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# Opioid use, pain intensity, age and sleep architecture in patients with fibromyalgia and insomnia

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## 1. Introduction

Approximately 80% of adults with chronic widespread pain experience insomnia [1]. Although opioids are commonly prescribed to treat pain and facilitate sleep, they are associated with adverse side effects [e.g., respiratory depression, physical dependence [22]], and there is a lack of evidence showing they improve chronic pain [5] or sleep [19]. Thus, further evaluation of opioid effects on physiological sleep, particularly in chronic pain populations such as Fibromyalgia, is warranted.

Few studies have examined opioid effects on sleep, with most studies employing small samples of healthy/non-pain participants. For instance, in healthy adults, opioids reduced deep/slow wave sleep (SWS; stages-3/4) and increased lighter stage-2 sleep [7; 25]. Opioid use also decreased amounts of rapid eye movement (REM) sleep in healthy younger adults without pain [25]. Collectively, these studies suggest that opioid use disrupts sleep architecture in healthy samples.

While some findings suggest associations between opioid use and improved sleep in chronic pain patients [29], most link opioids to sleep disruption [4]. In burn injury patients, opioid use was associated with more fragmented sleep assessed using actigraphy [21]. Similarly, a feasibility study on chronic back pain patients [23] found that higher doses (>100mg) were associated with increased stage-2 and decreased SWS/REM sleep. However, small sample sizes preclude strong conclusions regarding the impact of opioid use on sleep architecture in patients with chronic pain. In particular, the effect of opioid use and dosage on sleep assessed using polysomnography (PSG) is not established.

Opioids are thought to disrupt sleep due to their interaction with receptors and neurotransmitters involved in regulation of sleep/wake states [4; 15; 30; 31]. This is particularly problematic for Fibromyalgia patients, as long-term opioid use may exacerbate

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sleep architecture disturbance, which in turn may only promote pain symptoms [24]. Thus, it is critical to assess opioid-related effects on physiological sleep and the impact of other patient-specific factors on this relationship. Three potential moderators of the opioid/sleep association include opioid pain intensity, dosage, and age. We previously found that opioid use, relative to non-use, was associated with longer self-reported sleep onset latency (SOL) in patients with Fibromyalgia and insomnia, but only in patients reporting less pain [17]. We also found that higher opioid dosage predicted greater magnitude of discrepancies between self-reported/actigraphic SOL and sleep efficiency, and the direction of discrepancy depended on age [6].

The goal of this study was to assess associations between commonly prescribed oral opioid use/dosage on PSG-assessed sleep in adults with Fibromyalgia and insomnia. We hypothesized that opioid use would be associated with decreased SWS (stage-3/4) and REM sleep and increased lighter sleep (stage-1/2), and these effects would be more evident with increasing dosage. We also hypothesized that opioid use would be associated with longer SOL and wake after sleep onset (WASO), reduced total sleep time (TST), worse SE, and this would be exacerbated by increasing dosage. Given prior research documenting effects of age and pain on opioid-related associations with behavioral sleep, we explored whether opioid use/dosage interacted with age and pain intensity to predict sleep outcomes.

## 2. Methods

### 2.1. Participants

Participants were recruited as part of the baseline assessment of a parent clinical trial investigating efficacy of cognitive behavioral therapy for insomnia in Fibromyalgia (NCT02001077; PI: McCrae) [16]. During screening, participants ($N$=235) reported either a clinical diagnosis of Fibromyalgia or met criteria for Fibromyalgia during screening (widespread pain in 4 body quadrants that has persisted for a duration of 3 months or greater, and no indication of other disorder that may cause the chronic pain [33]). During screening, participants also reported symptoms of insomnia (i.e., answered “yes” to the question “are you currently experiencing difficulty with your sleep at night” and reported >30 minutes of SOL or WASO at least 3 days/week for at least 6 months as well as daytime dysfunction due to insomnia in mood, cognition, social/occupational functions). During screening, none of the participants reported symptoms or diagnosis of sleep apnea, or use of an oral appliance or Continuous Positive Airway Pressure (CPAP) device for sleep apnea. All procedures were approved by the University of Florida Institutional Review Board. Data were collected at the University of Florida in Gainesville, FL, and the surrounding area from February 2009 to August 2014.

