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Associations of nocturnal sleep with experimental pain and pain catastrophizing in healthy volunteers

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ABSTRACT

Strong alterations of night sleep (e.g., sleep deprivation, insomnia) have appeared to affect pain in inducing hyperalgesic changes. However, it has remained unclear whether everyday variations of night sleep in healthy individuals have any influence on pain processing. Forty healthy subjects were studied by portable polysomnography (PSG) and sleep questionnaire during two non-consecutive nights at home. Experimental pain parameters (pressure pain threshold, temporal summation = TS, conditioned pain modulation = CPM) and situational pain catastrophizing (Situational Catastrophizing Questionnaire = SCQ) were always assessed the evening before and the morning after sleep recording in a pain laboratory. Linear regression analyses were computed to test the prediction of overnight changes in pain by different sleep parameters. Significant prediction of changes in pain parameters by sleep parameters was limited (2 out of 12 analyses), indicating that everyday variations in sleep under non-pathological and low stress conditions are only weakly associated with pain.

1. Introduction

It is to date widely accepted that sleep alterations affect pain. Evidence for this belief stems mainly from studies in which the effects of sleep deprivation or substantial sleep fragmentation on experimental pain parameters were investigated (Karmann, Kundermann, & Lautenbacher, 2014; Kundermann and Lautenbacher, 2007; Lautenbacher, Kundermann, & Krieg, 2006). Insomnia as a clinical condition with sleep fragmentation as a symptom has appeared to corroborate this impression (Haack et al., 2012). These findings allow for the assumption that poor night sleep enhances pain sensitivity but not for the determination of the mechanisms of action.

Sleep is a highly complex state with multiple processes and different stages; thus, it appears unlikely that all sleep-indicative variables are equally linked with pain. For identification of the critical variables, more specific manipulations were used instead of total sleep deprivation. Lentz, Landis, Rothermel, & Shaver (1999) selectively disrupted slow wave sleep (SWS) with little effect on the total sleep duration and produced a substantial decrease in pain threshold. Onen, Alloui, Gross, Eschallier, & Dubray (2001) also interrupted SWS, again with the result of a decrease in pain threshold. These findings raised hope that a specific delta-wave related mechanism might be identified, which was, however, frustrated by a study by Older et al. (1998), who could not change pain threshold with three days of delta-wave interruption. The findings by Engstrøm et al. (2013, 2014); of inconsistent correlations between SWS duration and pain threshold also suggest that there might not be an easy answer claiming variations in SWS as major mediator of changes in pain processing.

Which other candidates are available and have been tested? Rapid eye movement (REM) sleep deprivation led to a decrease in pain threshold (Onen et al., 2001) in one study; however, in another study no changes in laser evoked potentials and ratings were observed (Azevedo et al., 2011). Roehrs, Hyde, Blaisdell, Greenwald, & Roth (2006) may have found an explanation for this inconsistency by demonstrating a rapid attenuation of the effect of REM sleep deprivation on pain after only one night. Landis, Lentz, Rothermel, Buchwald, & Shaver (2004) found a correlation of pain threshold with sleep spindle activity, with less activity being associated with lower thresholds, which is a finding awaiting further replication.

The impression that there are still open questions as regards the specific mechanisms implicated in sleep effects on pain was also supported by studies in which the conditioned pain modulation (CPM) paradigm for the study of pain inhibition was used. It seems very likely that CPM becomes deficient after sleep deprivation. However, it is still

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unclear which sleep stages are critically responsible for the naturally occurring nocturnal restoration of pain inhibition (Edwards et al., 2009; Smith, Edwards, McCann, & Haythornthwaite, 2007).

In summary, there is considerable evidence that substantial sleep interruption, either induced experimentally by total sleep deprivation or occurring as a consequence of insomnia, definitely leads to hyperalgesia. However, when less powerful interventions were used or non-pathological covariations were studied, results were much less consistent. One might assume that there is only a loose covariation between sleep and pain, which requires major changes of sleep to affect pain. Such an association might be functionally adaptive to avoid that smallest sleep disturbances can already dysregulate the pain system. Under this perspective, everyday variations of nocturnal sleep may have no impact on pain; it may be that the two functions remain disconnected as long as sleep varies within normal and non-pathological limits.

