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Original Article

Sleep extension reduces pain sensitivity☆

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ABSTRACT

Introduction: Insufficient sleep increases pain sensitivity in healthy individuals. Additionally, extending sleep (eg, increasing nocturnal sleep time or adding a mid-day nap) has been shown to restore pain sensitivity to baseline levels in sleep deprived/restricted individuals. Whether sleep extension can reduce pain sensitivity beyond baseline levels in non-sleep restricted/deprived individuals remains unknown.
Methods: In a sample of 27 healthy, pain-free, normally-sleeping individuals (17 males, mean age ~24 yrs), we examined the impact of five nights of sleep extension on pain sensitivity. Pain threshold (elapsed time until the participant reported pain) and pain tolerance (total time the participant kept the hand submerged in the cold water) were measured using the Cold Pressor Task. Furthermore, we assessed the extent to which self-reported sleep amount in relation to the minimal subjective sleep requirement for adequate performance (sleep credit) was associated with pain sensitivity changes.
Results: On average individuals slept almost 2 extra hours per night. Our results indicate that sleep extension increases pain tolerance beyond baseline levels. However, sleep extension did not impact pain threshold. We also found that individuals with a smaller sleep credit (ie, those who habitually obtain less sleep than they feel they need) experienced greater increases in pain tolerance after extending sleep.
Conclusions: The present findings suggest that sleep extension may increase pain tolerance but not pain threshold in healthy individuals who normally sleep the recommended amount. Our findings also support the idea that sleep credit may be a strong indicator of sleep debt in the context of pain sensitivity.

1. Introduction

The existence of a 'vicious circle' relationship between insufficient sleep and pain sensitivity has been shown for a number of disorders including rheumatoid arthritis [1], fibromyalgia [2,3]; and symptoms such as lower back pain [4] (reviewed in Ref. [5]). Likewise, it has been shown that sleep loss exacerbates pain sensitivity independently of pathology. In a large-scale study of more than 10,000 individuals in which the presence of pathology was controlled, self-reported sleep disturbances (eg, taking a long time to fall asleep, insomnia) were found to be a significant predictor of increased pain sensitivity [6].

In pain-free, healthy individuals total sleep deprivation has been shown to exacerbate self-reported pain measures [7], including (but not limited to) musculoskeletal tenderness [8,9], as well as heat and cold sensitivity [10]. Likewise, chronic sleep restriction (ie, multiple days with less-than adequate sleep) has been found to reduce pain thresholds [11,12] – effects that are reversed by recovery sleep (ie, extended sleep following sleep loss) [12–14]. However, to our knowledge, the effects of sleep extension (ie, increased nightly sleep durations relative to habitual, baseline sleep) on pain sensitivity have not been tested in healthy individuals.

Accordingly, in the present study we assessed the association between sleep extension and pain sensitivity (as measured on the Cold Pressor Task) within a healthy, pain-free non-sleep restricted sample of individuals with normal sleep habits. We hypothesized that sleep extension would improve pain sensitivity in non-sleep deprived individuals.

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2. Methods

2.1. Participants

Twenty-eight healthy, pain-free volunteers participated in our study. Participants were recruited via flyers posted at local colleges, universities and military installations. The Institutional Review Board at the Walter Reed Army Institute of Research approved the study. Participants provided written informed consent and were compensated monetarily for their participation. Study participants first completed questionnaires to determine eligibility based on physical and psychological health; as well as sleep habits and chronotype (described in more detail below). If eligible for our study, participants underwent a physical examination including a 12-lead electrocardiogram and evaluation of blood and urine samples to determine general health (including pregnancy and drug use). In order to reduce inter-subject variability in nighttime sleep, participants who self-reported habitual nightly sleep amounts outside the target range of 6–9 h nighttime lights-out times earlier than 2100 h on average during weeknights, morning wake-up times later than 0900 on average during weekdays, and habitual napping more than three times a week were excluded. Participants who reported consuming more than 400 mg of caffeine daily, on average, were also excluded. Participants were scheduled to complete a one-night in-laboratory overnight sleep screening, where sleep and breathing were monitored using a portable wearable device (Embletta MPR PG, Natus, Pleasanton, CA) to rule out sleep disorders. During the physical examination, participants who had a history of dermatological conditions that may increase risk and/or discomfort under cold temperatures (eg, open skin wounds, chilblains, skin and peripheral vascular diseases, etc.) were excluded. Participants with a history of neurological disorders, chronic pain, heavy alcohol use defined as fourteen drinks or more per week, tobacco use and psychiatric disorders were also excluded. Additionally, a score $\geq$41 on either side of the State Trait Anxiety Inventory a score $\geq$13 on the Beck Depression Inventory, and scores <31 or >69 on the Horne Ostberg Morningness-Eveningness Questionnaire (MEQ-indicative of extreme morning or evening preference) rendered the participants ineligible to participate in the study [15]. In total, 105 individuals were screened for this study, and 28 completed the protocol.

