Journal of Behavioral Medicine, Vol. 29, No. 2, April 2006 (© 2006)
DOI: 10.1007/s10865-005-9045-0

Sleep Disruptions Mediate the Relationship Between Early Postoperative Pain and Later Functioning Following Total Knee Replacement Surgery

Julie K. Cremeans-Smith,[1,5] Kendra Millington,[2] Eve Sledjeski,[1] Kenneth Greene,[3] and Douglas L. Delahanty[1,4]

Accepted for publication: December 16, 2005
Published online: February 22, 2006

Despite relatively standardized surgical procedures, patients undergoing total knee replacement (TKR) surgery differ dramatically in the speed of their recovery. Previous research has suggested a relationship between the experience of pain and sleep disruptions among patients with chronic pain or those undergoing surgery, such that more severe pain is associated with more frequent awakenings throughout the night. This study examined sleep disruptions 1 month following surgery as a mediator of the relationship between pain 1 month following surgery and functional limitations 3 months following surgery. A total of 110 patients scheduled to undergo unilateral TKR were examined at three time points: 2–3 weeks prior to surgery, 1 month following surgery, and 3 months following surgery. After controlling for presurgical levels of pain, sleep disruptions, and functional limitations, sleep disruptions 1 month following surgery partially mediated the relationship between pain 1 month following surgery and functional limitations 3 months following surgery. The present findings underscore the importance of adequate sleep during postsurgical recovery and suggest that interventions targeting sleep disruptions may improve the speed and quality of patients' recovery from TKR and other surgical procedures.

KEY WORDS: postoperative fatigue; pain; surgical recovery; total knee replacement surgery.

Total knee replacement (TKR) surgery is a relatively standardized surgical procedure, resulting in similar levels of physical trauma to patients. However, TKR patients differ greatly in length and quality of their recovery, as gauged by their reports of pain and the speed with which they are able to regain mobility (Lingard *et al.*, 2004). Medical variables appear to account for a limited percentage of the variance in recovery (e.g., Christensen and Kehlet, 1984; Edwards *et al.*, 1982; Kehlet, 1991), leading researchers to examine the extent to which psychological factors such as fatigue (DeCherney *et al.*, 2002), depression (Croog *et al.*, 1995), and anxiety (Boeke *et al.*, 1991) may impact surgical recovery. One of the most common complaints following surgery is difficulty in sleeping, and sleep difficulties have been related to reports of higher pain (McCracken and Iverson, 2002) and lower functioning (Acebo and Carksadon, 2002; Stepnowsky *et al.*, 2000) in chronic pain patients. However, the extent to which sleep disruptions may serve as a mechanism through which pain could lead to poorer recovery has not been examined. The present study used a prospective design to investigate the relationship between acute postoperative pain, sleep disruptions, and physical functioning in patients undergoing TKR surgery.

[1]Department of Psychology, Kent State University, Kent, Ohio.
[2]Department of Psychology, Taylor University, Upland, Indiana.
[3]Department of Orthopedics, Summa Health System, Akron, Ohio.
[4]Department of Psychology in Psychiatry, Northeastern Ohio Universities College of Medicine (NEOUCOM), Rootstown, Ohio.
[5]To whom correspondence should be addressed at Kent State University, Stark Campus, Canton, Ohio 44720; e-mail: jcremean@kent.edu.

SLEEP QUALITY FOLLOWING SURGERY

Following surgery, patients often experience impaired sleep quality and difficulty initiating or maintaining sleep (e.g., Brimacombe and Macfie, 1993; Cronin *et al.*, 2001; Kain and Caldwell-Andrews, 2003). For example, Kain and Caldwell-Andrews (2003) reported that 23% of patients undergoing outpatient surgery versus 2.9% of nonsurgical controls experienced clinically significant sleep disruptions during the first two postoperative days following surgery. However, research to date has focused primarily on documenting sleep impairments or changes within the sleep cycle without examining the impact that altered sleep may have on patients' long-term recovery (e.g., Brimacombe and Macfie, 1993; Cronin *et al.*, 2001; Kain and Caldwell-Andrews, 2003).

