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The Relationship between Self-reported Restless Sleep and Objectively Measured Physical Activity in Adults with Knee Osteoarthritis

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Abstract

Objective—Despite many health benefits of physical activity, inactivity is endemic among adults with knee osteoarthritis (KOA). Because sleep quality may be a target to improve physical activity behavior, we investigated the cross-sectional relationship between restless sleep and physical activity in participants with or at risk for KOA.

Methods—We analyzed accelerometer-measured physical activity and clinical data from Osteoarthritis Initiative (OAI) participants. We used multiple regression analysis to evaluate physical activity for participants grouped by the reported frequency of restless sleep adjusting for demographic and medical confounders.

Results—Of the 1892 OAI participants with complete data, 300 (16%) reported restless sleep 3 or more days in the past week. Participants reporting much (3-4 days/week) and most (5-7 days/week) restless sleep had 11.9% and 23.7% less weekly minutes of moderate-vigorous activity, respectively, compared to participants reporting rare restless sleep (less than 1 day/week) (p for trend 0.021). These differences persisted after accounting for age, gender, race, body mass index, medical comorbidity, KOA severity and pain (p for trend 0.023). Differences related to restless sleep were largely attenuated by the presence of high depressive symptoms and low energy levels.

Conclusion—Poor sleep quality is associated with less physical activity in persons with or at risk for KOA. Future studies are needed to determine the mechanisms of how poor sleep and physical activity are related, how energy and depression mediate these relationships, and whether interventions that improve sleep quality might result in increased physical activity.

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Introduction

One in ten adults over age 65 experiences knee osteoarthritis (KOA) and its progressive pain and disability.(1) Physical activity is well known to improve long-term functional status and to preserve independence in adults with KOA.(2) Despite current recommendations to promote physical activity as a primary treatment, almost half of adults with KOA are physically inactive, not even performing a single 10 minute session of moderate-intensity physical activity in a week.(2–4) Over half of individuals with KOA report sleep disturbance including difficulty initiating or maintaining nighttime sleep.(5) This is in contrast to one-third of all adults reporting sleep complaints.(6) Poor sleep quality is a modifiable risk factor (7) but is under-investigated as a determinant of physical activity. Improving sleep quality may be a novel target to increase physical activity behavior; the relationship between sleep quality and physical activity may be bidirectional and improving physical activity may also benefit sleep.

Good sleep quality is important for good health, yet chronic pain, including pain from osteoarthritis, interferes with sleep. In general populations, sleep and physical activity have been shown to have an association.(6, 8) However the relationship between sleep quality and physical activity in adults with knee osteoarthritis remains unknown. This is likely to be a complex relationship: sleep disturbance is associated with pain, depression, and fatigue with sleep disturbance exacerbating depression among individuals with high levels of pain.(5, 9) Individuals with major depressive disorder are less physically active than individuals without depression.(10) If restless sleep increases depressive symptoms and fatigue, and depression and fatigue lead to decreased physical activity, depressive symptoms and low energy may serve as mediators to explain the mechanism by which restless sleep results in less physical activity. The goal of this study was to investigate the relationship between sleep quality as measured by self-reported restless sleep and objectively-measured physical activity in adults with or at high risk for KOA. Our hypothesis was there is an inverse relationship between restless sleep and physical activity after controlling for confounders and that energy and depressive symptoms from sleep disturbance may explain the pathway between restless sleep and physical activity.