2.2. Experimental design

Participants wore a wrist actigraph device during the entire duration of this 24 days long study. Fig. 1 depicts the flow of events for this study. During the first 14 nights, participants slept at their home. During the subsequent two nights participants were requested to sleep in our sleep laboratory with a fix time in bed from 11PM to 7AM [Time in bed (TIB): 8 h]. During the subsequent five sleep extension nights, bedtime was 9PM to 7AM (TIB: 10 h).

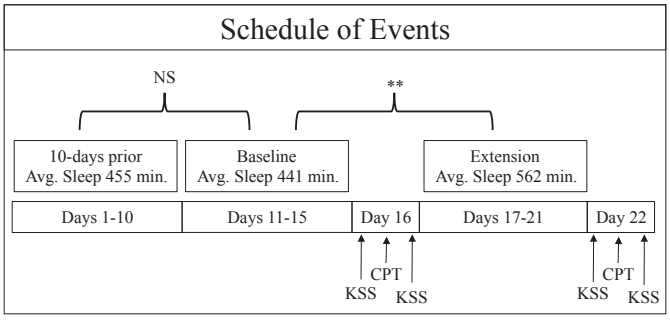

Fig. 1. Study design. Avg: average; NS Indicates p-value greater than 0.05; ** indicates p-value < 0.01; CPT = Cold Pressor Task; KSS = Karolinska Sleepiness Scale.

The Cold Pressor Task was administered at 10:00 AM following both (a) the first night that they slept in the laboratory and (b) the fifth night of extended sleep. Caffeine use was allowed for the first 12 days of the study but prohibited for the remainder of the study (ie, beginning 48 h prior to initiation of the full-time in-laboratory phase and continuing through the last day of sleep extension [confirmed with daily logs and urinalyses each time participants came to the lab]).

2.3. Measures

2.3.1. Actigraphy

For the entire duration of the study, participants wore an Actiwatch 2 (Philips Respironics, Murrysville, PA) wrist actigraph, on their non-dominant wrist. Activity data was collected in 30-s epochs. Sleep-wake status for each 30-s epoch was computed using the Actiware 6.0.9 scoring algorithm [16,17]. Average sleep duration was calculated for the 10-day period prior to the baseline sleep, five days of baseline sleep and five days of the extended sleep period.

2.3.2. Sleep credit

Participants reported their typical sleep duration during (a) weeknights and (b) weekend nights by responding to the following questions: (a) “How much do you typically sleep on weeknights?” and (b) “How much do you typically sleep on weekend nights?”. Furthermore, participants were asked to complete the following statements on subjective sleep need “If I get less than __ hours of sleep, I notice an impairment in my ability to function at work”. Self-reported average sleep duration for weeknights and weekend nights was then used to calculate the weighted average habitual sleep (in hours). “Sleep credit” was conceptualized as the difference between the weighted average habitual sleep and the subjective sleep needed [18]. Thus, sleep credit was calculated as the difference between how much sleep a person says they need to function normally versus how much they say they have been getting.

2.3.3. Karolinska Sleepiness Scale

The Karolinska Sleepiness Scale (KSS) is a validated 9-point Likert scale used for the assessment of sleepiness. The KSS was administered between 8 and 9AM (prior to the Cold Pressor Task) and in the evening 7–8PM on both the last day of the baseline phase and the last day of the extension phase. The two daily time points were averaged to determine sleepiness levels for that experimental day.

