Transient Effects of Sleep on Next-Day Pain and Fatigue in Older Adults With Symptomatic Osteoarthritis

Daniel Whibley,*,† Tiffany J. Braley,‡ Anna L. Kratz,* and Susan L. Murphy*,§

*Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, Michigan, †Epidemiology Group, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Scotland, UK, ‡Department of Neurology, University of Michigan, Ann Arbor, Michigan, §VA Ann Arbor Health Care System GRECC, Ann Arbor, Michigan

Abstract: Poor sleep quality has been associated with greater pain and fatigue in people living with osteoarthritis (OA). The objective of this micro-longitudinal study was to determine whether sleep impacts the diurnal pattern of next-day OA-related pain and fatigue. Community-dwelling older adults (≥65 years) with hip and/or knee OA provided data over 5 days using daily diaries and wrist-worn actigraphs. Pain and fatigue intensity were measured on awakening, at 11 AM, 3 PM, 7 PM, and bedtime. Subjective previous night sleep quality was measured on awakening. Multilevel linear regression models examined interactions between sleep variables and time of next-day symptom reports. One hundred sixty participants provided 785 days of data (median age = 71 years; 62% female). Analysis of time interaction effects identified an association between poor sleep quality and more morning pain and fatigue. Although the effect on awakening was more pronounced for fatigue, differences in both symptoms attributable to sleep quality attenuated as the day progressed. Investigation of actigraphy-based sleep parameters revealed no significant interactions with time of symptom measurement. These findings observed in a sample of older adults with mild-to-moderate OA symptoms warrant further investigation in a sample with more severe symptoms and more pronounced sleep dysfunction and/or sleep disorders.

Perspective: This article investigates the impact of sleep on next-day pain and fatigue of older adults with OA. On awakening from a night of poor quality sleep, pain and fatigue intensity were heightened. However, the effect was not sustained throughout the day, suggesting the morning may be an optimal time for symptom interventions.

Key words: Osteoarthritis, sleep, pain, fatigue, actigraphy.

Poor sleep quality, pain and fatigue are commonly experienced by older adults with osteoarthritis (OA).[1,40,48,65,66] Cross-sectional studies have demonstrated significant associations between poor sleep quality and higher OA-related pain intensity and/or fatigue[24,46] and sleep improvements after cognitive-behavioral therapy for insomnia have been associated with downstream and sustained reductions in pain and fatigue.[61,62] In older age adults with hip or knee OA, weekly fluctuations in sleep interference and OA-related pain have been shown to track with each other.[26] These cross-sectional and prospective studies have provided some clues about the association between sleep, pain, and fatigue in OA; however, there is a lack of research regarding the influence of nocturnal sleep experiences on the course of pain and fatigue throughout the following day in this population.

Studies using ecological momentary assessment and actigraphy methods that intensively collect data throughout the day have provided compelling evidence

for the importance of sleep on next-day pain experiences in people living with chronic pain conditions. A bidirectional relationship between sleep and pain has been identified in women with fibromyalgia, with an indication for a stronger prospective relationship from poor sleep to worse pain rather than vice versa.[3] Building on this research, in a mixed-pain sample of working-age adults, better self-reported sleep quality was associated with less pain on awakening but more pain later in the day, and actigraphy-assessed poor sleep efficiency was, surprisingly, related to less next-day pain.[56] In contrast, in a sample of people with low back pain, better self-reported sleep quality was associated with lower pain intensity on awakening and less average next day pain,[6] but actigraphy-assessed poor sleep efficiency was, as expected, related to worse next-day pain. Data collected from a gender-balanced sample of middle-age adults with chronic low back pain found a night of poor sleep to be followed by a day of higher, relatively unwavering pain intensity.[19] Conversely, a night of good sleep was followed by lower pain intensity on awakening, although the beneficial effect when compared with a night of poor sleep dissipated over the course of the day. Taken together, these studies suggest that sleep is related to next-day pain, but there is equivocal evidence as to the direction and duration of the effects and to the association between actigraphy-assessed sleep parameters and pain.

Less attention has been focused on the relationship between sleep and next-day fatigue experiences in people with OA. Fatigue is a subjective experience, described as a feeling of overwhelming tiredness, exhaustion, and lack of energy.[53] OA-related fatigue is associated with older age, pain intensity, physical activity, physical function, and mental health.[55] Previous examinations of the daily fatigue patterns of those living with lower extremity OA have demonstrated symptom increases across the course of the day.[39]

The relationship between sleep, pain, and fatigue may differ depending on pain etiology[56] and to date we are unaware of research that has examined the impact of sleep on next-day pain in community-dwelling older adults with hip and/or knee OA. Furthermore, there is a paucity of research using ecological momentary assessment designs investigating the sleep to next-day fatigue relationship, which seems a crucial area of inquiry given the common and dynamic overlap in pain and fatigue in OA.[50]

The aim of this study was to investigate the association of self-reported sleep quality and actigraphy-based sleep parameters (sleep duration, sleep efficiency, onset latency, and time awake after initial sleep onset) with pain and fatigue throughout the following day using 5 consecutive days of data from a community-dwelling cohort of older adults with hip and/or knee OA. Specifically, the aim was to investigate the association of sleep with diurnal changes in pain and fatigue to answer the question of whether there are specific times of the day when symptoms are most susceptible to the effects of poor sleep. We hypothesized that, within a sample of community-dwelling older adults with hip or knee OA, poor self-reported sleep quality would be associated with greater next-day pain and fatigue intensity and that this difference would be sustained across the day. We also hypothesized that poorer objective measures of sleep, collected using actigraphy, would be associated with worse pain and fatigue throughout the following day.

