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An Actigraphy Study of Sleep and Pain in Midlife Women – The SWAN Sleep Study

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Abstract

Objective—We examined whether women reporting nighttime pain would have more actigraphy-measured evidence for disturbed sleep and report feeling less rested compared to women without nighttime pain.

Methods—Up to 27 consecutive nights of actigraphy and sleep diary data were analyzed from each participant in this community-based study of 314 African-American (n=118), White (n=141),

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and Chinese (n=55) women, aged 48-58 years, who were pre-, peri- or post-menopausal and participating in the Study of Women's Health Across the Nation (SWAN) Sleep Study. Dependent variables were actigraphy-measured movement and fragmentation index, total sleep time, and sleep efficiency, and diary self-report of feeling rested after waking up. All outcomes were fit using linear mixed effect models to examine covariate-adjusted associations between the independent variable, nighttime pain severity, and sleep outcomes.

Results—Higher pain severity scores were associated with longer sleep duration but reduced sleep efficiency and feeling less rested. Women reporting nocturnal vasomotor symptoms had more sleep-related movement and sleep fragmentation, reduced sleep efficiency, and were less likely to feel rested after wakening, regardless of whether they reported pain.

Conclusions—Midlife women who report higher nighttime pain levels have more objective evidence for less efficient sleep, consistent with self-reported less restful sleep. Nocturnal vasomotor symptoms also can contribute to restlessness and wakefulness in midlife women.

Keywords

actigraphy; linear mixed effects model; menopausal transition; pain; sleep

Introduction

Pain, including somatic symptoms such as arthralgias, bodily aches and pains, musculoskeletal pain, and joint pain, is commonly reported by women transitioning through menopause.[1] Individuals with nonmalignant pain conditions commonly report sleep disturbances, with prevalences as high as 50% to 88% in association with chronic pain.[2] In cross-sectional studies, self-reported insomnia is related to pain severity,[2-11] and in longitudinal population-based studies, pain severity is associated with the incidence and/or persistence of insomnia.[12,13] Notably, the literature focuses on chronic pain, yet manifestations of acute and chronic pain differ. Moreover, not every patient with acute pain progresses to persistent/chronic pain, and most sleep complaints resolve when the pain abates.

Wrist actigraphy, a non-invasive method for objectively monitoring sleep-wake patterns,[11,14] can provide unique information regarding temporal interrelations between sleep and pain. Specifically, actigraphy can detect disturbed rest-activity patterns and night-to-night variability in sleep,[15] which may be associated with pain. Thus, actigraphy can be an ecologically valid procedure for assessing longitudinal within-subject sleep-wake patterns. [16,17]

Actigraphy-pain relationships have been studied mainly in individuals with specific conditions, particularly fibromyalgia syndrome (FMS). These studies have been relatively brief, generally 1 week or less, which may not be long enough to detect covariation in sleep and pain. Other studies have averaged actigraphy measures across several nights to examine sleep – pain relationships (eg, [11,18]). Kop et al[19] monitored activity levels and concurrent symptom reports 5 times daily over a period of 5 days. Sleep fragmentation, TST, and sleep efficiency (SE) did not differ significantly between FMS and non-pain control groups, but

average nocturnal activity level was higher and sleep latency was longer in the FMS group. In a week-long daily process study that modeled day-to-day within-person changes in pain and sleep, Tang et al[20] found that presleep pain predicted subsequent poorer sleep efficiency (SE) based on self-report, but not SE based on actigraphy or subjective sleep quality. A PSG study of sleep-related muscle activity in FMS detected disturbances in some measures of sleep continuity and increased muscle activity, but no reductions in SE.[21]

Women are increasingly likely to experience pain symptoms during the menopausal transition.[22] Analyzing data from the Australian Longitudinal Study on Women's Health, Berecki-Gisolf et al[23] observed that, compared with premenopause, women transitioning to peri- and through 7 years post-menopause had higher odds of “often” experiencing painful/stiff joints. However, we are aware of no published data that have examined the association between pain and sleep in women during this life cycle phase that have used repeated nightly objective measures of sleep and controlled for the effects of menopausal stage and vasomotor symptoms, which also can be associated disturbed sleep.

The current analysis focuses on a generally healthy, racially/ethnically diverse cohort of midlife women participating in a multi-site study of sleep during the menopausal transition. Participants wore a wrist actigraph for approximately one month in their home sleep environment to capture sleep patterns during one menstrual cycle. The aim of this analysis was to model night-to-night variation in actigraphic sleep measures and feeling rested in relation to self-reported pain severity during the sleep period. We hypothesized that on nights on which pain was reported, as compared with nights without pain, actigraphy would show more movement during sleep (higher movement and fragmentation index) and more disturbed sleep (less total sleep time, lower sleep efficiency), and women would report feeling less rested after waking up in the morning.

