The association between pain and sleep in fibromyalgia

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ABSTRACT

The association between pain and sleep in fibromyalgia is a common complaint among patients with fibromyalgia. The objective of this study was to clarify the relationship between pain and sleep in fibromyalgia.

Methods: Electronic databases, including PsycINFO, the Cochrane database for systematic reviews, PubMed, EMBASE, and Ovid were searched to identify eligible articles. Databases independently screened, and the quality of evidence using a reliable and valid quality assessment tool was assessed.

Results: In total, 16 quantitative studies fulfilled the inclusion criteria. According to the results, increased pain in fibromyalgia was associated with reduced sleep quality, efficiency, and duration and increased sleep disturbance and onset latency and total wake time. Remarkably, depressive symptoms were also related to both pain and sleep in patients with fibromyalgia.

Conclusion: Management strategies should be developed to decrease pain while increasing sleep quality in patients with fibromyalgia. Future studies should also consider mood disorders and emotional dysfunction, as comorbid conditions could occur with both pain and sleep disorder in fibromyalgia.

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Fibromyalgia (FM) is a complicated musculoskeletal syndrome that affects between 0.7% and 4.8% of the global population. Most (90%) individuals with FM are women. According to the American College of Rheumatology (ACR), the criteria for FM diagnosis include pain for at least 3 months, but FM patients also experience poor sleep, fatigue, depression, stress, and anxiety. Most (90%) FM patients experience sleep disorder, which exerts a negative effect on health-related quality of life, leading to issues such as unrefreshing sleep and daytime tiredness, causing difficulties with wakefulness. Observational evidence indicates that FM patients’ pain is directly related to poor sleep. Several aspects of sleep, including duration, disturbance, and efficiency, could be related to pain. In addition, poor sleep has been shown to decrease both pain thresholds and cognitive skills in pain management. Moreover, a longitudinal analysis showed that interactivity between pain and sleep disturbance was associated with depression in patients with rheumatoid arthritis, and patients with FM have...
also been found to experience comorbid conditions such as depression, anxiety, and stress.\(^3,15\)

Although sleep and pain have been evaluated frequently in patients with chronic pain, the nature of the relationship between these variables remains unclear in FM. Identifying the relationship between pain and sleep in FM could provide insight for the development of efficient interventions. Therefore, the goal of this systematic review was to 1) determine whether pain is related to sleep, 2) identify the sleep dimensions related to pain in FM, and 3) provide information regarding future research directions, to facilitate the achievement of better health outcomes in FM.

**Methods.** This systematic review aimed to examine the relationship between pain and sleep in FM. While the studies included in the review were not based on the assessment of interventions, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines\(^16\) were considered during the review. The methodology used in the review was similar to strategies used in previous research\(^11,17\) and involved 3 stages. Stage 1 consisted of a systematic examination of the literature using keywords. Stage 2 involved a) scanning related article titles and abstracts according to particular inclusion criteria, and b) examination of full papers and extraction of evidence. Stage 3 involved the use of a valid quality assessment instrument to classify the included studies according to quality.

**Literature search.** The literature search was completed between November 2011 and March 2016. Electronic databases, including PsycINFO (until December 2012), the Cochrane database of systematic reviews, PubMed, EMBASE, and Ovid (from October 2015 to March 2016), were searched. The database search was performed using a combination of several keywords including “fibromyalgia,” “fibromyalgia syndrome,” “chronic pain,” “pain,” “sleep,” “sleep quality,” “problematic sleep,” and “sleep disturbance/s.” Moreover, the reference lists of all related articles were scanned to identify additional relevant articles.

**Inclusion criteria.** Studies were selected according to language (English), year of publication (from 1990 to 2015), research methods (quantitative), and variables (pain and sleep in FM). The inclusion criteria were as follows: FM patients aged 18 years or older and diagnosed with FM according to ACR criteria as participants 3). The results of the included studies were retrieved according to the significance level for the results, which was set at \(p<0.05\). The included studies used different measurement tools to assess sleep and pain. The studies could include measurement of other FM symptoms such as depression, stress, physical functioning, fatigue, and anxiety. However, the review focused mainly on remarkable findings regarding pain and sleep, to improve understanding of these variables in FM. Several studies that did not fulfill the inclusion criteria, such as those that did not measure pain and sleep simultaneously, were excluded from the review. In addition, studies examining only facial pain in FM were excluded to avoid misconception.

**Assessment of evidence quality.** Authors used the Effective Public Health Practice Project (EPHPP) quality assessment instrument\(^18\) to categorize the selected studies according to quality. Classifications were then compared to make final decisions regarding the quality of each study. The EPHPP quality assessment instrument was used to analyze the following 6 factors: selection bias, allocation bias, confounders, blinding, data collection methods, and withdrawals and drop-outs.\(^18\) Quality for each factor was rated as “high,” “medium,” or “low.” Overall research quality was considered high, medium, and low if these factors received only high ratings, <4 high ratings and one low rating, and ≥2 low ratings, respectively. This tool has been identified as a suitable quality assessment instrument for the evaluation of randomized controlled trials and non-randomized controlled trials.\(^19\) In addition, it has been used in >30 systematic reviews.\(^18\)

This systematic review aimed to answer current research questions by systematically specifying, selecting, and critically evaluating related research and analyzing the evidence from the included studies. Systematic reviews may or may not include statistical analysis (meta-analysis) to summarize the findings.\(^16\) As the included studies varied in terms of methodology, participants’ sociodemographic characteristics, and other factors, statistical analysis was not included in the current systematic review, and the evidence was synthesized qualitatively.