### 2.2. Polysomnography Recording

To obtain physiological measures of sleep, participants completed one night of ambulatory PSG recording (using a 25-channel AURA Portable Recording System, Grass Technology) in their own homes. Consistent with ambulatory PSG recommendations [3], monitoring consisted of 10 electroencephalography (EEG) measures (F2, C2, O2, ground, reference, M1, M2), 2 electro-oculography (EOG), and 3 chin electromyography (EMG) measures in

standard placements [10]. PSG monitoring also included respiratory inductance plethysmography (thoracic & abdominal effort), oximeter application (pulse & oxygen saturation), electrocardiogram (ECG), right and left anterior tibialis EMG, oral-nasal airflow thermocouple, and nasal cannula pressure transducer. PSG records were scored by a registered polysomnographic technologist, according to standardized scoring procedures as described in the Sleep Heart Health Study [10]. The following objective sleep outcomes were computed: SOL, WASO, TST, sleep efficiency (SE), arousal index, % Stage 1 sleep, % Stage 2 sleep, % Stage 3 and 4 sleep (slow wave sleep, SWS), % rapid eye movement sleep (REM), and the apnea/hypopnea index (AHI).

### 2.3. Medication and Pain Ratings

Participants completed sleep diaries daily during the 14-day baseline portion of clinical trial, and recorded (yes/no) whether they used sleep medications or prescription oral opioid medication. Medication names and dosages were recorded. Consistent with previous studies [14], milligrams of opioids were converted into the lowest recommended dosage units per day (LRD; e.g., codeine: 15mg = 1; 30mg = 2) using values in the Physician's Desk Reference [27]. On daily diaries, participants also recorded their level of evening pain intensity on a 0 (no pain at all) to 100 (worst pain imaginable) scale, with higher scores representing worse pain intensity.

### 2.4. Statistical Analyses

Multiple linear regressions were carried out using the PROCESS macro [9] in SPSS (Version 25). Criterion variables included PSG-assessed sleep parameters: SOL, WASO, TST, SE, % Stage 1, % Stage 2, % SWS, % REM. Separate analyses were carried out for models including either opioid use (dichotomous variable coded as opioid users vs. non-users variable) or average LRD amongst opioid users. Other predictor variables in the models included: age, average evening pain intensity ratings, interaction between opioid use/dosage and age, and interaction between opioid use/dosage and evening pain ratings. All analyses controlled for use of sleep medication (dichotomous yes/no variable). Given research documenting associations between opioids and sleep-disordered breathing [28], all analyses also controlled for AHI. Significant interactions were clarified by calculating simple slopes of the association between opioid use/dosage and PSG outcomes at values 1 standard deviation (SD) above and below the mean of the moderator variable. In these analyses, age was characterized as younger adults (1 SD below mean age, ~40 years), middle-aged adults (~52 years) and older adults (1 SD above mean age, ~64 years). Pain intensity was characterized as low pain (1 SD below mean pain rating, ~41), average pain (~58), and high pain (1 SD above mean pain rating, ~75).

## 3. Results

### 3.1. Participant Characteristics

Participant demographics and descriptive statistics for sleep, pain, and medications, provided in Table 1. A total of 193 participants ($M_{age}$=51.70, $SD$=11.73) provided complete data for predictor and outcome variables and were included in the full sample opioid usage analyses.

A total of 65 participants (34%) participants reported using opioids ($M_{age}$=52.75, $SD$= 11.27) across the 14 days of baseline and were included in analyses regarding opioid dosage.

## 3.2. Multiple regression

**3.2.1. Opioid use—**Models evaluating opioid use (vs. non-use) as a predictor are shown in Table 2. Opioid use was associated with longer SOL, greater % stage 2 sleep, and reduced % SWS. However, opioid use interacted with age to predict SOL, and this interaction accounted for 2% unique variance in SOL. Specifically, opioid use was associated with longer SOL for older ($B$ = 35.46, SE= 11.20, $p$ = .002) and middle-aged adults ($B$ = 21.89, SE= 8.66, $p$ = .01), but was not associated with SOL in younger adults ($B$ = 5.49, SE= 11.84, $p$ = .64). Opioid use was not associated with WASO, TST, SE, arousal index, % stage 1 sleep, or % REM sleep.