Methods

This secondary analysis used data that were collected for a study designed to examine the relationship between momentary changes in fatigue and subsequent physical activity in persons with symptomatic OA.[38]

Participants

Adults aged ≥65 years were recruited from the community via online, newspaper, and radio advertisements, and the placement of flyers in medical centers, senior housing, and community centers in Ann Arbor, Michigan, and the surrounding areas. This study was approved by Human Subjects Review Boards at the University of Michigan and Ann Arbor VA Health Care System. For the primary study, people with clinically important levels of fatigue were recruited because the aim was to better understand fluctuations in this symptom in those most affected. In brief, participants were eligible if they had 1) knee or hip pain of at least mild to moderate severity on the Western Ontario and McMaster Universities Osteoarthritis Index pain scale[20]; 2) OA in the corresponding joint according to the American College of Rheumatology clinical criteria[7,8]; 3) evidence of significant fatigue (defined by endorsing a response of "a moderate amount of the time" to any 1 of 2 questions from the Center for Epidemiological Studies Depression Scale: during the past week, "I felt that everything I did was an effort" or "I could not get going"; 4) adequate cognitive function to participate in the study (defined as scoring >5 on a 6-item screening tool[14]); 5) able to enter symptom ratings on a wrist-worn accelerometer; and 6) a normal sleep schedule, defined as usual awakening before 11 AM and bedtime before 2 AM. Exclusion criteria included 1) an inability to walk, with or without an assistive device; 2) bed rest for >2 days in the past month; 3) change in medication regimen in the past 2 weeks; 4) reported diagnosis of sleep apnea, multiple sclerosis, lupus, fibromyalgia, chronic fatigue syndrome, rheumatoid arthritis, cancer, lung disease, or heart failure; or 5) diagnosis of any other condition known to cause fatigue.

For the current analysis, inclusion was restricted to participants who provided ≥3 nights of sleep data, in accordance with recommendations from the American Academy of Sleep Medicine.[31] No participants were excluded based on this criterion.

Procedures

Volunteers who were screened as eligible via telephone were invited to a laboratory visit where a study team member conducted informed consent procedures. Informed consent was provided by all study participants. After study enrollment, participants were examined by

trained research staff for further screening (including confirmation of OA as defined by American College of Rheumatology criteria) and completed a battery of self-report measures. Participants deemed eligible after in-person screening returned for a second lab visit where they were trained in actigraph use (Actiwatch-Score, Philips Respironics, Mini Mitter, Murrysville, Pennsylvania). Participants were instructed to continuously wear the actigraph on their nondominant wrist for 5 days (Monday through Friday), except when bathing, showering, or swimming. Participants were instructed to enter self-report ratings of symptoms into the actigraph: pain and fatigue 5 times a day (on awakening, at 11 AM, 3 PM, 7 PM, and bedtime) and sleep quality once a day (on awakening). Sleep ratings were completed each day on a paper survey diary. On completion of data collection, participants were instructed to return the actigraphs to the laboratory using prepaid postage. Once returned, all data were downloaded and processed.

Measures

Demographic and Clinical Variables

Demographic and clinical information collected at the laboratory visit included age, sex, marital status, race, and body mass index. Pain intensity was measured using the Western Ontario and McMaster Universities Arthritis Index 5-item pain subscale,[10] with higher scores indicating more severe pain. Fatigue was measured using the Brief Fatigue Inventory, a 9-item instrument that evaluates fatigue severity and interference over the past week.[36] Responses on an 11-point scale are averaged to generate a total score, with ≥7 denoting severe fatigue. Symptoms of depression were measured using the Center for Epidemiological Studies-Depression Scale,[9] where a score of ≥16 denotes clinically significant symptoms.[30] Symptoms of anxiety were measured using the State Anxiety Inventory, with higher values indicating greater current anxiety.[27]

Ecological Momentary Assessments

Sleep was assessed each morning with 2 questions: "Please enter the number that best describes how well you slept last night" (5-point scale: 0 [very bad], 1 [bad], 2 [fair], 3 [good], 4 [very good]); and "Please enter the number that best describes how rested you felt this morning when you woke up" (5-point scale: 0 [not at all], 1 [a little bit], 2 [somewhat], 3 [quite a bit], 4 [very]). A total sleep quality score was calculated by averaging each participant's responses to these 2 items (good internal consistency in the current sample: Cronbach's alpha = .81).

Pain Intensity was assessed 5 times a day with an 11-point Numeric Rating Scale that asked participants to respond to the statement: "Please enter the number that best describes how bad your pain is right now" (from 0 [no pain at all] to 10 [pain as bad as I can imagine]).

Fatigue intensity, defined for respondents as tiredness or weariness, was also assessed 5 times a day with an 11-point Numeric Rating Scale, which asked participants to respond to the statement: "Please enter the number that best describes how fatigued or tired you are right now" (from 0 [not fatigued at all] to 10 [fatigued as badly as I can imagine]).

To guide the interpretation of the meaningfulness of findings, 1 point on the pain and fatigue intensity scales was taken as representing a minimal clinically important difference,[49,52] in line with a study of determination of minimal clinically important change specific to people with hip or knee OA.[47]

Actigraphy Sleep Measures

The Actiwatch-Score (Philips Respironics, Mini Mitter) is an accelerometer commonly used in sleep research and has been validated in a number of clinical and non-clinical populations.[15,32−35,44,63] Sleep variables are computed with onboard software, using measurement of physical activity, assessed in 15-second epochs. Four actigraph-derived sleep variables were examined in this study. Sleep duration (total sleep time) is the time, in minutes, the individual was asleep. Sleep onset latency is the time in minutes that it takes for an individual to go from a wake state to sleeping. Sleep efficiency is the percentage of time spent asleep relative to total time spent in bed. Wake after sleep onset is the time spent awake in bed after initially falling asleep. Processing and scoring of actigraphy data was conducted using a predefined protocol, informed by published recommendations.[12] In brief, sleep intervals were established by corroborating self-report of lights off and wake-up times with actigraphy activity counts. The consistency of the data was assessed using published guidelines.[13] In cases where consistency was deemed good (self-report and actigraphy data matched within 11−30 minutes) or excellent (data matched within 10 minutes), software-generated sleep intervals were not manipulated. In cases of fair data consistency (matched within 31−60 minutes) or poor consistency (≥61 minutes difference), activity data were adjusted according to a standardized procedure[28]; activity that exceeded 50% of the average daytime activity level for an individual was marked as awake, and activity that was 50% below the person's average nocturnal level was marked as sleep. Daytime napping was reported, documented, and cross-referenced in a separate actigraphy analysis.