**Results.** **Literature search.** Of 1,842 database citations, 16 studies fulfilled the inclusion criteria for the systematic review (Figure 1). The publication years for the included studies ranged from 1996 to 2015. In addition, the research designs used in the selected studies varied (Table 1). The studies were conducted in the United States\(^20-29\), Spain\(^30-32\), the United Kingdom\(^33,34\), and Turkey.\(^35\)

**Assessment of the quality of included studies.** According to the EPHPP assessment tool, one study demonstrated high,\(^23\) 11 studies demonstrated medium\(^20,21,24,27-32,34,35\), and 4 studies demonstrated as low quality.\(^25-27,33\) (Table 1).
Outcome measures. Pain assessment tools. Most of the studies (n=6) measured pain using the McGill Pain Questionnaire, which has demonstrated very good reliability and validity, and one study used the shorter version of this scale, which has shown good reliability and validity. Three studies used the visual analog scale, which has shown good reliability and validity in various populations. Two studies used sensory testing, which evaluates pain threshold on the fingers. One study used the pain rating index, which is known to be an effective instrument. Two studies used ecological momentary assessment, which involves multiple assessments of individuals in their natural environments. Two studies used ecological momentary assessment, which involves multiple assessments of individuals in their natural environments. In addition, 2 studies used 3 pain subscales from various validated questionnaires, and one study used the Health-Related Quality of Life Questionnaire, which measures several health domains including pain.

Sleep assessment tools. Subjective tools. Most of the studies (n=10) assessed sleep using the Pittsburgh Sleep Quality Index, which has demonstrated reliability and validity. In addition, 2 studies used different reliable, valid questionnaires, and 2 studies used sleep diaries via ecological momentary assessment, which has been identified as effective assessment method. Another study used a sleep subscale from a different validated questionnaire. However, several studies used multiple measurement tools to evaluate sleep.

Objective tools. Two studies used polysomnography (PSG) recording, which allows objective assessment of sleep parameters. Polysomnography is a very reliable means of assessing sleep in patients with chronic conditions. In addition, one study used actigraphy,
### Table 1 - Descriptive characteristics of the studies and comparison of the outcomes.