2.3.4. Cold Pressor Task

The cold pressor task (CPT) is a pain stressor task that induces pain by the submersion of the hand in a bath of cold water (5 °C) [19]. For this assessment we used the Thermo Scientific™ A28 refrigerated bath circulator (Thermo Scientific Waltham, MA). Participants verbally reported when they first perceive the cold-water stimulus as causing discomfort (pain threshold) by saying “Now,” and then removed their hand when the pain became unbearable (pain tolerance). Unknown to the participants, the maximum permitted immersion time was 300 s. Pain threshold (elapsed time until the participant reported pain) and pain tolerance (total time the participant kept the hand submerged in the cold water) were expressed in seconds, and using the raw values for each time point, we calculated the difference between baseline and extension (extension values minus baseline values), or delta (Δ), for each variable.

2.4. Statistical analyses

SPSS 23 (Armonk, NY) was used for statistical analyses. One participant was excluded from analyses because of a large circadian shift during the two-week period prior to participation (detected via actigraphy). Ten participants were at ceiling for pain tolerance at baseline. For the main statistical analyses, repeated measures ANOVA tests were used to assess whether sleep extension influenced within-subject change in pain sensitivity (including both pain threshold and tolerance). In our main model, the within-subject factors were sleep condition (baseline, extension) and pain sensitivity (tolerance, threshold). Two sets of tests were conducted – one including the whole sample and one excluding individuals at ceiling for tolerance during baseline.

Correlations were determined for several factors: sleep credit (a lower number indicates a lower sleep reserve prior to experimentation), change in sleepiness levels between baseline and extension (sleepiness Δ; a lower number indicates sleepiness decreased), change in pain tolerance (To Δ; a lower number indicates pain tolerance decreased), and change in pain threshold (Th Δ; a lower number indicates pain threshold decreased).

3. Results

Of the 27 individuals who participated, 17 were males. Average age was 24.41 years old (*SD* = 5.29, 19–39 years). Table 1 shows the general demographics of the sample. Sleep duration was significantly higher during the sleep extension phase (average 562.4 ± 32.9 min) than during five-day baseline (441.9 ± 60.8 min) and during the 10 days prior to the baseline period (455.1 ± 52.2 min). There were no differences in terms of sleep duration between the five-day baseline period and the 10 days prior. There was a small improvement in subjective sleepiness ratings following sleep extension, although not statistically significant [baseline average 3.86 ± 1.28; extension average 3.48 ± 1.72; t (25) = 1.38; p = 0.18].

Ten participants were at ceiling for pain tolerance at baseline (300 s). These participants did not differ from the others in terms of their sleep durations during the first night in lab [t (25) = 0.16, p = 0.88], or during the 14 days prior to testing [t (25) = −0.85, p = 0.41].

A repeated measures ANOVA was applied to determine whether sleep extension affected pain tolerance and threshold. A main effect of condition [F (1,26) = 6.21, p = 0.019; partial eta squared = 0.19] revealed that sleep extension increased both pain tolerance and pain threshold. There was no significant condition by pain measure interaction [F (1,26) = 1.89, p = 0.18]. When participants who were at ceiling for pain tolerance at baseline were removed from the analyses, the main effect of condition remained significant [F (1,16) = 7.58, p = 0.014; partial eta squared = 0.32], and a significant condition by pain measure interaction was found [F (1,16) = 4.55, p = 0.049; partial eta squared = 0.22]. Post-hoc paired-sample t-tests revealed that pain tolerance increased significantly following sleep extension, although there was no significant effect on pain threshold. The average pain tolerance at baseline was 63.70 ± 12.45 s compared to an average of 96.64 ± 21.22 s following sleep extension [t (16) = −2.45, p = 0.026]. The average pain threshold at baseline was 18.29 ± 3.40 s compared to an average of 21.23 ± 3.65 s following sleep extension [t (16) = −1.88, p = 0.08].

Finally, there was a significant negative correlation between sleep credit and pain tolerance with lower sleep credit associated with greater sleep extension-induced increases in pain tolerance. In other words, individuals who reported habitually not satisfying their subjective sleep need at baseline (low sleep credit) experienced a larger pain tolerance increase following sleep extension (ie, experienced a greater benefit from sleep extension) (see Table 2).

Table 1
Participant demographics.

Metric	Mean or N	Std. Dev. or %
Age (Mean, SD)	24.41	5.29
Women (n, %)	10	37.04%
Body Mass Index (Mean, SD)	24.59	3.12
Weekly Self reported sleep duration [hours] (Mean, SD)	53.93	6.96
10 days prior mean sleep duration [minutes][a] (Mean, SD)	455.1	52.2
5 nights baseline mean sleep duration [minutes][a] (Mean, SD)	441.9	60.85
5 nights sleep extension mean sleep duration [minutes][a] (Mean, SD)	562.4	32.87

[a] Actigraphy measures.