Data Analyses

All analyses were conducted using Stata (version 15.1, StataCorp LLC, College Station, Texas). Descriptive statistics, informed by inspection of histograms, characterized the study sample and summarized missing data (means and standard deviations calculated for variables that displayed normal distributions; medians and inter-quartile ranges for non-normal distributions; proportions for categorical variables). Mean pain and fatigue scores at each time point over 5 days of data collection were plotted with 95% confidence intervals for the means, and aggregate means for pain and fatigue scores were calculated (across all available days, for the 5 within-day time points: on awakening, and at 11 AM,

3 PM, 7 PM, and bedtime). To investigate the possibility that sleep parameters affected pain and fatigue scores differently at different times of the following day, multilevel linear models were constructed that included an interaction term between the sleep variable and the time of symptom data collection (treated as categorical and nested within participants). Participant and day of data collection were modelled as random effects and models were adjusted for key covariates, age, sex, body mass index, and baseline symptoms of depression and anxiety.[46] Significant interactions were examined and illustrated using Stata's marginsplots command.

Results

One hundred sixty participants were eligible for the current study and the sample was representative of study that provided the data. The median age was 71 years (interquartile range = 67−75.5 years, range = 65−90 years), 61.9% were female, 58% were married, and most (82.5%) were white. Body mass index was just within the obese range. Depression and anxiety scores were not indicative of clinically significant symptoms. Pain and fatigue were, on average, of mild to moderate severity. Over the 5-day course of data collection, average self-reported sleep quality was fair and objectively measured sleep variables were suggestive of good sleep, comparable with healthy community-dwelling older adults[51] and a U.S. national probability sample.[29] The median total sleep time was 7.35 hours, median sleep efficiency of 83.8%, median sleep latency of 16 minutes, and median wake time after sleep onset of 42 minutes. Descriptive statistics are summarized in Table 1 and bivariate correlations of study variables are provided in Supplementary Table 1. Minimal rates of missing data were observed: 158 of 160 participants provided all 5 nights of sleep data (self-report or actigraphy) and there was a small amount of within-day missing data for pain (5% of all possible data collection points) and fatigue (4% of all possible data collection points).

Trajectories of Pain and Fatigue Over 5 Days

On average, pain and fatigue intensity demonstrated diurnal patterns (Fig 1), with pain exhibiting less within-day variation. Across an average day, mean pain intensity ranged from 3.04 to 3.39 and the mean fatigue intensity ranged from 3.27 to 4.97 (Table 2). However, plots of each individual's daily symptom trajectories revealed much variation (Supplementary Fig 1), thereby supporting a case for the analysis of a possible interaction between sleep variables and time of symptom measurement.

Impact of Sleep Quality on the Diurnal Pattern of Pain and Fatigue Intensity

Results from multilevel linear regression models that included interaction terms between sleep quality and time of day of data collection are presented in Table 3; graphs illustrate the relationships in Fig 2.

Table 1. **Descriptive Statistics**

CHARACTERISTICS	TOTAL SAMPLE (N = 160*)
Baseline variables	
Age, years	71 (67−75.5)
Female sex	99 (61.9)
Married	93 (58)
Race	
White	132 (82.5)
Black/African American	17 (10.6)
Asian	5 (3)
More than 1 race	2 (1.3)
American Indian/Alaskan native	1 (.6)
Unknown/chose not to report	3 (1.9)
Body mass index	29.6 (26.2−33.4)
Knee OA	143 (89)
Hip OA	46 (29)
Hip OA and knee OA	31 (19)
WOMAC pain scale score at baseline (possible range = 0−20)	8.6 ± 3.1
BFI total score (possible range = 0−10)	4.5 ± 2.0
Symptoms of depression (CES-D; possible range = 0−60)	9 (5−15)
Symptoms of anxiety (STPI-ANX; possible range = 10−40)	12 (10−16)
Sleep variables (average of 5 days of data collection)	
Quality (composite variable; possible range = 0−4)	2.3 ± .6
Duration, minutes	441.8 (395.7−487.4)
Efficiency, %	83.8 (77.7−88.3)
Onset latency, minutes	16.1 (8.7−29.3)
Wake after sleep onset, minutes	42.3 (29.6−55.6)

Abbreviations: BFI, Brief Fatigue Inventory; CES-D, Center for Epidemiological Studies Depression Scale; STPI-ANX, State-Trait Personality Inventory - anxiety subscale.
Values are median (IQR), number (%), or mean ± standard deviation.
*All statistics for N = 160, except body mass index, marital status, and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale scores (all based on n = 159 owing to missing data).

Pain Intensity

Ninety-five percent of the sample (n = 152) contributed 745 days of data, resulting in a total of 3,570 unique observations for analysis. A test of the overall interaction of sleep quality and time of next-day pain report was statistically significant (χ^2 = 27.2, df = 4, P < .001). After computing simple slopes, inspection of margins plots identified an association between better sleep quality and lower pain intensity on awakening (Fig 2). The magnitude of the difference in pain intensity scores after taking sleep quality thresholds into consideration was not statistically significant at all other time points (Fig 2, Table 3).

Fatigue

Ninety-five percent of the sample (n = 152) contributed 745 days of data, resulting in a total of 3,572 unique observations for analysis. A test of the overall interaction of sleep quality and time of next-day fatigue report was statistically significant (χ^2 = 153.9, df = 4, P < .001). After computing simple slopes, inspection of margins plots identified an association between better sleep
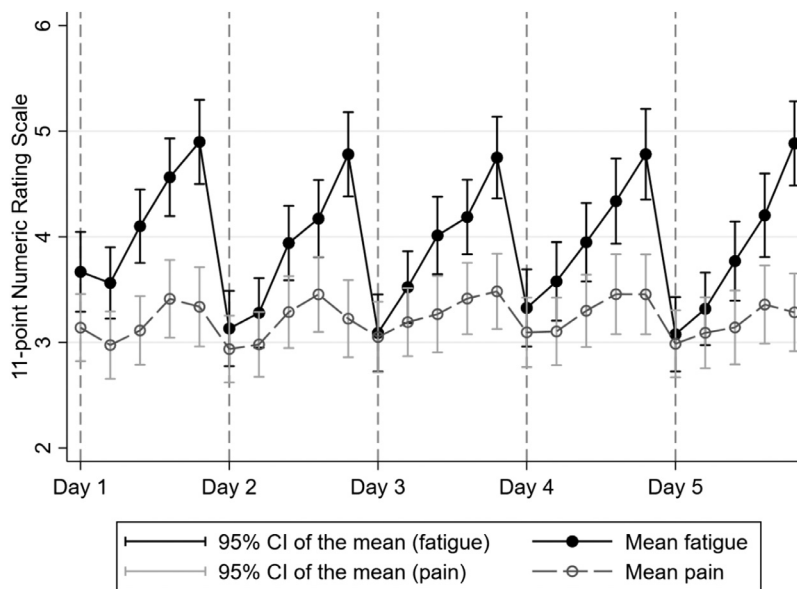
Figure 1. Mean pain and fatigue over 5 days.