| Study                        | Design                                                      | Participants | Sleep assessment method | Findings                                                                                          | Quality of the study |
|------------------------------|-------------------------------------------------------------|--------------|-------------------------|--------------------------------------------------------------------------------------------------|----------------------|
| Affleck et al20 (1996)       | Repeated measures                                           | 50 with FM   | All female              | a) Pain intensity: 39.75 (17.02; max = 84)  
    b) Sleep duration: 6.47 (0.86) h:m  
    c) Waking episodes: 1.76 (0.98; max = 6)  
    d) Refreshing sleep: 2.59 (1.02; max = 6)  
    e) Pain was related to pain attention (p<0.01) and sleep quality (p<0.05), but pain attention was not significantly associated with sleep quality  
    f) Pain attention was related to pain intensity the following day (p<0.001)  
    g) Sleep quality at night was associated with pain intensity during the day (p<0.001)  
    h) Greater daytime pain intensity was associated with poorer sleep quality (p<0.05) | Medium       |
| Ağargün et al35 (1999)       | Cross-sectional                                             | 16 with FM   | 13 female, 3 male       | a) Sleep quality: 1.3 (1.1; max = 3 for each component)  
    b) Sleep disturbance: 1.9 (0.9)  
    c) Habitual sleep efficiency: 0.6 (1.0)  
    d) Pain threshold was negatively associated with subjective sleep quality (p=0.018), habitual sleep efficiency (p=0.021), and sleep disturbance (p=0.019) scores  
    e) Pain threshold was not significantly related to sleep duration (p=0.055), sleep latency (p=0.06), or daytime dysfunction (p=0.35) | Medium       |
| Nicassio et al21 (2002)      | Cross-sectional & repeated measures                        | 105 with FM  | 96 female, 6 male       | a) Pain was positively related to depression (p<0.001), but sleep quality was negatively related to pain (p<0.01) and depression (p<0.01)  
    b) Daytime pain intensity was associated with poorer sleep quality (p<0.001)  
    c) Poorer sleep quality was related to stronger pain intensity during the day or evening (p<0.001) | Medium       |
| Theadom et al33 (2007)       | Cross-sectional                                             | 101 with FM  | 94 female, 7 male       | a) Poor sleep (99%)  
    b) Pain: 30.77 (18.56; max health = 100)  
    c) Sleep duration: 6.57 (1.82) h:m  
    d) Unrefreshing sleep: 7.97 (1.89; 10 = very unrefreshing)  
    e) Low levels of enjoyment of sleep: 6.88 (2.33; 10 = very unenjoyable)  
    f) Significant relationship between poor sleep and pain and negative affect (p<0.01)  
    g) Sleep quality predicted pain (p<0.05) | Low          |
| Hamilton et al22 (2007)      | Ecological momentary assessment                             | 27 with RA   | 19 female, 8 male; 22 with FM | 19 female, 3 male | a) Pain: 3.05 (0.93; max = 6)  
    b) Sleep duration: 7.20 (1.01) h:m  
    c) Sleep quality: 3.36 (1.25) (max = 7)  
    d) Sleep quality was significantly associated with pain (p<0.01)  
    e) Participants with FM reported greater pain intensity (p<0.05) and lower sleep quality (p<0.05) relative to those with RA  
    f) Sleep disturbance mediated the relationship between pain and stress (p<0.01)  
    e) Sleep quality was associated with pain (p<0.005)  
    f) Sleep disturbance was significantly related to sleep quality (p<0.001) | Low          |
| Bigatti et al23 (2008)       | Randomized controlled trial                                | 600 with FM  | 571 female, 29 male     | a) Pain: 1.68 (0.68; max = 6)  
    b) Poor sleep quality: 11.22 (3.96) (max = 21)  
    c) Significant relationship between sleep quality and pain (p<0.01)  
    d) Poor sleep was associated with greater pain intensity (p<0.05)  
    e) Pain was associated with depression (p<0.01) and poor physical functioning  
    f) Sleep was associated with depression (p<0.01) | High         |
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| Study | Design | Sample Size | Female | Mean Age (SD) | Subjective Measures | Findings |
|-------|--------|-------------|--------|---------------|---------------------|----------|
| Theadom et al (2008) | Cross-sectional | 83 with FM, 83 HC | 91.6% | 52.59±11.42 | a) Pain: 29.58 (18.10; max health = 100) | Medium |
|        |        |             |        |               | b) DBAS: 65.21 (16.42) (max = 100) |          |
|        |        |             |        |               | c) Sleep quality: 2.06 (0.76) (max = 3 for each sleep component) |          |
|        |        |             |        |               | d) Sleep latency: 3.25 (1.57) |          |
|        |        |             |        |               | e) Sleep duration: 1.27 (1.17) |          |
|        |        |             |        |               | f) Sleep efficiency: 1.86 (1.22) |          |
|        |        |             |        |               | g) Sleep disturbance: 2.39 (0.62) |          |
|        |        |             |        |               | h) Overall sleep quality: 14.71 (4.29) |          |
|        |        |             |        |               | i) Participants with FM had significantly higher levels of DBAS, pain, and poor sleep (c, d, e, f, g, h) relative to healthy controls (p<0.01) |          |
|        |        |             |        |               | j) Higher levels of DBAS were significantly related to greater pain intensity (p<0.05) and poorer sleep quality (p<0.05) in participants with FM |          |
|        |        |             |        |               | k) Higher levels of perceived stress were significantly related to greater pain intensity (p<0.01) and sleep disturbance (p<0.05) in participants with FM |          |
| O’Brien et al (2010) | Cross-sectional | 116 with FP, 55 with BP, 121 with FM | 241 female, 51 male | 46.67±12.05 | a) Overall sleep quality: 13.83 (4.19; max = 21) | Medium |
|        |        |             |        |               | b) Sleep onset latency: 53.18 (51.71) min |          |
|        |        |             |        |               | c) Total sleep time: 5.68 (1.59) hours |          |
|        |        |             |        |               | d) Patients with FM reported significantly longer sleep onset latency relative to those with FP (p<0.05) and BP |          |
|        |        |             |        |               | e) Participants with FM and BP showed poorer sleep quality relative to those with FP (p<0.001) |          |
|        |        |             |        |               | f) Participants with FM reported greater sleep disturbance relative to those with BP (p<0.05) and FP (p<0.001) |          |
|        |        |             |        |               | g) Participants with FM and BP reported shorter total sleep time relative to those with FP (p<0.01 and p<0.001, respectively) |          |
|        |        |             |        |               | h) 61.6% of participants with chronic pain reported poor sleep |          |
|        |        |             |        |               | i) Pain was significantly related to poor sleep (p<0.01) |          |
|        |        |             |        |               | j) Poorer sleep exerted a significant effect on pain (p<0.01) |          |
| Miro et al (2011) | Cross-sectional | 104 with FM, 86 HC | All female | 46.39±7.60 | a) Pain intensity: 7.41 (1.67; max = 10) | Medium |
|        |        |             |        |               | b) Sleep quality: 2.10 (0.79; max = 3 for each sleep component) |          |
|        |        |             |        |               | c) Sleep latency: 2.06 (0.94) |          |
|        |        |             |        |               | d) Sleep duration: 2.11 (1.01) |          |
|        |        |             |        |               | e) Sleep efficiency: 2.08 (1.16) |          |
|        |        |             |        |               | f) Sleep disturbance: 2.15 (0.61) |          |
|        |        |             |        |               | g) Daily dysfunction: 2.42 (0.81) |          |
|        |        |             |        |               | h) Overall sleep quality: 15.15 (3.99; max = 21) |          |
|        |        |             |        |               | i) 98% of participants with FM reported poor sleep |          |
|        |        |             |        |               | j) Participants with FM showed significantly higher pain intensity and poorer sleep quality relative to healthy controls (p<0.001) |          |
|        |        |             |        |               | k) Poorer sleep quality was significantly associated with greater pain intensity (p<0.01) and depression (p<0.01) in participants with FM |          |
|        |        |             |        |               | l) Pain exerted a significant effect on sleep quality (p<0.001) |          |
| Schaefer et al (2011) | Cross-sectional | 203 with FM, 192 female, 11 male | 47.9±10.9 | 47.9±10.9 | a) 91% of participants reported pain | Low |
|        |        |             |        |               | b) 85.7% of participants who were severely affected by FM reported sleep disturbance |          |
|        |        |             |        |               | c) Increased sleep-related problems were associated with greater FM intensity (p<0.001). |          |
|        |        |             |        |               | d) 58% reported depressive symptoms |          |

