Deciphering the Temporal Link between Pain and Sleep in a Heterogeneous Chronic Pain Patient Sample: A Multilevel Daily Process Study

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Objectives: Because insomnia is a common comorbidity of chronic pain, scientific and clinical interest in the relationship of pain and sleep has surged in recent years. Although experimental studies suggest a sleep-interfering property of pain and a pain-enhancing effect of sleep deprivation/fragmentation, the temporal association between pain and sleep as experienced by patients is less understood. The current study was conducted to examine the influence of presleep pain on subsequent sleep and sleep on pain reports the next day, taking into consideration other related psychophysiologic variables such as mood and arousal.

Design: A daily process study, involving participants to monitor their pain, sleep, mood, and presleep arousal for 1 wk. Multilevel modeling was used to analyze the data.

Setting: In the patients' natural living and sleeping environment.

Patients: One hundred nineteen patients (73.9% female, mean age = 46 years) with chronic pain and concomitant insomnia.

Measurement: An electronic diary was used to record patients' self-reported sleep quality/efficiency and ratings of pain, mood, and arousal at different times of the day; actigraphy was also used to provide estimates of sleep efficiency.

Results: Results indicated that presleep pain was not a reliable predictor of subsequent sleep. Instead, sleep was better predicted by presleep cognitive arousal. Although sleep quality was a consistent predictor of pain the next day, the pain-relieving effect of sleep was only evident during the first half of the day.

Conclusions: These findings challenge the often-assumed reciprocal relationship between pain and sleep and call for a diversification in thinking of the daily interaction of these 2 processes.

Keywords: Chronic pain, sleep, presleep arousal, mood, daily process, temporal relationship

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INTRODUCTION

Pain and sleep are often assumed to be reciprocally linked, whereby pain adversely affects sleep and poor sleep aggravates pain. Although intuitive, evidence accrued so far suggests the temporal relationship may be more complex.

Laboratory studies using healthy volunteers have found that, although the induction of nociceptive stimuli alters the microstructure of sleep,[1] it does not always increase the frequency of sleep-stage shift or actual awakening[2]; i.e., changing the macrostructure of sleep. Furthermore, although some studies noted increased pain perception after sleep deprivation/fragmentation,[3-8] other studies did not observe the same effect despite using similar research methodology.[1,9,10]

Prospective studies have been conducted to examine pain and sleep as interacting daily processes.[11] At the general population level, pain was found to predict subsequent sleep duration and the hours of reported sleep were a significant predictor of pain fre-

quency the next day.[12] Notably, the latter relationship was curvilinear such that both long (≥ 9 hr) and short (< 6 hr) sleep duration were predictive of higher pain frequency. In clinical settings, sleep quality (SQ) was found to be a significant predictor of next-day pain ratings in hospitalized acute burn patients.[13] However, the relationship did not appear to be reciprocal, as pain ratings during the day did not predict subsequent SQ, although in a follow-up study of a longer assessment period (and therefore more observations) SQ was predicted by daytime pain ratings.[14] Recently, the daily pain-sleep relationship was examined in a group of adolescents with and without chronic pain, using both actigraphy and self-report measures.[15] In contrast with previous findings, daytime pain did not predict nighttime sleep, and neither actigraphically-measured sleep efficiency (SE) nor self-reported SQ were found to predict pain the next day. Instead, higher pain was predicted by longer sleep duration and lengthy awakenings the night before. These results highlight the complexity of the pain-sleep relationship, which apparently varies according to the characteristics of the sample (acute versus chronic pain; adults versus adolescents), presence or types of pain (e.g., fibromyalgia, burn pain), setting (hospital versus home), and method of assessment (subjective versus objective). Moreover, the interaction between pain and sleep may be mediated by confounding processes not measured. This point is clearly illustrated in the now classic study by Affleck et al.,[16] in which women with fibromyalgia were asked to provide daily ratings of their sleep, pain, and attention to pain for 1 mo. Although SQ of the previous night predicted pain the next day and pain during the day predicted quality of sleep that subsequently
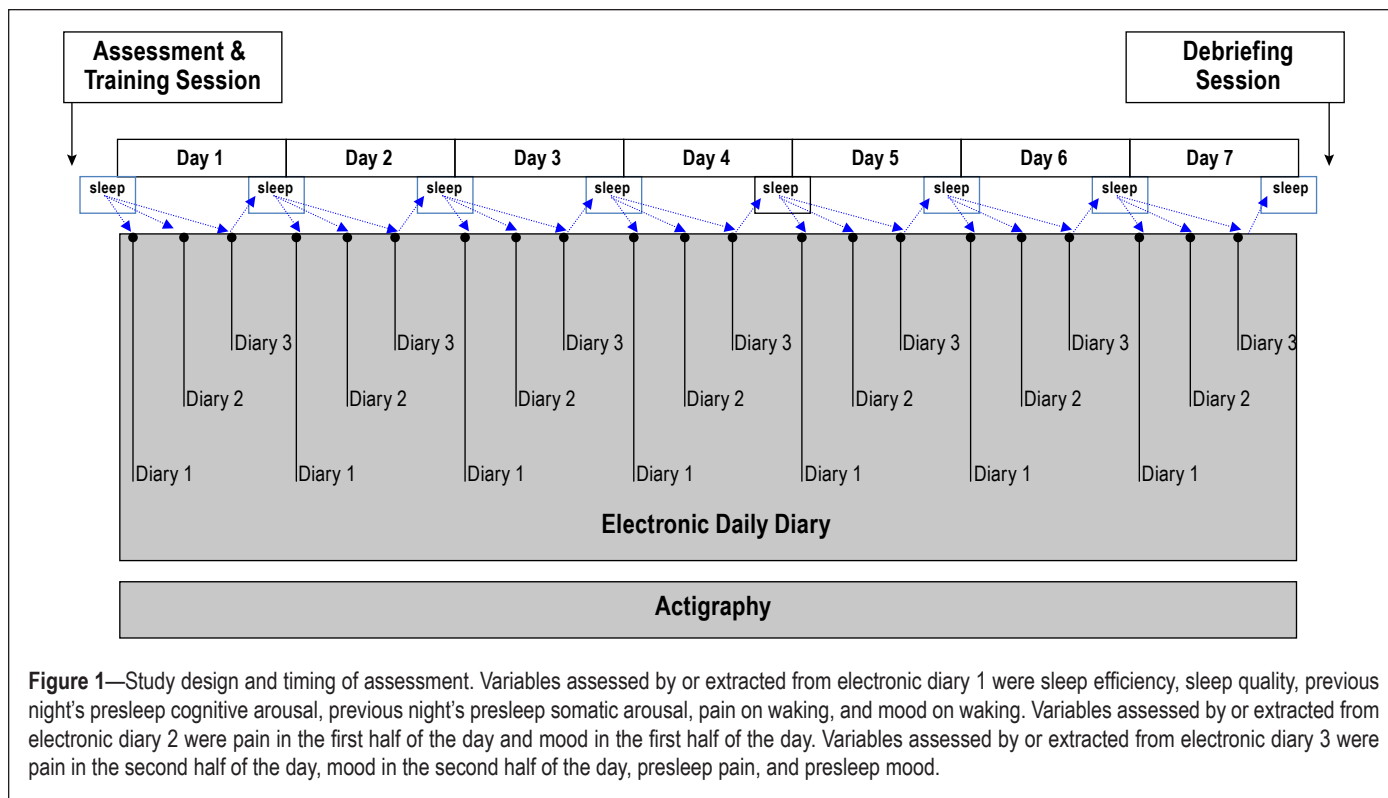
Figure 1—Study design and timing of assessment. Variables assessed by or extracted from electronic diary 1 were sleep efficiency, sleep quality, previous night's presleep cognitive arousal, previous night's presleep somatic arousal, pain on waking, and mood on waking. Variables assessed by or extracted from electronic diary 2 were pain in the first half of the day and mood in the first half of the day. Variables assessed by or extracted from electronic diary 3 were pain in the second half of the day, mood in the second half of the day, presleep pain, and presleep mood.

occurred, neither of these relationships remained significant once the effect of pain attention was controlled for.