Table 2
Correlations between sleep credit, sleepiness and pain outcomes.

	Sleep Credit	KSS Sleepiness Δ	Pain Threshold Δ
KSS sleepiness	0.23		
Pain threshold Δ	−0.12	**0.43**	
Pain tolerance Δ	**−0.5***	−0.19	−0.41

Bold indicates trend level significance (p-value between 0.05 and 0.1). Bold and * indicates p-value < 0.05. KSS Sleepiness morning and evening values are averaged.

4. Discussion

The present findings indicate that sleep extension may result in increased pain tolerance in healthy individuals with normal sleep habits. Pain threshold, however, was not significantly affected by sleep extension. Additionally, individuals with a smaller sleep credit (ie, those who habitually obtain less sleep than they feel they need) realized greater increases in pain tolerance from sleep extension. Those with the greatest subjective habitual sleep debt might therefore obtain greatest benefit from extending sleep.

The current study replicates and extends results from prior work in which sleep duration and pain sensitivity were studied. To our knowledge, there have been only two previous studies on sleep extension and pain sensitivity [14,20]. In the first, which was conducted in a laboratory setting, mildly sleepy (based on a Multiple Sleep Latency Test (MSLT) score < 8 min) individuals were randomly assigned to one of two groups: the control group maintained their normal nighttime sleep routine, and the experimental group extended their nighttime sleep (by a mean of 105 min) [14]. This study revealed that four nights of sleep extension reduced pain sensitivity, using a radiant heat method. However, an important difference between that study and the present study is that the aforementioned study sample consisted of mildly sleepy individuals, whereas all subjects in the present study had self-reported nighttime sleep durations and subjective daytime sleepiness levels that were within normal limits. Our results replicate their findings using different but conceptually related methods. First, we utilized a different quantitative pain testing modality, but also observed decreased sensitivity to pain attributable to extended sleep. Second, although our sample consisted of normal sleepers, our finding that sleep credit covaries with pain tolerance following sleep extension dovetails nicely with their results, and suggest that sleep extension might be most fruitful for those who objective or subjectively carry some sleep debt.

A second extant study was performed in a clinical setting on patients undergoing knee replacement surgery [20]. Prior to

surgery, patients were randomized into two groups: the first group was instructed to maintain their habitual nighttime sleep schedule, and the second group to extend their sleep. The sleep extension group, extended their sleep by an average of one hour and reported lower pain ratings (on a visual analog scale), and less pain management medication use relative to the group who maintained their typical nighttime sleep schedule. However, in this study, there was no objective sleep data prior to starting the intervention. It is therefore not known whether these patients' habitual sleep was within normal limits prior to intervention.

The present study is the first to report that sleep extension seems to reduce pain sensitivity in non-sleepy, healthy young adults – ie, in individuals free of pain-inducing pathology with normal sleep/wake habits. Similarly, the present study is the first to link sleep credit with an improvement in a behavioral task. This finding is noteworthy, as it may indicate that in the context of recommended hours of sleep, sleepiness may not be a suitable subjective tool to assess individuals sleep reservoir.

4.1. Sleep, emotion and pain

Pain threshold and tolerance are functionally distinct: although pain threshold seems to be determined predominantly by physiological factors, it is thought that pain tolerance is influenced by both physiological and cognitive/emotional factors [21]. Therefore, it is possible that sleep's positive impact on pain tolerance is, at least partially, mediated by the well-established effects of sleep on emotion regulation [22].

Sleep modulates the brain response to aversive emotional stimuli in humans [23]. Functional brain imaging studies have shown that sleep loss results in reduced prefrontal cortical activity [23,24], which in turns results in apparent disinhibition of activity in the amygdala, and increased emotional lability [24–26]. Likewise, recent work has suggested that sleep extension increases prefrontal-amaygdala connectivity [27]. Of course, it is also known that prefrontal cortices mediate the cognitive and emotional regulation of pain [28,29]. In fact, it has been suggested that this brain region is the primary mediator of downstream analgesic activity and/or emotional responsivity [21]. Thus, it is reasonable to hypothesize that increased sleep leads to increased top-down regulation of pain.