Methods

Study Population

Participants were a subcohort of the Osteoarthritis Initiative (OAI) enrolled into an accelerometer ancillary study conducted at the OAI 2008-2010 clinic visit (OAI 4-year follow-up).(4) The OAI is a multi-center prospective study investigating risk factors and biomarkers for the progression and/or onset of knee OA (see http://www.oai.ucsf.edu/datarelease/About.asp). OAI study design and eligibility criteria have been described in detail elsewhere.(11) At enrollment, the OAI recruited 4796 men and women between 45 to 79 years of age from four clinical sites, with or at high risk for developing symptomatic, radiographic knee OA. High risk was defined as the presence of two or more eligibility risk factors (e.g. age greater than 70 years, meeting gender-age-specific overweight criteria, prior knee injury, prior knee surgery, family history of total knee replacement for OA, Heberden's nodes, and/or frequent knee symptoms). The study population was drawn from 2127 people

enrolled in an OAI accelerometer monitoring substudy at the OAI 48-month follow-up visit (2008-2010). 1705 participants were not invited to participate due to their 48 month visit not during the study dates, 585 participants declined to participate in the accelerometer study, 70 were deceased, and 309 were not available as they did not attend the 48 month visit. Approval was obtained from the institutional review board at each OAI site and at Northwestern University, Chicago, IL. Each participant provided written informed consent. A subgroup of 2127 OAI participants participated in an accelerometer study at the 48 month clinic visit.

Restless Sleep

Frequency of restless sleep was evaluated by participants' responses to the Center for Epidemiologic Studies Depression Scale (CES-D) question that asked how often in the past week their sleep was restless, rarely: rarely or none of the time (less than 1 day), some: some or a little of the time (1-2 days), moderate/much: occasionally or a moderate amount of time (3-4 days), and most: most or all of the time (5-7 days). (12) Accelerometer monitoring and the CES-D results were both from the substudy baseline (i.e. the OAI 48-month study visit).

Covariates

Demographic factors included age, gender, and race.(4) Medical covariates included body mass index (BMI), medical comorbidity, knee osteoarthritis severity, and pain. (4)BMI was calculated as weight [kg]/height [m^2]. Height was measured using calibrated wall-mounted stadiometers. Body weight was measured in kilograms on all participants using calibrated standard balance beam scales. Medical comorbidity was ascertained using the Charlson index, a validated self-administrated questionnaire evaluating comorbid chronic conditions. Knee osteoarthritis severity was identified by the worst Kellgren-Lawrence grade score of both knees assessed from "fixed-flexion" knee radiography protocol. Self-reported knee pain was measured by a 5-point Likert scale from the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) modified to ask about the right and left knee symptoms separately in the past 7 days. The WOMAC pain score range is 0 to 20; a higher number represents worse symptoms. Energy level was based on a Likert scale response to the question "did you have a lot of energy" during the past four weeks ascertained from an item on the 12-Item Short Form Health Survey (SF-12). CES-D scores were calculated excluding the question of restless sleep and included the remaining 19 questions from the full 20-item scale. Patients were considered to have evidence of a high level of depressive symptoms if they had a score of ≥16 on the modified CES-D.(12)

Physical Activity Assessment

Physical activity was monitored using the ActiGraph GT1M uniaxial accelerometer. Trained research personnel gave uniform scripted in-person instructions to wear the accelerometer for seven consecutive days on a belt at the natural waistline in line with the right axilla upon arising in the morning until retiring, except during water activities. Accelerometer data were analytically filtered using validated methodology.(13) Nonwear periods were defined as ≥ 90 minutes with zero activity counts (allowing for 2 consecutive interrupted minutes with counts <100).(14) We identified participants with 4-7 valid monitoring days (i.e., 10 or more wear hours per day) needed for reliable physical activity estimates.(14) Thresholds used by

the National Cancer Institute (NCI) on a minute-by-minute basis were applied to identify moderate-to-vigorous (counts/minute ≥ 2020) intensity activity. Weekly moderate-vigorous activity minutes were summed from the daily totals over the monitoring hours and averaged across valid monitored days; for individuals with 4, 5, or 6 valid days of monitoring, weekly activity minutes were estimated as 7 average daily activity minutes spent in moderate-vigorous activity.