To develop a more sophisticated understanding of the pain-sleep relationship, the current study further examined the temporal link using the daily process approach. The target population of this study was working-age adults with chronic pain. This specific focus was motivated by the huge individual, economic, and societal costs associated with this condition in this population.[17-19] Maximizing the clinical relevance and ecologic validity of the findings, a heterogeneous sample of patients with chronic pain and concomitant insomnia were asked to monitor pain and sleep in their natural sleeping and waking environment for 1 wk. The decision to use a heterogeneous pain patient sample was based on the clinical reality that most patients presenting for treatment reported more than 1 cause of pain (i.e., multiple etiologies) and it was not always possible (and appropriate) to partition patients into ideologically defined pain subgroups. Sleep was assessed by both actigraphy and self-report using an electronic diary to capture possible differences between these technologies. Previous cross-sectional research has suggested that mood and different forms of presleep arousal may be better predictors of subsequent sleep than pain intensity.[8,20-25] We thus included daily measures of these variables and built separate models to evaluate their values in predicting sleep relative to pain. To examine whether the effect of sleep on pain varies across the day, pain ratings were taken at various time points so comparisons could be made.

METHOD

Overview

A daily process study was conducted with 119 patients with chronic pain and insomnia. Figure 1 illustrates the design and assessment procedure of the study. Participants who consented to taking part in this study were asked to monitor their pain and sleep for 1 wk by wearing an actigraph throughout the duration of the study and by completing a short electronic diary 3 times a day. The repeated measurement of pain and sleep, as well as mood and arousal during the presleep period, minimized recall bias and enabled us to document real-life changes in these processes as they happened. Applying the multilevel modeling technique with days as level 1 units and participants as level 2 units,[26,27] this design allowed an analysis of the within-person changes in these processes on a day-to-day basis while taking into account the issues of autocorrelation between responses and the influence of between-subjects variations in the relationships of interest. The research protocol had received full ethical approval.

Participants

Participants were recruited from a pain clinic located within an inner-city hospital in London, United Kingdom. An experienced member of the research team (C.E.G.) approached patients in the waiting room. Those who expressed interest in taking part were provided further information about the study and administered a short screening checklist. Those who passed the initial screening were offered an assessment interview, during which the Duke structured interview schedule for Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, text revision (DSM-IV-TR) and International Classification of Sleep Disorders, Second Edition (ICSD-2) was administered.[28] The interview took approximately 1-1.5 hr to complete. The purpose of this additional procedure was to confirm that the patients' insomnia complaints met diagnostic criteria for duration, frequency, and severity, and that they had no other medical, psychiatric, or sleep disorders that could better account for their sleep disturbance, aside from their pain.

Inclusion criteria were as follows: 18-65 yr of age; English-speaking; nonmalignant pain of at least 6 months' duration; scoring 15 or higher on the Insomnia Severity Index[29] (i.e., indicating clinical insomnia; description provided later in this article). Patients were not invited to proceed with the study if they reported having received an injection or undergone surgery for their pain in the past month or were scheduled to receive an injection or surgery during the duration of the study; were suffering from a life-threatening medical condition (e.g., cancer, human immunodeficiency virus/acquired immunodeficiency syndrome) or a severe psychiatric/psychologic problem causing acute distress (e.g., psychosis, depression with suicidal intent); or visual/cognitive impairments that rendered completing the electronic diary and sleep monitoring procedure unfeasible (e.g., poor vision, dementia).

Patients were recruited consecutively from the pain clinic. A total of 614 patients who attended the clinic were screened for eligibility. Among these individuals, 396 did not meet the basic study inclusion criteria (269 patients fell outside the age bracket, 54 were not proficient in English, 1 was unable to read, 2 reported experiencing pain for less than 6 months, 11 reported no difficulty sleeping, 25 had severe psychopathology or substance dependency, 25 had cancer or human immunodeficiency virus, and 9 had an identified organic sleep disorder). Of the 218 patients invited to take part in the study, 73 declined (22 did not give a reason, 21 were too busy, 13 did not want to travel to the appointments, 7 did not believe their sleep problems were severe enough, 3 were scheduled for surgery, 3 did not want to have their sleep monitored, 2 were recently bereaved, and 2 cited dissatisfaction with their medical treatment as the reason for not participating). Of the 145 patients who attended the assessment interview, 4 were excluded because of suspected restless legs syndrome, 2 participants withdrew after the initial assessment because they did not think they could manage the electronic diary, and an additional 6 patients withdrew halfway through the study due to time constraints. A total of 133 patients entered into the study and completed the monitoring procedure. Fourteen participants had to be excluded from the analysis due to incomplete data collection (caused by either technical failure of the recording devices or noncompliance with instructions). The final sample thus comprised 119 chronic pain patients with clinical insomnia.

A range of pain conditions was reported, with most patients having pain in more than 1 location (86.8%). The most common location of pain was lower back (72.8%), followed by legs (54.4%), neck (37.7%), shoulder (32.5%), knee (35.1%), arms (21.1%), upper back (21.9%), and joints (21.9%). In line with the multifactorial etiology of chronic pain, half of the participants identified more than one cause of their pain. The most commonly cited cause of pain was disc/cartilage damage (52.9%), followed by trauma/injury (32.8%), arthritis/osteoarthritis (24.4%), nerve damage (22.7%), surgery (8.4%), rheumatoid arthritis (7.6%), migraine and headaches (5.9%), fibromyalgia (5%), endometriosis (2.5%), ankylosing spondylitis (1.7%), tendinitis (1.7%), sickle cell anemia (1.7%), neurofibromatosis (0.8%), irritable bowel syndrome (0.8%), leg ulcer (0.8%), and spina bifida occulta (0.8%). A subset of the participants identified no specific cause for their pain (10.9%).

Procedure

The study took place in the participants' natural living and sleeping environment. The participants were asked to monitor their pain and sleep for 1 wk; 117 patients completed 7 days, 118 completed 6 days, and 119 completed 5 days of monitoring.

Prior to commencing the study, all participants completed a set of questionnaires (discussed later in this article) and attended a training session during which the rationale and procedure of the study were explained. Specifically, the participants were told that we were interested in studying their pain experience and natural sleep pattern over the course of 1 wk. To minimize unwanted confounders, the participants were explicitly asked not to change their usual sleep-wake pattern, consumption of substances (e.g., coffee, tea, alcohol, tobacco), and use of medication during the study. To enable the participants to perform the monitoring task as designed, they were given one-to-one training on wearing the actigraph and on completing the electronic diary using a handheld computer (see subsequent paragraphs). The participants were sent home with the equipment to start the monitoring task once they had demonstrated competence in using the actigraph and had successfully completed a full set of training diaries. They were also given a participant handbook, which contained step-by-step photographic instructions, to take home and refer to when necessary.