Table 1 - Descriptive characteristics of the studies and comparison of the outcomes (Continuation)
The association between fibromyalgia pain and sleep-related problems was studied in several research articles. Keskindag et al. (2017) reported that 63.05% of participants with fibromyalgia (FM) demonstrated multiple sleep-related problems. They also indicated significantly greater sleep difficulty relative to healthy controls ($p<0.001$) and each of pain $p<0.01$, respectively. Pain intensity in FM increased with the number of sleep-related problems (19.08%, 30.77%, and 43.26% for those with 0, 1, and 2 sleep-related problems, respectively).

Wagner et al. (2012) conducted a cross-sectional study with 2,196 participants with FM and 2,194 healthy controls (HC). Subjective sleep-related problems were assessed, and it was found that 63.05% of participants with FM had multiple sleep-related problems. They also indicated significantly greater sleep difficulty relative to healthy controls ($p<0.001$). The effect of pain helplessness on the association between sleep quality and pain was significant ($p<0.01$) and affected ($p<0.01$). Pain exerted a significant effect on the relationship between sleep quality and depression ($p<0.05$).

Hamilton et al. (2012) conducted a study with 35 participants with FM, all female. Subjective measures showed that poor sleep quality was significantly associated with sensory ($p<0.01$) and affective ($p<0.01$) pain. Pain was significantly related to objective total wake time ($p<0.001$) and negative mood ($p<0.05$). Negative mood significantly affected pain ($p<0.01$). Pain also significantly related to subjective poor sleep ($p<0.01$) and depression ($p<0.05$).

Anderson et al. (2012) conducted a repeated measures study with 74 participants with FM, 70 female and 4 male. Objective and subjective measures showed that pain intensity was 53.0 (20.3; max = 100) and total sleep time was 390.1 (66.8) minutes. Pain was significantly related to objective total sleep time ($p=0.05$) and negative mood ($p=0.002$). Pain was significantly related to negative mood ($p<0.01$). Negative mood significantly affected pain ($p<0.01$) and pain exerted a significant effect on the relationship between sleep quality and activity interference ($p<0.001$).

Diaz-Piedra et al. (2014) conducted a cross-sectional study with 55 participants with FM, all female. Objective and subjective measures showed that objective total sleep time was 425.69 (67.24) minutes, wake percentage was 16.22% (10.69), sleep efficiency was 83.76% (10.72), and sleep latency was 28.63 (27.66) minutes. Pain was significantly related to objective total sleep time ($p<0.005$), wake percentage ($p<0.01$), objective sleep efficiency ($p<0.005$) and objective sleep latency ($p<0.01$). Pain was also significantly related to subjective poor sleep ($p<0.01$) and pain was significantly related to objective total wake time ($p<0.001$).

Kothari et al. (2015) conducted a repeated measures study with 220 participants with FM, 195 female and 25 male. Subjective measures showed that sleep duration was 6:37 (1.93) hours and moderate sleep quality was 2.432 (1.175; max = 5). Participants with FM reported poor sleep (98.1%). Objective total wake time ($p<0.001$) and depression ($p=0.009$) exerted significant effects on subjective sleep quality in participants with FM.

Diaz-Piedra et al. (2015) conducted a cross-sectional study with 53 participants with FM and 36 healthy controls (HC). Objective and subjective measures showed that objective total sleep time was 7:09 (1:08) hours and sleep latency stage was 24:10 (20:52) minutes. Pain intensity was 21.2 (9.4; max = 45). Participants with FM reported poor sleep (98.1%). Objective total wake time ($p<0.005$) and subjective sleep quality ($p<0.05$) differed significantly between participants with FM and healthy controls. Objective total wake time ($p<0.001$) and depression ($p<0.009$) exerted significant effects on subjective sleep quality in participants with FM.
which is strongly associated with PSG with respect to sleep duration.60,61

**Dimension of sleep.** Sleep duration was subjectively assessed in 8 studies20,22,24,29,30,33-35 and objectively assessed in 2 studies31,32 One study28 assessed sleep duration both objectively and subjectively. In addition, 4 studies24,28,31,32 indicated reductions in total sleep time in FM patients. One study31 reported that objective total sleep time was significantly associated with pain, while another study35 found that this relationship was non-significant. In total, 9 studies of medium quality and 2 studies of low quality consistently demonstrated reduced sleep duration in FM patients.

Sleep quality was subjectively evaluated by 13 studies20,24,27,29,35 Studies of high (n=1), medium (n=9), and low quality (n=2) reported poor sleep quality in FM. Most studies found a significant relationship between pain and poor sleep quality in individuals with FM. Sleep disturbance was assessed subjectively in 8 studies22,24,26,29,30,34,35 In total, medium (n=5) and low quality (n=3), consistently reported that FM patients experienced pain and sleep disturbance. In addition, 4 studies reported subjective24,30,34,35 and 2 studies reported objective31,32 sleep onset latency. In total, 6 studies of medium quality reported that sleep onset latency ranged between approximately 24 and 58 min. Three studies of medium quality examined objective total wake time;28,31,32 of these, 2 studies reported that total wake time was significantly associated with pain in individuals with FM.28,31

Moreover, 3 and 2 studies of medium quality reported reduced subjective30,34,35 and objective31,32 sleep efficiency, respectively. In addition, 2 of these studies31,35 found that sleep efficiency was significantly associated with pain in FM patients. One medium quality study34 showed relationships between dysfunctional beliefs and attitudes about sleep and poor sleep quality and pain in FM (Table 1).

