SLEEPJ, 2020, 1–8

doi: 10.1093/sleep/zsz310
Advance Access Publication Date: 21 December 2019
Original Article

ORIGINAL ARTICLE

How stress affects sleep and mental health: nocturnal heart rate increases during prolonged stress and interacts with childhood trauma exposure to predict anxiety

Yasmine Azza[1,2,3], Marcus Grueschow[4], Walter Karlen[5], Erich Seifritz[3] and Birgit Kleim[1,2,3,*]

[1]Department of Psychology, University of Zurich, Zurich, Switzerland, [2]Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital, University of Zurich, Zurich, Switzerland, [3]Sleep & Health Zürich, University of Zurich, Zurich, Switzerland, [4]Zurich Center for Neuroeconomics, Department of Economics, University of Zurich, Zurich, Switzerland and [5]Mobile Health Systems Lab, Institute of Robotics and Intelligent Systems, Department of Health Sciences and Technology, ETH Zurich, Zurich, Switzerland

*Corresponding author. Birgit Kleim, Department of Experimental Psychopathology and Psychotherapy, Psychiatric University Hospital, University of Zurich, Lenggstrasse 32, 8032 Zurich, Switzerland. Email: birgit.kleim@ uzh.ch.

Abstract

Study Objectives: Stress can adversely impact sleep health by eliciting arousal increase and a cascade of endocrine reactions that may impair sleep. To date, little is known regarding continuous effects of real-world stress on physiological sleep characteristics and potential effects on stress-related psychopathology. We examined effects of stress on heart rate (HR) during sleep and total sleep time (TST) during prolonged real-world stress exposure in medical interns. Moreover, we investigated the influence of previous stress and childhood trauma exposure on HR during sleep, TST, and its interaction in predicting anxiety.

Methods: We examined a sample of 50 medical students prior to and during their first internship, a well described real-world stressor. HR and TST were continuously collected over 12 weeks non-invasively by a wrist-worn activity monitor. Prior to starting the internship, at baseline, participants reported on their sleep, anxiety, and childhood trauma exposure. They also tracked stress exposure during internship and reported on their anxiety symptoms 3 months after this professional stress.

Results: Mean HR during sleep increased over time, while TST remained unchanged. This effect was more pronounced in interns exposed to childhood trauma exposure. In multilevel models, childhood trauma exposure also moderated the relation between individual HR increase and development of anxiety.

Conclusions: Prolonged stress may lead to increased HR during sleep, whereas individuals with childhood trauma exposure are more vulnerable. Childhood trauma exposure also moderated the relation between individual HR increase and development of anxiety. These findings may inform prevention and intervention measures.

Statement of Significance

Longitudinal trajectories of sleep health have rarely been investigated during prolonged stress exposure. Little is thus known about continuous effects of real-world stress on physiological sleep characteristics and on stress-related psychopathology. Here we show that prolonged stress exposure may lead to increased heart rate during sleep. Interestingly, trauma exposure during childhood may add to the effects, affect adult sleep quality, and increase anxiety. The interactions are instrumental for prevention and intervention measures.

Key words: anxiety; childhood trauma; sleep; heart rate; medical students

Submitted: 17 July, 2019; **Revised:** 17 October, 2019

Elevated stress levels may adversely impact sleep quality and quantity [1]. Sleep naturally occurs in regular intervals and allows the organism to restore energy and consolidate experiences made during waking [2]. A complex and bi-directional relationship between stress and sleep has been suggested: stressful and emotional experiences may elicit increased arousal at encoding and insufficient integration of experiences into hippocampal–cortical networks, as well as introducing a cascade of endocrine reactions involving the release of glucocorticoids, such as cortisol [3]. Cortisol, in turn, hinders the production of melatonin which supports falling asleep. Sleep fragmentation or insufficient time asleep affects emotional reactivity [4] and has been linked to negative mental health consequences, such as anxiety and mood disorders [5]. To date, few studies have examined continuous effects of stress on sleep over time. Much of the previous evidence is based on associations between real-life stress and sleep indexed either via questionnaires or via EEG or actigraphy during short periods, such as hours or days [6–9]. Moreover, only few investigations have focused on more complex relationships, for instance, by including further key influences on sleep that, possibly in interaction with stress, impact on sleep, such as previous stress or exposure to trauma during childhood or adulthood.

Stress-related disturbances of the sleep architecture may not only be characterized by several indices, such as alterations of total sleep time (TST), increased sleep fragmentation, and awakenings, but also by additional physiological indices, such as lower heart rate variability (HRV) during sleep [10] and an increased nocturnal heart rate (HR) [11]. Nocturnal HR was furthermore found to correlate with micro-arousals during sleep [12]. Such prolonged cardiovascular effects during sleep after various kinds of stressors have indeed been observed, but to our knowledge never studied continuously over time [13].