quality and lower fatigue severity on awakening (Fig 2). The difference when compared with poorer sleep quality attenuated at each subsequent time point across the course of the day (Table 3, Fig 2).

Actigraphy-Based Sleep Parameters

Of the 4 objectively measured sleep variables that were assessed, an overall test of interaction was only statistically significant for the relationship between sleep duration and time of next-day pain report ($\chi^2 = 16.5$, df = 4, $P = .003$), and time spent awake after initial sleep onset and time of next-day pain report ($\chi^2 = 111.3$, df = 4, $P = .02$). However, regardless of actigraphy-based sleep parameters and pain or fatigue outcomes, computation and plotting of simple slopes identified no meaningful differences across the course of a day (full results provided in Supplementary Table 2).

Discussion

The aim of this study was to investigate whether measures of sleep were associated with pain and fatigue

Table 2. Mean Pain and Fatigue at Different Times of the Day

	PAIN (NRS, RANGE 0−10)			FATIGUE (NRS, RANGE 0−10)		
TIME POINT	N	MEAN	SD	N	MEAN	SD
Awakening	785	3.05	2.07	785	3.27	2.33
11 AM	756	3.04	2.02	756	3.39	2.18
3 PM	777	3.24	2.18	777	3.90	2.28
7 PM	754	3.38	2.24	755	4.21	2.34
Bedtime	746	3.39	2.29	747	4.97	2.46

Abbreviations: NRS, Numeric Rating Scale; SD, standard deviation.

the following day in a community-dwelling cohort of older adults with hip and/or knee OA and specifically to investigate whether some times of day would be more affected than others. Pain and fatigue intensity demonstrated diurnal patterns, and time interaction effects indicated that a night of good sleep was followed by a morning of significantly lower symptom scores, yet similar symptom scores to a night of poor sleep later in the day. Notably, sleep quality had a more pronounced effect on fatigue than on pain intensity. When measured using actigraphy, no sleep variables impacted differentially on next-day pain and fatigue trajectories.

Our finding that pain is heightened after a night of poor sleep but that the effect dissipates across the course of a day is in agreement with previous research in different chronic pain populations.[19,56] However, we found that, although pain intensity varied across a given day, on average, the variation did not meet criteria for clinically important differences.[16,47,49,52] We used 1 point on the numeric rating scales to define minimal clinically important differences, based on findings from previous research, including a study of adults with hip or knee OA.[47,49,52] We acknowledge that there is variation regarding the threshold to define clinically meaningful change using these scales[43] and that the majority of research to date has focused on pain intensity and not fatigue. However, our interpretation using this guidance is also informed by the fact that within-day micro-processes may have a greater cumulative effect over time, even when observed associations are very small.[2] Revisiting previous literature, the magnitude of the effect of sleep on pain has, arguably, been consistently small,[3,6,19,56] echoing results from trials of cognitive-behavioral therapy for insomnia interventions for patients with non-cancer chronic pain which have demonstrated improvements in sleep but modest effects on pain intensity.[57] We have extended the

Table 3. **Multilevel Linear Regressions for Interactions Between Sleep Quality and Time of Day of Pain and Fatigue Intensity**

|	DEPENDENT VARIABLE: PAIN INTENSITY				DEPENDENT VARIABLE: FATIGUE INTENSITY			
	COEFFICIENT (95% CI)	SE	z	P VALUE	COEFFICIENT (95% CI)	SE	z	P VALUE
Fixed effects								
Sleep quality	−.48 (−.62 to −.34)	.07	−6.73	<.001	−1.20 (−1.35 to −1.05)	.08	−15.4	<.001
Time of day								
Awakening	Reference							
11 AM	−.77 (−1.16 to −.38)	.20	−3.83	<.001	−1.15 (−1.60 to −.70)	.23	−5.05	<.001
3 PM	−.54 (−.92 to −.15)	.20	−2.70	.007	−1.22 (−1.67 to −.78)	.23	−5.44	<.001
7 PM	−.55 (−.94 to −.15)	.20	−2.72	.007	−1.26 (−1.70 to −.81)	.23	−5.54	<.001
Bedtime	−.19 (−.58 to −.20)	.20	−.95	.34	−.57 (−1.01 to −.12)	.23	−2.49	.01
Interaction: Time of day × Sleep quality								
Awakening	Reference							
11 AM	.32 (.16 to .48)	.08	3.96	<.001	.54 (.36 to .72)	.09	5.82	<.001
3 PM	.31 (.16 to .47)	.08	3.88	<.001	.79 (.61 to .97)	.09	8.56	<.001
7 PM	.38 (.22 to .54)	.08	4.64	<.001	.95 (.77 to 1.13)	.09	10.26	<.001
Bedtime	.22 (.06 to .37)	.08	2.64	.008	.98 (.80 to 1.16)	.09	1.62	<.001
Covariates								
Age	−.003 (−.05 to .04)	.02	−.14	.89	−.008 (−.05 to .03)	.02	−.36	.72
Sex (ref: male)	−.09 (−.60 to .42)	.26	−.36	.72	.57 (.07 to 1.08)	.26	2.23	.03
Body mass index	.04 (−.005 to .08)	.02	1.75	.08	.02 (−.03 to .06)	.02	.75	.45
CES−D	.04 (−.0006 to .08)	.02	1.93	.054	.06 (.02 to .10)	.02	3.18	.001
STPI−ANX	.07 (.0007 to .15)	.04	1.98	.048	.02 (−.06 to .09)	.04	.44	.66
	ESTIMATE (95% CI)	SE			ESTIMATE (95% CI)	SE		
Random effects								
Participant	2.23 (1.75 to 2.83)	.27			2.17 (1.70 to 2.76)	.27		
Day	.30 (.24 to .39)	.04			.28 (.21 to .38)	.04		
Residual	1.54 (1.46 to 1.62)	.04			1.98 (1.88 to 2.08)	.05		