Methods

Study Design and Participants

The Study of Women's Health Across the Nation (SWAN), initiated in 1996, is a multi-ethnic, community-based, cohort study of the menopausal transition. A total of 3,302 women were enrolled at seven sites in the Core SWAN: Boston, MA, Chicago, IL, Detroit area, MI, Los Angeles and Oakland, CA, Newark, NJ, and Pittsburgh, PA. The study design and recruitment of the main cohort have been described in detail.[24] Each site recruited White women and a minority group sample. SWAN cohort eligibility criteria required women to be aged 42-52, premenopausal or early perimenopausal, have an intact uterus and at least 1 ovary, have at least one menstrual period in the previous three months, not be using any sex steroid hormone in the previous three months, and not be pregnant.

The SWAN Sleep Study was a cross-sectional study of sleep patterns over a one-month period, conducted at four of the seven study sites (Chicago, the Detroit area, Oakland, Pittsburgh) from 2003-2005 and included 370 women aged 48-59 years. This sub-cohort included 328 pre- and peri-menopausal and 42 post-menopausal White (all sites), African-American (Chicago, Detroit area, Pittsburgh), and Chinese (Oakland) women; two women did not have a sleep study. Each site's institutional review board approved both the Core

SWAN study and the Sleep Study protocols and all women gave written informed consent to participate. Women were paid for participating in the study.

Eligibility for the Sleep Study was determined prior to and during participants' annual Core SWAN assessment. Efforts were focused on recruiting women who were pre- and peri-menopausal as defined by the SWAN Core Study, but eligibility criteria were relaxed during the final year of the study to allow inclusion of postmenopausal women. Surgically menopausal women (< 1%) and women using hormone therapy but not yet postmenopausal at the annual SWAN Core examination (approximately 23% of the cohort) were excluded; the latter were excluded because use of these products affects bleeding patterns and classification of menopausal status. Exclusion criteria also included factors known to affect sleep, including active cancer chemotherapy or radiation; regular shift work/night shift employment; oral corticosteroid use; regular consumption of more than four alcoholic drinks daily; and noncompliance with Core SWAN procedures (eg, missed more than 50% of annual visits, refused annual visit blood draw).

All Core SWAN participants meeting the eligibility criteria at the four Sleep Study sites were approached regarding participation. Of these, 30% declined to participate in the Sleep Study, mostly because of protocol time burden. As previously reported,[25] Sleep Study participants did not differ markedly from Core SWAN participants at annual visit 05 on self-reported demographic characteristics, health status, depressive symptoms, or sleep quality. Sleep Study participants reported hot flashes slightly less frequently over a 2-week time period preceding Sleep Study participation than did study non-participants ($p<.02$), but frequency of night sweats or cold sweats did not differ.

Procedures and Measures

Data for SWAN Sleep Study participants included five to seven years of hormonal, behavioral, social and psychological measures collected during the 5th through 7th annual Core SWAN visits. Core SWAN data used in this report were from the baseline visit and the closest visit preceding the Sleep Study.

The SWAN Sleep Study protocol was initiated within 7 days of beginning the follicular phase of the menstrual cycle in women who were still menstruating. Sleep data were collected for an entire menstrual cycle or 35 days, whichever was shorter, in order to capture the influence of hormone fluctuation and vasomotor symptoms changes, which vary across the menstrual cycle and may affect sleep architecture or quality over the menstrual cycle. Non-cycling women were scheduled at their convenience.

Measures of sleep described in this report included subjective sleep symptoms, daily sleep diaries, wrist actigraphy, and PSG-assessed apnea-hypopnea index (AHI) and periodic leg movement with arousal index (PLMAI) scores. Menopausal characteristics were assessed by self-report. Diaries were completed twice daily, at bedtime and after awakening (variables described below). PSG sleep studies were conducted in participants' homes during the first 3 days of the protocol (Vitaport-3 [TEMEC VP3] ambulatory PSG monitor; TEMEC Instruments B.V., Kerkrade, Netherlands); see Hall et al[25] for details.

The wrist actigraph (Actiwatch-64 [AW-64]; Philips Respironics, MiniMitter, Bend, OR) was worn concurrently with the completion of sleep diaries to provide a behavioral assessment of participants' habitual sleep. Analyses were limited to actigraphy days 4-30 (27 days) because instrumentation for the concurrent PSG recordings on the first 3 nights may have introduced additional movement during sleep and because data were sparse after 30 days. Analyzable actigraphy data were from 314 women and available for a mean (sd) of 23.1 (5.1) days and a median (IQR; interquartile range = difference between upper quartile and lower quartile) of 26.0 (7.0) days for each woman. A total of 185 women (58.9%) had data for all 27 nights and 292 women (92.9%) had data for ≥15 nights. Actigraphy data were collected in one-minute sampling epochs and sleep-wake variables were calculated using the Actiware Version 5.04 software program time above threshold mode, using medium sensitivity. Bedtimes and rise times recorded in participants' diaries were used to set the parameters for total time in bed in the actigraphy software.