The participants were instructed to wear the actigraph on the nondominant wrist during the day and at night, except when coming into contact with water (e.g., when taking a bath or shower). They were also instructed to report their experience of pain, sleep, mood, and/or arousal on the electronic diary 3 times a day. The timing of these 3 diaries was individually determined based on the participants' self-reported normal daily routine; diary 1 was programmed to be completed at the participant's typical rise time, diary 2 at the midpoint between diary 1 and diary 3, and diary 3 at the participant's typical bedtime. The alarm of the handheld computer was programmed to go off at these prespecified times, prompting the participant until the diary was completed or expired (diaries not completed before the next one was to be used were considered expired). Each completed diary was time-stamped, locked, and saved in the handheld computer for later extraction. Expired diaries were also automatically locked and saved, so it was not possible for the participant to complete missed diaries retrospectively.

The participants came back to the laboratory 1 wk later to return the equipment and download the data. They were debriefed and each given a £20 gift voucher as reimbursement.

Materials

Electronic daily diary

The electronic daily diaries were operated on handheld computers (Palm PDA, model: Z22, Palm, Inc., Sunnyvale, CA) that had a touch-screen interface, allowing the participants to enter their response using a stylus pen. The diaries were specifically designed and customized for this study using Satellite Forms version 7.2 (Thacker Network Technologies Inc, Canada). Diary 1 was to be completed upon waking. It contained questions asking the participants to record their bedtime and rise time. Participants were also asked to estimate – based on the sleep they had the previous night – how long it had taken them to fall asleep (i.e., sleep-onset latency, SOL), how many times and for how long they had been woken up after sleep onset (i.e., wake after sleep onset, WASO; duration of wake after sleep onset,

WASO duration), and how long they had slept all together (i.e., total sleep time, TST). To enhance precision, all participants were instructed to make their estimates to the nearest minute. These data were then used to calculate an overall index of SE based on the formula: [TST / (SOL + WASO duration + TST)] × 100%. The SE figure thus represents the percentage of time spent asleep while in bed and is a recognized indicator of sleep consolidation/fragmentation. In addition, the participants were asked to rate the quality of their sleep ("How would you rate the quality of sleep obtained last night?"; 0-10 numeric rating scale (NRS): 0 "very poor," 10 "very good"), their experience of cognitive arousal ("As you were trying to go to sleep last night, did thoughts keep running through your mind?"; 0-10 NRS: 0 "not at all," 10 "very much so") and somatic arousal ("As you were trying to go to sleep last night, did you experience a jittery, nervous feeling in your body?"; 0-10 NRS: 0 "not at all," 10 "very much so") as they were trying to go to sleep, and the level of pain ("How much pain do you have right now?"; 0-10 NRS: 0 "no pain at all," 10 "a lot of pain") and mood ("How would you describe your mood right now?"; 0-10 NRS: 0 "very bad mood," 10 "very good mood") they experienced on waking. Diary 2 was to be completed at the midpoint between Diaries 1 and 3. All questions in Diary 2 started with the time referent: "Overall, with reference to the first half of your day…," such that the ratings the participants provided on pain ("…how much pain did you have?") and mood ("…how would you rate your mood?") would represent their experience during this time frame. Diary 3 was to be completed at the participant's usual bedtime. All questions in Diary 3 started with the time referent: "Overall, with reference to the second half of your day,…" such that the ratings the participants provided on pain ("…how much pain did you have?") and mood ("…how would you rate your mood?") would represent their experience during this time frame. Diary 3 also contained questions asking the participants to rate their experience of pain and mood as they prepared themselves for bed. The time referents for these questions were altered to "Right now, at this minute,…" so the participants' ratings represented the state of their experience during the presleep period.

Actigraphy

Actigraphy was used to provide an objective estimate of sleep, based on physical activity. It is a lightweight, nonintrusive device to be worn on the nondominant wrist, similar to a normal wristwatch. The device contains a piezoelectric accelerometer set up to record the integration, amount, and duration of movements in all directions. The corresponding voltage is then converted and stored as activity count data, which are then downloaded for sleep analysis using the software, Actiwatch Activity and Sleep Analysis (Cambridge Neurotechnology Ltd., Cambridge, UK) version 5.43. Actigraphy is widely used as an adjunct measure of sleep in behavioral sleep medicine research.[30,31] Sleep estimates provided by actigraphy have good agreement with those provided by polysomnography (78%-85% agreement[32]) although, compared with polysomnography, actigraphy tends to misidentify quiet wakefulness as sleep, resulting in discrepancies between these estimates. The Actiwatch-Insomnia model (Cambridge Neurotechnology, Ltd.) was therefore used in this study as an attempt to improve accuracy in detecting quiet wakefulness. A small pressure sensor, which is not a device used with conventional actigraphs, is at-

tached to the watch to be held by the wearer between the thumb and the finger until muscle tone relaxes at the onset of sleep. This additional behavioral measure of sleep onset facilitates the scoring of SOL and has been shown to improve accuracy in the estimation of wakefulness, and thus the calculation of SE.[33] As per the standard protocol, participants were asked to depress the event marker once when they switched off the light and got ready for bed and once when they got up in the morning. To facilitate the scoring and detection of awakenings, the participants were also asked to hold the pressure sensor with their fingers as they tried to fall asleep and every time when they woke up from sleep. The SE index as calculated by the computer software was used in subsequent analyses.

Questionnaires

The questionnaire contained a selection of measures that collect data on the participants' demographics (age, sex, body mass index, ethnicity, educational level, employment and marital status, pain types, pain duration, and insomnia duration) and physical conditions using the Brief Pain Inventory (BPI)[34] and Insomnia Severity Index (ISI).[29] Participants' general psychologic characteristics were assessed with the Hospital Anxiety and Depression Scale (HAD) [35] and the Short Health Anxiety Inventory (SHAI).[36] Scores on these questionnaires, briefly described in the following paragraphs, were used to characterize the sample.

Brief Pain Inventory: The interference subscale of the BPI contains 7 items to assess to what extent pain has interfered with a person's general activity, mood, walking ability, work, relationships, sleep, and enjoyment of life. Responses are made on 0–10 NRS, with 0 representing "Does not interfere" and 10 representing "Interferes completely." Responses are summed to give a global interference score between 0 and 70, with higher ratings indicating greater levels of interference. The interference subscale of the BPI has shown to have good internal consistency (Cronbach $\alpha = 0.88$).

Insomnia Severity Index: The ISI is a 7-item scale validated with reference to the diagnostic criteria for primary insomnia in the DSM-IV.[37] Participants in the current study were instructed to respond to the questions based on their sleep patterns in the past month. Each item is rated on a 5-point scale (0 = "Not at all," 4 = "Extremely") and summed to generate a total score that ranges from 0 to 28. A score of 7 or lower indicates no clinical insomnia, whereas a score of 15 or higher identifies cases of clinical insomnia with excellent sensitivity (94%) and specificity (94%). The ISI has good levels of internal consistency (Cronbach $\alpha = 0.76$–0.78; item-total $r = 0.36$–0.67) and concurrent validity (correlation with sleep diary variables = 0.32–0.91; correlation with polysomnography variables = 0.07–0.45; correlation with clinician's ratings = 0.50–0.71).