To test this assumption, we studied healthy individuals (sleep and pain disorders were explicitly excluded) as regards their pain psychophysics (pain threshold, temporal summation, CPM) before and after having had night sleep at home, i.e., in a familiar and non-stressful situation. We added pain catastrophizing as subjective state variable known to influence both sleep quality and pain processing (Byers, Lichstein, & Thorn, 2016; Campbell et al., 2015). Night sleep was recorded via portable polysomnography and sleep quality was assessed via questionnaires. We hypothesized that sleep parameters would not substantially relate to pain parameters in our healthy sample under these non-pathological and low stress conditions.

2. Materials and methods

2.1. Subjects

The 40 participants (female: N = 20) between the ages of 19 and 59 years (mean age: 38.8 years; SD = 13.5) were recruited via university news posted in the local newspapers. Exclusion criteria were acute and chronic pain, psychological disorders or medical diseases, including sleep disorders. Participants taking psychotropic drugs or analgesics were also excluded from participation. A trained psychologist verified the exclusion criteria in a standardized clinical interview. All participants provided written informed consent before testing and received monetary compensation for their participation. The study protocol was approved by the ethics committee of the University of Bamberg.

2.2. Procedures

Nocturnal sleep quality was assessed in two non-consecutive nights (1–13 days interval) at the participant's home via objective (portable polysomnography (PSG) recordings) and subjective (questionnaire) measures. In addition, four procedurally equal test sessions were run in the pain laboratory at the University of Bamberg in order to assess several parameters of pain processing. These sessions took always place at 6 p.m. before and at 8 a.m. after the test nights. The test protocol for these sessions included the assessment of several physiological, behavioral and psychological measures. At the start and end of each session, subjects provided saliva samples for determination of cortisol levels. In a second part, the participants completed a dot-probe task and an eye tracking paradigm, both presenting emotional facial stimuli (in a randomized order). The last part of each session – which will be the subject of the current publication – was run to measure pain processing. First, pressure pain thresholds were assessed. The assessment of temporal summation of pressure pain and conditioned pain modulation (CPM) followed. Given this protocol, the impact of stimuli slowly increased, starting with pain cues (pictorial facial expression of pain), being followed by slightly painful stimuli (pain threshold) and ending with moderately painful stimuli (temporal summation, CPM), in order to minimize order effects. After pain stimulation, participants were asked to fill out the Situational Catastrophizing Questionnaire (SCQ; 17), whereupon the last cortisol sampling followed.

2.3. Assessment of pain-related measures

2.3.1. Apparatus

Pressure stimuli were administered with a computer-controlled pressure algometer (Noxitest Biomedical, Aalborg, Denmark; see also Nie, Arendt-Nielsen, Andersen, & Graven-Nielsen, 2005 for a detailed description). A rounded aluminum foot plate with a padded probe area of 1 cm^2 was fixed to the tip of a piston, which was moved by an electric motor. The pressure stimulation was controlled by a built-in force transducer. Pressure stimuli were applied to the fingertip of the middle and index finger of the left hand. The pressure algometer was mounted on a table in front of the participants in such a way that the participant could place her/his fingertips comfortably below the probe.

A heat stimulus was administered as conditioning stimulus in the CPM paradigm by using a circulating water bath (Witeg GmbH, WiseCircu WCB-22, Wertheim, Germany), containing 46 °C hot water. The subject immersed her/his hand up to 2 cm above the wrist in this water bath. The water temperature was controlled by a thermostat, and the water was stirred with a force and suction pump to avoid layers of lower temperature around the hand. The heat stimulus was always applied to the right hand.