A diverse range of factors may influence the association between sleep and stress, such as negative affectivity, maladaptive coping style, circadian misalignment, and others [14–16]. One key factor linked to sleep disturbances in adulthood is exposure to stressful or traumatic events experienced earlier in life [17, 18]. Adverse childhood trauma may shape brain systems that govern stress responsivity affecting the sympathetic nervous system's (SNS) reactivity to psychological stress years later [19]. Such heightened SNS responses could serve as adaptive mechanism to increase vigilance and attention to potentially threatening situations at the time of trauma exposure that may become dysfunctional and maintain stress-related psychopathology, such as posttraumatic stress disorder, in later life [20]. Cardiovascular reactivity is proposed to be a central mechanism connecting childhood trauma exposure to developing psychopathology [21]. Students with a history of emotional neglect, for instance, indicated a lower self-reported sleep quality mediated by greater psychological distress during a stressful period of life [6]. Current stress may lead to additional increases in arousal and, among other symptoms, may reduce feelings of safety and disrupt sleep [21, 22]. However, the impact of the interaction between childhood trauma, sleep-related cardiovascular reactivity during real-world stress on psychopathology has not been studied in detail.

The current study aims to close this gap by parsing physiological indices of sleep over an extended period of real-world stress, as well the consequences on symptoms of anxiety. We investigate this in a sample of medical interns, who just commence their first medical rotation, a well-known real-world stressor associated with acute and chronic stress, as well as increased psychopathology [22–25]. We indexed sleep quality continuously between just before the start of the medical rotation until 3 months into the rotation. We acquired data on HR during sleep and TST longitudinally from a wearable (FitbitChargeHR) over the first 3 months of medical internship. This is relevant to understand the impact of stress on psychopathology as well as resilience. In the group of interns studied here, consequences of fatigue and elevated work stress during their internship may not only have an impact on interns physical and mental health, but may also result in compromised patient care [26]. Here we investigated individual differences in TST and HR during sleep over 3 months of internship-related stress exposure. Specifically, we hypothesized that (1) TST decreases while individual slopes of nocturnal HR increase over time, (2) increased rate of childhood trauma exposure is associated with decreased TST and increased nocturnal HR. Finally, we investigated whether (3) sleep pattern predict later anxiety symptoms and whether increased childhood trauma may enhance this relationship.

Methods

Participants

The study sample comprised 50 subjects, while they were medical students and during their first 12 weeks of internship at the University of Zurich by information in lectures, emails, and a bulletin in the medical faculty. We recruited medical students enrolled in their fifth year of medical training, just prior to their internship representing a well described real-world stressor [25–27]. Exclusion criteria for the participation in this study were self-reported psychiatric disorders, including sleep disorders, suicidality, or severe physical conditions. Participants were reimbursed for their time (100 CHF, equivalent to 100 US dollars) at the end of the study in exchange for participation. In addition, participants could keep their personal FitbitChargeHR that they had worn during the study.

Study procedures

Prior to the start of the internship (t_0, baseline), participants were screened for the presence of current depression, psychosis, or suicidality by means of a structured diagnostic interview; (SCID-I) [28]. Severity of sleep disturbances at t_0 was examined using the Insomnia Severity Index (ISI) [29]. If they met the inclusion criteria of being a fifth year medical student undergoing their first clinical internship), and after providing informed consent, they answered the first questionnaire battery. It contained questions about demographic information, health situation, sleep quality, and anxiety symptoms. They also received a FitbitChargeHR (Fitbit Inc., San Francisco, CA, USA) that they were instructed to wear for continuous recording of HR and their sleep/wake cycle over the 3 month period. At 3 months follow up (t_1, midterm of the internship), a second questionnaire on anxiety was administered. The local ethics review board at the University of Zurich approved the study.

Longitudinal sleep and HR recordings

The FitbitChargeHR provided mean HR in beats per minute (bpm) at minute intervals and TST at the end of each night. HR was estimated using the optical photoplethysmographic method where

blood volume changes are detected by measuring the absorption of light that had passed through perfused tissues [30]. Nocturnal HR was defined as the mean over all HR values from sleep onset to sleep offset as defined by the device. In addition, the FitbitChargeHR registers movement via a microelectronic triaxial accelerometer. Proprietary algorithms of the company further classify pattern of motion to identify sleep [31]. The device had to be recharged every 4–5 days with a charging duration of approximately 2 h. In a previous study, overall good agreement with polysomnography (PSG) and electrocardiography (ECG) in measuring sleep indices and HR during sleep was documented [32].

Questionnaire measures

A sociodemographic questionnaire was employed to assess basic demographic information such as age, gender, and relationship status. Traumatic experiences during childhood were measured by the Childhood Trauma Questionnaire (CTQ) [33] which includes 28 items with 6 subscales, namely abuse (emotional, physical, or sexual), neglect (emotional or physical), and denial. Each item was measured by a 5-point Likert scale ranging from 1 ("not at all") to 5 ("very often"). As an indicator of the overall childhood trauma load, the CTQ sum score was applied (range: 25–125). The Beck Anxiety Inventory (BAI) [34] was used to assess anxiety. All 21 items were applied and measured on a 4-point scale ranging from 0 ("not at all") to 3 ("strongly, I could barely stand it"). To examine sleep quality and disturbances, the Pittsburgh Sleep Quality Index (PSQI) [35] was used, asking participants about their sleep situation in the last 4 weeks by a 4-point scale ranging from 0 ("never in the last 4 weeks") to 3 ("three times or more per week"). The 7 subscales of its 19 self-assessment items were sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, sleep medication, and sleepiness during the day. We asked participants to indicate their perceived distress during the internship, that is, "How distressed were you during the internship?" Participants were also asked to describe their most stressful events using a free text entry panel.