PAIN AND SLEEP QUALITY

Prior research has revealed a robust relationship between subjective experiences of pain and impaired sleep quality among a variety of chronic pain patients, including those with chronic back pain (Atkinson *et al.*, 1988), rheumatoid arthritis (Nicassio and Wallston, 1992), and severe burns (Raymond *et al.*, 2001). Specifically, patients who report more severe pain experience poorer sleep, as indicated by patients' self-reported poorer overall sleep quality, delayed sleep onset, increased number of awakenings due to pain, and fewer hours of sleep per night (Agargun *et al.*, 1999; Atkinson *et al.*, 1988; McCracken and Iverson, 2002; Morin *et al.*, 1998; Pilowsky *et al.*, 1985; Raymond *et al.*, 2001). Although these studies document the negative consequences of chronic pain on sleep, these findings may not generalize to a patient's experience during postoperative recovery.

Following TKR surgery, several months of exercise and rehabilitation are necessary to regain functionality. Early aggressive mobilization of the joint has been found to speed recovery and shorten the hospital stay (Rohr and Hungerford, 1992), and exercise-related muscle contraction aids in the movement of fluids, decreases pain, stabilizes and protects the joint and overall improves functioning (Gradisar *et al.*, 1996). Prior research has found that subjective pain reports are associated with difficulty in completing the tasks associated with every day living in chronic pain patients (e.g., Jakobsson *et al.*, 2003; Scudds and Robertson, 1998). Therefore, it follows that, to the extent that pain interferes with necessary exercise and rehabilitation following TKR, postsurgical pain may impede postsurgical recovery.

Current Study

This study prospectively examined the relationship between sleep, pain, and functional limitations in male and female patients undergoing TKR surgery. The examination of participants undergoing an elective surgery allowed for the collection of preoperative (2–3 weeks presurgery) measures of sleep and pain, and the prospective design allowed for the examination of predictors of surgical outcome. We hypothesized that sleep disruptions 1 month postsurgery would be significantly related to poorer functioning 3 months postsurgery. We further hypothesized that self-reported sleep disruptions would act as mediator between early postoperative pain and subsequent functioning. More specifically, we proposed a mediational model where sleep disruptions 1 month postsurgery would mediate the relationship between 1 month postsurgical pain and functional limitations 3 months following surgery.

METHODS

Participants

Participants consisted of 123 patients over the age of 18 seeking unilateral TKR surgery through the Department of Orthopedics at Summa Health System, Akron, Ohio. Of the 123 patients who agreed to participate in the study, 6 dropped out for health-related reasons (e.g., development of other conditions prior to surgery, hospitalization for other medical conditions), 5 decided they were no longer interested in participating, and 2 patients postponed their surgeries. Therefore, the final sample consisted of 110 patients (35 males and 75 females) between the ages of 49 and 90 ($M = 69.2 \pm 10.2$) who completed all assessment time points. Patients who initially agreed to participate, but later withdrew from the study, did not differ from those patients who completed the study on age ($t[121] = -1.45$, $p = 0.15$), gender($\chi^2[1] = 0.30$, $p = 0.59$), race/ethnicity($\chi^2[1] = 0.934$, $p = 0.334$), income($t[111] = 1.12$, $p = 0.26$), level of education ($t[119] = 0.53$, $p = 0.60$) or surgeon ($\chi^2[3] = 1.77$, $p = 0.62$). The majority of the sample was Caucasian

(92.8%; 7.2% African American). Patients undergoing revision TKR were not eligible to participate. The majority of patients were undergoing TKR for the first time (75.5%); 24.5% had previously undergone TKR on the other knee.