Dependent Variables

Dependent variables were derived from wrist actigraphy and morning sleep diary reports. Three actigraphy variables were defined and computed as follows: (1) Movement and fragmentation index (MFI) is a composite measure of movement and brief (less than one minute) immobility intervals and is expressed as a percentage of the sleep period, with higher values indicating greater restlessness during sleep. (2) Actual sleep time is the amount of time between sleep start and sleep end that is scored as sleep, a measure of total sleep time (TST). (3) Sleep efficiency (SE) is the percentage of time in bed that is scored as sleep, calculated by dividing the actual sleep time by the time in bed (x 100). Pittsburgh Sleep Diary (PghSD)[26]-derived “feeling rested” (FR), is a subjective report of how rested one feels upon waking up in the morning, coded from 0 (not at all) to 4 (extremely).

Independent Variables

Pain measure—The primary independent variable was nighttime pain severity, which was added to the original PghSD, and was measured by waketime diary ratings. Participants were instructed to record every morning the level of pain severity (0 = not at all – 4 = extremely) experienced the previous night. Two response categories (‘3’ [quite] and ‘4’ [extremely]) were combined because together they accounted for only 4% of the responses.

Covariates

Covariate data were obtained from the PghSD and Core SWAN assessments, as indicated below.

Sociodemographics—Age was a continuous variable recorded at the time of the Sleep Study. Race/ethnicity was determined by self-identification as African-American, White, or Chinese. Site was recorded as Chicago, University of California Davis (Oakland), Michigan (Detroit area), or Pittsburgh. Due to heterogeneity within site and race/ethnicity, a variable with 8 categories was created to represent each site and race/ethnicity category (ie, African-American and Chicago, White and Chicago, etc.). Education (a 5-level categorical variable indicating the highest level attained) was obtained from Core SWAN baseline and marital status (a 3-level categorical variable defined as single, separated/divorced/widowed, or

married) was obtained from the most recent Core SWAN visit preceding the Sleep Study assessment.

Menopausal status and use of hormone therapy (HT)—Transition status was determined using bleeding criteria,[27] and participants were classified into one of four categories: (1) premenopausal (no change in menstrual bleeding regularity) or early perimenopausal (menses in the preceding 3 months with an increase in bleeding irregularity), (2) late perimenopausal (menses in the previous 12 months, but not the previous 3 months), (3) postmenopausal (at least 12 months of amenorrhea), or (4) indeterminant status. The latter group consisted of women not yet postmenopausal but reporting any HT use following their last Core SWAN assessment visit preceding Sleep Study participation. The women were categorized as "undetermined" menopausal status because HT use affects bleeding patterns.

Vasomotor and menstrual symptoms—Nocturnal vasomotor symptoms (nVMS) were assessed using the PghSD.[26] Each morning, participants recorded the frequency and severity of three symptoms (cold sweats, hot flashes or flushes, night sweats) that they may have experienced during the previous night. Nocturnal VMS were coded as a binary variable, yes ('1' if at least 1 of the 3 symptoms)/no ('0' if none of the symptoms). If data were missing for only one of the three symptoms, the nVMS score was based on the two available symptoms, but if data were missing for two symptoms, we scored that night's VMS as 'missing' unless the one available symptom recorded was present. Nocturnal menstrual symptoms/cramps also were coded as present or absent.

Bodily Pain (SF-36 BP) over the Core SWAN visits—To index each participant's pain level over the years prior to the Sleep Study, we computed the median SF-36 BP score for each woman based on all of her bodily pain percentile scores. The BP subscale of the SF-36, a widely used self-report measure of health-related quality of life,[28] consists of two questions that assess the level of pain severity and the extent to which pain has interfered with function. It was administered in the Core SWAN study at baseline and at follow-up visits 1-4, 6 and 8. The original coding algorithm was used, in which raw scores are transformed to a percentile score (range = 0–100), with higher scores indicating less pain. The subscale has good reliability and construct validity,[29,30] and norms have been published.[31,32]

Body mass index (BMI)—BMI was a continuous measure computed as measured weight in kilograms/height in meters squared) at the nearest Core SWAN visit preceding the Sleep Study.