Statistical analyses

Preprocessing of HR data was conducted in MATLAB 2016b (The MathWorks, Natick, MA) extracting the bpm values from sleep onset to sleep offset and calculating the individual mean HR per night. We chose to identify the individual mean HR per night to best quantify the change of nocturnal arousal level within participants over a duration of 3 months. To exclude poor recordings with a small number of measures, only sleep episodes with a minimum sleep duration of 240 min were included into our analyses. Visual assessments for outliers on the minute by minute resolution were conducted and showed no univariate outliers. As repeated HR and TST measurements were nested within participants, we employed multilevel regression analyses. We first calculated intraclass correlations (ICC) to test whether measures within participants were non-independent. We expected inter-individual differences in slopes of HR and TST over time. We calculated either models featuring random intercept only as well as models featuring both random intercept and slopes. To identify the best fitting model, we use the R-nlme package [36]. We controlled for autocorrelation by incorporating an autoregressive correlation structure of order 1 (AR(1)) into our models. We visually assured no homoscedasticity violations in our temporal data (HR and TST, respectively) and included gender and age as covariates in our analyses. All of the multilevel analyses steps were conducted in R (version 3.3.3) [37].

Results

Descriptive statistics

Sample characteristics are displayed in Table 1. The final sample consisted of 50 individuals, including 72% women with overall good self-reported sleep quality at baseline. One participant dropped out of the study before midterm of the internship and could therefore not be included in the respective analyses. Another two participants did not wear the activity tracker and were excluded from the longitudinal sleep analyses. For one participant, the questionnaires were missing. In four cases of the CTQ and in three cases of the BAI, a single item was not answered and we replaced them by the individual mean score. In total, we collected 3,491 days of sleep data with a mean of 6 h and 58 min of sleep per night and an average HR during sleep of 60.04 (*SD* = 8.57, see Table 1). The measured means of nocturnal HR and TST in our study resembled previously reported typical values [32]. Exposure of traumatic childhood experiences in our overall sample was rather low, with a mean sum score of 31.4 (*SD* = 3.83, range 26–40). Anxiety levels increased from baseline to midterm of the internship across the sample ($t(46) = -2.02$, $p = 0.049$). With regards to perceived stress in their rotation, 15 students reported being "not distressed" during the internship, 27 reported being "somewhat distressed", 6 participants entered "very distressed", while no participant indicated "extreme stress". A total of 12 participants provided detailed descriptions of experienced specific stress events (e.g. "rapid deterioration of physical state of a patient" or "reanimation of a patient").

Change in HR during sleep and TST during internship

Repeated measures of HR during sleep within participants were non-independent (ICC(1) = 0.65, $F(47,3189) = 126.6$, $p < 0.0001$). A random intercept and slope model was employed as this fitted our data better than the random intercept model ($\chi^2_{diff(1)} = 7.62$,

Table 1. Demographic and clinical sample characteristics

	Mean(*SD*)
Age (years)	23.61 (1.27)
Gender (1 = male, 2 = female)	1.72 (0.45)
BMI	21.86 (2.38)
Prior medical experience (1 = no, 2 = yes)	1.64 (0.48)
Smoking (1 = never, 2 = sometimes, 3 = daily)	1.2 (0.40)
Alcohol (1 = never, 2 = sometimes, 3 = weekly, 4 = daily)	2.22 (0.71)
Relationship status (1 = single, 2 = in a relationship)	1.66 (0.48)
Mean HR during sleep (bpm)	60.04 (8.57)
Total sleep time (min)	418.19 (90.51)
Total sleep time (h)	6.97 (1.51)
CTQ (sum)	31.40 (3.83)
PSQI	4.22 (1.71)
BAI t_0	4.25 (3.27)
BAI t_1	5.99 (6.59)

N = 50, 36♀. BAI = Beck Anxiety Inventory; BMI = Body mass index; bpm = beats per minute; CTQ = Childhood Trauma Questionnaire; HR = Heart rate; PSQI = Pittsburgh Sleep Quality Index.

$p = 0.02$). There was a significant main effect of time, such that HR increased significantly from baseline to midterm of the internship (see Table 2, model 1 and Figure 1, A). Female students showed a significant higher HR during sleep compared with males. HR was not affected by age (Table 2, model 3).

Repeated measures of TST within persons were also non-independent (ICC(1) = 0.17, $F(47,3443) = 16.36$, $p < 0.0001$). The random intercept and slope model fitted our data not significantly better than the random intercept model, so we employed the more parsimonious model ($\chi^2_{diff(1)} = 0.08$, $p = 0.96$). There was no significant main effect for TST over time (Figure 1, B). TST was not affected by age nor gender over time (Table 2, model 4).

Association of childhood trauma exposure with stress-related nocturnal HR change and TST

As a next step, we examined the influence of the CTQ score on HR and TST in our models. Childhood trauma exposure moderated the effect of increasing HR over time. That is, those with higher childhood trauma scores showed a steeper increase of HR during sleep over time compared with those with childhood trauma exposure, see Table 2, model 2 and Figure 2. This model fitted our data better than the model without the CTQ score included, Table 2. There was no association of CTQ scores with TST over time, Table 2, model 4.