4.2. Strengths and weaknesses

The present study is the first in which both baseline sleep and sleep extension were conducted in a highly controlled laboratory environment with normal, healthy volunteers who had been screened for sleep disorders and pain history, and whose habitual sleep was within recommended limits. Another strength of this study is the use of the CPT, an instrument with excellent two-week test-retest stability for pain threshold and pain tolerance, at least in a young population, similar to the one in this study [30,31].

There are some limitations that warrant discussion. First, there was no control group to rule out the possibility that the observed changes in pain tolerance were due to other unmeasured factors. For instance, improvement pain tolerance could have been due to a habituation effect rather than sleep extension. Without a control group, we are unable to conclusively state that sleep extension benefits pain tolerance. However, the high test-retest reliability of the CPT is actually restrictive in terms of statistical power and we observed an effect of the extension manipulation and the sleep credit index. Moreover, a habituation-based interpretation of enhanced pain tolerance does not fit with the observed and robust covariance between sleep credit and post-sleep extension changes in pain tolerance. Future research should aim to replicate these findings with a matched control group and preferably with a crossover design. Second, our study was restricted to healthy young adults, therefore potentially limiting the generalizability of our results to other populations (eg, chronic pain conditions, older adults, etc.). Finally, we did not use the MSLT, the current gold standard for the assessment of sleepiness. However, the KSS, a validated tool used to assess situational sleepiness [32], indicated that our participants were overall alert – their scores were within normal limits at baseline, and improved only slightly following sleep extension. This was expected because one of the study eligibility requirements was self-reported habitual sleep duration of at least 7 h per night – consistent with the nightly sleep durations recommended by the American Academy of Sleep Medicine and the Sleep Research Society [33]. The habitual sleep duration of 7 h for our sample was also confirmed with actigraphy.

5. Conclusions

The present findings suggest that sleep extension may increase pain tolerance but not pain threshold in normal, healthy, young adults with normal sleep/wake schedules. Our findings also support the idea that sleeping in relation to the minimal subjective sleep requirement for adequate performance may be a strong indicator of sleep debt in the context of pain sensitivity. The implications of these preliminary findings are broad, and include, for example, the possibility that interventions to enhance sleep might prove useful as part of a prophylactic pain management strategy that is initiated prior to surgery, physical therapy, physically demanding tasks or intense athletic performance.

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Disclaimer

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Conflicts of interest

None of the authors have any relevant conflicts of interest to report.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.10.023.

References

[1] Drewes AM, Nielsen KD, Hansen B, et al. A longitudinal study of clinical symptoms and sleep parameters in rheumatoid arthritis. Rheumatology (Oxford) 2000;39:1287–9.

[2] O'Brien EM, Waxenberg LB, Atchison JW, et al. Intraindividual variability in daily sleep and pain ratings among chronic pain patients: bidirectional association and the role of negative mood. Clin J Pain 2011;27:425–33.

[3] Affleck G, Urrows S, Tennen H, et al. Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. Pain 1996;68:363–8.

[4] Alsaadi SM, McAuley JH, Hush JM, et al. The bidirectional relationship between pain intensity and sleep disturbance/quality in patients with low back pain. Clin J Pain 2014;30:755–65.

[5] Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. J Pain 2013;14:1539–52.

[6] Sivertsen B, Lallukka T, Petrie KJ, et al. Sleep and pain sensitivity in adults. Pain 2015;156:1433–9.

[7] Haack M, Sanchez E, Mullington JM. Elevated inflammatory markers in response to prolonged sleep restriction are associated with increased pain experience in healthy volunteers. Sleep 2007;30:1145–52.

[8] Lentz MJ, Landis CA, Rothermel J, et al. Effects of selective slow wave sleep disruption on musculoskeletal pain and fatigue in middle aged women. J Rheumatol 1999;26:1586–92.

[9] Moldofsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. Psychosom Med 1976;38:35–44.

[10] Kundermann B, Spernal J, Huber MT, et al. Sleep deprivation affects thermal pain thresholds but not somatosensory thresholds in healthy volunteers. Psychosom Med 2004;66:932–7.

[11] Simpson NS, Scott-Sutherland J, Gautam S, et al. Chronic exposure to insufficient sleep alters processes of pain habituation and sensitization. Pain January 2018;159(1):33–40. https://journals.lww.com/pain/Abstract/2018/01000/Chronic_exposure_to_insufficient_sleep_alters.7.aspx.

