0.65 and the intraindividual variability of SD (SD_std) was 1.251 ± 0.35 . The intraindividual strength of the phase relationship between REM sleep with total sleep (ICC50REM) was 0.64 ± 0.02 . For further sample characteristics and interconnections among the variables refer to our previous publications [21,23,24] (Tables 4 and 5).

3.2 Correlation-based network analysis

Relationships between the variables were analyzed by Spearman correlations (Figure 1a) and illustrated in a correlation-based network analysis (Figure 1b). Biological sex was not associated with any other variable (Figure 1a) and thus not included in the network analysis. The only association of age and caffeine consumption was with each other (not shown).

The BMI was negatively correlated with subjective workload (Figure S1), suggesting a relationship between

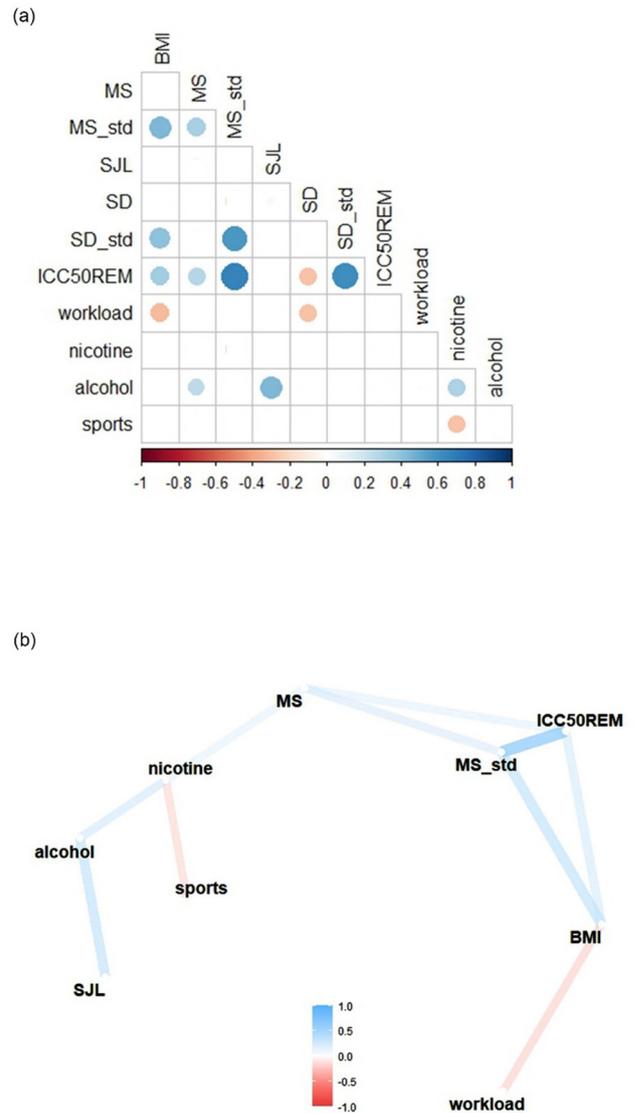


Figure 1: Relationship of BMI with sleep variables and life style factors. (a) Plot of Spearman correlation coefficients for significant ($p < 0.05$) correlations. The color code and size of circles represent the value of correlation coefficients. (b) Network analysis of the most relevant variables based on significant ($p < 0.05$) Spearman correlations. Variables that are more highly correlated appear closer together and are joined by stronger paths. Positive and negative correlations are indicated in blue and red paths, respectively. BMI, body mass index; ICC50REM, measure for phase relationship between REM sleep and total sleep; MS, midpoint of sleep on workdays; MS_std, intraindividual variability of MS; SD, sleep duration on workdays; SD_std, intraindividual variability of SD; SJL, social jet lag.

metabolic homeostasis and resilience to psychological stress in our cohort. Moreover, the BMI was positively correlated with the intraindividual variability in midpoint of sleep (MS_std) and sleep duration (SD_std) and the intraindividual strength in the phase relationship between REM sleep and total sleep (ICC50REM) (Figure S1), which are

interconnected and connected with the midpoint of sleep. This suggests a relationship between metabolic homeostasis with variability in sleep timing and robustness of REM sleep timing.

MS was positively correlated with nicotine use (Figure 1), which is positively correlated with alcohol consumption and negatively correlated with sports. Alcohol consumption was also associated with SJL. BMI was not correlated with any of the life style factors.