Procedures

The following procedures were approved by the Institutional Review Boards of Kent State University and Summa Health System. Potential participants were initially informed about the study by their orthopedic surgeon at the time of referral for surgery. Researchers subsequently contacted patients by mail and telephone to solicit their participation. The time 1 assessment ($T1$, baseline) was conducted 2–3 weeks prior to surgery at the participants' homes. At this time, informed consent was obtained, and participants completed a packet of questionnaires including measures of depression (The Center for Epidemiological Studies—Depression scale, CES-D: Radloff, 1977), general pain (Arthritis Impact Measurement Scale, AIMS: Meenan *et al.*, 1992), functional limitations (The Western Ontario and McMaster Universities Osteoarthritis Index, WOMAC: Bellamy *et al.*, 1988), and sleep quality (Pittsburgh Sleep Quality Index, PSQI: Buysse *et al.*, 1989). The time 2 ($T2$) and time 3 ($T3$) assessments occurred 1 and 3 months following the surgery, and were also conducted in participants' homes. Participants completed the PSQI (Buysse *et al.*, 1989) and AIMS (Meenan *et al.*, 1992) at $T2$ and the WOMAC (Bellamy *et al.*, 1988) at $T3$.

Measures

Depression

Given established relationships between depression, pain, and sleep (e.g., McCracken and Iverson, 2002), depression at $T2$ was analyzed as a potential control variable using the Center for Epidemiological Studies—Depression Scale (CES-D; Radloff, 1977). The CES-D is a 20-item questionnaire assessing depressive symptomatology experienced during the week prior to the assessment. Depressive symptoms were rated on a 4-point Likert scale from 0 (*never*) to 3 (*most of the time*). Items were summed to yield a total depression score (Cronbach's alpha at $T2 = 0.84$).

Pain

The pain subscale of the Arthritis Impact Measurement Scale 2 (AIMS: Meenan *et al.*, 1992) was used to measure frequency of pain experienced over the last month at $T1$ and $T2$. The pain subscale of the AIMS consists of 5 items on which participants rate the frequency of experienced on a 5-point Likert scale from 1 (*no days*) to 5 (*all days*). Items were summed to yield a total pain score (Cronbach's alpha at $T1 = 0.81$ and $T2 = 0.74$).

Functional Limitations

To assess functional limitations, The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC: Bellamy *et al.*, 1988) was administered at $T1$ and $T3$. The WOMAC is a general measure of functionality which assesses functional limitations, stiffness, and pain in the knee (e.g., difficulty in ascending/descending stairs, putting on socks, getting in and out of a car). The WOMAC asks individuals to rate the severity of their difficulty/pain while completing a variety of daily tasks involving knee movement on a 5-point Likert scale from 0 (*none*) to 4 (*extreme*). Greater values on the WOMAC indicate more severe limitations, pain, and stiffness (Cronbach's alpha at $T1 = 0.95$ and $T3 = 0.96$).

Sleep Disruptions

Sleep quality during the past month was measured at $T1$ and $T2$ using the PSQI (Buysse *et al.*, 1989). The PSQI consists of seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disruptions, use of sleeping medication, and daytime dysfunction. The present analyses focused on the 9-item sleep disruptions subscale as it was hypothesized, based on previous research (e.g., Agargun *et al.*, 1999; Atkinson *et al.*, 1988; Hart *et al.*, 1970) that postsurgical pain would be most likely to interfere with sleep by contributing to multiple awakenings during the night, thereby interfering with patients' ability to maintain sleep. The items on the sleep disruptions subscale include inability to fall asleep and waking up in the middle of the night, among others (Cronbach's alpha at $T1 = 0.72$ and $T2 = 0.96$).