2.3.2. Assessment of pressure pain thresholds

Pressure pain thresholds were assessed using the method of limits. The piston was lowered until the probe touched the skin of the fingertip. Then, the pressure increased at a rate of 50 kPa/s until the subjects felt the stimulus to be slightly painful and responded by pressing a stop button. Each time they pressed the button, the probe lifted and returned the pressure to zero. After two practice trials, five trials were presented at each finger (middle and index fingers) with an inter-stimulus interval (ISI) of > 8 s. These 5 trials were averaged to get the estimate of pressure pain threshold for each finger. For the correlation analysis with sleep parameters, the average pain threshold computed over both fingers was used.

2.3.3. Assessment of temporal summation

Temporal summation was tested by comparing the sensations evoked by single pulses of pressure stimulation to sensations evoked by a series of five pulses (only the last pulse was rated), which were applied with a repetition frequency of 0.5 Hz. The series of five pulses was always delivered 60 s after the single pulse. Stimulus intensity was tailored to the individual pain threshold (50% above threshold) and increased with a rate of rise of 75% of the target intensity per second. The stimuli had a saw-tooth shape with stimulus duration at maximum of only 0.1 s. The three runs of single pulses and pulse series were separated by intervals of 60 s. In each run, either the index or the middle finger were stimulated, alternating always with the other finger in the next run. This sequence was counterbalanced over the participants, with half of the participants starting with the index finger. The three runs were presented once in each of the two experimental conditions (baseline, CPM).

2.3.4. Assessment of conditioned pain modulation (CPM)

The CPM effect was tested using water of painful heat (46 °C) as conditioning stimulus whereas the pressure stimuli (single and series) served as test stimuli. The perceived intensity of the latter was supposed to be modulated by the former stimulus. For assessing this CPM effect, the ratings evoked by the pressure stimuli during concurrent presentation of the conditioning stimulus (CPM condition) were compared to ratings without conditioning stimulation (baseline condition). The temperature of 46 °C was selected as the painful intensity of the conditioning stimulus based on the results of previous studies (Lautenbacher, Roscher, & Strian, 2002; Willer, Roby, & Le Bars, 1984).

The immersion time of the hand was set to 6 min in order to allow for concurrent application of all pressure stimuli (three single pulses and three series of five pulses).

2.3.5. Rating scale

After the application of each single pulse and each series of five pulses, participants were asked to rate the perceived pain intensity. For this purpose a numerical rating scale (NRS) was used, reaching from "0" representing "no pain" to "10" representing "extremely strong pain", respectively. In addition, subjects also rated the perceived intensity of the conditioning stimulus in the CPM paradigm (hot water of 46 °C), using the same scale. Ratings of the water bath always followed the ratings of the pressure stimuli, resulting in six ratings for pressure stimulation (three single pulses and three series of five pulses) and six ratings for heat stimulation. For further analyses, the ratings of pressure stimulation were averaged for each experimental condition (baseline, CPM), separately for ratings of single pulses and ratings of last pulses in the series of five pulses. The six ratings of the heat stimuli during conditioning stimulation were also averaged.

Using these NRS scores, the effects of temporal summation as well as CPM were calculated as follows. Temporal summation (TS) was determined as the averaged differences between sensations evoked by the series of stimuli and the single stimuli in a way that high scores indicate strong temporal summation. The TS parameter was computed from the data of the baseline condition (without conditioning stimulation) only in order to avoid confounding of TS and CPM effects.

CPM effects were determined as the averaged differences in pain intensity ratings of test stimuli between the baseline condition (i.e., test stimuli applied alone) and the CPM condition (i.e., test stimuli applied during conditioning stimulation). Thus, high scores indicate a strong CPM effect. CPM effects were computed separately for single stimuli and series of stimuli and in turn averaged, resulting in only one parameter for CPM.

2.3.6. Situational catastrophizing questionnaire (SCQ)

The SCQ is an adaptation of the Pain Catastrophizing Scale (Sullivan, Bishop, & Pivik, 1995) and consists of six items assessing catastrophizing specifically with respect to the noxious stimuli previously applied (Edwards, Smith, Stonerock, & Haythornthwaite, 2006). Accordingly, participants were instructed to reference the mechanical and thermal pain procedures received when filling out the SCQ.