**Overall sleep.** Nine studies (one high, 5 medium, and 3 low quality) found that sleep exerted a significant effect on pain in FM;20,24,26,27,29,33 however, one study of medium quality28 failed to demonstrate this effect. In contrast, 4 studies of medium quality21,30,31,35 showed that pain significantly influenced sleep. However, in 2 studies of medium quality,23,32 this effect was nonsignificant (Table 1).

**Pain, sleep, and mood.** A few studies (2 medium and one low quality) demonstrated that negative affect and stress were associated with sleep quality29,33 and pain.29,34 Similarly, one study of medium quality showed that negative mood was significantly related to pain and objective and subjective total wake time.28

In addition, one study of medium quality showed that negative mood mediated the relationship between pain and sleep in FM.24 In contrast, 7 studies (one high, 5 medium, and one low quality) reported that FM patients experienced depression.21,23,25,27,30,32 Moreover, depression was independently associated with pain and sleep in FM.21,23,27 Two studies of moderate quality indicated that pain and sleep quality influenced depression independently;31,32 however, only one of these studies demonstrated that depression influenced sleep directly22 (Table 1).

**Summary.** The findings demonstrated a significant association between pain and poor sleep in FM patients. In addition, pain exerted a significant effect on sleep, and sleep exerted a significant effect on pain. However, although only half of the studies included in the review analyzed psychological variables, the finding that depression was associated with both pain and sleep in FM patients was remarkable (Table 1).

**Discussion.** The objective of this systematic review was to enhance understanding regarding the relationship between pain and sleep in FM. The findings showed that FM patients who experienced intense pain also experienced poor sleep. More specifically, several sleep dimensions, including total wake time and sleep quality, disturbance, efficiency, onset latency, and duration, were associated with pain in FM patients.

The results of the review indicated that FM patients experienced greater pain intensity and poorer sleep (manifested as sleep disturbance, daytime sleepiness, and daytime dysfunction) relative to healthy individuals.26,30,32,34 In addition, overall sleep was negatively associated with pain in FM patients. Disorders in the dimensions of sleep could affect overall sleep, which could interact with pain.11

The findings identified sleep disturbance, which was associated with pain,35 as a sleep dimension that FM patients experienced frequently.22,24-26,29,30,34,35 Sleep disturbance could be regarded as failure of the reparative function of sleep,62-64 which could cause hyperalgesia.13,65-68 Patients with chronic pain, including FM, rheumatoid arthritis, osteoarthritis, cancer pain, headaches, and chronic fatigue syndrome, reported different types of sleep disturbance.11,69,70 Moreover, sleep disturbance has been identified as a principal symptom of FM5,71 and associated with both sleep quality and pain intensity.72-74 Sleep disturbance in FM has been defined as difficulty falling asleep and maintaining sleep, reductions in sleep time, multiple interruptions to sleep during the night, and unfreshing sleep.72,75-77 These problems could result in poor sleep quality,
reduced sleep efficiency, and increased sleep onset latency. The results of this review are consistent with those of previous studies that reported increased sleep onset latency, reduced sleep duration, and poor sleep efficiency in FM patients. Sleep efficiency was associated with both subjective and objective pain, while total wake time was associated solely with objective pain, in FM patients. The review also included one study indicating that pain was objectively related to sleep duration and sleep onset latency. However, another study did not observe subjective relationships between these sleep dimensions and pain. Although both studies were of medium quality, various findings in the review could have resulted from differences between objective and subjective sleep measurements.

The association between pain and sleep is complicated. Clinical and experimental evidence has indicated that chronic pain is associated with increased levels of irritability during sleep, resulting in awakening. Several longitudinal studies involving patients with chronic pain have established that pain and poor sleep could affect one another. The findings of this review support the results of previous research suggesting that pain and sleep share a bidirectional relationship, which is difficult to understand in FM. The number of studies indicating that sleep influenced pain was higher relative to that of studies suggesting that pain influenced sleep.