Statistical Analyses

Pearson product moment correlations, chi-square tests, and initial analyses of variance (ANOVAs), where appropriate, were calculated to test for possible relationships between the variables of interest and sociodemographic variables. Next, initial bivariate correlations were conducted to examine the relationships between sleep disruptions and pain 1 month following surgery, and functional limitations 3 months following surgery. Initial hierarchical linear regressions were used to examine the extent to which predictor variables accounted for variance in functional limitations after accounting for confounding variables. Additional hierarchical linear regressions were used to test the hypothesis that sleep disruptions 1 month postsurgery mediated the relationship between 1 month postsurgical pain and 3 month postsurgical functioning. Briefly, mediational models require that the following criteria be met: (a) in zero-order relationships, the predictor variable must be significantly related to the outcome variable and the potential mediator; (b) the mediator must significantly predict the outcome variable; and (c) the standardized regression coefficient for the relationship between the predictor and the outcome variable must lose significance when controlling for the effects of the mediator (Baron and Kenny, 1986). Finally, a product coefficient test (selected for its statistical power with small sample sizes) was employed to examine the significance of the mediation effect (MacKinnon *et al.*, 2002).

RESULTS

Determination of Covariates

Analyses of potential covariates are displayed in Table I. Reported sleep disruptions, pain at 1 month, and arthritis severity at 3 months did not differ by race/ethnicity ($ps > 0.1$). However, age was significantly related to sleep disruptions 1 month following surgery ($r = -0.258$, $p = 0.007$), such that younger participants reported greater levels of sleep disruptions. In addition, females rated their pain as more severe than males at *T*2 ($t(109) = 2.55$, $p = 0.035$). Patients experiencing their first TKR surgery did not differ from patients who had previously undergone TKR on the other knee in reports of pain ($p = 0.535$) or sleep disruptions ($p = 0.799$) 1 month following surgery, or on functional limitations 3 months following surgery ($p = 0.271$). As expected, depression 1 month following surgery was significantly related to pain ($r = 0.383$, $p = 0.000$) and sleep disruptions ($r = 0.251$, $p = 0.010$) 1 month following surgery, and functional limitations 3 months following surgery ($r = 0.367$, $p < 0.001$). Therefore, age, gender, and depression (1 month following surgery) were included as control variables in the first step of the regression analyses. Similarly, presurgical reports of pain, sleep disruptions, and functional limitations were also included as control variables. Using a total of eight predictors (two independent variables and six control variables), a power analysis (GPower; Faul and Erdfelder, 1992) indicated that the present sample size (110) would provide adequate power (0.80) to detect medium effect sizes (0.15) in the final model. Bivariate correlations between the study variables are displayed in Table II.

Individual Regression Analyses

Prior to examining the hypothesized mediation model, separate regressions were conducted to investigate the strength of the predictive relationships between 1-month postoperative pain and sleep disruptions and functional limitations 3 months following surgery (see Table III). After controlling for age, gender, preoperative pain, preoperative functional limitations, and postoperative depression, pain

Table I. Analysis of Potential Control Variables

	Pain	Sleep disruptions	Functional limitations
Age	$r = -0.077$	$r = -0.258^{**}$	$r = 0.107$
Gender	$t(105) = -2.133^{*}$	$t(105) = 1.075$	$t(105) = -0.904$
Race/ethnicity	$t(105) = -1.029$	$t(105) = 1.075$	$t(105) = -0.904$
Previous TKR	$t(103) = -0.622$	$t(103) = 0.256$	$t(103) = -1.107$
Depression	$r = 0.383^{**}$	$r = 0.251^{*}$	$r = 0.367^{**}$

Note. Pain and sleep disruptions were assessed at 1 month following surgery, functional limitations was assessed at 3 months following surgery.
$^{*}p < 0.05$; $^{**}p < 0.01$.

Table II. Correlations Between Baseline and Follow-Up Measures

	1	2	3	4	5	6	7
Baseline measures							
1. Pain	—	0.199*	0.667**	0.400**	0.193	0.112	0.298**
2. Sleep disruptions	—	—	0.183	0.148	0.444**	0.166	0.109
3. Functional limitations	—	—	—	0.364**	0.244*	0.169	0.390**
1-Month postoperative follow-up							
4. Pain	—	—	—	—	0.258**	0.383**	0.440**
5. Sleep disruptions	—	—	—	—	—	0.251*	0.298**
6. Depression	—	—	—	—	—	—	0.367**
3-Month postoperative follow-up							
7. Functional limitations	—	—	—	—	—	—	—

*$p < 0.05$; **$p < 0.01$.