Antidepressant, sleep, and pain medication—Daily medication use (prescription and over-the-counter), recorded at Sleep Study protocol inception and in the PghSD, was coded according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification.[33] For these analyses, concurrent use of medications for pain, sleep or depression from the following drug classes was coded: antiinflammatory/antirheumatic products, non-steroids (M01A), muscle relaxants, centrally acting agents (M03B), opioids (N02A), other analgesics and antipyretics (N02B), antimigraine preparations (N02C),

antiepileptics (N03A), anxiolytics (N05B), hypnotics and sedatives (N05C), antidepressants (N06A), psycholeptics and psychoanaleptics in combination (N06C), and antihistamines for systemic use (R06A).

Polysomnogram sleep disturbances—AHI and PLMAI were obtained from the PSG performed on the first actigraphy night, and both indices were scored according to standard criteria.[34,35]

Actigraphy recordings—Actigraphy study night and whether each individual actigraphy day was a weekday or weekend were included as time-varying covariates.

Data Analysis

A total of 331 women completed actigraphy data collection. Because concurrent PSG instrumentation during the first 3 nights could interfere with a “usual night's sleep”, we excluded these nights from the analysis, leaving 327 women eligible for this analysis (4 had data on only these 3 days). Although there was no reported equipment failure, 13 women were excluded from this analysis because the majority (> 50%) of their observed values for fragmentation index was zero. Because this is not a valid value for a participant wearing a functioning actigraph, it was presumed that they were not wearing the device. Thus, 314 women contributed longitudinal data for the analysis, for a total of 7472 nights (∼23.8 nights per woman).

Univariate statistics, including means, standard deviations, medians and interquartile ranges (IQR) were computed for continuous variables and frequencies were determined for categorical variables. Variables with highly skewed distributions were transformed or categorized. To reduce the skewness, square root transformation was conducted for the movement and fragmentation index (MFI). Sleep efficiency was treated as dummy variables (≥85% or <85%).

Linear mixed effect modeling (SAS, Proc Mixed) with random intercept and slope was used to evaluate the associations between self-reported nighttime pain severity scores and continuous variables (MFI, TST; data presented as β (SE)) while generalized linear mixed effect modeling (SAS, Proc GLIMMIX) with random intercept and slope was used to model the effects of self-reported nighttime pain on the dichotomized feeling rested (FR) in morning (moderate/quite a bit/extremely vs not at all/a little) and dichotomized sleep efficiency (SE) (≥85% vs <85%) (data presented as OR (95% CI)). We chose this SE cut point because <85% is below the lower limit of the normative range for middle-aged women.[36] The mixed effects modeling approach combined the cross-sectional (between women) and longitudinal (within women) estimates of association while correcting those estimates for multiple and correlated measures within women. All models used the auto-regressive AR(1) structure except for the model with dichotomized sleep efficiency and feel rested as the outcome, which used the unstructured covariance matrix structure. The models were evaluated using Akaike information criterion (AIC) and likelihood ratio statistics.

Three mixed-effects regression models were fit for each actigraphy outcome. The first (“unadjusted”) model analyzed the pain severity variable on sleep outcomes. In the second

("forced covariates") model the following covariates were added: study site and race/ethnicity, subject age (at beginning of Sleep Study), menopausal status, nVMS, and SF-36 BP score. In the third ("fully adjusted") model, BMI, AHI, PLMAI, weekend/weekday actigraphy night, medications, educational level, and marital status were added. Sleep study night for each participant was included in the fully adjusted model to capture night-to-night variations.

All analyses were conducted in SAS (SAS, version 9.3, Cary, NC). Two-tailed p-values < 0.05 were considered statistically significant.

Results

Sample characteristics

Table 1 shows characteristics for the 314 participants included in this analysis, as well as comparisons between the group that reported pain on at least one night (n = 211, 67%) and the group that reported no pain on any night (n = 103, 33%). These two groups were similar on most characteristics, except for menopausal status (higher percentages of pre- and perimenopausal in no pain group, p = 0.02), difficulty paying for basics (higher percentage reporting 'not very' in no pain group, p < 0.05), and BMI (greater in pain group, p = 0.01). A larger percentage of women in the pain group reported taking pain medication (68% of the pain group, 45% of the no pain group; p < 0.0001). Those who reported taking pain medication averaged 12.1 (sd=10.0) days of use. A larger percentage in the no pain group reported taking medication for sleep during the study (p = 0.04). The mean SF-36 BP percentile score was 72.2 (sd=18.6; N = 298), similar to published age- and sex-standardized scale scores,[31,32] but the median score was lower (ie, more pain) in the pain group (p < 0.0001). Women reported nVMS on a median of 9 (IQR=15) nights, and the pain and no pain groups did not differ significantly on the median number of nights with nVMS.