Abbreviations: CI, confidence interval; SE, standard error; CES-D, Center for Epidemiological Studies Depression scale; STPI-ANX, State-Trait Personality Inventory - anxiety subscale.

naturalistic research by identifying a larger, and arguably more clinically meaningful effect of sleep quality on next-day fatigue intensity compared with its effect on pain intensity.

One possible mechanism whereby poorer sleep quality could have a marked effect on pain and fatigue on awakening rather than later in the day may be through lower mood, greater irritability, or decreased motivation to initiate effortful cognitive or behavioral coping strategies on awakening after a night of poor sleep.

This interpretation is supported by findings from Affleck et al[3] that described attenuation of the sleep-to-pain relationship in women with fibromyalgia after adjusting for attention to pain, and a study by Harrison et al[23] that provided some support for the hypothesis that depressive symptoms and increased attention to pain mediate the sleep disturbance−pain intensity relationship. We speculate that our observation of a decrease in the difference in symptom reports with temporal distance from awakening may be attributable to the
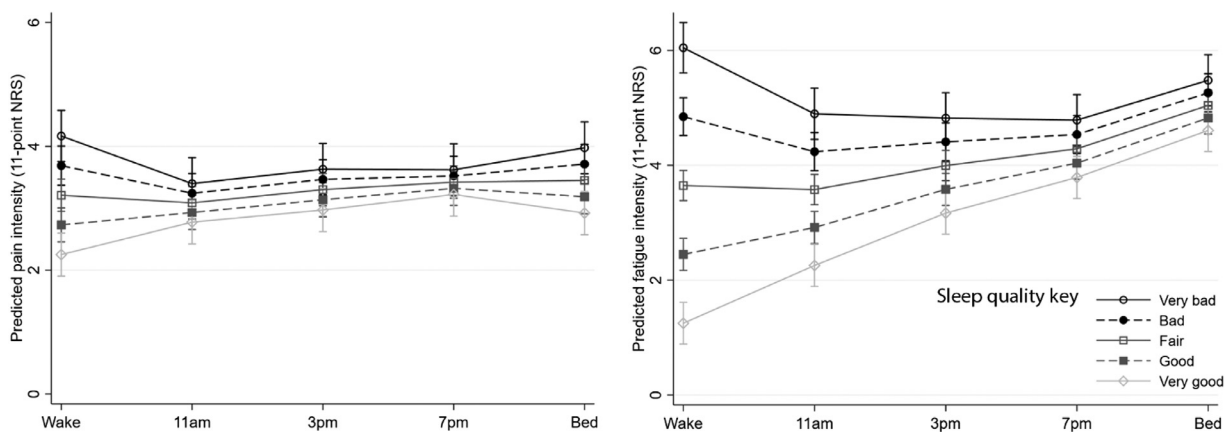
Figure 2. Interaction between time of day and effect of sleep quality on pain and fatigue intensity.

possibility that heightened somatic vigilance on awakening attenuates as the day progress. Alternatively, it may be that after a good night's sleep hypervigilance is initially muted, but increases throughout the day, possibly with increasing levels of mental fatigue. These interpretations are offered cautiously; indeed, it is possible that perceptions of sleep quality simply influenced contemporaneous pain and fatigue intensity reports on awakening. Further focused research that collects data on attention to pain throughout the day to examine a potentially mediating effect is required, alongside measures of both physical and mental fatigue.

These findings should be interpreted within the context of the limitations of our study. As a secondary analysis of data collected for a different purpose, the sample had on average mild to moderate OA symptoms, relatively good subjective sleep quality, and adequate objective markers of sleep. Although inspection of individual trajectories revealed substantial within- and between-person variability for the variables of interest, it is possible that our findings may be amplified or different in a sample that includes more individuals with on average severe pain and fatigue and more impaired sleep. Also, our measure of sleep quality was an average of responses to 2 questions. The possibility of shared method variance of the constituent items and imprecise measurement of sleep quality cannot be ruled out. Although the validity and reliability of this measure is yet to be established, a test of the internal consistency in our sample supported its use. Upon re-running our models for the 2 sleep questions in separate analyses, the interpretations did not change, although it seemed that self-reported sleep restfulness contributed more to pain and fatigue diurnal patterns than perception of sleep quality.

Our data collection period of 5 days could be argued as short and particularly susceptible to reactivity given the regularity of symptom reporting. However, the diurnal periodicity of pain and fatigue intensity observed was consistent with existing evidence from the wider OA literature, with pain increasing throughout the day then decreasing in the evening (possibly owing to decreased activity),[4,11] and fatigue increasing until bedtime.[39] This finding stands in contrast with the diurnal pattern of fatigue observed in non-clinical samples, where fatigue has been observed to decrease throughout the morning, reach its lowest point at the middle of the day, and then steadily increase until bedtime.[25] The diurnal patterns observed in our study provided support for the decision to treat each individual day as a separate unit for analysis, thereby maximizing use of the available data. Examination of cross-day lagged effects in studies of longer duration would shed light on the carry-over effects of poor nights of sleep on symptoms of OA. Although not the aim of our study, we also conducted an exploratory, post hoc analysis of whether previous day's pain and fatigue impacted on subsequent sleep experiences. Neither average day pain or fatigue, or pain and fatigue at bed time predicted that night's sleep quality or actigraphy assessed sleep characteristics (all $P > .16$).