[12] Faraut B, Leger D, Medkour T, et al. Napping reverses increased pain sensitivity due to sleep restriction. PloS One 2015;10, e0117425.

[13] Onen SH, Alloui A, Gross A, et al. The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. J Sleep Res 2001;10:35–42.

[14] Roehrs TA, Harris E, Randall S, et al. Pain sensitivity and recovery from mild chronic sleep loss. Sleep 2012;35:1667–72.

[15] Jankowski KS. Morning types are less sensitive to pain than evening types all day long. Eur J Pain 2013;17:1068–73.

[16] Neurosleep. Manual for actigraphy standardisation. Data acquisition, analysis and reporting. Australia: National Health and Medical Research Council Centre of Research Excellence; 2017.

[17] Jobert M, Wilson FJ, Roth T, et al. Guidelines for the recording and evaluation of pharmaco-sleep studies in man: the International Pharmaco-EEG Society (IPEG). Neuropsychobiology 2013;67:127–67.

[18] Weber M, Webb CA, Deldonno SR, et al. Habitual 'sleep credit' is associated with greater grey matter volume of the medial prefrontal cortex, higher emotional intelligence and better mental health. J Sleep Res 2013;22:527–34.

[19] Edens JL, Gil KM. Experimental induction of pain: utility in the study of clinical pain. Behav Ther 1995;26(2):197–216. https://www.sciencedirect.com/science/article/abs/pii/S0005789405801029?via%3Dihub.

[20] Roehrs TA, Roth T. Increasing presurgery sleep reduces postsurgery pain and analgesic use following joint replacement: a feasibility study. Sleep Med 2017;33:109–13.

[21] Bingel U, Tracey I. Imaging CNS modulation of pain in humans. Physiology (Bethesda) 2008;23:371–80.

[22] Altena E, Micoulaud-Franchi JA, Geoffroy PA, et al. The bidirectional relation between emotional reactivity and sleep: from disruption to recovery. Behav Neurosci 2016;130(3):336–50. https://doi.org/10.1037/bne0000128. http://psycnet.apa.org/record/2016-07215-001.

[23] Yoo SS, Gujar N, Hu P, et al. The human emotional brain without sleep–a prefrontal amygdala disconnect. Curr Biol 2007;17:R877–8.

[24] Gujar N, Yoo SS, Hu P, et al. Sleep deprivation amplifies reactivity of brain reward networks, biasing the appraisal of positive emotional experiences. J Neurosci 2011;31:4466–74.

[25] Goldstein AN, Greer SM, Saletin JM, et al. Tired and apprehensive: anxiety amplifies the impact of sleep loss on aversive brain anticipation. J Neurosci 2013;33:10607–15.

[26] Gujar N, Yoo SS, Hu P, et al. The unrested resting brain: sleep deprivation alters activity within the default-mode network. J Cogn Neurosci 2010;22:1637–48.

[27] Motomura Y, Kitamura S, Nakazaki K, et al. Recovery from unrecognized sleep loss accumulated in daily life improved mood regulation via prefrontal suppression of amygdala activity. Front Neurol 2017;8:306.

[28] Kong J, Gollub RL, Rosman IS, et al. Brain activity associated with expectancy-enhanced placebo analgesia as measured by functional magnetic resonance imaging. J Neurosci 2006;26:381–8.

[29] Wager TD, Rilling JK, Smith EE, et al. Placebo-induced changes in FMRI in the anticipation and experience of pain. Science 2004;303:1162–7.

[30] Koenig J, Jarczok MN, Ellis RJ, et al. Two-week test-retest stability of the cold pressor task procedure at two different temperatures as a measure of pain threshold and tolerance. Pain Pract 2014;14:E126–35.

[31] Saab PG, Llabre MM, Hurwitz BE, et al. The cold pressor test: vascular and myocardial response patterns and their stability. Psychophysiology 1993;30:366–73.

[32] Akerstedt T, Anund A, Axelsson J, et al. Subjective sleepiness is a sensitive indicator of insufficient sleep and impaired waking function. J Sleep Res 2014;23:240–52.

[33] Consensus Conference P, Watson NF, Badr MS, et al. Joint consensus statement of the american Academy of sleep medicine and sleep research society on the recommended amount of sleep for a healthy adult: methodology and discussion. Sleep 2015;38:1161–83.