Covariates

Aside from the site-race variable, the only covariate that was significantly associated with at least 3 of the sleep-related outcome measures in the fully adjusted analyses was nighttime VMS. In fully adjusted models, nights on which VMS were reported were associated with higher odds of motor restlessness, and lower odds of SE ≥ 85% and of feeling moderately, quite or extremely rested in the morning. Other statistically significant associations (p < 0.05) between covariates and actigraphy or PghSD outcomes were as follows. Compared with married women, single women had a significantly higher movement and fragmentation index and lower odds of SE ≥ 85%. PLMAI and taking antidepressant medication also were associated with a higher MFI, and sleep on weekends and use of sleeping medication were associated with a longer TST, 17.5 and 17.6 minutes, respectively. Reporting less past bodily pain (SF-36 BP score) and weekend sleep both were associated with a higher odds of feeling "moderately," "quite" or "extremely" rested in the morning.

Pain severity and actigraphy-assessed sleep measures

Associations between self-reported nighttime pain severity scores and the continuous sleep variables (MFI, TST) are shown in Table 2A, and the effects of self-reported nighttime pain

on the dichotomized “feeling rested upon awakening” (FR) and sleep efficiency (SE) variables are shown in Table 2B. As expected, the pain severity parameter estimates (beta coefficients) for the MFI outcome were larger for each successively greater pain level, but neither the unadjusted nor the adjusted models showed statistically significant associations. TST was significantly associated with nighttime pain, but in the opposite direction expected – women reporting nighttime pain averaged 5.2 -12.1 minutes more sleep than women reporting no pain. In the fully adjusted model, pairwise comparisons with ‘no pain’ showed that both ‘slight’ and ‘moderate’ pain were associated with more sleep time (6.7 minutes, $p < .05$, and 12.1 minutes, $p = .001$, respectively).

SE, an estimate of the percentage of time in bed actually spent sleeping, was significantly associated with nighttime pain in the fully adjusted model ($p = .02$). For successively higher levels of nighttime pain, the odds ratios for SE ≥ 85% were monotonically lower. In the fully adjusted model the pairwise comparison was significant between nights with ‘quite/ extreme’ pain versus none (OR = .51, 95% CI = .31, .82; $p < .006$), indicating that nights with extreme pain were associated with a 49% reduction in the odds of sleeping at least 85% of the time spent in bed compared with nights with no pain.

In unadjusted and adjusted models, the effects of pain severity on FR were reflected in the sleep efficiency data, and the overall P values were highly significantly related to FR ($p < .0001$). On average, the no pain group felt at least moderately well rested on 2.3 nights more than the pain group (19.1 [SE=0.7] vs 16.8 [SE=0.5], $p < 0.006$). In all models, higher levels of nighttime pain severity were related to significantly lower odds (29 – 72% lower in fully adjusted models) of feeling well-rested on awakening in the morning.

Discussion

Experiencing pain during sleep may be a relatively common experience for middle-aged women, as about two-thirds of our sample reported at least slight pain or discomfort on at least one actigraph-recorded night, and was reported on 24% of the 7,472 nights. To our knowledge, this is the first study to examine associations between night-to-night pain self-reports and actigraphy-assessed sleep disturbances in community-dwelling middle-aged women. Linear mixed model analysis is a useful approach for examining variability in temporal patterns of sleep measures across multiple nights within individuals as well as for comparing differences between individuals.[37] After adjusting for other variables that could influence sleep in midlife women, pain severity was associated with two components of sleep, a lower percentage of time in bed spent asleep (lower SE) and longer sleep duration (TST) in women reporting “slight” or “moderate” pain. Subjectively, women who reported higher levels of pain severity felt less rested on awakening in the morning.

Pain can produce repetitive arousals and disrupt the continuity of sleep, resulting in sleep deprivation, which can heighten pain perception the next day.[14,38-40] However, we did not find differences in our actigraphy-assessed measure of restlessness (MFI) during sleep, nor did we find a significant TST effect in the severe pain group as we did in the ‘slight’ and ‘moderate’ pain severity groups. This non-linear relationship between pain severity and TST, as well as the unexpectedly and perhaps paradoxically significant association in the

direction opposite to what we had hypothesized, raises a question regarding whether women with milder pain stay in bed longer trying to sleep despite pain, thereby accumulating more sleep time but at the expense of spending a disproportionately greater time in bed not sleeping, and hence a lower SE. Another consideration is that actigraphy can overestimate sleep when someone is lying in bed awake, so higher actigraphy TST on pain nights may also reflect longer time lying quietly awake. Therefore, despite our surprise, the result is plausible and should be explored in future studies.

Others have studied the sleep – pain relationship using both actigraphy and self-report measures. Using an analytic approach similar to ours, O'Brien et al[18] examined daily intra-individual variations in sleep and pain over a 2-week period with hierarchical linear modeling to compare “good” and “poor” sleepers with chronic pain. However, they analyzed an “average daily pain rating,” which combined daytime and nighttime pain measures, and examined conventional actigraphy measures of sleep duration and continuity but not movement/restlessness indices. In insomniacs with chronic pain, Wilson et al[11] observed that pain severity was associated only with sleep diary measures and suggested that actigraphy could be insensitive to the magnitude of the sleep disturbance in individuals with high-severity pain if they were immobile during periods of extended wakefulness. However, only 2 nights of actigraphy were recorded. Our middle-aged women were not selected for sleep or pain problems as were O'Brien et al's and Wilson et al's samples, which included younger groups of men and women with chronic musculoskeletal pain.