2.4. Assessment of sleep quality

2.4.1. Nocturnal polysomnography (PSG)

PSGs were run in two non-consecutive nights by a portable PSG recorder (SOMNO-watch plus EEG by SOMNOmedics; Randersacker, Germany) and analysed according to the standard PSG protocol (Rechtschaffen and Kales, 1968). PSG recording was prepared in the lab of the University of Bamberg directly after the evening pain testing session. Thereafter, participants left the lab to sleep at home. The PSG montage included the following: four EEG channels (C4, C3, O1, O2), bilateral electro-oculogram (EOG; left and right) and two EMGs channels (m. sub-mentalis). All channels were referenced towards Cz. EEG, EOG and EMG channels were recorded using Grass gold electrodes, which were filled and attached to the head with Grass EC2 electrode cream. Prior to application of the electrodes, skin was cleaned with Nuprep abrasive gel to reduce electrode resistance. The acquired data were analysed as follows. In a first step, the DOMINO light software automatically scored sleep and wake stages in 30-s epochs. Afterwards, all epochs were visually inspected to check whether the automatic analysis performed correctly according to the Rechtschaffen and Kales criteria (Rechtschaffen and Kales, 1968). In case of discrepancy, the automatic analysis was overruled and stages were rescored.

The following parameters, extracted from the PSG recordings, were used for further analysis: Total sleep time (TST; time from "lights off" to "lights on" without the time spent awake), sleep efficiency (SE; TST/time spent in bed after sleep onset * 100%), sleep latency (time from "lights off" to first occurrence of Non-REM stage 2), awakenings (total number and total duration), durations of Non-REM stage 1, stage 2, slow-wave sleep (SWS) and rapid eye-movement sleep (REM). "Lights off" and "lights on" were marked by button press on the recorder.

For one subject, technical problems of the PSG recording during the first night prevented the assessment of all sleep parameters except sleep latency.

2.4.2. Self-reported sleep quality

In order to assess self-reported sleep quality, participants were asked to fill out the evening/morning protocol of the German Sleep Society (DGSM). Only the morning protocol, which covers the night and well-being in the morning and was filled out right after waking up in the morning, were considered for the present report. Three questions assessing the subjective state in the morning had to be filled out on a 6-point scale (Mood – ranging from depressed to untroubled; Freshness – ranging from run down to refreshed; Tension – ranging from tense to relaxed); the question assessing restfulness of the sleep had to be answered on a 5-point scale (ranging from very restful to not restful at all). These items were chosen for further analysis. Scale properties were misunderstood by one participant, whose data could not be used for further analysis.

2.5. Statistical analysis

First, descriptive statistics (mean, standard deviation) were calculated for all pain and sleep parameters for both nights. In order to determine whether there was a difference between the first and second test night, *t*-tests for dependent samples, comparing the sleep parameters of the two nights, were calculated.

Second, the overnight changes in pain processing were predicted by use of linear regression analyses with sleep parameters (for both nights) as predictors and pain parameters as criteria. The overnight changes in pain processing were indicated by computing the difference between morning and evening sessions. In a first step, *Night* coded as a dummy variable (first night vs. second night) was entered to determine any differences in overnight changes in pain parameters between the first and the second night. In a second step, the sleep parameters were entered in three groups of predictors: (i) *General PSG* (TST, SE; sleep latency, number and duration of awakenings), (ii) *Sleep Stage Specific PSG* (durations of Non-REM stage 1, stage 2, slow-wave sleep (SWS) and rapid eye-movement (REM) sleep) as well as (iii) *Subjective Sleep Quality* (4 items of the morning/evening protocol). In each of these 2-step regression analyses, only one of the three predictor groups was entered. Thus, this protocol resulted into 12 regression analyses (3 sleep predictor groups × 4 pain parameters).

SPSS 23 (IBM) was used for all calculations; the significance level was set to alpha = 0.05. Bonferroni corrections for multiple testing were applied.