However, pain and sleep might not share a direct relationship in FM. This relationship could be affected by various factors, including mood disorders, in patients with chronic pain. The current findings indicated that FM patients experienced depression in parallel with pain and poor sleep. In addition, few studies in the review considered the significant role of pain-related cognition, such as pain attention and pain helplessness, in pain intensity. Moreover, negative effect has been associated with poor sleep in individuals with chronic pain. Consistent with the results of previous research, the current findings suggest that negative mood in FM patients could affect the association between pain and sleep disturbance, as a covariate. Considering that these patients generally experience greater stress relative to healthy individuals, it is not surprising that negative emotional functioning interacts with FM symptoms. Although this review provides important insights into the association between pain and sleep in FM, it was subject to several limitations that should be noted. Most studies included in the review used the Pittsburgh Sleep Quality Index to assess sleep subjectively, while few studies used objective measures such as PSG and actigraphy. However, some differences were observed between the studies that used objective and subjective sleep assessments. Despite the finding that objective and subjective sleep assessment methods are moderately related, they have different functions in sleep assessment. Moreover, the observational findings of some studies did not allow inference of a causal relationship between pain and sleep. Although we used the EPHPP, which is a valid, reliable quality assessment tool, the studies included in the review were generally of lower quality because of their study designs. Overall, the findings should be considered with caution, as some studies of the same quality reported contradictory results. This could be explained by differences in research methods between the studies or authors’ misconceptions regarding the quality assessment process. Furthermore, some studies in the review regarding sleep quality as a sleep dimension, while others considered it an overall sleep score. Therefore, the results were difficult to interpret. In addition, the relationship between pain and sleep could be influenced by other FM symptoms that were not identified in the review. The studies in the review differed in terms of sample size, participants’ sociodemographic characteristics, reporting of control variables, and research methods. These differences could have affected both the interpretation and summary of the results.

The review indicated that the relationship between pain and sleep could be bidirectional in FM. In addition, this relationship could interact with depressive symptoms. Findings suggested that several dimensions of sleep, including sleep disturbance, onset latency, and efficiency, were associated with pain in FM. More specifically, sleep disturbance was identified as the most important sleep dimension and should be the focus of FM research. This review is significant, as it sought to enhance understanding of the association between sleep and pain in FM in the context of subjective and objective sleep dimensions. This could guide future research that aims to improve health-related quality of life in FM patients. The enhancement of sleep could reduce pain, and reductions in pain could enhance sleep in FM patients. However, additional studies involving mixed designs are required to determine whether 1) pain drives poor sleep, 2) poor sleep leads to greater pain intensity, and 3) pain and sleep share an indirect relationship that interacts with depression in FM. In addition, further studies examining sleep should use both objective and subjective measurement tools where available, as differences between sleep assessment tools could lead to misconceptions. In light of comprehensive research, multidisciplinary interventions should be
developed to reduce pain and depressive symptoms and enhance sleep quality, which could improve health outcomes for patients with FM.

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References

1. Bergman S. A general practice approach to management of chronic widespread musculoskeletal pain and fibromyalgia (Revised). In: Adebafo OA, Dickson J, editors. Collected Reports on the Rheumatic Diseases. Series 4 (Revised). Halmstad (SW): Arthritis Research Campaign; 2005. p. 129-139.

2. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, reviewers for their valuable recommendations.

3. Wolle F. New American College of Rheumatology Criteria for Fibromyalgia: A Twenty-Year Journey. Arthritis Care Res 2010; 62: 583-584.

4. Cote KA, Moldofsky H. Sleep, daytime symptoms, and cognitive performance in patients with fibromyalgia. J Rheumatol 1997; 24: 2014-2023.

5. Shaver JL, Lentz M, Landis CA, Heitkemper MM, Buchwald DS, Woods NE. Sleep, psychological distress, and stress arousal in women with fibromyalgia. Res Nurs Health 1997; 20: 247-257.

6. Lashley FR. A review of sleep in selected immune and autoimmune disorders. Holist Nurs Pract 2003; 17: 65-80.

7. Mease P, Arnold LM, Choy EH, Clauw DJ, Crofford LJ, Glass JM, et al. Fibromyalgia syndrome module at OMERACT 9: domain construct. J Rheumatol 2009; 36: 2318-2329.

8. Consoli G, Marazziti D, Ciapparelli A, Bazzichi L, Massimetti G, Giacomelli C, et al. The impact of mood, anxiety, and sleep disorders on fibromyalgia. Res Nurs Health 2012; 53: 962-967.

9. Affleck G, Tennen H, Urrows S, Higgins P, Abeles M, Hall C, et al. Fibromyalgia and women's pursuit of personal goals: a daily process analysis. Health Psychol 1998; 17: 40-47.

10. Arnold LM, Crofford LJ, Mease PJ, Burgess SM, Palmer SC, Abetz L, et al. Patient perspectives on the impact of fibromyalgia. Patient Educ Couns 2008; 73: 114-120.

11. Kelly GA, Blake C, Power CK, O'Keeffe D, Fullen BM. The association between chronic low back pain and sleep: a systematic review. Clin J Pain 2011; 27: 169-181.

12. Chiu YH, Silmana AJ, Macfarlane GJ, Ray D, Gupta A, Dickens C, et al. Poor sleep and depression are independently associated with a reduced pain threshold. Results of a population based study. Pain 2005; 115: 316-321.

13. Kundermann B, Sperral J, Fluber MT, Krieg JC, Lautenbacher S. Sleep deprivation affects thermal pain thresholds but not somatosensory thresholds in healthy volunteers. Psychosom Med 2004; 66: 932-937.

14. Nicassio PM, Wallston KA. Longitudinal relationships among pain, sleep problems, and depression in rheumatoid arthritis. J Abnorm Psychol 1992; 101: 514-520.

15. Arnold LM, Hudson JJ, Keck PE, Auchenbach MB, Javars KN, Hess EV. Comorbidity of fibromyalgia and psychiatric disorders. J Clin Psychiatry 2006; 67: 1219-1225.

16. Liberati M, Tetzlaff AJ, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA Statement. PLoS Med 2009; 6: e1000097.