**3.2.2. Opioid dosage—**Models with opioid dosage (amongst opioid users, $n$ = 65) are shown in Table 3. Opioid dosage interacted with age to predict SOL, and this interaction accounted for 9% of unique variance in SOL. Specifically, higher dosage was associated with longer SOL for older adults ($B$ = 34.42, SE= 12.84, $p$ = .01), whereas this association was not observed for middle-aged ($B$ = 12.59, SE= 9.60, $p$ = .20) or younger adults ($B$ = −20.74, SE= 16.03, $p$ = .20). Similarly, opioid dosage interacted with age to predict SE, and this interaction accounted for 7% of the unique variance in SE. Specifically, higher dosage was associated with worse SE for older adults ($B$ = −6.40, $SE$ = 2.68, $p$ = .02), whereas this association was not observed for middle-aged ($B$ = −2.48, $SE$ =2.01, $p$ =.22) or younger adults ($B$ = 3.50, $SE$ = 3.35, $p$ = .30). Additionally, opioid dosage interacted with pain intensity to predict % SWS, accounting for 15% of unique variance in % SWS. Specifically, for individuals with lower pain, higher opioid dosage was associated with reduced % SWS ($B$ = −5.47, SE= 2.02, $p$ = .009). For individuals with high pain intensity, higher opioid dosage was associated with increased % SWS ($B$ = 3.71, SE= 1.76, $p$ = .04). Opioid dosage did not predict % SWS for patients with average/moderate pain intensity ($B$ = −1.01, SE= 1.26, $p$ = .43). Opioid dosage also interacted with pain intensity to predict arousal index, accounting for 7% of the unique variance. Specifically, for individuals with lower pain, higher opioid dosage was associated with greater arousal index ($B$ = 3.10, $SE$ = 1.15, $p$ = .01), whereas opioid dosage was not associated with arousal index for individuals with average/moderate pain intensity ($B$ =1.32, $SE$=.72, $p$ = .07) or high pain intensity ($B$ = −.47, $SE$ = 1.00, $p$ = .64). Opioid dosage was not associated with WASO, TST, % stage 1 sleep, % stage 2 sleep or % REM sleep.

## 3.3. Exploratory Analyses

Although AHI was controlled for in all analyses, and exerted no independent effect on sleep architecture results in the present sample (see Tables 2 and 3), we conducted additional exploratory analyses to further examine the potential impact of opioids on sleep disordered breathing. We computed the odds ratio for opioid use and risk of exhibiting sleep apnea (i.e., meeting criteria for sleep apnea as outlined in Table 1). The odds ratio was 1.81 (95% CI 0.53–6.15). As the 95% CI included the neutral value of 1, this suggests that opioid use does not increase risk of sleep disordered breathing in this sample.

## 4. Discussion

This study examined associations between commonly prescribed oral opioid usage/dosage and physiological sleep outcomes in adults with Fibromyalgia and insomnia. Data suggest that opioid use is associated with longer SOL among middle-aged and older adults and disruptions to sleep architecture across age groups. Opioid dosage was also associated with longer SOL among older adults. However, the beneficial versus detrimental effects of opioid dose on slow-wave “deep” sleep depended on self-reported pain intensity.

Hypotheses that opioid use would be associated with reduced deep and REM sleep and increased lighter-stage sleep were generally supported. Results were mostly consistent with studies in healthy adults, which found associations between opioid use and reduced SWS/increased lighter-stage sleep [7; 25]. However, unlike results from other studies in healthy adults [25] and patients with chronic back pain [23], we did not observe associations between opioid use and reduced % REM sleep. Given that endogenous opioid receptors are activated during SWS [11; 31], it is possible that use of exogenous opioids was associated with selective disruption of this stage of sleep in our sample of patients with Fibromyalgia and insomnia. As SWS disruption has been associated with lower pain thresholds [13] and increased pain ratings [20], our results suggest that opioid use should be carefully monitored and considered in the management of pain symptoms in Fibromyalgia. It is possible that long-term opioid use may lead to a paradoxical effect that results in worsening of pain severity through the mechanism of increased sleep disruption.

Our hypothesis that use of opioids would be associated with greater SOL and WASO and reduced TST and SE was only partially supported. While opioid use was associated with increased SOL, it was not associated with WASO, SE, or TST. Results for PSG-assessed SOL are consistent with previous findings regarding opioid use and self-reported SOL in patients with chronic pain [18]. However, this association depended on patient age, with middle-aged and older adults showing the greatest disruption to SOL. While opioids are thought to have sedative effects and are often prescribed to reduce pain and promote sleep onset, our results suggest that they may have the opposite effect in patients with Fibromyalgia, particularly as patients become older.

Our hypothesis that opioid-related disruptions to PSG-assessed sleep parameters would increase with opioid dosage was only partially supported, as these associations varied as a function of pain level and/or age. The association between increasing opioid dose and longer SOL in older adults is consistent with our prior findings regarding self-reported SOL in patients with fibromyalgia [6]. Given the consistency of these findings for subjective and objective SOL, as well as our finding that higher dosage is also associated with lower SE in older adults, more research is needed to determine mechanism(s) by which higher opioid dose may prolong SOL and reduce SE in older adults.