Hospital Anxiety and Depression Scale: The HADS contains 14 items describing anxiety and depression symptoms in nonpsychiatric medical contexts. Participants were asked to rate the severity of their symptoms during the past week on a 4-point scale (0–3), generating a score for both "Anxiety" (range: 0-21) and "Depression" (range: 0-21). Higher scores indicate greater symptom severity. The HADS has demonstrated good internal consistency (mean Cronbach $\alpha > 0.8$ for both subscales) and concurrent validity (agreement with clinician ratings of anxiety: $r = 0.54$ and depression: $r = 0.79$).

Short Health Anxiety Inventory: The SHAI comprises 14 groups of 4 statements concerning health anxiety (ranked 0–3). Participants were asked to select the statement most appropriate for them from each group. The rank scores were then summed to give a total score (range: 0-42), with a higher score indicative of a higher level of health anxiety. The SHAI has demonstrated good internal consistency (Cronbach α = 0.89).

Data Analysis

Descriptive statistics were used to characterize the sample. Means and standard deviations were reported for continuous variables, whereas frequencies and percentages were used in reporting categoric variables.

To evaluate the within-person temporal link between pain and sleep, as well as the psychophysiologic variables of interest, we pooled the daily monitoring data from all participants, generating an aggregate data set of 830 observations. MLwiN (Centre for Multilevel Modeling, University of Bristol, Bristol, UK) version 2.20[38] was used to carry out multilevel analysis on the observations, taking into account variations in the relationship between pain and sleep at both the "day" level (level 1) and the "participant" level (level 2). However, instead of just evaluating the significance of coefficients within models, we performed a between-model comparison. The results of this comparison enabled us to determine the relative strength of the various predictors of interest.

Following the natural order of the events, we first fit multilevel models to examine whether the level of pain reported during the presleep period of the previous night (i.e., presleep pain) predicted various indices of sleep subsequently obtained (i.e., "sleep quality," "sleep efficiency," and "actigraphy sleep efficiency"). We also examined whether presleep pain was the best predictor of subsequent sleep, in comparison with other potential predictors (i.e., "presleep mood," "presleep cognitive arousal," and "presleep somatic arousal"). Next, we examined whether any of the sleep indices predicted pain ratings given by the participants at different points of the following day (i.e., "pain upon waking," "pain during the first half of the day" and "pain during the second half of the day"). In each set of the analyses, the first model was always one that only included a constant term, set to be a random effect at both the "day" and "participant" levels.

In the Results section, we assessed the significance of each predictor by comparing it to the model with only a constant, using a likelihood ratio test (LRT). In addition, we directly compared the strengths of the predictors to each other using Akaike Information Criterion (AIC) values, which trade off goodness of fit with a penalty for model complexity. Smaller AIC values indicate better models. The difference between the model AIC values indicates the relative strength of predictors, which are assessed in the form of probabilities, where larger values are better. Details of this method are provided in the Appendix. In Tables 2 through 8, we also reported the fixed coefficients for the best models to indicate the direction of the effect.

RESULTS

Participant Characteristics

Demographic, pain, sleep and psychologic characteristics of the participants are presented in Table 1. The mean age was 46

Table 1—Participant characteristics

	M (SD)
Demographic variables	
Age	46.0 (10.9)
Body mass index	27.7 (6.1)
Sex (female %)	73.9%
Ethnicity (Caucasian %)	75.6%
Education (degree or above %)	22.7%
Marital status (married or living as married %)	47.9%
Employment (unemployed/sick leave %)	47.9%
Benefit (receiving benefit %)	49.6%
Pain variables	
Pain duration (yr)	10.4 (9.6)*
Pain interference (BPI interference score)	47.0 (13.1)
Sleep variables	
Insomnia duration (yr)	7.9 (8.3)**
Insomnia severity (ISI total score)	20.1 (3.7)
Psychological variables	
Anxiety (HADS-anxiety)	9.8 (3.9)
Depression (HADS-depression)	8.4 (4.5)
Health anxiety (SHAI)	14.6 (7.4)

Means are presented with standard deviations in parantheses, unless otherwise stated. *Median = 8 yr. **Median = 5 yr. BPI, Brief Pain Inventory; HADS, Hospital Anxiety and Depression Scale; ISI, Insomnia Severity Index; SHAI, Short Health Anxiety Inventory.

yr for these participants, who reported an average pain duration of 10.4 yr (median = 8) and insomnia duration of 7.9 yr (median = 5). The levels of pain interference experienced by these patients were high (BPI = 47) and their mean ISI score (20.1) was well above the cutoff for clinical insomnia (15).[29] The mean body mass index of this sample was 27.7. Similar to studies conducted in other pain clinics in the United Kingdom,[39] most of the participants were female (73.9%), Caucasian (75.6%), and without university education (77.3%). Approximately half of them were unemployed (47.9%) and/or receiving benefits (49.6%) at the time of the study. Their mean scores on the HADS (anxiety = 9.8; depression = 8.4) and SHAI (14.6) were high, given the suggested cutoffs for probable cases of anxiety and mood disorders were 8 for the HADS[40] and 15 for the SHAI.[41]

Predicting Nighttime Sleep Using Presleep Variables

Models exploring the effect of previous night's variables (i.e., presleep pain, mood, cognitive arousal, and somatic arousal) on subsequent sleep used the outcome variables of sleep diary SQ, SE based on self-reports, and SE as calculated from actigraphy data. Tables 2 through 4 give the model components, fixed coefficients of the predictor(s), the values and significance of the negative log maximum likelihood, the AIC values, and the relative probability of each model as determined from the AIC values.

Sleep quality

As can be seen from Table 2, presleep pain was not a significant predictor of SQ (P = 0.09). Instead, presleep mood, cognitive arousal, and somatic arousal were independently found to be significant predictors of SQ (all P values < 0.001), whereby

Table 2—A summary of model outcomes in predicting sleep quality

Model terms	Fixed coefficients	LRT		AIC	
		-Log likelihood	Significance	Value	Relative probability
C	4.40	1,870	n/a	3,747	0.00
Presleep pain + C	0.066, 4.05	1,869	P = 0.09	3,746	0.00
Presleep mood + C	0.227, 3.33	1,852	P < 0.001	3,716	0.00
Presleep cognitive arousal + C	-0.306, 5.17	1,819	P < 0.001	3,651	1.00
Presleep somatic arousal + C	-0.281, 4.68	1,848	P < 0.001	3,711	0.00

LRT = Likelihood Ratio Test, which assessed the significance of each predictor of interest (e.g., presleep pain) by comparing the alternative model (e.g., presleep pain + C; -log likelihood = 1,869) with the null model with only a constant term (C; -log likelihood = 1,870). A smaller -log likelihood value indicated a better fitting model. The P value adjacent indicated whether the alternative model was significantly better. AIC = Akiake Information Criterion, unlike LRT, compared the alternative models directly (e.g., presleep pain + C versus presleep mood + C), taking into account each model's complexity. Smaller AIC values indicated better models, but the absolute sizes of the AIC values were not informative. Instead the difference between them indicated the relative strength of predictors, which were then assessed in the form of relative probabilities, where larger values were better. C, constant; n/a, not applicable.