3. Results

3.1. Description of sleep and pain parameters

Descriptive data for the pain parameters are given in Table 1. Compared with norms for pressure pain thresholds (see Fischer, 1987; Magerl et al., 2010; Pfau et al., 2014), the findings of the present study were within normal limits during all test sessions. As planned, the conditioning stimulus was rated as painful during all sessions. In addition, Table 1 descriptively shows that CPM (inhibition) as well as temporal summation (augmentation) effects could be detected in all sessions. Significant deviations from 0 (= no change) to be interpreted as inhibition and temporal summation were confirmed for both

Table 1
Descriptive statistics (Mean, *(SD)*) for pain parameters in all test sessions and overnight changes (morning–evening).

	Evening – 1st night	Morning – 1st night	Overnight change – 1st night	Evening – 2nd night	Morning – 2nd night	Overnight change – 2nd night
Pressure Pain Threshold – Index Finger (kPa)	333.48 *(155.37)*	327.48 *(129.00)*	−6.00 *(82.61)*	359.68 *(169.11)*	355.18 *(149.21)*	−4.50 *(55.80)*
Pressure Pain Threshold – Middle Finger (kPa)	327.50 *(140.06)*	311.38 *(126.31)*	−16.13 *(68.71)*	350.03 *(157.13)*	327.35 *(138.33)*	−22.68 *(54.92)*
Pressure Pain Threshold – Average (kPa)	330.49 *(143.11)*	319.43 *(125.07)*	−11.06 *(66.07)*	354.85 *(160.82)*	341.26 *(141.33)*	−13.59 *(49.87)*
Pain rating for conditioning stimulus (CS)	6.25 *(2.80)*	5.78 *(2.59)*	−0.48 *(1.00)*	5.64 *(2.67)*	5.43 *(2.62)*	−0.21 *(0.77)*
Temporal Summation	1.05 *(.93)*	1.20 *(.88)*	0.15 *(1.10)*	0.94 *(.73)*	0.90 *(.84)*	−0.04 *(0.76)*
Conditioned Pain Modulation (CPM)	0.56 *(1.36)*	0.09 *(1.29)*	−0.47 *(1.48)*	0.17 *(.99)*	0.23 *(1.19)*	0.06 *(1.21)*
Situational Catastrophizing Questionnaire (SCQ)	5.63 *(5.02)*	4.63 *(4.67)*	−1.00 *(2.86)*	3.65 *(3.28)*	3.53 *(3.10)*	−0.13 *(1.98)*

Temporal summation = mean rating (pressure pulse series) – mean rating (pressure single pulses); CPM = mean rating (baseline of pressure pulses) – mean rating (CS concurrent with pressure pulses), averaged over single pulses and pulse series; all rating data refer to a Numerical Rating Scale (NRS; 0–10) as artificial unit.

measures (averaged across the four measurements) by one-sample *t*-tests (CPM: $T(39) = 1.811$, $p = 0.039$; TS: $T(39) = 10.403$, $p < 0.001$; one-tailed). Thus, parameters for experimental pain reached sufficient quality for further analysis.

Descriptive statistics for the sleep parameters of both nights are illustrated in Table 2. According to several sleep parameters, sleep appeared to have been slightly poorer in the first night. TST as well as duration of REM-sleep were significantly shorter in the first than in the second night. In addition, participants felt subjectively less relaxed after the first night. Therefore, there was a clear necessity to control for differences between the two nights in producing overnight changes in the pain parameters.

3.2. Regression analyses for predicting overnight changes in pain parameter by sleep parameters

The regression analyses are depicted in Table 3,[1] grouped by pain parameters. Already a quick look at Table 3 shows that *Night* was not a significant predictor in any of the 12 regression analyses, which means that the overnight changes in pain parameters were not different between the two recording nights. Thus, the two nights could be considered replication in the sense of the study, strengthening statistical power.