Determining the causal role of the various factors that can influence sleep and pain is challenging.[41] In our sample, we statistically controlled for a number of factors that may be associated with pain and sleep disturbance in midlife women, including sociodemographics, menopausal symptoms, polysomnographic measures of common sleep disturbances (sleep apnea, periodic leg movements in sleep), and medication use. Although we had no information on specific acute/chronic pain conditions, we controlled for history of bodily pain using participants' SF-36 BP scores obtained annually for up to six years prior to the Sleep Study. Women reporting nighttime pain tended to report more severe and impairing pain in previous years (Table 1). This indicator of pain chronicity also was significantly associated with feeling (less) rested in the morning.

A number of other factors also were associated with the sleep outcomes. As might be expected in women traversing the menopausal transition, nVMS was significantly associated with motor restlessness in bed (ie, MFI), and less likely to have good sleep efficiency or feeling at least moderately rested in the morning. The effect of nVMS on sleep-related restlessness was significant even after controlling for the effects of PLMAI, which also involves motor activity during sleep and was significantly associated with MFI.

Marital status also correlated with the actigraph measures of MFI and SE. Consistent with another analysis from this sample,[42] single women had significantly more nighttime movement/restlessness and were less likely to sleep at least 85% of the night in bed than did married women. However, we hesitate to speculate on its implications because we do not know what proportion of single or married/cohabiting women slept alone in our cohort.

Nights that preceded a weekend were significantly associated with actigraphy- measured longer sleep duration (TST) and subjectively feeling rested, but not with sleep efficiency or movement/restlessness (MFI). Together, these observations seem to suggest that the subjective benefit of "sleeping in" on weekends may extend to lengthening the time in bed but not necessarily to how efficiently one sleeps.

Among the medication groups examined, antidepressant use was associated with more restlessness in bed and sleep medication was associated with longer sleep duration. The latter finding is consistent with their advertised goal of treatment, and the former has been reported to be due to the pharmacologic effects of certain agents in this group of medications on processes governing sleep and wakefulness, such as the serotonin reuptake inhibitors.[43,44]

Limitations of our study are related to the lack of information on the acute/chronic nature, specific type, and location of pain, as well as the known limitations of actigraphy.[15,17] Nevertheless, actigraphy is the most convenient and ecologically valid means to objectively measure habitual sleep. Because our sample was limited to middle-aged women, it remains unclear whether the results can be generalized to men or other age groups. Also, we acknowledge that despite the statistically significant associations for pain and VMS with sleep outcomes, both accounted for little variance in these measures (R^2 for pain, 0.18-1.57%; for VMS, 0.10-0.20%). Nevertheless, in the case of pain, even small influences could have a meaningful impact on public health since an estimated 100 million persons in the United States are affected by chronic pain.[45] VMS (especially severe VMS) can affect sleep, and sleep problems increase across the menopausal transition. However, other factors, such as mood, may account for associations between VMS and sleep.[46-48] Finally, due to the lack of information about the onset or chronology of pain or sleep symptoms we could not examine the bidirectionality hypothesis in regard to sleep – pain relationships in this cross-sectional design. Our approach was to model night-to-night variation in actigraphic sleep measures as a function of self-reported nighttime pain over the course of one menstrual cycle. Experimental models have shown that sleep and pain interact in complex ways, suggesting that the relationship can be bidirectional, but perhaps not in a reciprocal relationship such as has been described.[20,41]

This study has significant and unique strengths. First, we studied a large community sample of women unselected for the presence of pain or sleep problems to enhance the generalizability of the results. Second, we analyzed actigraphy data collected for up to 27 consecutive nights, longer than any other study of sleep – pain relationships, and taking inter- and intra-individual variability into account. Third, our large sample and the large number of observations afforded by this longitudinal data analysis provided sufficient statistical power to control for the effects of a number of covariates known or suspected to be associated with sleep and/or pain.

Conclusions

In conclusion, we found that midlife women who reported more severe pain levels demonstrated more actigraphy-assessed sleep disturbance and subjectively less restful sleep.

However, pain is just one of a host of factors that disturbs sleep. Thus, complaints of sleep problems in patients with pain require a thorough clinical assessment of other possible contributing factors, particularly if controlling pain does not improve sleep.