Table 3—A summary of model outcomes in predicting sleep efficiency

Model terms	Fixed coefficients	LRT		AIC	
		-Log Likelihood	Significance	Value	Relative probability
C	-0.005	950	n/a	1,906	0.00
Presleep pain + C	0.009, -0.061	940	P < 0.01	1,895	0.00
Presleep mood + C	0.016, -0.081	949	P = 0.33	1,907	0.00
Presleep cognitive arousal + C	-0.111, 0.254	904	P < 0.001	1,825	1.00
Presleep somatic arousal + C	-0.101, 0.089	925	P < 0.001	1,864	0.00

LRT = Likelihood Ratio Test, which assessed the significance of each predictor of interest (e.g., presleep pain) by comparing the alternative model (e.g., presleep pain + C; -log likelihood = 940) with the null model with only a constant term (C; -log likelihood = 950). A smaller -log likelihood value indicated a better fitting model. The P value adjacent indicated whether the alternative model was significantly better. AIC = Akiake Information Criterion, unlike LRT, compared the alternative models directly (e.g., presleep pain + C versus presleep mood + C), taking into account each model's complexity. Smaller AIC values indicated better models, but the absolute sizes of the AIC values were not informative. Instead the difference between them indicated the relative strength of predictors, which were then assessed in the form of relative probabilities, where larger values were better. C, constant; n/a, not applicable.

worse mood and greater presleep arousal predicted poorer SQ. Among all predictors considered in this set of analyses, presleep cognitive arousal was by far the best predictor of SQ, with a relative probability of 1.00.

Sleep efficiency

As shown in Table 3, results returned from the prediction of SE were largely consistent with those from the prediction of SQ, with the exception that presleep mood was no longer a significant predictor (P = 0.33), whereas presleep pain was a significant predictor (P < 0.01). Again, among all predictors, presleep cognitive arousal was by far the best predictor of SE, with a relative probability of 1.00.

Actigraphy sleep efficiency

As presented in Table 4, results returned from the prediction of actigraphy SE (A-SE) were similar to those from the prediction of SE, despite the intrinsic difference in sleep-estimating technology. The results were similar in the sense that previous night's presleep cognitive and somatic arousal were again significant predictors of A-SE (both P values less than 0.01),

with greater presleep arousal predicting lower A-SE. Previous night's presleep cognitive arousal was found to be the best predictor (relative probability = 0.75), although previous night's presleep somatic arousal achieved a similar AIC value and a reasonably large relative probability in its predictions. Neither pain nor presleep mood was a significant predictor of A-SE.

Predicting Daytime Pain Using Previous Night's Sleep Variables

For the prediction of pain, the outcome variables were "pain upon waking," "pain during the first half of the day," and "pain during the second half of the day". The predictors in this case were the SQ, SE, and A-SE. Again, models were built for constants and individual predictors. Tables 5 through 7 give the model components, fixed coefficients of the predictor(s), the values and significance of the negative log maximum likelihood, the AIC values, and the relative probability of each model as determined from the AIC values.

Pain upon waking

As can be seen from Table 5, SQ (P < 0.001) and SE (P < 0.001) were significant predictors of pain upon waking,

Table 4—A summary of model outcomes in predicting actigraphy sleep efficiency

		Tests for model selection			
		LRT		AIC	
Model terms	Fixed coefficients	-Log Likelihood	Significance	Value	Relative probability
C	0.001	881	n/a	1,767	0.00
Presleep pain + C	-0.011, 0.065	878	P = 0.16	1,768	0.00
Presleep mood + C	0.009, -0.040	881	P = 0.53	1,769	0.00
Presleep cognitive arousal + C	-0.035, 0.072	873	P < 0.01	1,757	0.75
Presleep somatic arousal + C	-0.009, 0.012	875	P < 0.01	1,759	0.24

LRT = Likelihood Ratio Test, which assessed the significance of each predictor of interest (e.g., presleep pain) by comparing the alternative model (e.g., presleep pain + C; -log likelihood = 878) with the null model with only a constant term (C; -log likelihood = 881). A smaller -log likelihood value indicated a better fitting model. The P value adjacent indicated whether the alternative model was significantly better. AIC = Akiake Information Criterion, unlike LRT, compared the alternative models directly (e.g., presleep pain + C versus presleep mood + C), taking into account each model's complexity. Smaller AIC values indicated better models, but the absolute sizes of the AIC values were not informative. Instead the difference between them indicated the relative strength of predictors, which were then assessed in the form of relative probabilities, where larger values were better. C, constant; n/a, not applicable.

Table 5—A summary of model outcomes in predicting pain upon waking

		Tests for model selection			
		LRT		AIC	
Model terms	Fixed coefficients	-Log Likelihood	Significance	Value	Relative probability
C	5.06	1,597	n/a	3,200	0.00
SQ + C	-0.178, 5.87	1,544	P < 0.001	3,103	1.00
SE + C	-2.09, 6.73	1,579	P < 0.001	3,172	0.00
A-SE + C	0.05, 4.57	1,597	P = 0.60	3,202	0.00

LRT = Likelihood Ratio Test, which assessed the significance of each predictor of interest (SQ) by comparing the alternative model (e.g., SQ + C; -log likelihood = 1,544) with the null model with only a constant term (C; -log likelihood = 1,597). A smaller -log likelihood value indicated a better fitting model. The P value adjacent indicated whether the alternative model was significantly better. AIC = Akiake Information Criterion, unlike LRT, compared the alternative models directly (e.g., SQ + C versus SE + C), taking into account each model's complexity. Smaller AIC values indicated better models, but the absolute sizes of the AIC values were not informative. Instead the difference between them indicated the relative strength of predictors, which were then assessed in the form of relative probabilities, where larger values were better. A-SE, actigraphy sleep efficiency; C, constant; n/a, not applicable; SE, sleep efficiency; SQ, sleep quality.

whereby high SQ and SE predicted less pain the following morning. Of all 3 sleep predictors, SQ had the smallest AIC value and a very high relative probability (1.00), and thus was the best predictor of pain upon waking in this set of analyses.

Pain during the first half of the day

As shown in Table 6, only SQ (P < 0.001) was a significant predictor of pain during the first half of the day, with higher SQ predicting less pain during the day. Of all 3 sleep predictors, it had the smallest AIC value and highest relative probability (0.99) and thus was the best predictor of pain during the first half of the day in this set of analyses.

Pain during the second half of the day

As with pain during the first half of the day, SQ was a significant predictor of pain during the second half of the day. However, here A-SE was a significant predictor (P < 0.01) and also the strongest predictor, with a strong relative probability of 0.72. The direction of A-SE and SQ predictions were surprising, with a higher A-SE and a higher SQ predicting more pain during the second half of the day.

Post Hoc Analysis

Although not a stated objective of the current study, we conducted a *post hoc* analysis, given the availability of data, to explore whether individual differences in anxiety, depression, and health anxiety would affect the predictions of pain and sleep. As indicated in previous research,[22] anxiety, depression, and health anxiety were elevated in patients with chronic pain reporting sleep disturbance relative to those who did not report any problem sleeping.