Our findings of pain-related opioid dosage effects on SWS and arousal index lend themselves to several interpretations. In individuals with minimal or low pain, increasing dosage may be associated with greater SWS and increased arousals disruption because these patients may be overmedicating for their current pain level. Therefore, instead of having the

intended sedative effect in patients with less severe pain, increased opioid dosage may exacerbate SWS disruption and lead to more arousals/hour throughout the night. It is possible that this disruption is observed in SWS due to the endogenous opioid networks known to be involved in this stage of sleep [11; 31]. Conversely, in individuals with high pain intensity, increasing opioid dosage may have the intended effect, facilitating deep sleep. Changes in central pain processing may also explain our observed interactive effect of pain intensity and opioid dosage on % SWS. Prior research has shown that increased pain intensity and disrupted pain processing networks in the central nervous system (CNS) (i.e., disrupted endogenous pain inhibition) are associated with more fragmented sleep in patients with chronic joint pain [8] and women with Fibromyalgia [26]. Therefore, it is possible that patients with more severe pain have greater disruption of their endogenous pain inhibitory system in the CNS and, as a result, show greater sleep improvement at higher opioid doses. Although we did not observe an association between clinical pain ratings and any of the PSG-assessed sleep parameters, it will be important to examine associations between central pain mechanisms, opioid use/dosage, and physiological sleep in future work.

Although prior work has shown that opioid use depresses respiration during sleep [28], findings from this study are unlikely related to sleep disordered breathing, as opioid effects on sleep architecture were independent of AHI, which did not independently predict any of the PSG outcomes. More work is needed to explore the mechanisms by which opioids may selectively disrupt certain sleep stages. In order to understand the impact of opioids in Fibromyalgia, it will also be important to examine the impact of opioid-related sleep architecture disruption on other aspects of daytime functioning (e.g., cognition, mood, quality of life).

The present study has several limitations. First, given that we did not compare results to a healthy pain-free control group, we cannot be certain that results are specific to patients with Fibromyalgia. Additionally, the results of the present study may not apply to Fibromyalgia patients diagnosed under the new 2016 criteria [32]. Second, because we examined effects in patients with self-reported symptoms of insomnia, results may not generalize to Fibromyalgia patients without insomnia. However, the high prevalence of insomnia in the general population of patients with Fibromyalgia [~80% [1]] mitigates this concern. Third, although we did not have data available for sleep stage shift indices, given prior research suggesting that opioids increase the amount of stage shifts throughout the night in chronic opioid users [12], it will be important for future research to examine the effects opioid use and dosage on these outcomes in patients with Fibromyalgia. Fourth, our sample consisted mainly of women (94%), so results may not generalize to men with Fibromyalgia. Fifth, although we did not evaluate the potential effects of season on PSG outcomes, given that the study location (Florida) generally has more consistent levels of light throughout the year, it is unlikely that season would impact results. However, results may not translate to patients in areas with more seasonal variation, particularly in terms of light exposure. Sixth, it is possible that unequal sample sizes of opioid users ($n = 128$) vs. non-users ($n = 65$) may have biased results of the first regression analyses regarding effects of opioid usage on sleep outcomes; therefore, results should be replicated in larger samples of patients with Fibromyalgia and insomnia with equal numbers of users and non-users. Finally, although exploratory analyses suggest no increased risk of sleep apnea for opioid users with

Fibromyalgia and insomnia, it will be important to further examine a potential effect of opioids on sleep disordered breathing using larger sample sizes.

### 4.1. Conclusion

Opioid use disrupts sleep architecture in patients with Fibromyalgia and insomnia complaints, specifically disrupting SWS and increasing the amount of lighter stage 2 sleep. Depending on clinical pain ratings, opioid dosage may have opposite effects on SWS, with individuals with less severe pain showing the greatest disruption at higher opioid dosage. Older adults may also be most vulnerable to opioid dosage-related worsening of SOL and SE. Clinicians should monitor opioid use and dosage in patients with Fibromyalgia, and consider patient pain levels and age in order to understand and treat sleep symptoms. Non-pharmacological pain treatments (e.g., cognitive behavioral therapy for pain) may be a better alternative to manage pain in patients with Fibromyalgia and mitigate further sleep disruption. Prospective studies that take into consideration potential patient-related factors such as age and pain intensity are needed to assess the causal effects of opioid use and dosage on sleep.