Statistical analysis

We compared moderate-vigorous physical activity minutes per week across 4 self-reported restless sleep categories. The outcome of weekly minutes of moderate-vigorous physical activity was log-transformed due to the skewed distribution. For 13 participants with 0 weekly moderate-vigorous physical activity minutes, we added 0.1 and then log-transformed. Multiple linear regression was used to estimate the difference between restless sleep groups in outcome using the reference group which reported rarely having restless sleep. Regression findings on log-transformed outcomes can be validly translated as the percent difference in the weekly minutes of moderate-vigorous physical activity among each restless sleep group and reference group by using the equation $(e^{\wedge(\text{coefficient})}-1)*100\%$, where the coefficient is estimated for each restless sleep group from the log-transformed regression model.(15) Hierarchical multiple regression adjusted for potential confounders: first adjusting for demographic factors (age, gender, and race as prior studies have demonstrated that women, older individuals, and nonwhite individuals are less likely to be physically active),(4) then additionally adjusting for medical characteristics (BMI, KOA severity, WOMAC pain, and medical comorbidity as individuals who have high BMI, more knee pain, and have more medical comorbidities are more likely to be physically inactive).(16) To explore if depressive symptoms and low energy mediate the relationship between restless sleep and physical activity, we added the presence of high depressive symptoms and low energy to the final model to see if the magnitude of the restless sleep-physical activity relationship was diminished. Gender, race, and presence of high depressive symptoms were entered as categorical variables, all others were treated as continuous. All statistical analyses were completed using SAS 9.4 (Cary, NC).

Results

Of the 2127 accelerometer participants, 1927 (91%) had complete physical activity outcomes (4-7 valid days of monitoring). Less than 2% had incomplete covariate data. The analysis sample included 1892 participants. As shown in Table 1, 168 (8.9%) participants reported moderate restless sleep much of the time (3-4 days in the past week), and 132 (7.0%) participants reported restless sleep most of the time (5-7 days in the past week). Participants who reported restless sleep most or all of the time had high depressive symptoms (40.2%) compared to only 3.6% of those who rarely reported restless sleep. Table 2 shows participants who reported moderate and most restless sleep had 14.9% and 25.2% less weekly minutes of moderate-vigorous physical activity, respectively, compared to participants reporting rare restless sleep (p for trend 0.019). After adjusting for potential demographic confounders (age, gender, and race), the trend became stronger for spending less time in moderate-vigorous physical activity with more frequently reported restless sleep

(p for trend <0.001). Compared to the reference group which reported rarely/none of the time, the participants had 23.8% and 36.3% less likely weekly MVPA for participants in much of the time and for participants in most/all of the time, respectively. This translates to 19 and 29 weekly MVPA minutes less for each restless sleep group compared to the reference group (reporting restless sleep rarely/none of the time) participating on average in 80 minutes of weekly MV minutes. The significant trend persisted with additional adjustment for potential confounders relating to general health, pain, and KOA severity (p for trend 0.020). When we evaluated if energy and high depressive symptoms mediate this relationship, we showed that adjusting for these variables largely attenuated the relationship between increased frequency of restless sleep and less time spent in moderate-vigorous physical activity with individuals with restless sleep much of the time and individuals with restless sleep most of the time respectively performing 2.0% (95% CI: −17.3%, 25.7%) and 1.8% (95% CI: −20.0%, 29.7%) more physical activity (p for trend 0.950).

Discussion

In this study, we evaluated the relationship between the frequency of self-reported restless sleep and objectively measured physical activity in adults with or at high risk for KOA. We demonstrated a significant trend between greater frequency of restless sleep and less time engaged in moderate-vigorous physical activity after adjusting for potential demographic and medical confounders. The difference in physical activity was attenuated by differences in how often participants reported having a lot of energy and the frequency of participants reporting high depressive symptoms.