We first determined the significance of each of these individual difference variables (i.e., anxiety, depression, and health anxiety) by running LRTs as previously discussed for each of the outcome variables (i.e., SQ, SE, A-SE, pain on waking, pain in the first half of the day, and pain in the second half of the day). In this set of analyses, which involved comparing a Constant model to a model with a constant and a predictor, only depression was found to be a significant predictor of self-reports of SQ using a strict criterion (P < 0.001). Examining this relationship more closely, we did a further *post hoc* analysis to determine whether depression interacted with presleep cognitive arousal in the prediction. As described in the section on SQ, presleep

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Table 6—A summary of model outcomes in predicting pain during the first half of the day

| Model terms | Fixed coefficients | Tests for model selection | | | |
| | | LRT | | AIC | |
		-Log Likelihood	Significance	Value	Relative probability
C	5.04	1,614	n/a	3,234	0.00
SQ + C	-0.029, 5.19	1,605	P < 0.001	3,222	0.99
SE + C	0.018, 5.02	1,613	P = 0.34	3,236	0.00
A-SE + C	0.019, 3.35	1,613	P = 0.07	3,233	0.00

LRT = Likelihood Ratio Test, which assessed the significance of each predictor of interest (e.g., SQ) by comparing the alternative model (e.g., SQ + C; -log likelihood = 1,605) with the null model with only a constant term (C; -log likelihood = 1,614). A smaller -log likelihood value indicated a better fitting model. The P value adjacent indicated whether the alternative model was significantly better. AIC = Akiake Information Criterion, unlike LRT, compared the alternative models directly (e.g., SQ + C versus SE + C), taking into account each model's complexity. Smaller AIC values indicated better models, but the absolute sizes of the AIC values were not informative. Instead the difference between them indicated the relative strength of predictors, which were then assessed in the form of relative probabilities, where larger values were better. A-SE, actigraphy sleep efficiency; C, constant; n/a, not applicable; SE, sleep efficiency; SQ, sleep quality.

Table 7—A summary of model outcomes in predicting pain during the second half of the day

| Model terms | Fixed coefficients | Tests for model selection | | | |
| | | LRT | | AIC | |
		-Log Likelihood	Significance	Value	Relative probability
C	5.26	1,649	n/a	3,304	0.04
SQ + C	0.073, 4.93	1,645	P < 0.05	3,301	0.22
SE + C	-0.017, 5.27	1,649	P = 0.96	3,306	0.02
A-SE + C	0.014, 3.94	1,643	P < 0.01	3,299	0.72

LRT = Likelihood Ratio Test, which assessed the significance of each predictor of interest (e.g., SQ) by comparing the alternative model (e.g., SQ + C; -log likelihood = 1,645) with the null model with only a constant term (C; -log likelihood = 1,649). A smaller -log likelihood value indicated a better fitting model. The P value adjacent indicated whether the alternative model was significantly better. AIC = Akiake Information Criterion, unlike LRT, compared the alternative models directly (e.g., SQ + C versus SE + C), taking into account each model's complexity. Smaller AIC values indicated better models, but the absolute sizes of the AIC values were not informative. Instead the difference between them indicated the relative strength of predictors, which were then assessed in the form of relative probabilities, where larger values were better. A-SE, actigraphy sleep efficiency; C, constant; n/a, not applicable; SE, sleep efficiency; SQ, sleep quality.

cognitive arousal was found to be the best day-to-day predictor of SQ. In Table 8, we show that the 2 predictors together were better than they were apart. Both presleep cognitive arousal and HADS depression provided separate predictive power, as the model that included both of these effects was relatively much more likely than models with either of these components alone. The model containing both predictors and the model with the interaction had similar relative probabilities, but the interaction model was not a significantly better predictor of SQ as determined by a separate LRT (P = 0.32).

DISCUSSION

Although it is now an established finding that insomnia often co-occurs with chronic pain,[5,25,42,43] research has only just begun to unravel the intricate relationship between pain and sleep. Several daily process studies have been conducted with different samples to examine their sequential association on a day-to-day basis. Equivocal results were obtained and it remains obscure whether daytime pain is the primary precursor of insomnia and whether sleepless nights are necessarily followed by days of more pain. The current study aimed to clarify this

issue, with a design that enhanced the testing power (with more than 800 observations for each analysis) and ecologic validity of the findings (monitoring sleep and pain of a heterogeneous group of patients with chronic pain in their natural sleeping and living environment). The specific goal was to test not only the association of pain with subsequent sleep but also its relative value in predicting sleep in comparison with mood and arousal. Using different parameters and assessment technologies, the relative ability of different dimensions of sleep in predicting next day pain reports was also examined.

Presleep Cognitive Arousal, Not Pain, was a Reliable Predictor of Subsequent Sleep

Despite the potentially sleep-interfering properties of pain,[1,3-8] pain reported during the presleep period was not found to be a reliable predictor of subsequent sleep in this sample. Although presleep pain was a significant predictor of poorer SE, it did not predict SQ and A-SE. The failure to reliably predict sleep with pain is consistent with the mixed/negative findings reported in Raymond et al.[13,14] and Lewandowski et al.,[15] and lends support to the idea that pain may not be the primary factor deter-

Table 8—Prediction of self-reports of sleep quality by presleep cognitive arousal, depression, and their combination

Model terms	Fixed coefficients	LRT		AIC	
		-Log Likelihood	Significance	Value	Relative probability
C	4.42	1,861	n/a	3,729	0.00
PCA + C	-0.308, 5.19	1,810	P < 0.001	3,633	0.01
DEP + C	-0.121, 5.42	1,851	P < 0.001	3,710	0.00
PCA + DEP + C	-0.290, -0.09, 5.90	1,805	P < 0.001	3,623	0.59
PCA + DEP + Interaction + C	-0.372, -0.118, 0.009, 6.14	1,804	P < 0.001	3,624	0.41

LRT = Likelihood Ratio Test, which assessed the significance of each predictor of interest (e.g., PCA) by comparing the alternative model (e.g., PCA + C; -log likelihood = 1,810) with the null model with only a constant term (C; -log likelihood = 1,861). A smaller -log likelihood value indicated a better fitting model. The P value adjacent indicated whether the alternative model was significantly better. AIC = Akiake Information Criterion, unlike LRT, compared the alternative models directly (e.g., PCA + C versus DEP + C), taking into account each model's complexity. Smaller AIC values indicated better models, but the absolute sizes of the AIC values were not informative. Instead the difference between them indicated the relative strength of predictors, which were then assessed in the form of relative probabilities, where larger values were better. C, constant; DEP, depression; n/a, not applicable; PCA, presleep cognitive arousal.

mining subsequent sleep in people with chronic pain. In fact, the importance of pain declined in comparison with presleep cognitive and physiologic arousal, both of which were found to be significant predictors of subsequent SQ, SE, and A-SE. In particular, cognitive arousal stood out from the rest of the competing predictors as the best predictor of all 3 sleep parameters. These findings corroborate the emerging evidence from cross-sectional studies suggesting a role for presleep rumination in pain-related insomnia.[23-25] They also tie in nicely with the hyperarousal concept of insomnia,[44] which suggests – at the cognitive-behavioral level – that arousal may be expressed in the form of excessive negative worry and rumination,[45] negative beliefs and interpretation about sleep and the consequences of not sleeping,[46,47] and explicit efforts to control or promote sleep.[48] Arousal during the presleep period is considered to be a sleep-interfering factor because it may delay sleep onset, heighten sensory and information processing during sleep, and motivate the development of compensatory behaviors that may disrupt sleep over the long term (e.g., extending time in bed, taking naps). The current findings also help explain why treatments seeking to reduce presleep cognitive arousal had success in promoting sleep despite patients' ongoing pain.[49-52]

Better Perceived Sleep Quality was Associated with Less Pain in the Earlier, But Not Later, Part of the Following Day

Regarding the association between sleep and next day's pain reports, a negative relationship was found such that higher perceived SQ was predictive of less pain the following day, and lower SQ was predictive of more pain. This finding is consistent with the idea that sleep is recuperative.[53] Whereas low-quality sleep can heighten pain perception[8] and intensify other relevant symptoms such as fatigue,[54] good-quality sleep may facilitate the resolution of pain complaints.[55] Interestingly however, the pain-relieving effect of sleep appeared to be short-lived in this sample; although higher SQ significantly predicted lower levels of pain upon waking and during the first half of the day, the prediction did not apply to the second half of the day. The loss of effect may be attributed to the longer time gap, where variables introduced as the day unfolded might have weakened/altered the pain-sleep relationship. As has been identified in previous

daily process studies,[11,16] changes in attentional focus and in the use of different pain coping strategies can influence a person's pain perception.