A further limitation of our study is a lack of comprehensive screening for a range of sleep disorders. Although people with a known diagnosis of obstructive sleep apnea were excluded, it is possible that some participants may have had undiagnosed obstructive sleep apnea or a diagnosis of other primary sleep disorders, such as restless leg syndrome, REM behavior disorder, or circadian phase disorders. These disorders often impact the symptoms of musculoskeletal disease and quality of life[37] and are not uncommon in this patient group.[1] By not excluding participants with these disorders, our sample could be argued to be generalizable to a heterogeneous, older population with OA. However, the relationship between sleep experiences of people with specific sleep disorders comorbid with OA and the impact of their nightly sleep experiences on next-day symptoms warrants more specialized study.

Residual confounding is also an issue. We did not have data for a number of potentially important psychological variables that have been shown to be important correlates of the sleep-pain relationship, such as negative and positive affect,[18,41,60] pain helplessness,[22] and attention to pain.[23] However, evidence suggests that these variables may lie on the causal path between sleep and pain, therefore making these statistical adjustments would have removed their contribution to the total effect of sleep on next-day symptom reports.

Our sample was predominantly white. Within the context of evidence for racial/ethnic differences in pain and fatigue experiences in people living with OA,[5,45,54] as well as impacts on the sleep−fatigue relationships,[21,59] our findings are not generalizable to diverse populations. Further research that specifically recruits a broader demographic is required to examine the potential role that racial, ethnic, and culture differences play in the sleep−pain and sleep−fatigue relationships.

Notwithstanding these limitations, our study has a number of strengths. We measured both subjective and objective sleep parameters and our use of multilevel modelling allowed us to make maximal use of the data, with each participant able to contribute up to 5 person-days. This approach took into consideration autocorrelation of symptom scores within an individual and allowed retention of participants' data, even if some time points were missed or skipped. The ecological momentary assessment methodology decreased the likelihood of recall bias and, with 5 data collection time points per day, we were able to well characterize the daily trajectories of pain and fatigue intensity in our sample.

Discordance between the association between subjectively and objectively measured sleep variables on symptoms of musculoskeletal disorders has been well-described.[64] Disparity has also been reported between report of symptoms of insomnia and actigraphy-based sleep characteristics in older, non-clinical populations.[17] Our finding of a lack of an association between objective measures of sleep and next-day pain intensity specifically is in accordance with earlier research in this area.[42] However, reports are not equivocal. Although Tang et al[56] identified more pain later in the day after an objectively efficient night's rest, we found no such

relationship in older adults with OA. Tang et al reasonably speculated that their finding may be attributable to a boom-or-bust activity pattern, whereby individuals with greater sleep efficiency, guided by lower pain intensity on awakening, may see this as an opportunity to be more active, potentially over-reaching and then experiencing more pain later in the day. Their study recruited adults with a mixture of chronic pain conditions with a mean age of 46. A relationship between sleep efficiency and differential trajectory of pain intensity was not replicated in our study. We also found no association with differential change in fatigue over the day based on the previous night's sleep efficiency. However, given our sample of older, community-dwelling adults with OA (median age = 71 years), this result is not incongruent with the tentative supposition of Tang et al.[56] The disparity does, however, support arguments for future investigations of the sleep—pain and sleep—fatigue relationships in specific populations in both clinical and non-clinical contexts.

Our findings suggest potentially important implications for future studies of time-based interventions. If supported by further research, people living with OA may be counselled about the likely outcome of a poor night's sleep on their symptoms, and this information may be used to inform the optimal timing of pharmacologic and/or nonpharmacologic interventions to reduce pain and fatigue (ie, on awakening). Indeed, there is the potential for these findings to be incorporated into the content of hybrid cognitive-behavioral therapy for insomnia and cognitive-behavioral therapy interventions for pain and/or fatigue[58] specific to those with OA-related symptoms. This information may also be used to guide research practice. Observational studies that ask participants to report on their pain or fatigue right now may wish to consider the time of day that the question is asked, and trials that restrict inclusion to specific pain and/or fatigue severity levels, or use then to underpin randomization minimization algorithms, may wish to take this factor into consideration. Given the absence of evidence in our study across multimodal sleep measurements and relatively small effects, more research is required before such translation to practice is warranted. However, the more robust association we observed between self-reported sleep quality and diurnal fatigue pattern may provoke discussions between older adults living with OA and health care providers focused on the role of sleep and time optimization of daily tasks.

In summary, in older community-dwelling adults with hip or knee OA, good subjective sleep quality was associated with less pain and fatigue intensity on awakening; however, this beneficial effect dissipated as the day progressed.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2019.04.011.

References

1. Abad VC, Sarinas PS, Guilleminault C: Sleep and rheumatologic disorders. Sleep Med Rev 12:211-228, 2008

2. Abelson RP: A variance explanation paradox - when a little is a lot. Psychol Bull 97:129-133, 1985

3. Affleck G, Urrows S, Tennen H, Higgins P, Abeles M: Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. Pain 68:363-368, 1996

4. Allen KD, Coffman CJ, Golightly YM, Stechuchak KM, Keefe FJ: Daily pain variations among patients with hand, hip, and knee osteoarthritis. Osteoarthritis Cartilage 17:1275-1282, 2009

5. Allen KD, Helmick CG, Schwartz TA, DeVellis RF, Renner JB, Jordan JM: Racial differences in self-reported pain and function among individuals with radiographic hip and knee osteoarthritis: The Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 17:1132-1136, 2009

6. Alsaadi SM, McAuley JH, Hush JM, Lo S, Bartlett DJ, Grunstein RR, Maher CG: The bidirectional relationship between pain intensity and sleep disturbance/quality in patients with low back pain. Clin J Pain 30:755-765, 2014

7. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, Brown C, Cooke TD, Daniel W, Feldman D: The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 34:505-514, 1991

8. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M: Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum 29:1039-1049, 1986

9. Andresen EM, Malmgren JA, Carter WB, Patrick DL: Screening for depression in well older adults: Evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). Am J Prev Med 10:77-84, 1994

10. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW: Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 15:1833-1840, 1988