Previous studies in general adult populations have examined the relationship between sleep quality and physical activity and found a bidirectional relationship: participants with higher levels of physical activity are less likely to report sleep complaints and conversely better sleep efficiency is associated with more daily physical activity.(6, 17) Only one study that we are aware of has examined the relationship between sleep quality and physical activity in individuals with KOA: in contrast to our study, Mesci et. al. did not find an association between self-reported sleep quality (as measured by the Pittsburgh Sleep Quality Index) and physical activity (classified by meeting physical activity guidelines by self-report).(18) Whereas the Pittsburgh Sleep Quality Index evaluates several different sleep components, our study focuses solely on restless sleep. In addition, our study objectively measured physical activity and was analyzed on a continuous scale which is likely more powerful than the self-reported, categorical physical activity classification used by Mesci and colleagues.

Our study demonstrated that depression and energy were important mediators in the relationship between restless sleep and physical activity. Prior studies have shown that increased fatigue is associated with reduced physical activity in individuals with knee or hip osteoarthritis and fatigue.(19) It is likely that participants who reported restless sleep experience significant fatigue. Fatigue and depression may be part of the causal pathway explaining the mechanism by which restless sleep resulted in decreased physical activity. Individuals with major depressive disorder are known to have decreased physical activity compared to individuals without depression.(10) In individuals with KOA, sleep disturbance is known to exacerbate depression in individuals with high levels of pain.(5) It is likely that

increased depressive symptoms and low energy are both part of the causal pathway partially explaining the relationship between restless sleep and decreased physical activity. However, individuals who are physically inactive may experience more restless sleep and low energy and be more vulnerable to depression as a result of low levels of physical activity. Thus the relationships are likely to be bidirectional. Future research should explore if improving sleep quality may help individuals experience less depressive symptoms and have more energy, resulting in more participation in physical activity. Future studies could also more fully evaluate how fatigue and depression mediate the relationship between sleep and physical activity.

Our study had some limitations. Due to log-adjustments for skewed data, we are unable to directly transform the results of the regression analyses back to absolute minutes, limiting our results to percent difference between restless groups. CES-D has not previously been examined as a measure of sleep quality and information regarding sleep duration was unavailable. We are not aware of any studies validating using the SF-12 question as a measure of energy or any studies validating the CES-D using 19 of the 20 questions. Although we adjusted for known confounders (e.g., demographic, medical covariates including depression), some of the differences in physical activity may be explained by residual confounding between the groups. Finally, we were unable to assess the temporal relationship between restless sleep and physical activity given the cross-sectional nature of this analysis. Future studies are needed to better characterize the bidirectional relationship between sleep and physical activity. Strengths of our study include a large cohort with objectively measured physical activity.

In conclusion, we demonstrated a significant relationship between greater frequency of restless sleep and less time engaged in moderate-vigorous physical activity among participants with or at high risk for KOA. Future research is needed to characterize mechanisms of how poor sleep quality might result in less physical activity or vice versa, and to determine if improving sleep quality alone or in conjunction with other interventions can increase physical activity in those with restless sleep.

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Significance and Innovations: (2-4 bullets)

- Physical inactivity is endemic in individuals with knee osteoarthritis, and increasing physical activity has been shown to improve long-term functional status.
- The relationship between sleep and physical activity in individuals with knee osteoarthritis remains unknown.
- This study examining the cross-sectional relationship between self-reported restless sleep and objectively measured physical activity in adults with or at risk for knee osteoarthritis demonstrated a significant trend between greater frequency of restless sleep and less time engaged in moderate-vigorous physical activity.
- Future research should characterize the mechanisms of how sleep disturbance and physical activity are related, and should evaluate if focusing on sleep as part of a multi-targeted intervention results in more sustainable increases in physical activity.

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Table 1

Participant characteristics by self-reported restless sleep during the past week (n=1892).