Childhood trauma exposure moderates the association between HR increase and anxiety

We tested whether individual slopes of HR increase and childhood trauma exposure, as well as their interaction, predicted change in anxiety levels. There was no significant main effect of individual HR increase over time on anxiety symptom change, and there was also no main effect of childhood trauma exposure, see Table 3. However, we identified a significant interaction between childhood trauma exposure and HR increase in predicting change in anxiety over the course of the internship (Table 3, model 8). As depicted in Figure 3, for those exposed to no or low childhood trauma exposure, the simple slope test revealed a significant negative association between HR increase and anxiety increase ($b = -149.13$, $t(47) = -2.5$, $p = 0.02$), indicating that a rise in HR was associated with lower anxiety scores in this group. For high CTQ, there was no significant relationship between HR increase and anxiety change ($b = 35.6$, $t(47) = 0.72$, $p = 0.47$).

Table 2. Linear mixed model regressing HR during sleep and TST on time

	Heart rate			Total sleep time		
	1	2	3	4	5	6
Model	β (*SE*)	β (*SE*)	β (*SE*)	β (*SE*)	β (*SE*)	β (*SE*)
Intercept	59.21*** (1.06)	59.41*** (1.07)	52.53*** (1.82)	418.55*** (6.20)	419.55*** (6.28)	415.04*** (12.01)
Time (day)	0.03*** (0.01)	0.03*** (0.01)	0.03*** (0.01)	−0.08 (0.05)	−0.08 (0.05)	−0.08 (0.05)
CTQ score		−0.13 (0.30)	−0.07 (0.26)		−0.88 (1.74)	−1.37 (1.79)
Sex			9.21*** (2.11)			6.04 (13.66)
Age			−0.68 (0.75)			6.02 (4.82)
Time × CTQ score		0.004** (0.001)	0.004** (0.001)		0.004 (0.01)	0.004 (0.01)
Marginal pseudo-Δ R^2	0.01	0.01	0.19	<0.01	<0.01	0.01
Conditional pseudo-Δ R^2	0.68	0.69	0.69	0.18	0.18	0.19
Akaike Inf. Crit.	20	20	20	41	41	41
Bayesian Inf. Crit.	20	20	20	41	41	41

Standard errors (SE) are in parentheses. CTQ = Childhood trauma questionnaire; mc = mean centered; CTQ and age are grand-mean centered. Phi ranged between 0.005 and 0.19.

**$p < 0.01$.

***$p < 0.001$.

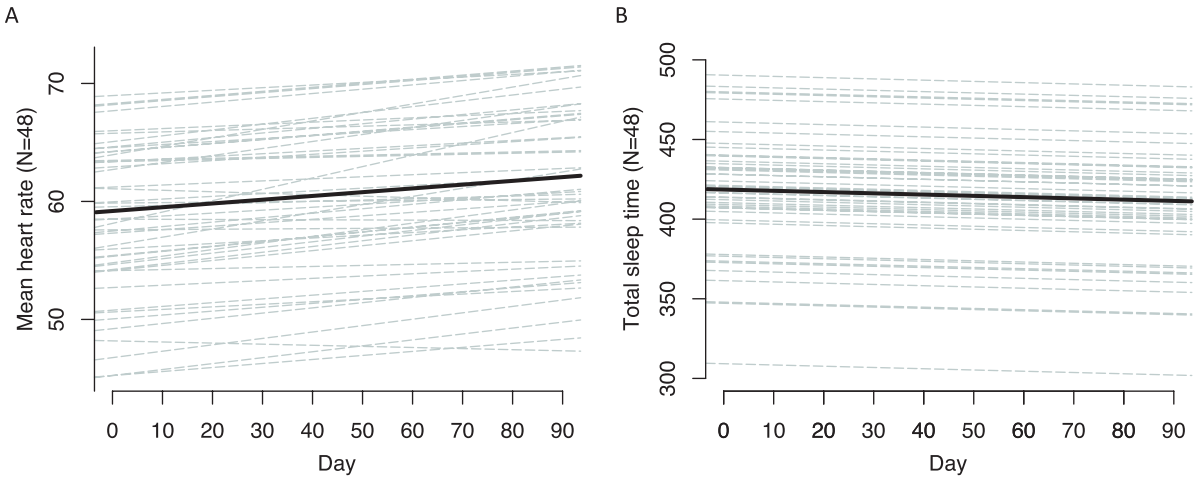

Figure 1. Mean HR at night (A) and TST (B) over 90 days of medical internship (N = 48).

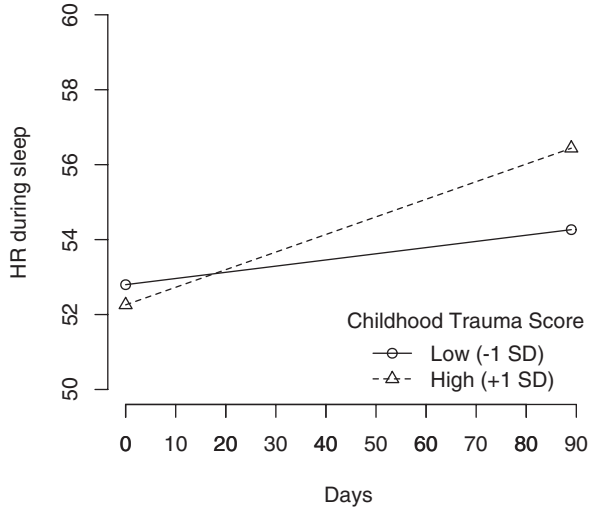

Figure 2. Association between childhood trauma load and increase in HR at night over time ($N = 48$).