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Table 1

Sample Characteristics (N = 314)[a]

Characteristic	Total	Any Pain[b]	No Pain[b]	P value < 0.05[c]
	N = 314	N = 211	N = 103	
Age in years, mean (sd)	51.6 (2.1)	51.7 (2.1)	51.6 (2.1)	
Race/Ethnicity, N (%)				
African American	118 (37.6)	80 (37.9)	38 (36.9)	
Chinese	55 (17.5)	34 (16.1)	21 (20.4)	
White	141 (44.9)	97 (46.0)	44 (42.7)	
Site, N (%)				
Chicago	71 (22.6)	48 (22.8)	23 (22.3)	
Davis/Kaiser	100 (31.8)	64 (30.3)	36 (35.0)	
Michigan	64 (20.4)	43 (20.4)	21 (20.4)	
Pittsburgh	79 (25.2)	56 (26.5)	23 (22.3)	
Marital status, N (%)				
Married	195 (62.1)	127 (60.2)	68 (66.0)	
Single	50 (15.9)	32 (15.2)	18 (17.5)	
Separated/widowed/divorced	69 (22.0)	52 (24.6)	17 (16.5)	
Education, N (%)				
< High School	7 (2.2)	4 (1.9)	3 (2.9)	
High school	43(13.7)	31 (14.7)	12 (11.7)	
Some college	122(38.9)	86 (40.8)	36 (35.0)	
College degree	76(24.2)	48 (22.8)	28 (27.2)	
Post College	66(21.0)	42 (19.9)	24 (23.3)	
Menopausal status, N (%)				0.0212
Pre-/Early Perimenopausal	196 (62.4)	125 (59.2)	71 (68.9)	
Late Perimenopausal	64 (20.4)	40 (19.0)	24 (23.3)	
Postmenopausal (includes 2 hormone users)	37 (11.8)	31 (14.7)	6 (5.8)	
Undetermined (non-postmenopausal hormone users)	17 (5.4)	15 (7.1)	2 (1.9)	
Difficulty paying for basics, N (%) (N=275)				0.0496
Not very	202 (73.5)	124 (68.9)	78 (82.1)	

Characteristic	Total	Any Pain[b]	No Pain[b]	P value < 0.05[c]
Somewhat	60 (21.8)	45 (25.0)	15 (15.8)	
Very	13 (4.7)	11 (6.1)	2 (2.1)	
Medical comorbidities, N (%), (N=310)				
0	156 (50.3)	100 (47.4)	56 (56.6)	
1	84 (27.1)	59 (28.0)	25 (25.2)	
2 or more	70 (22.6)	52 (24.6)	18 (18.2)	
Body mass index, kg/m^2 median (IQR)	27.9 (9.6)	28.2 (11.5)	26.6 (8.0)	0.0120
Nights with nVMS, median (IQR)	9 (15)	10 (14)	5 (15)	
Apnea + hypopnea index, per hour of sleep, median (IQR)	5.4 (7.2)	5.4 (7.4)	5.0 (5.6)	
Periodic leg movement index (movements with arousal), per hour of sleep, median (IQR)	2.0 (3.9)	2.0 (4.2)	2.0 (3.5)	
SF-36 Bodily Pain Score over previous years, median (IQR), (N= 298)	74 (22)	72 (23)	84 (12)	<0.0001
Took at least 1 Sleep Medication during study, N (%)	75 (23.9)	50 (23.7)	25 (24.3)	0.0423
Took at least 1 Antidepressant Medication during study, N (%)	40 (12.7)	26 (12.3)	14 (13.6)	
Took at Least 1 Pain Medication during study, N (%)	189 (60.2)	143 (67.8)	46 (44.7)	<0.0001

Abbreviations: N, number; nVMS, nocturnal vasomotor symptoms; sd, standard deviation; IQR, interquartile range; SF-36 BP, SF-36 Bodily Pain score.

[a] N is specified if not equal to 314 due to missing data. Percentages are calculated after excluding participants with missing data. Columns may not sum to 100% due to rounding.

[b] "Any pain" was defined as reporting nighttime pain/discomfort in the sleep diary on at least one actigraph-recorded night during the whole study; "No pain" was defined as reporting no nighttime pain/discomfort in the sleep diary on any actigraph-recorded night during the whole study.

[c] P values: Chi-square test for categorical variables; non-parametric one-way analysis for medians (BMI, SF-36 Bodily Pain Score).