Only two out of 12 regression analyses suggest significant influence of sleep parameters on overnight changes in pain (see Table 3). The overnight change in CPM was significantly predicted by the *Sleep Stage Specific PSG* (as a group of predictors with $p = 0.045$[2]). Amongst the four predictors of this group, it was the duration of SWS which predicted the overnight change in CPM significantly (beta = −0.248, $T = -2.185$, $p = 0.032$[3]). This means that a long duration of SWS was associated with a low CPM inhibition on the next morning relative to the evening before, suggesting a non-restorative function of SWS for CPM.

SCQ was significantly predicted by *General PSG* measures (see Table 3). The significant three out of five predictors were SE (beta = 1.079, $T = 2.658$, $p = 0.010$[4]), sleep latency (beta = −0.371, $T = -2.642$, $p = 0.010$) and duration of awakenings (beta = 1.029, $T = 2.287$, $p = 0.025$). This means that those individuals with a decline in SCQ overnight had a short duration of awakenings but also a low SE and a long sleep latency. The interpretation of these sleep-related influences on SCQ is complicated by the fact of very high and significant (all $p \leq 0.001$) correlations amongst the significant predictors (SE with sleep latency: $r = -0.496$, SE with duration of awakenings: $r = -0.965$, sleep latency with durations of awakenings: $r = 0.629$).

4. Discussion

As to be expected the study produced regular and non-pathological results as regards the pain parameters (pain thresholds within normal limits, temporal summation and CPM inhibition occurred as expected) and the sleep parameters (all sleep parameters within normal limits with a tendency to better nocturnal sleep in the second night of two). Thus, our approach of including only healthy and pain-free individuals without sleep disorders and using portable PSG to allow for recording of sleep parameters in the home environment was successful in reproducing non-pathological pain responses and sleep patterns.

Furthermore, the tests on differences between the first and second night as regards overnight changes in pain parameters were altogether negative, which allowed us to combine both nights in order to enhance statistical power. Therefore, we had ideal conditions for testing the hypothesis that variations of sleep and pain processing are unrelated in healthy individuals under everyday conditions.

The results of our regression analyses testing the prediction of overnight changes in experimental pain responses by sleep parameters supported this hypothesis. Only one of the 9 regression analyses yielded a significant finding: The *sleep stage specific PSG* predictors, i.e., the duration of SWS, were significantly associated with CPM inhibition. This finding should be interpreted with caution as it would not withstand a Bonferroni correction. However, the trend towards longer SWS being associated with less CPM efficiency is in line with findings reported by Matre, Andersen, Knardahl, & Nilsen (2016) who found enhanced CPM after partial sleep restriction. These observations seem counterintuitive as the related literature suggests positive effects of good night sleep on CPM and not the opposite (Edwards et al., 2009; Haack et al., 2012; Smith et al., 2007); future research should try to clarify this issue by directly testing the effects of SWS on CPM. Overall, our findings indicate at most weak associations between sleep and pain processing as assessed by psychophysical paradigms under non-pathological and low stress conditions.

The relationship between sleep and situational pain catastrophizing (SCQ), a psychological variable relating to negative cognitive-emotional responses to pain, appeared to be more pronounced. SCQ was significantly predicted by the predictor group *General PSG* with five single predictors with $p = 0.010$ for the whole model, which passed a Bonferroni correction. Amongst these five predictors, SE, sleep latency and duration of awakening were the significant single predictors (even after Bonferroni correction). In light of previous findings associating poor night sleep with higher levels of trait and state measures of pain catastrophizing (Byers et al., 2016; Campbell et al., 2015; Goodin et al., 2011), the directions of prediction by the single predictors were,

[1] Detailed information (B, beta) for all single predictors is provided in Table S1 (Supplement).
[2] Bonferroni corrected alpha = 0.006.
[3] Bonferroni corrected alpha = 0.013.
[4] Bonferroni corrected alpha = 0.017.

Table 2
Descriptive statistics and *t*-tests for the sleep parameters in both nights.