No Clear Link Between Sleep Efficiency Estimates and Subsequent Pain Reports

No specific pattern of association was observed for the prediction of pain by previous night's SE indices. Consistent with the finding for SQ, higher SE was predictive of less pain immediately upon waking. However, when SE was estimated with actigraphy (A-SE), the opposite result was obtained with higher A-SE being predictive of more pain during the second half of the day. Although the observation that higher SE was predictive of less pain upon waking was in line with findings from previous experiments showing that sleep fragmentation increased spontaneous pain reports,[8] the observation that higher A-SE was predictive of more pain during the second half of the day was unexpected and required some further thinking. One possible explanation we can offer is concerned with suboptimal activity regulation, which is commonly observed in the boom-and-bust activity pattern among patients with chronic pain.[56] Overactivity typically occurs on days when people are feeling better or when the pain is less severe. If better sleep indeed led to less pain upon waking and during the first half of the day, it is plausible that some of the patients in this sample, especially those who use pain as a guide of how much they do, might have capitalized on this brief spell of wellness and undertaken more activity than they could physically manage. A likely outcome of overactivity is increased pain, and thus the observation of an increase in pain during the second half of the day. To explore the validity of this speculation, a *post hoc* analysis was carried out to determine whether there was a trend for pain patients to increase their physical activity on days when they awakened feeling refreshed. Specifically, we determined whether nights of better SQ or higher SE/A-SE were followed by higher levels of physical activity (as measured with actigraphy) in the first half of the day (roughly defined as 09:00 to 16:00). SE was the only significant predictor of activity in the first half of the day. We found a positive coefficient for this predictor, meaning

that higher SE predicted a higher level of physical activity. Although intriguing, these *post hoc* findings were far from conclusive and should be interpreted with caution. Our research team is now planning a more detailed analysis of the data to explore the tripartite relationship between sleep, activity, and pain in a separate study. In future investigations, it might be interesting to collect additional data on the content and duration of people's daily activity. This, we believe, would enrich (and contextualize) our understanding of the interrelationship between sleep, activity and pain.

Different Sleep Parameters had Different Associations with Pain

It is noted that, among the 3 sleep parameters, the sequential relationship with pain was more consistently reflected in SQ than in SE and A-SE. The differential relationships suggest that these parameters are probably measuring different aspects of the sleep experience, which may or may not be related to the differences in sleep-estimating technologies. Despite SE being an important index of sleep continuity, the data appear to suggest that people's evaluation of their SQ is more receptive to the influence of pain, and reversely, has a stronger influence on people's subsequent pain reports. In the insomnia literature, it is a robust finding that the way people think they sleep does not always agree with the objective estimates of sleep provided by polysomnography and/or actigraphy.[57-71] A similar subjective-objective discrepancy has also been observed in patients with chronic pain who have problems sleeping.[72] It is of scientific interest and clinical benefit to identify the factors, other than sleep, that shape people's perception of SQ. In a recent review article on this topic,[73] a range of mechanisms were proposed to explain the sleep misperception phenomenon and these included the level of psychologic distress experienced by the sleeper, the presence of different forms of presleep arousal (cognitive, physiologic, and cortical), the amount of brief awakenings, the context in which sleep occurs, and the presence of beliefs and symptoms that influence memory and recall. Potentially, the effectiveness of treatments seeking to improve sleep in patients with chronic pain can be enhanced by also addressing the factors that influence patients' sleep perception.[74] Moreover, research applying power spectral analysis to deconstruct complex waveform data into their constituent frequencies (e.g., alpha, beta, theta, and delta) has revealed that certain spectral measures maybe associated with SQ perceptions. For example, Perlis et al.[65] found that, in comparison with good sleepers, individuals with primary insomnia exhibited more average nonrapid eye movement beta (14-35 Hz) and gamma (35-45 Hz) activity. These authors also found a significant correlation ($r = 0.46$) between the enhanced beta electroencephalographic activity and the discrepancy between subjective and objective estimates of sleep (i.e., sleep misperception). Consistently, Krystal et al.[75] observed that individuals with subjective insomnia (defined as those with relatively long TST and relative underestimation of TST) displayed lower delta and greater alpha, sigma, and beta nonrapid eye movement electroencephalographic activity in comparison with those with objective insomnia. Together, these findings called for more attention to the phenomenon of sleep misperception and the effect of these spectral abnormalities on SQ perception.

Depression Interacted with Precognitive Arousal in Manifesting Sleeplessness

A *post hoc* analysis was conducted to examine the extent to which individual characteristics of the participants influenced the prediction of pain and sleep. Of the 3 variables tested, depression was the only individual difference factor that was significantly associated with the prediction of sleep in this sample. In line with findings from previous cross-sectional studies,[22-24,76] depression was found to be an independent predictor of SQ. Including depression in the model considerably improved the prediction of SQ by presleep cognitive arousal, although the interaction between depression and presleep cognitive arousal did not significantly enhance the prediction. Future research may want to delineate the different pathways through which depression exerts its influence on sleep. One possibility illustrated in the current study is the effect of depression on transitory mood. Negative mood during the presleep period was found to be predictive of poorer SQ, although the same effect was not observed for SE and A-SE.

Methodologic Strengths and Limitations

Several methodologic features of the current study should be discussed. Different from experimental studies, the current study was a daily process study that was concerned with understanding the relationship between different variables across days within an individual, rather than the scientific association between variables across groups of people. In a way, it may be fair to say that the current study asked/answered questions that more closely approximate those of a clinician, to whom it may be more relevant to know whether a person with chronic pain would have a poorer night's sleep on days when the pain is high, than knowing the general effect of nociceptive stimuli on sleep architecture. Although in a daily process study the associations observed did not imply causation between variables, the lagged design in the data analysis did help establish temporal precedence within a naturalistic setting. In contrast with previous experimental studies demonstrating a sleep-interfering effect for painful stimuli, the current study did not see a strong and consistent association between presleep pain and subsequent sleep. This may in part be explained by the design of the study, as several advocates of daily process studies have cautioned that between-persons and within-person association can differ in both magnitude and direction.[11]

Repeated measurements were taken for pain, sleep, mood, and arousal in the current study. Although this method enabled us to capture changes in these processes over time, the act of frequent assessments may have interfered with the processes being observed despite explicit instructions to the participants not to alter their daily routine because of the experimental procedure. This issue of reactivity has been reported in previous studies.[77,78] Although there is evidence to suggest that electronic diary assessment of pain-related variables is nonreactive,[79] a *post hoc* analysis was conducted to determine if there was a trend of change in pain, mood, arousal, and sleep over the course of 1 wk. No significant trend of change was observed for any of these variables (all P values greater than 0.01). Thus, it may be argued that reactivity was not a significant issue in the current study. The use of an electronic diary may have helped minimize reactivity, as it saved and locked the data as soon as they were entered.

The participants had no retrospective access to the data and thus reactivity was less of an issue in the absence of feedback.