1 month following surgery predicted functional limitations at 3 months following surgery ($\beta = 0.225$, $p = 0.034$). As expected, postoperative pain and functional limitations were positively related. Similarly, after accounting for the variance in control variables, sleep disruptions 1 month following surgery accounted for a significant percentage of the variance (approximately 6%) in functional limitations at 3 months following surgery ($\beta = 0.282$, $p = 0.008$). The relationship between postoperative sleep disruptions and functional limitations was also positive, indicating that patients who reported more sleep disruptions reported more functional limitations 3 months following surgery.

Mediational Analysis

To test the hypothesis that sleep disruptions would mediate the relationship between 1 month postoperative pain and functional limitations 3 months following surgery, initial zero-order correlations between reported pain and sleep quality 1 month following surgery and arthritis severity 3 months following surgery were calculated. Pain 1 month following surgery (the independent variable) was significantly related to the mediator (sleep disruptions; $r = 0.258$, $p = 0.009$) and the outcome variable (arthritis severity; $r = 0.440$, $p < 0.001$). In addition, the mediator (sleep disruptions) was significantly correlated with the outcome variable (arthritis severity; $r = 0.298$, $p = 0.002$). A hierarchical multiple regression was conducted to test the mediation model, with functional limitations 3 months following surgery serving as the dependent variable. Control variables (age and gender; baseline pain, sleep disruptions, and functional limitations; and depression 1 month following surgery) were entered on the first step, sleep disruptions (1 month following surgery) were entered on the second step,

Table III. Initial Regression Analyses Examining Pain and Sleep Disruptions as Predictors of Functional Limitations

		Functional limitations (3 months postoperative)				
Step no	Variables	B	SE	β	ΔR^2	F of ΔR^2
1	Age	0.265	0.096	0.260**		
	Gender	−0.111	1.953	−0.005	0.301	9.701
	Presurgical functional limitations	0.272	0.108	0.310*		
	Depression (1 month postoperative)	0.274	0.097	0.266**		
2	Presurgical pain	0.109	0.253	0.053	0.077	0.965
3	Pain (1 month postoperative)	0.544	0.253	0.225*	0.035	4.632*
	Significance of the regression model, $F(6, 94) = 7.672$**					
2	Presurgical sleep disruptions	−2.547	1.803	−0.144	0.001	0.098
3	Sleep disruptions (1 month postoperative)	6.225	2.296	0.282**	0.057	7.353**
	Significance of the regression model, $F(6, 93) = 6.951$**					

*$p < 0.05$; **$p < 0.01$.

Table IV. Hierarchical Regression Analyses to Test Sleep Disruptions as a Mediator of the Relationship Between Pain and Functional Limitations

		Functional limitations (3 months postoperative)				
Step no	Variables	B	SE	β	ΔR^2	F of ΔR^2
1	Control variables	0.285	5.441**			
2	Sleep disruptions (1 month postoperative)	6.005	2.231	0.286**	0.059	7.252**
	Significance of the regression model, $F(7, 88) = 6.052$**					
3	Pain (1 month postoperative)	0.469	0.267	0.197	0.024	3.083
	Significance of the regression model, $F(7, 88) = 5.817$**					

Note. Control variables in step 1 include age, gender, presurgical functional limitations, presurgical pain, presurgical sleep disruptions, and depression 1 month postoperative.
$^*p < 0.05$; $^{**}p < 0.01$.

and pain (1 month following surgery) was entered on the third step (see Table IV). The overall regression model was significant, $F(7, 88) = 5.817$, $p < 0.001$, accounting for 37% of the variance in functional limitations 3 months following surgery (see Table IV). In addition, sleep disruptions 1 month following surgery partially mediated the relationship between pain (1 month following surgery, the independent variable) and functional limitations (3 months following surgery, the dependent variable) as the relationship between pain and functional limitations became nonsignificant once the mediator was added to the model (change from $\beta = 0.225$, $p = 0.034$ to $\beta = 0.197$, $p = 0.083$; see Table IV). A product coefficient test (MacKinnon *et al.*, 2002) revealed that sleep disruptions significantly mediated the relationship between pain and functional limitations ($z = 1.85$, $p < 0.05$).