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**Table 1**

Demographics and Sleep Outcomes of Study Sample of Patients with Fibromyalgia and Insomnia[a]

| Variable | Mean (*SD*) | Range | Mean (SD) | Range | Mean (SD) | Range |
|---|---|---|---|---|---|---|
| | ***Full sample (n=193)*** | | ***Opioids users (n=65)*** | | ***Opioid non-users (n=128)*** | |
| Age | 51.70 (11.73) | 18–77 | 52.75 (11.27) | 25–74 | 51.13 (12.05) | 18–77.00 |
| Sex (F:M) | 182:11 | -- | 60:5 | -- | 122:6 | -- |
| Duration of chronic pain (months) | 97.40 (85.15) | 2.00–324.00 | 108.07 (93.47) | 3.00–324.00 | 91.24 (79.81) | 2.00–304.00 |
| Use of Opioids (n, %) | 65 (35%) | -- | 65 (100%) | -- | -- | -- |
| Morphine (n, %) | 6 (3%) | -- | 6 (9%) | -- | -- | -- |
| Methadone (n, %) | 2 (1%) | -- | 2 (3%) | | -- | -- |
| Darvocet/Darvon | 5 (3%) | -- | 5 (8%) | | -- | -- |
| Hydrocodone | 12 (6%) | -- | 12 (18%) | | -- | -- |
| Nucynta | 1 (1%) | -- | 1 (2%) | | -- | -- |
| Oxycodone | 15 (8%) | -- | 15 (23%) | | -- | -- |
| Oxycontin | 3 (2%) | -- | 3 (5%) | | -- | -- |
| Tramadol | 10 (5%) | -- | 10 (15%) | | -- | -- |
| Codeine | 2 (1%) | -- | 2 (3%) | | -- | -- |
| Percocet | 1 (1%) | -- | 1 (2%) | | -- | -- |
| Toradol | 1 (1%) | -- | 1 (1%) | | -- | -- |
| LRD Opioids | .43 (.82) | 0.00–1.85 | 1.23 (.98) | .07–4.00 | -- | -- |
| Days of opioid use during baseline[b] | 3.18 (5.31) | 0.00–14.00 | 9.06 (5.19) | 1.00–14.00 | -- | -- |
| Duration of Opioid use (months) | 22.02 (66.20) | 0.00–512.00 | 31.64 (90.67) | 0.00–512.00 | -- | -- |
| Use of sleep meds (*n*, %) | 85 (44%) | -- | 37 (57%) | -- | 48 (38%) | -- |
| Benzodiazepines (n, %) | 33 (17%) | -- | 23 (35%) | -- | 10 (8%) | -- |
| Benzodiazepine-like hypnotics (n, %) | 20 (10%) | -- | 6 (9%) | -- | 14 (11%) | -- |
| Antidepressants (n, %) | 44 (23%) | -- | 18 (28%) | -- | 26 (20%) | -- |
| Antihistamines (n, %) | 30 (16%) | -- | 15 (23%) | -- | 15 (12%) | -- |
| Evening pain severity | 51.54 (18.97) | 4.71–95.71 | 57.96 (16.92) | 17.33–94.86 | 48.53 (19.66) | 4.71–95.71 |
| Presence of Depression[c] | | | | | | |

| Variable | Mean (*SD*) | Range | Mean (SD) | Range | Mean (SD) | Range |
|---|---|---|---|---|---|---|
| | ***Full sample (n=193)*** | | ***Opioids users (n=65)*** | | ***Opioid non-users (n=128)*** | |
| Mild (n,%) | 26 (13%) | -- | 11 (17%) | -- | 15 (12%) | -- |
| Moderate (n,%) | 42 (22%) | -- | 16 (25%) | -- | 26 (20%) | -- |
| Severe (n,%) | 31 (16%) | -- | 13 (20%) | -- | 16 (13%) | -- |
| *PSG Sleep Measures* | | | | | | |
| SOL (minutes) | 27.58 (54.00) | 0.00–382.00 | 39.46 (75.22) | 1.00–382.00 | 20.53 (32.72) | 0.00–223.00 |
| WASO (minutes) | 68.99 (46.49) | 4.0–321.00 | 71.89 (53.73) | 6.00–321.00 | 67.43 (42.49) | 4.00–226.00 |
| TST (minutes) | 385.51 (103.37) | 78.00– 800.00 | 375.75 (104.27) | 143.00–648.00 | 389.40 (103.13) | 78.00–800.00 |
| SE (%) | 80.35 (12.69) | 23.00–97.00 | 78.06 (15.45) | 23.00–97.00 | 81.49 (10.96) | 38.00–97.00 |
| REM latency | 132.57 (87.33) | 10.00–430.00 | 142.57 (94.45) | 19.00–430.00 | 127.61 (83.50) | 10.00–408.00 |
| Arousal Index | 8.46 (4.32) | 0.00–35.00 | 9.17 (5.62) | 0.00–35.00 | 8.11 (3.49) | 0.00–18.00 |
| % Stage 1[d] | 8.55 (4.33) | 1.00–32.00 | 9.57 (5.27) | 1.00–32.00 | 8.02 (3.67) | 1.00–21.00 |
| % Stage 2[d] | 58.29 (12.2) | 22.00–90.00 | 61.00 (13.31) | 22.00–90.00 | 56.92 (11.36) | 31.00–90.00 |
| % SWS (stage 3 and 4)[d] | 15.40 (9.5) | 0.00–44.00 | 12.28 (9.68) | 0.00–39.00 | 16.97 (9.24) | 0.00–44.00 |
| % REM[d] | 17.60 (7.9) | 0.00–41.00 | 16.48 (8.80) | 2.00–41.00 | 18.17 (7.25) | 0.00–38.00 |
| AHI | 4.47 (6.80) | 0.00–49.00 | 5.35 (8.30) | 0.00–44.00 | 3.99 (5.84) | 0.00–49.00 |
| AHI mild (0–9; n,%) | 174 (90%) | -- | 55 (85%) | | 117 (91%) | |
| AHI moderate (10–29; n, %) | 18 (9%) | -- | 8 (12%) | -- | 10 (8%) | -- |
| AHI severe (30+; n,%) | 3 (2%) | -- | 2 (3%) | | 1 (8%) | |
| *Criteria met for apnea/PLMD* | | | | | | |
| PLMD[e] (n,%) | 2 (1%) | -- | 2 (3%) | -- | 0 (0%) | -- |
| Sleep Apnea[f] (n,%) | 11 (6%) | -- | 5 (8%) | -- | 6 (5%) | -- |