Related to the use of the electronic diary, the mean age of the current sample was 46 yr, most of whom did not receive university education. We were initially concerned that participants in the study may find the experience overwhelming or technically challenging. However, our concern was mainly unjustified as – with only a single training session – most patients could master the use of the handheld computer, and only 2 participants withdrew after the initial assessment because they did not think they could handle the technology. Missing data were a concern, with approximately 12.5% of the entries having 1 or more missing observations. We reduced the effect of these missing observations as much as possible by not initially discarding every observation in which there was a missing variable. A fair comparison requires evaluating each predictor against the same set of data, so within a comparison only those observations in which the predictors (e.g., SQ, SE, and A-SE in Table 5) or the predicted variable (e.g., pain upon waking in Table 5) contained missing data were ignored. This resulted in only 4% of entries being ignored on average across the different comparisons of predictors.

The decision to use both sleep diary and actigraphy to measure sleep was to enable us to capture differences between these sleep-estimating technologies. The sleep diary was based on the person's subjective perception of sleep, whereas actigraphy generated estimates of sleep based on the person's level of wrist activity. Each method of estimation has its own advantages and disadvantages. Self-reported sleep estimates are unique in the sense that they represent the participants' subjective experience of sleep. However, these estimates are susceptible to recall and reporting biases, and typically, people have a tendency to round up their estimates to the nearest quarter of an hour, half-hour, or hour, resulting in low precision (and unnecessary loss of information). In the current study, we tried to minimize these problems by asking the participants to report their sleep, on a daily basis, as soon as practical upon waking and by instructing the participants to estimate different sleep parameters to the nearest minute. Frequency analyses of their sleep estimates indicated that we achieved the intended purpose of improving precision in these estimates, but it would be interesting for future research to investigate what data collection/analysis method may be used to enhance validity and reliability of these self-reported sleep estimates. Some researchers have examined the possibility of using a range estimate (e.g., a fuzzy response format[80]) to increase reliability of responses to a sleep questionnaire, but the applicability of this method to sleep diary data is yet to be determined. Actigraphy is an indirect estimate of sleep based on physical activity data. Although it does not provide information about sleep architecture and/or spectral abnormality of the electroencephalogram activities as does polysomnography, it is a non-interfering, cost-effective method to collect data on people's sleep-wake schedule in their natural living and sleeping environment. Relative to polysomnography, actigraphy has a tendency to underscore wake and overscore sleep. This is one of the reasons why we chose the Actiwatch-Insomnia model over other models of actigraphy, as an attempt to improve measurement precision. The Actiwatch-Insomnia model has an additional pressure sensor attached to the watch. The sensor is to be held by the wearer between the thumb and the finger until muscle tone relaxes at sleep onset. Pilsworth et al.[33] reported a significant improvement in the accuracy of estimating wakefulness with the addition of this behavioral device. Moreover, to facilitate the scoring and detection of wakefulness during the night, the participants were also asked to hold the pressure sensor with their fingers every time they awoke from sleep. Although these measures should improve the precision of the actigraphy data collected in the current study, caution should still be applied when interpreting the actigraphic estimates of sleep.

Finally, in terms of the generalizability of the findings, it should be noted that most of the participants were middle-aged, female Caucasians. Accordingly, findings of the current study may be more applicable to individuals of these demographic characteristics than others. It should also be emphasized that, in an attempt to maximize clinical relevance of the study, we decided to focus our investigation on a heterogeneous sample of patients with chronic pain. There is a possibility that the daily pain-sleep-pain relationship may systematically vary between individuals and between patients with pain who are given different diagnoses (e.g., fibromyalgia, rheumatoid arthritis, osteoarthritis, low back pain), although contamination across diagnoses is not uncommon in clinical reality. Future research that compares the pain-sleep-pain relationship between different clearly defined ideologic pain subgroups is required to answer this question.

CONCLUSION

Within the confines of the limitations discussed previously, the results of the current study suggest that, in this heterogeneous sample of chronic pain patients, although SQ is a fairly consistent predictor of pain the next day, presleep pain is not a particularly reliable predictor of subsequent sleep. Instead, sleep quality and efficiency are best predicted by the presence of presleep cognitive arousal. These findings appear to contradict the often-assumed reciprocal relationship between pain and sleep and call for a diversification in our conceptualization of the daily interplay between these 2 processes.

DISCLOSURE STATEMENT

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APPENDIX

Multilevel models provide exceptional flexibility in how to model the relationship between the predictor and predicted variable. As in standard linear regression analyses, the predictor can be either a fixed or random effect. In addition to standard linear regression analysis, the predictor can be fixed or random at either or both the "day" and "participant" levels. A final degree of flexibility in this modelling framework is the capacity to have a covariance term to allow for a nonadditive relationship between the variances. Of course, different model structures can lead to different results. To allow our results to reflect the patterns in the data, rather than a particular choice of model structure, we compared the predictors across all possible model structures. There were altogether nine possible model structures for each predictor. We used Iterated Generalized Least Square (IGLS) to remove any bias introduced by autocorrelation in the predicted variable. This iterative method was able to find the maximum likelihood solution for 98% of the models, and these models were used in the remaining analysis. Instead of showing the maximum likelihood values, we presented the -log maximum likelihood values for better readability. The 2 SE variables were negatively skewed, so we monotonically transformed them to normally distributed variables, by replacing each score with its expected rank under a normal distribution. A total of 107 observations of the 830 total had 1 or more missing fields. To enable fair comparisons between models while using as much of the data as possible, we removed only those observations that had missing data for the predicted variable or any of the predicting variables associated with that predictor. On average, 36 observations of the 107 possible missing observations were excluded from each analysis.

The significance of individual predictors was assessed by between-model comparisons using maximum likelihood fits. As the constant model, M_C, was nested within the constant + predictor model, M_{C+P}, we could assess whether the addition of the predictor made the fit significantly better via a LRT, LRT = $-2\log p(M_C) + 2\log p(M_{C+P})$, where $p(M_C)$ is the maximum likelihood of the constant model and $p(M_{C+P})$ is the maximum likelihood of the constant + predictor model. The probability of finding this LRT value was then determined by comparing it to a χ^2 distribution with degrees of freedom equal to the difference in the number of parameters between the 2 models. The number of parameters here is not the number of predictors, but is instead the number of terms that were fit for each model. For example, the constant model, M_C, had a total of 3 parameters; 1 parameter for the mean, 1 for the level 1 variance, and 1 for the level 2 variance.

Assessing the relative strength of the predictors requires a comparison of non-nested models. A standard method for doing so is the AIC,[81] which rewards goodness of fit and penalizes a model for flexibility. The AIC value of a model is calculated from the maximum likelihood fit and the number of parameters, $AIC_i = -2\log p(M_i) + 2V_i$ where $p(M_i)$ is the likelihood of model i and V_i is the number of parameters in the model. AIC gives us a scale for comparing models: lower AIC values indicate a better model.

To assist in the interpretation of the raw AIC values, we transformed them to relative model probabilities[82-84] where a relative probability is equal to the ratio of the exponentiated AIC value of a particular predictor against the sum of the exponentiated AIC values of all of the predictors

$$\text{Relative Probability} = \frac{\exp(-\frac{1}{2}AIC_i)}{\sum_{k=1}^{K} \exp(-\frac{1}{2}AIC_k)}$$

These relative probabilities tell us how likely a model is given the data, in comparison with the other models that we are considering.

An alternative to taking the best model is to find structure-agnostic probabilities by averaging the probabilities for each predictor over the different model structures and renormalizing. The orderings of relative model probability, as we found, were the same between the 2 approaches.