11. Bellamy N, Sothern RB, Campbell J: Rhythmic variations in pain perception in osteoarthritis of the knee. J Rheumatol 17:364-372, 1990

12. Berger AM, Wielgus KK, Young-McCaughan S, Fischer P, Farr L, Lee KA: Methodological challenges when using actigraphy in research. J Pain Symptom Manage 36:191-199, 2008

13. Blackwell T, Ancoli-Israel S, Gehrman PR, Schneider JL, Pedula KL, Stone KL: Actigraphy scoring reliability in the study of osteoporotic fractures. Sleep 28:1599-1605, 2005

14. Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC: Six-item screener to identify cognitive impairment

among potential subjects for clinical research. Med Care 40:771-781, 2002

15. Cellini N, McDevitt EA, Mednick SC, Buman MP: Free-living cross-comparison of two wearable monitors for sleep and physical activity in healthy young adults. Physiol Behav 157:79-86, 2016

16. Cepeda MS, Africano JM, Polo R, Alcala R, Carr DB: What decline in pain intensity is meaningful to patients with acute pain. Pain 105:151-157, 2003

17. Chen JH, Waite L, Kurina LM, Thisted RA, McClintock M, Lauderdale DS: Insomnia symptoms and actigraph-estimated sleep characteristics in a nationally representative sample of older adults. J Gerontol A Biol Sci Med Sci 70:185-192, 2015

18. Evans S, Djilas V, Seidman LC, Zeltzer LK, Tsao JCI: Sleep quality, affect, pain, and disability in children with chronic pain: Is affect a mediator or moderator? J Pain 18:1087-1095, 2017

19. Gerhart JI, Burns JW, Post KM, Smith DA, Porter LS, Burgess HJ, Schuster E, Buvanendran A, Fras AM, Keefe FJ: Relationships between sleep quality and pain-related factors for people with chronic low back pain: Tests of reciprocal and time of day effects. Ann Behav Med 51:365-375, 2017

20. Goggins J, Baker K, Felson D: What WOMAC pain score should make a patient eligible for a trial in knee osteoarthritis? J Rheumatol 32:540-542, 2005

21. Grandner MA, Hale L, Jackson N, Patel NP, Gooneratne NS, Troxel WM: Perceived racial discrimination as an independent predictor of sleep disturbance and daytime fatigue. Behav Sleep Med 10:235-249, 2012

22. Hamilton NA, Pressman M, Lillis T, Atchley R, Karlson C, Stevens N: Evaluating evidence for the role of sleep in fibromyalgia: A test of the sleep and pain diathesis model. Cognit Ther Res 36:806-814, 2012

23. Harrison L, Wilson S, Heron J, Stannard C, Munafò MR: Exploring the associations shared by mood, pain-related attention and pain outcomes related to sleep disturbance in a chronic pain sample. Psychol Health 31:565-577, 2016

24. Hawker GA, French MR, Waugh EJ, Gignac MA, Cheung C, Murray BJ: The multidimensionality of sleep quality and its relationship to fatigue in older adults with painful osteoarthritis. Osteoarthritis Cartilage 18:1365-1371, 2010

25. Hülsheger UR: From dawn till dusk: Shedding light on the recovery process by investigating daily change patterns in fatigue. J Appl Psychol 101:905-914, 2016

26. Hutchings A, Calloway M, Choy E, Hooper M, Hunter DJ, Jordan JM, Zhang Y, Baser O, Long S, Palmer L: The Longitudinal Examination of Arthritis Pain (LEAP) study: Relationships between weekly fluctuations in patient-rated joint pain and other health outcomes. J Rheumatol 34:2291-2300, 2007

27. Julian LJ: Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). Arthritis Care Res (Hoboken) 63(Suppl. 11)):S467-S472, 2011

28. Kop WJ, Lyden A, Berlin AA, Ambrose K, Olsen C, Gracely RH, Williams DA, Clauw DJ: Ambulatory monitoring of physical activity and symptoms in fibromyalgia and chronic fatigue syndrome. Arthritis Rheum 52:296-303, 2005

29. Kurina LM, Thisted RA, Chen JH, McClintock MK, Waite LJ, Lauderdale DS: Actigraphic sleep characteristics among older Americans. Sleep Health 1:285-292, 2015

30. Lewinsohn PM, Seeley JR, Roberts RE, Allen NB: Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. Psychol Aging 12:277-287, 1997

31. Littner M, Kushida CA, Anderson WM, Bailey D, Berry RB, Davila DG, Hirshkowitz M, Kapen S, Kramer M, Loube D, Wise M, Johnson SF, Standards of Practice Committee of the American Academy of Sleep Medicine: Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: An update for 2002. Sleep 26:337-341, 2003

32. Mantua J, Gravel N, Spencer RM: Reliability of sleep measures from four personal health monitoring devices compared to research-based actigraphy and polysomnography. Sensors (Basel) 16, 2016

33. Meltzer LJ, Walsh CM, Peightal AA: Comparison of actigraphy immobility rules with polysomnographic sleep onset latency in children and adolescents. Sleep Breath 19:1415-1423, 2015

34. Meltzer LJ, Walsh CM, Traylor J, Westin AM: Direct comparison of two new actigraphs and polysomnography in children and adolescents. Sleep 35:159-166, 2012

35. Meltzer LJ, Wong P, Biggs SN, Traylor J, Kim JY, Bhattacharjee R, Narang I, Marcus CL, Caffeine for Apnea of Prematurity - Sleep Study Group: Validation of actigraphy in middle childhood. Sleep 39:1219-1224, 2016

36. Mendoza TR, Wang XS, Cleeland CS, Morrissey M, Johnson BA, Wendt JK, Huber SL: The rapid assessment of fatigue severity in cancer patients: Use of the Brief Fatigue Inventory. Cancer 85:1186-1196, 1999

37. Moldofsky H: Rheumatic manifestations of sleep disorders. Curr Opin Rheumatol 22:59-63, 2010

38. Murphy SL, Alexander NB, Levoska M, Smith DM: Relationship between fatigue and subsequent physical activity among older adults with symptomatic osteoarthritis. Arthritis Care Res (Hoboken) 65:1617-1624, 2013