17. Khan KS, Kunz R, Kleijnen J, Antes G. Five steps to conducting a systematic review. J R Soc Med 2003; 96: 118-121.

18. Effective Public Health Practice Projec. Quality Assessment Tool for Quantitative Studies. [cited 2009]. Available from http://www.ephpp.ca/tools.html

19. Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, et al. Evaluating non-randomised intervention studies. Health Technol Assess 2003; 7: 1-173.

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

21. Nicassio PM, Moxham EG, Schuman CE, Gevirtz RN. The contribution of pain, reported sleep quality, and depressive symptoms to fatigue in fibromyalgia. Pain 2002; 100: 271-279.

22. Hamilton N, Catley D, Karlson C. Sleep and the affective response to stress and pain. Health Psychol 2007; 26: 288-295.

23. Bigatti SM, Hernandez AM, Cronan TA, Rand KL. Sleep disturbances in fibromyalgia syndrome: Relationship to pain and depression. Arthritis Care Res 2008; 59: 961-967.

24. O’Brien EM, Waxenberg LB, Achinson JW, Gremillion HA, Staud RM, McCrave CS, et al. Negative mood mediates the effect of poor sleep on pain among chronic pain patients. Clin J Pain 2010; 26: 310-319.

25. Schaefer C, Chandran A, Hufstader M, Baik R, McNett M, Goldenberg D et al. The comparative burden of mild, moderate and severe fibromyalgia: results from a cross-sectional survey in the United States. Health Qual Life Outcomes 2011; 9: 71.

26. Wagner JS, DiBonaventura MD, Chandran AB, Cappelleri JC. The association of sleep difficulties with health-related quality of life among patients with fibromyalgia. BMC Musculoskelet Disord 2012; 13: 199.

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

28. Anderson RJ, McCrae CS, Staud R, Berry RB, Robinson ME. Predictors of clinical pain in fibromyalgia: Examining the role of sleep. J Pain 2012; 13: 350-358.

29. Kothari DJ, Davis MC, Yeung EW, Tennen HA. Positive affect and pain: mediators of the within-day relation linking sleep quality to activity interference in fibromyalgia. Pain 2015; 156: 540-546.

30. Miro E, Martinez MP, Sanchez AI, Prados G, Medina A. When is mediated by objective and subjective sleep characteristics in fibromyalgia patients. Clin J Pain 2014; 30: 852-859.
Association between fibromyalgia pain and sleep... Keskindag et al

32. Diaz-Piedra C, Catena A, Sánchez AI, Miró E, Pilar Martínez M, Bucla-Casal G. Sleep disturbances in fibromyalgia syndrome: The role of clinical and polysomnographic variables explaining poor sleep quality in patients. *Sleep Med* 2015; 16: 917-925.

33. Theadom A, Copley M, Humphrey KL. Exploring the role of sleep and coping in quality of life in fibromyalgia. *J Psychosom Res* 2007; 62: 145-151.

34. Ağargün MY, Tękeoğlu I, Güneş A, Adak B, Kara H, Ercan M. Dysfunctional beliefs, stress and sleep disturbance in fibromyalgia. *Sleep Med* 2008; 9: 376-381.

35. Ağargün MY, Tękeoğlu I, Güneş A, Adak B, Kara H, Ercan M. Sleep quality and pain threshold in patients with fibromyalgia. *Compr Psychiatry* 1999; 40: 226-228.

36. Love A, Leboeuf C, Crisp TC. Chiropractic chronic low back pain sufferers and self-report assessment methods. Part I. A reliability study of the Visual Analogue Scale, the Pain Drawing and the McGill Pain Questionnaire. *J Manipulative Physiol Ther* 1989; 12: 21-25.

37. Pearce J, Morley S. An experimental investigation of the construct validity of the McGill Pain Questionnaire. *Pain* 1989; 39: 15-121.

38. Burckhardt CS, Clark S, Bennett RM. The Fibromyalgia Impact Questionnaire: development and validation. *J Rheumatol* 1991; 18: 728-733.

39. Bryce TN, Budh CN, Cardenas DD, Dijkers M, Felix ER, Finnerup NB et al. Pain after spinal cord injury: an evidence-based review for clinical practice and research. Report of the National Institute on Disability and Rehabilitation Research Spinal Cord Injury Measures meeting. *J Spinal Cord Med* 2007; 30: 421-440.

40. Jensen MP. Measurement of Pain. In: Fishman SM, Ballantyne JC, Rathmell JP editors. Bonica’s management of pain. Philadelphia (PA): Williams & Wilkins; 2010. p. 251-270.

41. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. *Pain* 2011; 152: 2399-2404.

42. Raymond NC, de Zwaan M, Fails PL, Nugent SM, Ackard DM, Crosby RD, et al. Pain thresholds in obese binge-eating disorders subjects. *Biol Psychiatry* 1995; 37: 202-204.

43. Ağargün MY, Tękeoğlu I, Kara H, Adak B, Ercan M. Hypnotizability, pain threshold, and dissociative experiences. *Biol Psychiatry* 1998; 44: 69-71.

44. Nicassio PM, Radojevic V, Schoenfeld-Smith K, Dwyer K. The contribution of family cohesion and the pain-coping process to depressive symptoms in fibromyalgia. *Ann Behav Med* 1995; 17: 349-356.