Table 3. Linear model regressing BAI change on HR slope and CTQ score

	Dependent variable: change of anxiety	
	7	8
Model	β (*SE*)	β (*SE*)
Intercept	1.70 (0.88)	0.93 (0.88)
HR slope	−24.15 (40.64)	−54.15 (42.31)
CTQ sum mc		0.07 (0.25)
HR slope × CTQ sum mc		25.10* (9.37)
Observations	47	47
R^2	0.01	0.16
Adjusted R^2	−0.01	0.10
Residual std. error	5.97 ($df = 45$)	5.62 ($df = 43$)
F Statistic	0.35 ($df = 1; 45$)	2.67 ($df = 3; 43$)

Standard errors (*SE*) are in parentheses. Change of anxiety (t_1–t_0);
CTQ = Childhood trauma questionnaire; mc = mean centered. CTQ and age are grand-mean centered.
*$p < 0.05$.

Discussion

Stress exposure may affect sleep health and adversely impact stress reactivity and emotion regulation. In line with previous studies documenting immense stress and mental and physical health compromises in this population [26, 38, 39], we found that individual nocturnal HR slopes increased over time of continuous stress exposure during internship. TST, however, remained constant. Moreover, nocturnal mean HR increases over time were particularly pronounced in those with increased childhood trauma exposure rates. Childhood trauma exposure also significantly moderated the relation between individual HR increases and anxiety: While anxiety over time of the internship decreased markedly and despite nocturnal HR increase in those without childhood trauma exposure, our results showed a more positive association between HR increase and anxiety increase in those with childhood trauma exposure.

Mean nocturnal HR increased over time in the overall sample and this finding was paralleled by increased anxiety over the course of the internship, which is in line with reported stress and increases in depression, anxiety, and suicidality in medical

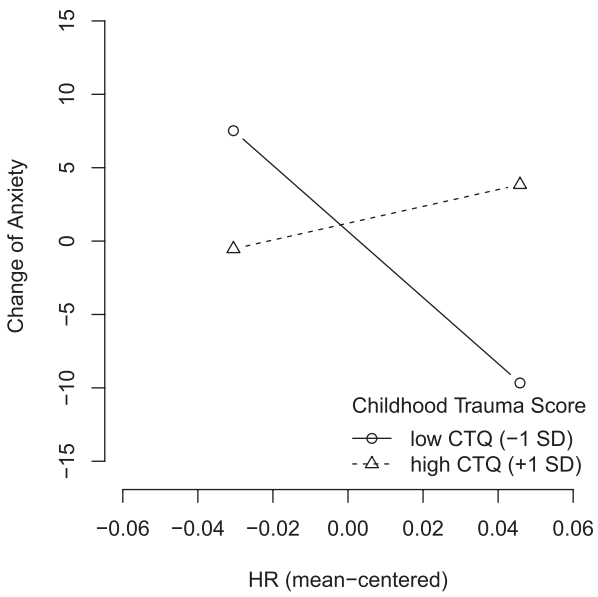

Figure 3. Childhood trauma moderates the association between HR increase over time and anxiety ($N = 47$).

interns [22, 38]. The increase in nocturnal HR might thus indicate less deep and successively less restful sleep over the first 3 months. Nocturnal HR dynamics may indeed characterize internal structures of sleep [40]. During slow wave sleep (SWS), when activity of the hypothalamic–pituitary–adrenal axis and cortisol secretion is inhibited [41], HR is typically lowest. SWS has been linked to processing of personally relevant memories, including emotional experiences thought to be selectively reactivated and reorganized during sleep [42, 43]. We obtained mean HR scores over an entire night over the 90 days of internship, rather than during specific sleep stages within these nights. Based on these data, we can thus not directly link HR increases to lower SWS or other sleep stages or sleep architecture characteristics. We can only speculate, however, that the increase in mean nocturnal HR may indicate less time spent in those stages where HR is typically lower, such as SWS, and that there was decreased recovery during sleep.

Our sample slept an average of nearly 7 h per night, a value that is broadly in accord with previous findings based on subjective reports of interns in the same working environment [7]. Overall, TST remained constant across the 90 days and this was in contrast to our hypothesis. We propose at least two interpretations of this finding: First, timing of sleep episodes may have varied across shifts and this was not assessed in detail, even though we measured fluctuations of TST within individuals. We obtained information on shift work indicating that most of the participants had to work in shifts, but we did not track specific shift hours over 90 days and our data on shift work is thus not detailed enough to be matched on a daily basis with sleep data. Based on previous reports, sleep durations may thus have been irregular due to shift work, at least in a significant subgroup of participants, and cardiovascular and metabolic consequences of such circadian misaligned sleep patterns have indeed been reported earlier [44]. Second, even though TST did not change overall, acute stress episodes might have been linked to deviations in sleep durations within participants [45] which were not assessed by our methods.