39. Murphy SL, Smith DM, Clauw DJ, Alexander NB: The impact of momentary pain and fatigue on physical activity in women with osteoarthritis. Arthritis Rheum 59:849-856, 2008

40. Neogi T: The epidemiology and impact of pain in osteoarthritis. Osteoarthritis Cartilage 21:1145-1153, 2013

41. O'Brien EM, Waxenberg LB, Atchison JW, Gremillion HA, Staud RM, McCrae CS, Robinson ME: Negative mood mediates the effect of poor sleep on pain among chronic pain patients. Clin J Pain 26:310-319, 2010

42. O'Brien EM, Waxenberg LB, Atchison JW, Gremillion HA, Staud RM, McCrae CS, Robinson ME: Intraindividual variability in daily sleep and pain ratings among chronic pain patients: Bidirectional association and the role of negative mood. Clin J Pain 27:425-433, 2011

43. Olsen MF, Bjerre E, Hansen MD, Tendal B, Hilden J, Hróbjartsson A: Minimum clinically important differences in chronic pain vary considerably by baseline pain and methodological factors: Systematic review of empirical studies. J Clin Epidemiol 101:87-106.e102, 2018

44. Paquet J, Kawinska A, Carrier J: Wake detection capacity of actigraphy during sleep. Sleep 30:1362-1369, 2007

45. Parmelee PA, Harralson TL, McPherron JA, DeCoster J, Schumacher HR: Pain, disability, and depression in osteoarthritis: Effects of race and sex. J Aging Health 24:168-187, 2012

46. Parmelee PA, Tighe CA, Dautovich ND: Sleep disturbance in osteoarthritis: Linkages with pain, disability, and depressive symptoms. Arthritis Care Res (Hoboken) 67:358-365, 2015

47. Perrot S, Bertin P: "Feeling better" or "feeling well" in usual care of hip and knee osteoarthritis pain: Determination of cutoff points for patient acceptable symptom state (PASS) and minimal clinically important improvement (MCII) at rest and on movement in a national multicenter cohort study of 2414 patients with painful osteoarthritis. Pain 154:248-256, 2013

48. Pickering ME, Chapurlat R, Kocher L, Peter-Derex L: Sleep disturbances and osteoarthritis. Pain Pract 16:237-244, 2016

49. Pouchot J, Kherani RB, Brant R, Lacaille D, Lehman AJ, Ensworth S, Kopec J, Esdaile JM, Liang MH: Determination of the minimal clinically important difference for seven fatigue measures in rheumatoid arthritis. J Clin Epidemiol 61:705-713, 2008

50. Power J, Badley E, Wheaton B, Hawker G: Investigating the overlap of fatigue, pain and depression in an osteoarthritis population. Osteoarthritis and Cartilage 22:S220-S221, 2014

51. Rowe M, McCrae C, Campbell J, Horne C, Tiegs T, Lehman B, Cheng J: Actigraphy in older adults: Comparison of means and variability of three different aggregates of measurement. Behav Sleep Med 6:127-145, 2008

52. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W: Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. Eur J Pain 8:283-291, 2004

53. Sandıkçı SC, Özbalkan Z: Fatigue in rheumatic diseases. Eur J Rheumatol 2:109-113, 2015

54. Smith DM, Parmelee PA: Within-day variability of fatigue and pain among African Americans and non-Hispanic whites with osteoarthritis of the knee. Arthritis Care Res (Hoboken) 68:115-122, 2016

55. Snijders GF, van den Ende CH, Fransen J, van Riel PL, Stukstette MJ, Defoort KC, Arts-Sanders MA, van den Hoogen FH, den Broeder AA, Group NOCS: Fatigue in knee and hip osteoarthritis: The role of pain and physical function. Rheumatology (Oxford) 50:1894-1900, 2011

56. Tang NK, Goodchild CE, Sanborn AN, Howard J, Salkovskis PM: Deciphering the temporal link between pain and sleep in a heterogeneous chronic pain patient sample: A multilevel daily process study. Sleep 35:675-687A, 2012

57. Tang NK, Lereya ST, Boulton H, Miller MA, Wolke D, Cappuccio FP: Nonpharmacological treatments of insomnia for long-term painful conditions: A systematic review and meta-analysis of patient-reported outcomes in randomized controlled trials. Sleep 38:1751-1764, 2015

58. Tang NKY: Cognitive behavioural therapy in pain and psychological disorders: Towards a hybrid future. Prog Neuropsychopharmacol Biol Psychiatry 87:281-289, 2018

59. Thomas KS, Bardwell WA, Ancoli-Israel S, Dimsdale JE: The toll of ethnic discrimination on sleep architecture and fatigue. Health Psychol 25:635-642, 2006

60. Valrie CR, Gil KM, Redding-Lallinger R, Daeschner C: Daily mood as a mediator or moderator of the pain-sleep relationship in children with sickle cell disease. J Pediatr Psychol 33:317-322, 2008

61. Vitiello MV, McCurry SM, Shortreed SM, Baker LD, Rybarczyk BD, Keefe FJ, Von Korff M: Short-term improvement in insomnia symptoms predicts long-term improvements in sleep, pain, and fatigue in older adults with comorbid osteoarthritis and insomnia. Pain 155:1547-1554, 2014

62. Vitiello MV, Rybarczyk B, Von Korff M, Stepanski EJ: Cognitive behavioral therapy for insomnia improves sleep and decreases pain in older adults with co-morbid insomnia and osteoarthritis. J Clin Sleep Med 5:355-362, 2009

63. Weiss AR, Johnson NL, Berger NA, Redline S: Validity of activity-based devices to estimate sleep. J Clin Sleep Med 6:336-342, 2010

64. Wilson KG, Watson ST, Currie SR: Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with chronic musculoskeletal pain. Pain 75:75-84, 1998

65. Wolfe F, Hawley DJ, Wilson K: The prevalence and meaning of fatigue in rheumatic disease. J Rheumatol 23:1407-1417, 1996

66. Zautra AJ, Fasman R, Parish BP, Davis MC: Daily fatigue in women with osteoarthritis, rheumatoid arthritis, and fibromyalgia. Pain 128:128-135, 2007