Sleep parameter		N	Mean	SD		N	Mean	SD	t	df	p
Total sleep time (TST)[a]	1st Night	39	6:36:58	1:14:26	2nd Night	40	7:04:05	0:49:50	−2.684	38	.011
Sleep efficiency (Percent)[b]		39	91.78	12.27		40	95.05	4.29	−1.851	38	.072
Sleep latency[a]		40	0:13:19	0:11:43		40	0:11:26	0:10:16	1.654	39	.106
Awakenings (Number)[c]		39	9.49	5.66		40	8.51	4.97	−0.958	38	.344
Awakenings (Duration)[a]		39	0:42:34	0:57:19		40	0:28:54	0:22:53	1.861	38	.070
Non-REM Stage 1 (Duration)[a]		39	0:22:44	0:13:16		40	0:19:04	0:10:23	1.754	38	.088
Non-REM Stage 2 (Duration)[a]		39	3:45:40	0:56:59		40	4:00:20	0:41:07	−1.766	38	.085
SWS (Duration)[a]		39	1:13:32	0:29:25		40	1:13:53	0:30:52	−0.233	38	.817
REM (Duration)[a]		39	1:15:11	0:28:55		40	1:31:04	0:19:39	−3.841	38	**< .001**
Mood		39	4.49	0.97		39	4.36	1.04	0.682	38	.499
Freshness		39	3.54	0.94		39	3.72	1.21	−1.045	38	.303
Tension		39	4.41	0.91		39	4.69	0.98	−2.056	38	**.047**
Restfulness of sleep		39	3.35	0.83		39	3.55	0.71	−1.433	39	.160

Parameters are given in [a] hours:minutes:seconds, [b] percentage, [c] total number; *t*-tests are calculated for differences between the two nights.

Table 3
Two step-regression analyses with inclusion of *Night* (first night vs. second night) in *step 1* and sleep parameters in *step 2* (three groups of predictors: (i) *General PSG* (TST, SE; sleep latency, number and duration of awakenings), (ii) *Sleep Stage Specific PSG* (durations of Non-REM stage 1, stage 2, slow-wave sleep (SWS) and rapid eye-movement (REM) sleep) as well as (iii) *Subjective Sleep Quality* (4 items of the morning/evening protocol)) and pain parameter as criteria (pressure pain threshold, temporal summation, Conditioned Pain Modulation (CPM) and Situational Catastrophizing Questionnaire (SCQ)).

Pressure pain threshold (criterion)			
Predictors	DF	F	p
Night (step 1)	1/77	0.122	0.728
General PSG (step2)	6/72	0.729	0.628
Night (step 1)	1/77	0.122	0.728
Sleep Stage Specific PSG (step2)	5/73	0.235	0.946
Night (step 1)	1/76	0.086	0.770
Subjective sleep quality (step 2)	5/72	0.606	0.695
Temporal summation (criterion)			
Predictors	DF	F	p
Night (step 1)	1/77	1.184	0.280
General PSG (step2)	6/72	0.552	0.767
Night (step 1)	1/77	1.184	0.280
Sleep Stage Specific PSG (step2)	5/73	1.433	0.223
Night (step 1)	1/76	1.004	0.320
Subjective sleep quality (step 2)	5/72	0.875	0.502
Conditioned Pain Modulation (CPM)			
Predictors	DF	F	p
Night (step 1)	1/77	2.808	0.098
General PSG (step2)	6/72	0.637	0.700
Night (step 1)	1/77	2.808	0.098
Sleep Stage Specific PSG (step2)	5/73	***2.402***	***0.045***
Night (step 1)	1/76	3.146	0.080
Subjective sleep quality (step 2)	5/72	1.352	0.252
Situational Catastrophizing Questionnaire (SCQ)			
Predictors	DF	F	p
Night (step 1)	1/77	3.187	0.078
General PSG (step2)	6/72	***3.041***	***0.010***
Night (step 1)	1/77	3.187	0.078
Sleep Stage Specific PSG (step2)	5/73	2.010	0.087
Night (step 1)	1/76	3.094	0.083
Subjective sleep quality (step 2)	5/72	0.904	0.483

however, puzzling. The expected direction was found for the duration of awakenings but not for SE and sleep latency. However, the high correlations between predictors suggest multicollinearity with the consequences of little risk for the whole regression model but of potentially erratic patterns amongst the individual predictors. Thus, it seems justified to conclude that objective sleep quality is related to overnight changes in pain catastrophizing. Such associated alterations in sleep quality and in cognitive affective processing related to pain

may be especially relevant for the understanding of functional chronic pain syndromes like fibromyalgia, as previous research has already suggested (Affleck, Urrows, Tennen, Higgins, & Abeles, 1996; Byers et al., 2016; Campbell et al., 2015). However, future research is needed to clarify the direction of these associations in clinical and non-clinical samples.