4 Discussion

Many epidemiological surveys in children and adults have investigated the association between body composition with sleep in the context of sleep deprivation and obesity [11–16,28]. In contrast, this study examines associations between BMI, sleep timing, psychological stress, and lifestyle factors in young, lean adults without sleep deprivation

In our cohort, the mean BMI is 22.03 kg/m² which corresponds to normal weight and it is normally distributed within the sample. None of the subjects were obese. In contrast to cross-sectional studies including overweight and obese subjects [29] physical activity is not related to BMI in our cohort. The mean sleep duration on workdays in our cohort is 7.88 h which is within the range of 7–9 h of sleep per night for healthy adults recommended by the American Academy of Sleep Medicine and Sleep Research Society [30] and it is normally distributed within the sample. None of the subjects had a mean sleep duration of less than 6 h. There is no association between sleep duration and BMI in our cohort, indicating that this association occurs primarily under non-physiological conditions [11–16,28].

However, using the same dataset, we previously reported an association between shorter sleep duration with higher subjective workload [21] and with a stronger temporal alignment between REM sleep and total sleep, which is associated with good sleep quality [24]. Although this seems contradictory, it is consistent with a reciprocal relationship between sleep and psychosocial stress and a balance between sleep quantity and sleep quality. Biological sex, age, and lifestyle factors, such as physical activity or the use of stimulants are not directly associated with BMI, subjective workload, or the PHQ-4 score. Alcohol consumption is associated with SJL, while later midpoint of sleep is associated with nicotine consumption. This is consistent with earlier studies on the effect of chronotype on the substance consumption [9,31]. However, there is an association of BMI with the intraindividual variability in

sleep timing and with ICC50REM, a marker for the temporal alignment between REM sleep and total sleep. Although we cannot establish causality, we assume that if sleep timing can be adjusted more flexibly according to an individual's specific needs, this has a positive effect on the phase adjustment of REM sleep and promotes anabolic metabolic processes during sleep. During sleep, numerous neurotransmitters, metabolites, and hormones are released that contribute to the regulation of metabolism and energy balance. Chronic sleep deprivation [32–35] and high sleep variability [10], e.g., in shift work, can therefore lead to metabolic imbalances with the corresponding risk factors and comorbidities. In addition, acute sleep restriction seems to increase the appetite for high-calorie foods [35]. Taken together, sleep times dictated by the environment that deviate significantly from intrinsically determined sleep time preferences appear to represent a major health problem in our society.

Epidemiological studies have also identified sleep disorders as a risk factor for metabolic and cardiovascular mortality/morbidity [36]. On the other hand, metabolic changes seem to be frequently associated with sleep disorders [36]. Metabolites also appear to play a role in the natural aging process, modulating brain function and sleep architecture with possible involvement of the circadian system [19]. Hence, metabolites may also influence the neuronal networks that control sleep architecture in young individuals, which, in turn, modulates various brain functions. Moreover, chronic inflammation is associated with disturbed sleep patterns and architecture [37,38] and sleep disorders have a negative impact on the immune system [38]. Our own results in mice support the hypothesis that chronodisruption induces a proinflammatory state in the brain [39] and affects neuronal plasticity and brain function [40]. By integrating wearable devices, new biomarkers can be identified to elucidate these interrelationships in humans [38].

Studies combining longitudinal Fitbit sleep data and questionnaire survey suggest a negative impact of short sleep and high sleep variability on mood and depression [41,42]. Using a similar approach, we have previously shown in the same cohort as in this study that short sleep duration on working days is associated with a higher PHQ-4 score, which is mediated by a higher perception of workload under comparable objective workload [21]. The current literature screening suggests that sleep architecture characteristics are endophenotypic traits which might serve to identify increased risk for depressive symptoms and metabolic disturbances [43]. This is consistent with this study showing that ICC50REM is associated with BMI which, in turn, is associated with the perception of

workload. Based on these associations, we cannot establish causality. However, we suspect that students with higher BMI may be more resilient to psychosocial stress than students with lower BMI. The relatively small and homogeneous sample limits the generalizability of the results. We suggest to further examine interactions between sleep timing, in general, and REM sleep timing, in particular, with metabolic homeostasis and resilience to psychosocial stress in larger cohorts.

In summary, in our sample of young healthy adults with a mean normal weight and sufficient sleep, BMI correlates with higher individual flexibility in sleep duration and timing, stronger relationship between REM sleep and total sleep, and lower subjective workload. This suggests that greater flexibility in sleep schedule and a stronger temporal alignment between REM sleep and total sleep is associated with anabolic metabolism and resilience to psychosocial stress.

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