In line with our hypothesis, nocturnal HR increase over the 3 months was most pronounced in participants who reported more trauma exposure during childhood, including emotional abuse, such as feeling hated by one's family, and neglect, such as not feeling important or loved, and not feeling close to one's family. This finding corroborates recent evidence of a greater decline in sleep quality during stressful life episodes in adults exposed to emotional neglect during childhood [6]. Early trauma is associated with alterations in threat processing and may constitute underpinning mechanisms accounting for the association. Elevated amygdala responses to negative emotional cues have been observed in children and in adults exposed to childhood trauma [46]. Resulting biases in information processing may enable rapid threat classification and maintain heightened emotional responses to threats and heightened arousal [47]. Elevated nocturnal HR could reflect such heightened arousal in childhood trauma survivors. Previous investigations of such effects have rarely been expanded to effects of childhood trauma on adult sleep and indexed physiological data [48], our findings thus provide additional confirmation to strengthen this suggested link [6].

Childhood trauma exposure also moderated the relationship between individual nocturnal HR increase over time and anxiety. In those interns reporting no or lower levels of childhood trauma exposure, there was a significant negative relationship between HR increase and anxiety, indicating better adaptation to the continuous stressor compared with those who reported higher childhood trauma exposure. This effect was small in size, hence indicating that additional factors may play a role. Heightened emotional and cognitive arousal is prevalent in individuals with anxiety and could result in increased HR and blood pressure during sleep and thus disturb sleep [49]. Disturbed sleep, on the other hand, may contribute to symptoms of anxiety [50]. The relationship is complex, however, and a number of additional factors play a role, such as responsible genetic vulnerabilities governing regulation of arousal and sleep-initiating brain activity [51].

Our study is not without limitations. Physiological sleep stage scoring and detailed sleep indices of interest, such as rapid eye movement sleep, sleep spindle density, cannot be inferred from our data collected via the FitbitChargeHR device. The use of this device provided a non-invasive opportunity to monitor participants' continuous sleep to examine the course of changes in sleep (HR during sleep and TST) longitudinally over an extensive period of time [31, 32] in interns' natural environment, including their work environment. Our data nevertheless warrant careful interpretation, as it is merely an approximation of sleep compared with the gold standard of sleep measurement, the sleep PSG. We also did not obtain HRV changes within a given night. Future studies should thus aim to obtain more specific assessments, including repeated EEG- and HRV-measurements over times of stress. Another limitation of the current study is the lack of detailed information and time-points regarding stressful situations experienced by the interns and potential coping strategies that might have been employed. Future studies should assess these information in greater detail, for example, by using ecological momentary assessment. This information could further clarify within- and between person dynamics of and estimate its effect on nocturnal HR. Regarding the evaluation of childhood trauma, our data did not include age of traumatization, which would add relevant information in terms of sensitive periods of exposure and their later effects [52]. Future studies should therefore investigate the impact of experiences made in specifically sensitive age groups on stress reactivity.

Taken together, we parsed sleep, HR, and symptoms of anxiety over an extended period in medical interns, a population afflicted with continued stress exposure and increased risk of psychopathology [22–25]. We identified childhood trauma exposure as contributing factor to nocturnal HR increases in stress-exposed populations and potential facilitator of mental health problems, such as anxiety [53, 54]. Together with data suggesting that up to 20% of adolescents report exposure to childhood trauma, such as emotional or physical neglect or violence [55], this calls for promotion of preventive and supportive prevention measures at early stages. The study also highlights a potential need in young medics, such as medical interns studied here, with stress-related sleep disturbances that may impact on their own well-being as well as affect patient safety [26, 39]. Our research underlines the importance of sleep as protective factor to increase stress resilience [26]. Sleep can be modified using evidence-based and accessible behavioral interventions such as cognitive–behavioral therapy for insomnia, hypnosis, mindfulness, and other behavioral techniques [56]. Other protective factors, such as social support and emotion regulation strategies should be identified and exploited to advance the impact of prevention and intervention science in these and other vulnerable populations.

Acknowledgments

We would like to thank the Medical Faculty, University of Zurich, Dean's office for valuable support to conduct this study, and Hans-Peter Landolt, Ines Wilhelm and Ian Clark for helpful comments on analysis and interpretation of our data. This work was conducted at the University of Zurich, Zurich, Switzerland.

Funding

This was not an industry-supported study. The research was funded by the Swiss National Science Foundation, grants PZ00P1_126597 and PZ00P1_150812 awarded to Birgit Kleim. Yasmine Azza was funded by the Clinical Research Priority Program "Sleep and Health" at the University of Zurich.
Conflict of interest statement. None declared.