Table 2

Effect of self-reported nighttime pain severity (4 categories) on Actigraphy Sleep and Sleep Diary Measures: N=314

Table 2A: Continuous outcomes using linear mixed effect models

Actigraphy utcome measures	Independent Night Pain Severity (Reference: no pain)[d]	Model 1 (Unadjusted)[a]		Model 2 (Forced Covariates)[b]		Model 3 (Fully Adjusted)[c]	
		β (SE)	P	β (SE)	P	β (SE)	P
Square root of Movement and fragmentation index (MFI)	Slight	0.1091 (0.0542)	0.0442	0.0940(0.0542)	0.0827	0.0908(0.0542)	0.0939
	Moderate	0.0749(0.0598)	0.2105	0.0486(0.0600)	0.4181	0.0505(0.0600)	0.4002
	Quite/Extremely	0.1441(0.0882)	0.1023	0.0978(0.0884)	0.2685	0.0932(0.0884)	0.2921
		Overall P (F test) for Pain = 0.1134		Overall P (F test) for Pain = 0.2943		Overall P (F test) for Pain = 0.3264	
Actual sleep time (Total sleep time, TST)	Slight	6.3548(3.3712)	0.0595	6.0915(3.3746)	0.0711	6.6592(3.3543)	0.0472
	Moderate	11.782(3.7191)	0.0015	11.8873(3.7374)	0.0015	12.0505(3.7140)	0.0012
	Quite/Extremely	4.6228(5.4695)	0.3980	5.2743(5.4942)	0.3371	5.2227(5.4636)	0.3392
		Overall P (F test) for Pain = 0.0109		Overall P (F test) for Pain = 0.0116		Overall P (F test) for Pain = 0.0082	

Table 2B: Odds ratio for “Sleep Efficiency ≥85%” and “Feel Rested in the Morning,” with “No Nighttime Pain” as the reference group using generalized linear mixed models; N = 314

Actigraphy outcome measures	Independent Night Pain Severity (Reference: no pain)[d]	Model 1 (Unadjusted)[a]		Model 2 (Forced Covariates)[b]		Model 3 (Fully Adjusted)[c]	
		Odds Ratio(95% CI)	P	Odds Ratio(95% CI)	P	Odds Ratio(95% CI)	P
Dichotomous Sleep efficiency (SE)[e]	Slight pain	0.8042(0.6157,1.0504)	0.1097	0.8156(0.6245,1.0652)	0.1345	0.8222(0.6296,1.0738)	0.1506
	Moderate pain	0.7278(0.5447,0.9726)	0.0317	0.7604(0.5686,1.0168)	0.0647	0.7703(0.5758,1.0306)	0.0789
	Quite/Extreme pain	0.4332(0.2666,0.7039)	0.0007	0.5338(0.3313,0.8602)	0.0099	0.5057(0.3127, 0.8180)	0.0055
		Overall P (F test) for Pain = 0.0025		Overall P (F test) for Pain = 0.0274		Overall P (F test) for Pain = 0.0205	
Dichotomous Feel rested in morning[f]	Slight pain	0.7109(0.5511, 0.9170)	0.0086	0.7161(0.5549, 0.9240)	0.0102	0.7097(0.5497, 0.9163)	0.0085
	Moderate pain	0.4901(0.3754, 0.6398)	<0.0001	0.5243(0.4012, 0.6850)	<0.0001	0.5179(0.3959, 0.6775)	<0.0001
	Quite/Extreme pain	0.2716(0.1836, 0.4018)	<0.0001	0.2896(0.1953, 0.4293)	<0.0001	0.2870(0.1933, 0.4261)	<0.0001
		Overall P (F test) for Pain < 0.0001		Overall P (F test) for Pain < 0.0001		Overall P (F test) for Pain < 0.0001	

Abbreviations: β, unstandardized beta estimate; SE, standard error; AHI, apnea+hypopnea index; BMI, body mass index; nVMS, nocturnal vasomotor symptoms; PLMAI, periodic leg movements with arousal; SF-36 BP, SF-36 bodily pain score

[a]Model 1 (“unadjusted”): β coefficient or Odds Ratio for the pain severity variable. Actigraphy variable transformations: MFI – square root transformation; SE – dichotomized; TST (Total Sleep Time) – not transformed; Feeling Rested – dichotomized.

[b] Model 2 (“forced covariates”): β coefficients and Odds Ratios were adjusted for age at beginning of Sleep Study, study site & race/ethnicity, menopausal status, nighttime vasomotor symptoms, SF-36 bodily pain score, and sleep study night {countc}. These covariates also are included in Model 3.

[c] Model 3 (“fully adjusted”): β coefficients and Odds Ratios were adjusted for the covariates in model 2, plus education, marital status, BMI, AHI, PLMAI, night preceded a weekend (weekend indicator), and sleep, antidepressant and pain medications.

[d] Nighttime Pain Severity: 0=not severe at all (Reference category); 1=slightly; 2=moderately; 3/4=quite/extremely.

[e] Probability of SE≥85% is modeled.

[f] Feeling Rested: 0=not at all/1=a little versus 2=moderately/3=quite a bit/4=extremely (Reference category: probability of being rested (mod/quite a bit/Extremely) is modeled).