*Note.* LRD = lowest recommended dosage; SOL = sleep onset latency; WASO = wake after sleep onset; TST = total sleep time; SE = sleep efficiency; AHI = apnea hypopnea index; PLMD = Periodic Leg Movement Disorder

[a]Average descriptive values of the full sample of participants (n = 235) who completed at least some of the baseline assessments in the parent clinical trial [15] were largely similar across all variables. Thus, it is unlikely that participants excluded from regression analyses due to incomplete data differed from those included in regression models.

[b]parent trial baseline period of 14 days

[c]Based on Beck Depression Inventory [2] scores of 14–19 (mild), 20–28 (moderate), 29–63 (severe)

*Pain*. Author manuscript; available in PMC 2020 September 01.

[d] expressed as percentage of TST

[e] met criteria for PLMD based on the following criteria = periodic limb movements (myoclonus arousals greater than 15/hr);

[f] met criteria for sleep apnea (apnea–hypopnea index greater than 15/hr or between 10 and 15 per hr with oxygen saturation below 88%)

## Table 2

Regression models including opioid use as predictor of polysomnographically assessed sleep in patients with chronic widespread pain and insomnia complaints (*N*=193)

| Sleep Parameter | *B* | *SE* | *t* | *p* |
|---|---|---|---|---|
| *SOL* | | | | |
| Opioid use (Y/N) | 21.10 | 8.72 | 2.42 | **.02** |
| Age | −.13 | .34 | −.37 | .71 |
| Opioid use × age | 1.41 | .71 | 1.98 | **.049** |
| Pain rating | −.28 | .21 | −1.33 | .19 |
| Opioid use × pain rating | −.51 | .47 | −1.11 | .27 |
| Use of sleep medications | −4.89 | 7.92 | −.62 | .54 |
| AHI[a] | 1.05 | .59 | 1.80 | .07 |
| *WASO* | | | | |
| Opioid use (Y/N) | .79 | 7.55 | .11 | .92 |
| Age | .86 | .30 | 2.90 | **.004** |
| Opioid use × age | .29 | .62 | .47 | .64 |
| Pain rating | .13 | .18 | .72 | .47 |
| Opioid use × pain rating | .40 | .40 | .98 | .33 |
| Use of sleep medications | .72 | 6.85 | .11 | .92 |
| AHI[a] | −.74 | .51 | −1.47 | .14 |
| *TST* | | | | |
| Opioid use (Y/N) | −22.21 | 16.82 | −1.32 | .19 |
| Age | −.66 | .66 | −1.01 | .32 |
| Opioid use × age | −2.25 | 1.38 | −1.63 | .10 |
| Pain rating | −.05 | .41 | 1.13 | .90 |
| Opioid use × pain rating | 1.24 | .90 | 1.38 | .17 |
| Use of sleep medications | 31.89 | 15.28 | 2.09 | **.04** |
| AHI[a] | .17 | 1.13 | .15 | .88 |
| *SE* | | | | |
| Opioid use (Y/N) | −3.25 | 2.10 | −1.55 | .12 |
| Age | −.13 | .08 | −1.52 | .13 |
| Opioid use × age | −.31 | .17 | −1.81 | .07 |
| Pain rating | −.00 | .05 | −.02 | .98 |
| Opioid use × pain rating | .02 | .11 | .18 | .86 |
| Use of sleep medications | 1.26 | 1.91 | .66 | .51 |
| AHI[a] | .00 | .14 | .02 | .98 |
| *Arousal Index* | | | | |
| Opioid use (Y/N) | 1.29 | .71 | 1.83 | .07 |
| Age | .02 | .03 | .80 | .43 |
| Opioid use × age | −.01 | .06 | −.25 | .80 |
| Pain rating | −.01 | .02 | −.85 | .39 |