Returning to the main focus of the present study, we obtained a lack of association between nocturnal sleep and pain processing when pain psychophysics were considered as outcome. This finding is in line with our hypothesis but might seem counterintuitive when considering the large body of evidence suggesting hyperalgesic effects of deficient sleep (Haack et al., 2012; Karmann et al., 2014; Kundermann and Lautenbacher, 2007; Lautenbacher et al., 2006; Lentz et al., 1999; Onen et al., 2001). There are two possible explanations for the divergence between these previous studies and our investigation. (i) The correlations between the two functions emerge only when the within-system variations reach a certain level (Lautenbacher, 2018). From this perspective, significant correlations may mainly emerge under pathological conditions (e.g., chronic pain in sleep disorders) or when exerting strong impact on one of the two functions (e.g., pain threshold changes after total sleep deprivation). (ii) Alternatively, one might assume that there is a continuous correlation between sleep and pain processing over the full range of within-system variations, which might, however, be masked by measurement error in case of only weak within-system variations. The data of the present study do not allow for deciding between the two theoretical alternatives because they only provide evidence for no substantial correlations between sleep and pain under non-pathological and low stress conditions.

It might be that we selected the wrong parameters to represent sleep and pain processing when looking for co-variations. However, given that we used a wide range of well-established parameters for both functions, it is highly unlikely that this could be an explanation for so many zero-correlations. Another limitation might be that we excluded elderly individuals which might have guaranteed larger within-system variations which are known for both sleep and pain from age studies (Crowley, 2011; Lautenbacher, 2012). However, as the mean age of our participants was 39 years, our study does definitely not belong to the many investigations using very young student samples but rather targets an age group with first prevalence increases in sleep and pain disorders (Fayaz, Croft, Langford, Donaldson, & Jones, 2016; Ohayon, 2002). This makes its results certainly informative and valid for the present context.

Two other limitations should be briefly addressed although the relevance of discussion would have been higher in case of positive findings, namely substantial correlations between sleep and pain parameters. The effects of night sleep and time of day are confounded by nature. Thus, differences between evening and morning sessions might be due to the nocturnal sleep in-between or due to circadian rhythms not related to sleep. However, previous findings concerning diurnal variations of pain processing are inconsistent which makes it difficult and elaborate to consider such variations in design planning (Aviram, Shochat, & Pud, 2015). Furthermore, these variations appear to be strong in some individuals and weak in others with different acrophases (Strian, Lautenbacher, Galfe, & Hölzl, 1989). Therefore, it is – as the second limitation – difficult to plan the schedule for data assessment in an interindividually comparable fashion.

From a clinical perspective, one important implication of the present findings might be that patients and clinicians should not be overly concerned as minor sleep disturbances do not necessarily increase pain vulnerability and – vice versa – minor variations in pain responsiveness do not necessarily affect night sleep. From an interventional perspective, i.e., when planning experimental modulations or therapeutic interventions, it should be borne in mind that strong modulations of sleep or pain might be necessary to uncover effects on the other variable.

In conclusion, everyday variations in sleep and pain processing did not appear to mutually affect each other when observed under low stress conditions in healthy individuals. The use of portable polysomnography for studying night sleep at home in a familiar environment might be helpful when aiming at minimizing sleep disturbances due to the study protocol. In future studies, gradual increases in disturbing night sleep should be used to determine the level of change at which sleep problems appear to affect pain processing and correlations between the two functions become apparent.

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Conflicts of interest

There are no conflicts of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.biopsycho.2018.02.015.

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