	Restless sleep during the past week				**P value for trend****
	Rarely/none of the time (<1 day)	Some of the time (1-2 days)	Moderate/much of the time (3-4 days)	Most/all of the time (5-7 days)	
N (%)	751 (39.7%)	841 (44.5%)	168 (8.9%)	132 (7.0%)	-
Age, years	65.4 (9.0)	65.5 (9.0)	63.7 (9.4)	63.0 (9.3)	0.003
Gender: % female	53.9%	55.1%	60.7%	60.6%	0.255
Race: % Caucasian	81.5%	86.0%	84.5%	82.6%	0.108
BMI[a], kg/m^2	28.2 (4.7)	28.4 (4.8)	28.5 (5.4)	29.7 (5.1)	0.011
Normal	25.6%	26.3%	28.6%	15.9%	0.059
Overweight	41.4%	38.4%	33.3%	43.9%	
Obese	33.0%	35.3%	38.1%	40.2%	
K/L[b] grade					
0-1	38.4%	38.8%	44.1%	41.7%	0.477
2-3	52.7%	52.9%	44.1%	50.0%	
4	8.9%	8.3%	11.9%	8.3%	
WOMAC pain[c]	2.1 (2.8)	2.8 (3.4)	3.5 (3.8)	4.6 (4.3)	<.001
Comorbidity[d]					
0	71.9%	71.3%	63.1%	65.9%	0.004
1-2	24.9%	23.2%	27.4%	27.3%	
3+	3.2%	5.5%	9.5%	6.8%	
Depression[e]	3.6%	7.3%	22.6%	40.2%	<.001
Energy level[f]: had a lot of energy					
All of the time	11.5%	3.6%	1.8%	0.0%	<.001
Most of the time	61.7%	58.7%	35.1%	25.0%	
Some of the time	21.4%	27.9%	39.3%	36.4%	
A little of the time	4.5%	7.7%	19.1%	23.5%	
None of the time	0.9%	2.0%	4.8%	15.2%	

	Restless sleep during the past week				P value for trend**
Weekly moderate-vigorous activity minutes, median (interquartile range)*	79 (28-188)	83 (27-192)	77 (22-200)	58 (19.4-142)	0.189

Mean (standard deviation) or column percent reported.

*Medians and interquartile range for weekly moderate-vigorous activity minutes

**Test for trend used a Mantel-Haenszel Chi-square test (1 d.f.) except for race and gender comparisons, which used chi-square test for overall differences, ANOVA for continuous factors age, BMI, and WOMAC pain, and quantile regression for physical activity minutes/week

[a]Body Mass Index (normal <25, overweight 25-30, obese≥30)

[b]Kellgren-Lawrence for severity of knee osteoarthritis

[c]WOMAC: Western Ontario and McMaster University Osteoarthritis Index pain score modified to ask about right and left knee symptoms separately, range 0-20, worse knee reported

[d]Charlson comorbidity index

[e]High Depressive symptoms as defined by modified Center for Epidemiological Studies Depression Scale ≥16

[f]Item from 12-Item Short Form Health Survey

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Table 2

Difference[a] in weekly moderate-vigorous physical activity minutes compared to restless sleep rarely or none of the time (n=1892)

	Rarely/none of the time (<1 day)	Some of the time (1-2 days)	Much of the time (3-4 days)	Most/all of the time (5-7 days)	p for trend
Unadjusted model	Reference	−1.1% (−14.5%, 14.4%)	−14.9% (−33.5%, 9.0%)	**−25.2% (−43.1 %, −1.7%)**	0.019
Adjusted[b] model 1	Reference	−1.5% (−13.2%, 11.7%)	**−23.8% (−38.5%, −5.6%)**	**−36.3% (−49.7%, −19.3%)**	<.001
Adjusted[c] model 2	Reference	4.9% (−7.0%, 18.4%)	−12.4% (−28.7%, 7.7%)	−20.4% (−36.8%, 0.3%)	0.020

[a]Percent difference for each restless sleep category compared to rarely or none of the time.

[b]Model 1: adjusted for age, gender, and race

[c]Model 2: adjusted for model 1 and body mass index, Kellgren-Lawrence grade, Charlson comorbidity index.