| Sleep Parameter | *B* | *SE* | *t* | *p* |
|---|---|---|---|---|
| Opioid use × pain rating | .03 | .04 | .83 | .41 |
| Use of sleep medications | −1.29 | .64 | −2.01 | .05 |
| AHI[a] | −.06 | .05 | −1.27 | .21 |
| *% Stage 1*[b] | | | | |
| Opioid use (Y/N) | 1.39 | .71 | 1.96 | .05 |
| Age | .01 | ..03 | .48 | .64 |
| Opioid use × age | .03 | .07 | .45 | .65 |
| Pain rating | −.003 | .02 | −.16 | .88 |
| Opioid use × pain rating | .04 | .04 | 1.02 | .31 |
| Use of sleep medications | −.53 | .64 | −.82 | .41 |
| AHI[a] | .08 | .05 | 1.59 | .11 |
| *% Stage 2*[b] | | | | |
| Opioid use (Y/N) | 4.16 | 1.99 | 2.09 | **.04** |
| Age | −.02 | .08 | −.24 | .81 |
| Opioid use × age | −.08 | .16 | −.49 | .62 |
| Pain rating | −.03 | .05 | −.57 | .57 |
| Opioid use × pain rating | −.06 | .11 | −.61 | .54 |
| Use of sleep medications | 3.03 | 1.80 | 1.68 | .10 |
| AHI | | | | |
| *% SWS (Stage 3 and 4)*[b] | | | | |
| Opioid use (Y/N) | −4.90 | 1.53 | −3.20 | **.002** |
| Age | −.03 | .06 | −.52 | .60 |
| Opioid use × age | .09 | .13 | .73 | .47 |
| Pain rating | .03 | .04 | .70 | .49 |
| Opioid use × pain rating | .02 | .08 | .30 | .76 |
| Use of sleep medications | −1.13 | 1.39 | −.81 | .42 |
| AHI[a] | .01 | .10 | .14 | .89 |
| *% REM*[b] | | | | |
| Opioid use (Y/N) | −1.61 | 1.28 | −1.26 | .21 |
| Age | .06 | .05 | 1.14 | .25 |
| Opioid use × age | .01 | .11 | .10 | .92 |
| Pain rating | .01 | .03 | .48 | .63 |
| Opioid use × pain rating | .04 | .07 | .54 | .59 |
| Use of sleep medications | −1.56 | 1.17 | −1.33 | .18 |
| AHI[a] | .05 | .09 | .54 | .59 |

*Note*. *SE* = Standard error; SOL= sleep onset latency; WASO=time awake after sleep onset; TST = total sleep time; SWS=slow wave sleep; REM=rapid eye movement sleep; AHI=apnea hypopnea index

[a]AHI expressed as continuous variable in regression models. Models with AHI expressed as a categorical variable (i.e., mild, moderate, severe; see Table 1) revealed similar results across all outcomes

[b] expressed as a percentage of TST

## Table 3

Regression models including opioid dosage as predictor of polysomnographically assessed sleep in patients chronic widespread pain and insomnia complaints ($n = 65$)