References

1. Vandekerckhove M, *et al*. The role of presleep negative emotion in sleep physiology. *Psychophysiology*. 2011;**48**(12):1738–1744. doi:10.1111/j.1469-8986.2011.01281.x
2. Rasch B, *et al*. About sleep's role in memory. *Physiol Rev*. 2013;**93**(2):681–766.
3. Meerlo P, *et al*. Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stress systems and stress responsivity. *Sleep Med Rev*. 2008;**12**(3):197–210. doi:10.1016/j.smrv.2007.07.007
4. Zohar D, *et al*. The effects of sleep loss on medical residents' emotional reactions to work events: a cognitive-energy model. *Sleep*. 2005;**28**(1):47–54.
5. Medic G, *et al*. Short- and long-term health consequences of sleep disruption. *Nat Sci Sleep*. 2017;**9**:151–161. doi:10.2147/NSS.S134864
6. John-Henderson NA, *et al*. Changes in sleep quality and levels of psychological distress during the adaptation to university: the role of childhood adversity. *Br J Psychol*. 2018;**109**(4):694–707.

7. Kalmbach DA, *et al*. Effects of sleep, physical activity, and shift work on daily mood: a prospective mobile monitoring study of medical interns. *J Gen Intern Med*. 2018;**33**(6):914–920. doi:10.1007/s11606-018-4373-2
8. Åkerstedt T, *et al*. Predicting sleep quality from stress and prior sleep—a study of day-to-day covariation across six weeks. *Sleep Med*. 2012;**13**(6):674–679. doi:10.1016/j.sleep.2011.12.013
9. Vahle-Hinz T, *et al*. Effects of work stress on work-related rumination, restful sleep, and nocturnal heart rate variability experienced on workdays and weekends. *J Occup Health Psychol*. 2014;**19**(2):217–230. doi:10.1037/a0036009
10. Brosschot JF, *et al*. Daily worry is related to low heart rate variability during waking and the subsequent nocturnal sleep period. *Int J Psychophysiol*. 2007;**63**(1):39–47. doi:10.1016/j.ijpsycho.2006.07.016
11. Monroe LJ. Psychological and physiological differences between good and poor sleepers. *J Abnorm Psychol*. 1967;**72**(3):255. doi:10.1037/h0024563
12. Ekstedt M, *et al*. Microarousals during sleep are associated with increased levels of lipids, cortisol, and blood pressure. *Psychosom Med*. 2004;**66**(6):925–931. doi:10.1097/01.psy.0000145821.25453.f7
13. Pieper S, *et al*. Prolonged stress-related cardiovascular activation: is there any? *Ann Behav Med*. 2005;**30**(2):91–103. doi:10.1207/s15324796abm3002_1
14. Pillai V, *et al*. Moderators and mediators of the relationship between stress and insomnia: stressor chronicity, cognitive intrusion, and coping. *Sleep*. 2014;**37**(7):1199–1208A. doi:10.5665/sleep.3838
15. Van Schalkwijk FJ, *et al*. Social support moderates the effects of stress on sleep in adolescents. *J Sleep Res*. 2015;**24**(4):407–413. doi:10.1111/jsr.12298
16. Wunsch K, *et al*. The effect of physical activity on sleep quality, well-being, and affect in academic stress periods. *Nat Sci Sleep*. 2017;**9**:117–126. doi:10.2147/NSS.S132078
17. Chapman DP, *et al*. Adverse childhood experiences and sleep disturbances in adults. *Sleep Med*. 2011;**12**(8):773–779. doi:10.1016/j.sleep.2011.03.013
18. Hanson MD, *et al*. Daily stress, cortisol, and sleep: the moderating role of childhood psychosocial environments. *Heal Psychol*. 2010;**29**(4):394. doi:10.1037/a0019879
19. Otte C, *et al*. Association between childhood trauma and catecholamine response to psychological stress in police academy recruits. *Biol Psychiatry*. 2005;**57**(1):27–32. doi:10.1016/j.biopsych.2004.10.009
20. Ellis BJ, *et al*. Biological sensitivity to context: II. Empirical explorations of an evolutionary–developmental theory. *Dev Psychopathol*. 2005;**17**(2):303–328. doi:10.1017/s0954579405050157
21. Heleniak C, *et al*. Cardiovascular reactivity as a mechanism linking child trauma to adolescent psychopathology. *Biol Psychol*. 2016;**120**:108–119. doi:10.1016/j.biopsycho.2016.08.007
22. Mata DA, *et al*. Prevalence of depression and depressive symptoms among resident physicians a systematic review and meta-analysis. *J Am Med Assoc*. 2015;**314**(22):2373–2383. doi:10.1001/jama.2015.15845
23. Kalmbach DA, *et al*. Insomnia symptoms and short sleep predict anxiety and worry in response to stress exposure: a prospective cohort study of medical interns. *Sleep Med*. 2019;**55**:40–47. doi:10.1016/j.sleep.2018.12.001
24. Rotenstein LS, *et al*. Prevalence of depression, depressive symptoms, and suicidal ideation among medical students: a systematic review and meta-analysis. *J Am Med Assoc*. 2016;**316**(21):2214–2236. doi:10.1001/jama.2016.17324
25. Slavin SJ. Medical student mental health: culture, environment, and the need for change. *J Am Med Assoc*. 2016;**316**(21):2195–2196. doi:10.1001/jama.2016.16396
26. Weinger MB, *et al*. Sleep deprivation and clinical performance. *J Am Med Assoc*. 2002;**287**(8):955–957. doi:10.1001/jama.287.8.955
27. Sen S, *et al*. A prospective cohort study investigating factors associated with depression during medical internship. *Arch Gen Psychiatry*. 2010;**67**(6):557–565. doi:10.1001/archgenpsychiatry.2010.41
28. Wittchen H-U, *et al*. *SKID. Strukturiertes klinisches Interview für DSM-IV. Achse I und II. Handanweisung*. 1997.
29. Bastien CH, *et al*. Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med*. 2001;**2**(4):297–307. doi:10.1016/S1389-9457(00)00065-4
30. Allen J. Photoplethysmography and its application in clinical physiological measurement. *Physiol Meas*. 2007;**28**(3):R1–R39. doi:10.1088/0967-3334/28/3/r01
31. Feehan LM, *et al*. Accuracy of Fitbit devices: systematic review and narrative syntheses of quantitative data. *JMIR mHealth uHealth*. 2018;**6**(8):e10527. doi:10.2196/10527
32. de Zambotti M, *et al*. Measures of sleep and cardiac functioning during sleep using a multi-sensory commercially-available wristband in adolescents. *Physiol Behav*. 2016;**158**:143–149. doi:10.1016/j.physbeh.2016.03.006
33. Bernstein DP, *et al*. *Childhood Trauma Questionnaire: A Retrospective Self-Report: Manual*. San Antonio, TX: Psychological Corporation; 1998.
34. Beck AT, *et al*. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol*. 1988;**56**(6):893–897.
35. Buysse DJ, *et al*. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;**28**(2):193–213.
36. Pinheiro J, *et al*. *nlme: Linear and Nonlinear Mixed Effects Models. R package version 3.1-143;* 2019. https://CRAN.R-project.org/package=nlme.
37. R Core Team. *R: A Language and Environment for Statistical Computing*. 2017. https://www.r-project.org/.
38. Mayer SE, *et al*. Chronic stress, hair cortisol and depression: a prospective and longitudinal study of medical internship. *Psychoneuroendocrinology*. 2018;**92**:57–65.
39. Sen S, *et al*. Effects of the 2011 duty hour reforms on interns and their patients: a prospective longitudinal cohort study. *JAMA Intern Med*. 2013;**173**(8):657–662. doi:10.1001/jamainternmed.2013.351
40. Penzel T, *et al*. Dynamics of heart rate and sleep stages in normals and patients with sleep apnea. *Neuropsychopharmacology*. 2003;**28**(Suppl 1):S48–S53.
41. Follenius M, *et al*. Nocturnal cortisol release in relation to sleep structure. *Sleep*. 1992;**15**(1):21–27.
42. Payne JD, *et al*. Napping and the selective consolidation of negative aspects of scenes. *Emotion*. 2015;**15**(2):176–186.
43. Payne JD, *et al*. Stress, sleep, and the selective consolidation of emotional memories. *Curr Opin Behav Sci*. 2018;**19**:36–43. doi:10.1016/j.cobeha.2017.09.006
44. Kervezee L, *et al*. Metabolic and cardiovascular consequences of shift work: the role of circadian disruption and sleep disturbances. *Eur J Neurosci*. 2018:1–17. doi:10.1111/ejn.14216
45. Seixas A, *et al*. Linking emotional distress to unhealthy sleep duration: analysis of the 2009 National Health Interview