DISCUSSION

This study examined the relationships between pain, sleep disruptions, and functional limitations following surgery. Bivariate correlations between the study variables supported the findings of previous studies, indicating that more severe pain is associated with impaired sleep quality (e.g., more sleep disruptions; Agargun *et al.*, 1999; Atkinson *et al.*, 1988; McCracken and Iverson, 2002; Morris *et al.*, 1998; Pilowsky *et al.*, 1985; Raymond *et al.*, 2001). Further, the present study expands upon the findings of previous studies by examining the relationship between pain and sleep disruptions in the context of functional limitations following surgery. Initial regressions indicated that (after controlling for presurgical differences in pain, sleep disruptions, and functional limitations) postoperative pain and sleep disruptions independently predicted functional limitations 3 months following surgery. Specifically, patients who reported greater levels of pain and sleep disruptions 1 month following surgery reported greater functional limitations 3 months following surgery. Interestingly, sleep disruptions accounted for a higher percentage of the variance in functional limitations than did self-reported pain. This finding suggests that sleep disruptions following surgery may more accurately predict 3-month postoperative functional limitations, compared to self-reported pain. Further, we examined whether sleep disruptions could serve as a mechanism through which pain would be related to decreased functioning in TKR patients. Results revealed that sleep disruptions 1 month following surgery partially mediated the relationship between 1-month postoperative pain and functional limitations 3 months following surgery. In other words, sleep disruptions served as a mechanism through which postoperative pain could result in functional limitations. It is important to note that these findings persisted even after controlling for presurgical levels of sleep disruptions, pain, and functional limitations.

The results of this study highlight the importance of targeting sleep disruptions in TKR patients to improve functional outcomes following surgery. Following TKR surgery, patients are prescribed a variety of medications to control their pain, but rarely are sleep difficulties actively targeted as part of postoperative therapeutic interventions. This study suggests that targeting sleep quality, particularly sleep disruptions, with psychopharmacological interventions may decrease pain-related functional limitations. Future research may consider examining the efficacy of the combination of pain and sleep medications at impacting postoperative recovery.

This study focused on a specific patient population undergoing a relatively standardized surgical procedure so as not to be confounded by factors that may differ across surgical procedures (e.g., extent of physical trauma, length of surgery, etc.). However, because this study focused solely on patients undergoing unilateral TKR surgery, the findings may not generalize to all surgical patients. In addition, this study is limited by a reliance on self-reported measures, particularly those of sleep disruptions and functional limitations. Confirmation of the present findings through future research incorporating objective assessments of these variables (e.g., polysomnography or observations of individual's ability to perform tasks of daily living with or without assistance) would increase confidence in the present results.

Despite these limitations, the current study provides valuable insight into possible contributors to variability in postoperative recovery. In addition, the patient population examined in this study provided researchers with the opportunity to consider baseline (presurgical) pain and functioning in models predicting postsurgical recovery, and further strengthen the current findings. Sleep is an essential part of the healing process, as it contributes to the relationship between pain and functioning. Consequently, future research should examine whether interventions aimed at alleviating postoperative sleep disruptions could potentially shorten patients' recovery period.

ACKNOWLEDGMENTS

This study was supported by a grant from the Center for the Treatment and Study of Traumatic Stress, Kent State University and Summa Health System. Preparation of this manuscript was supported, in part, by National Institutes of Mental Health grants R01 MH 62042 and R34 MH073012.

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