| Sleep Parameter | *B* | *SE* | *t* | *p* |
|---|---|---|---|---|
| *SOL* | | | | |
| Opioid dosage | 8.87 | 9.59 | .92 | .36 |
| Age | 1.11 | .86 | 1.29 | .20 |
| Opioid dosage × age | 2.59 | 1.00 | 2.58 | **.01** |
| Pain rating | −.34 | .54 | −.64 | .53 |
| Opioid dosage × pain rating | −.66 | .63 | −1.05 | .30 |
| Use of sleep medications | 3.46 | 18.29 | .19 | .85 |
| AHI[a] | .85 | 1.13 | .75 | .45 |
| *WASO* | | | | |
| Opioid dosage | 1.13 | 7.22 | .16 | .88 |
| Age | 1.10 | .65 | 1.71 | .09 |
| Opioid dosage × age | .87 | .76 | 1.15 | .26 |
| Pain rating | .50 | .40 | 1.25 | .22 |
| Opioid dosage × pain rating | −.42 | .47 | −.89 | .37 |
| Use of sleep medications | −6.00 | 13.78 | −.44 | .66 |
| AHI[a] | −.51 | .85 | −.60 | .55 |
| *TST* | | | | |
| Opioid dosage | −21.78 | 13.52 | −1.61 | .11 |
| Age | −1.75 | 1.21 | −1.45 | .15 |
| Opioid dosage × age | .17 | 1.41 | .12 | .90 |
| Pain rating | .78 | .75 | 1.03 | .31 |
| Opioid dosage × pain rating | −.32 | .89 | −.36 | .72 |
| Use of sleep medications | 53.96 | 25.77 | 2.09 | **.04** |
| AHI[a] | −.004 | 1.59 | −.002 | .99 |
| *SE* | | | | |
| Opioid dosage | −1.84 | 2.00 | −.92 | .36 |
| Age | −.38 | .18 | −2.11 | **.04** |
| Opioid dosage × age | −.46 | .21 | −2.22 | **.03** |
| Pain rating | −.03 | .11 | −.29 | .77 |
| Opioid dosage × pain rating | .08 | .13 | .62 | .54 |
| Use of sleep medications | 2.33 | 3.82 | .61 | .54 |
| AHI[a] | −.01 | .24 | −.04 | .97 |
| *Arousal Index* | | | | |
| Opioid dosage | 1.32 | .72 | 1.83 | .07 |
| Age | −.02 | .06 | −.34 | .73 |
| Opioid dosage × age | .06 | .08 | .80 | .42 |
| Pain rating | .03 | .04 | .62 | .54 |

| Sleep Parameter | *B* | *SE* | *t* | *p* |
|---|---|---|---|---|
| Opioid dosage × pain rating | −.11 | .05 | −2.24 | **.03** |
| Use of sleep medications | −2.35 | 1.37 | −1.71 | .09 |
| AHI[a] | −.00 | .08 | −.01 | .99 |
| *% Stage 1*[b] | | | | |
| Opioid dosage | .31 | .71 | .43 | .67 |
| Age | .02 | .06 | .30 | .76 |
| Opioid dosage × age | .05 | .07 | .62 | .54 |
| Pain rating | .04 | .04 | .93 | .36 |
| Opioid dosage × pain rating | −.09 | .05 | −1.84 | .07 |
| Use of sleep medications | −.88 | 1.35 | −.65 | .52 |
| AHI[a] | .08 | .08 | 1.00 | .32 |
| *% Stage 2*[b] | | | | |
| Opioid dosage | .75 | 1.82 | .41 | .68 |
| Age | −.15 | .16 | −.92 | .36 |
| Opioid dosage × age | −.22 | .19 | −1.13 | .26 |
| Pain rating | −.07 | .10 | −.64 | .52 |
| Opioid dosage × pain rating | −.15 | .12 | −1.26 | .21 |
| Use of sleep medications | 2.57 | 3.48 | .74 | .46 |
| AHI[a] | −.21 | .21 | −.96 | .34 |
| *% SWS (Stage 3 and 4)*[b] | | | | |
| Opioid dosage | −.90 | 1.26 | −.72 | .48 |
| Age | .10 | .11 | .90 | .37 |
| Opioid dosage × age | .07 | .13 | .58 | .57 |
| Pain rating | .01 | .07 | .17 | .87 |
| Opioid dosage × pain rating | .27 | .08 | 3.24 | **.002** |
| Use of sleep medications | −2.55 | 2.40 | −1.06 | .29 |
| AHI[a] | .03 | .15 | .17 | .86 |
| *% REM*[b] | | | | |
| Opioid dosage | .38 | 1.23 | .31 | .76 |
| Age | .07 | .11 | .59 | .56 |
| Opioid dosage × age | .07 | .13 | .57 | .57 |
| Pain rating | .05 | .07 | .77 | .44 |
| Opioid dosage × pain rating | −.06 | .08 | −.71 | .48 |
| Use of sleep medications | −.02 | 2.34 | −.01 | .99 |
| AHI[a] | .06 | .15 | .39 | .70 |

*Note*. *SE* = Standard error; SOL= sleep onset latency; WASO=time awake after sleep onset; TST = total sleep time; SWS=slow wave sleep; REM=rapid eye movement sleep; AHI=apnea hypopnea index

[a]AHI expressed as continuous variable in regression models. Models with AHI expressed as a categorical variable (i.e., mild, moderate, severe; see Table 1) revealed similar results across all outcomes.

[b] expressed as a percentage of TST