Survey. *Neuropsychiatr Dis Treat*. 2015;**11**:2425. doi:10.2147/NDT.S77909
46. Suzuki H, *et al*. Early life stress and trauma and enhanced limbic activation to emotionally valenced faces in depressed and healthy children. *J Am Acad Child Adolesc Psychiatry*. 2014;**53**(7):800–13.e10.
47. McLaughlin KA, *et al*. Child trauma exposure and psychopathology: mechanisms of risk and resilience. *Curr Opin Psychol*. 2017;**14**:29–34.
48. De Bellis MD, *et al*. The biological effects of childhood trauma. *Child Adolesc Psychiatr Clin N Am*. 2014;**23**(2):185–222, vii.
49. Espie CA, *et al*. The attention-intention-effort pathway in the development of psychophysiologic insomnia: a theoretical review. *Sleep Med Rev*. 2006;**10**(4):215–245.
50. Hertenstein E, *et al*. Insomnia as a predictor of mental disorders: a systematic review and meta-analysis. *Sleep Med Rev*. 2019;**43**:96–105.
51. Riemann D, *et al*. The hyperarousal model of insomnia: a review of the concept and its evidence. *Sleep Med Rev*. 2010;**14**(1):19–31. doi:10.1016/j.smrv.2009.04.002
52. Teicher MH, *et al*. Differential effects of childhood neglect and abuse during sensitive exposure periods on male and female hippocampus. *Neuroimage*. 2018;**169**:443–452.
53. Brindle RC, *et al*. The relationship between childhood trauma and poor sleep health in adulthood. *Psychosom Med*. 2018;**80**(2):200–207. doi:10.1097/PSY.0000000000000542
54. Kessler RC, *et al*. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. *Psychol Med*. 1997;**27**(5):1101–1119.
55. McLaughlin KA, *et al*. Trauma exposure and posttraumatic stress disorder in a national sample of adolescents. *J Am Acad Child Adolesc Psychiatry*. 2013;**52**(8):815–830.e14.
56. Friedrich A, *et al*. Let's talk about sleep: a systematic review of psychological interventions to improve sleep in college students. *J Sleep Res*. 2018;**27**(1):4–22.