45. Nicassio PM, Schoenfeld-Smith K, Radojevic V, Schuman C. Pain coping mechanisms in fibromyalgia: relationship to pain and functional outcomes. *J Rheumatol* 1995; 22: 1552-1558.

46. Nicassio PM, Schuman C, Radojevic V, Weisman MH. Helplessness as a mediator of health status in fibromyalgia. *Cognit Ther Res* 1999; 23: 181-196.

47. Stone A, Shiffman S. Ecological momentary assessment (EMA) in behavioral medicine. *Ann Behav Med* 1994; 16: 199-202.

48. Stone AA, Broderick JE, Porter LS, Kaell AT. The experience of rheumatoid arthritis pain and fatigue: Examining momentary reports and correlates over one week. *Arthritis Care Res* 1997; 10: 185-193.

49. Mason JH, Silverman SL, Weaver AL, Simms RW. Impact of fibromyalgia on multiple aspects of health status. *Scand J Rheumatol* 1992; 94: 33.
Association between fibromyalgia pain and sleep ... Keskindag et al

67. Edwards RR, Almeida DM, Klick B, Haythornthwaite JA, Smith MT. Duration of sleep contributes to next-day pain report in the general population. *Pain* 2008; 137: 202-207.

68. Dzierzewski JM, Williams JM, Roditi D, Marsiske M, McCoy K, McNamara J, et al. Daily variations in objective night sleep and subjective morning pain in older adults with insomnia: Evidence of covariation over time. *J Geriatr Soc Med* 2010; 58: 925-930.

69. Marty M, Rozenberg S, Duplan B, Thomas P, Duquesnoy B, Allaert, F. Quality of sleep in patients with chronic low back pain: a case-control study. *Eur Spine J* 2008; 17: 839-844.

70. Parrino L, Zucconi M, Terzano M. Sleep fragmentation and arousals in the pain patient. In: Lavigne G, Sessle B, Choiniere M, et al, editors. Sleep and Pain. Seattle: IASP Press; 2007. p. 213-231.

71. Moldofsky H. The contribution of sleep-wave physiology for fibromyalgia. *Adv Pain Res Ther* 1990; 17: 227-240.

72. Perlis ML, Giles DE, Bootzin RR, Dikman ZV, Fleming GM, Drummond SPA, et al. Alpha sleep and information processing, perception of sleep, pain and arousability in fibromyalgia. *Int J Neurosci* 1997; 89: 265-280.

73. MacDonald S, Linton SJ, Jansson-Frojmark M. Cognitive vulnerability in the development of concomitant pain and sleep disturbances. *Br J Health Psychol* 2010; 15: 417-434.

74. Moldofsky H. Rheumatic manifestations of sleep disorders. *Curr Opin Rheumatol* 2010; 22: 59-63.

75. Moldofsky H. Management of sleep disorders in fibromyalgia. *Rheum Dis Clin North Am* 2002; 28: 353-365.

76. White KP, Speechley M, Harth M, Ostbye T. The London Fibromyalgia Epidemiology Study: Comparing the demographic and clinical characteristics in 100 random community cases of fibromyalgia versus controls. *J Rheumatol* 1999; 26: 1577-1585.

77. Cohen MJM, Menefee LA, Doghramji I, Anderson WR, Frank ED. Sleep in chronic pain: Problems and treatments. *Int Rev Psychiatry* 2000; 12: 115-127.

78. Landis CA, Lentz MJ, Rothermel J, Buchwald D, Shaver JL. Decreased sleep spindles and spindle activity in midlife women with fibromyalgia and pain. *Sleep* 2004; 27: 741-750.

79. Wilson KG, Eriksson MY, D'Eon JL, Mikail SF, Emery PC. Major depression and insomnia in chronic pain. *Clin J Pain* 2002; 18: 77-83.

80. Smith MT, Haythornthwaite JA. How do sleep disturbance and chronic pain interrelate? Insights from the longitudinal and cognitive-behavioral clinical trials literature. *Sleep Med Rev* 2004; 8: 119-132.

81. Deardorff W. Breaking the cycle of chronic pain and insomnia. [cited 2005]. Available from http://www.spine-health.com/wellness/sleep/chronic-pain-and-insomnia-breaking-cycle

82. Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. *J Pain* 2013; 14: 1539-1552.

83. Ohayon MM. Relationship between chronic painful physical condition and insomnia. *J Psychiatr Res* 2005; 39: 151-159.

84. Carrette S. Fibromyalgia 20 years later: what have we really accomplished? *J Rheumatol* 1995; 22: 590-594.

85. Tang NK, Goodchild CE, Sanborn AN, Howard J, Salkovskis PM. Deciphering the temporal link between pain and sleep in a heterogeneous chronic pain patient sample: a multilevel daily process study. *Sleep* 2012; 35: 675A-678A.

86. Harrison L, Wilson S, Heron J, Stannard C, Munafò MR. Exploring the associations shared by mood, pain-related attention and pain outcomes related to sleep disturbance in a chronic pain sample. *Psychol Health* 2016; 446: 1-13.

87. Hall M, Buyssse DJ, Nowell PD, Nofzinger EA, Houck P, Reynolds CF et al. Symptoms of stress and depression ascorrelates of sleep in primary insomnia. *Psychosom Med* 2000; 62: 227-230.

88. Engel CC, von Korff M, Katon WJ. Back pain in primary care: Predictors of high health-care costs. *Pain* 1996; 65: 197-204.

89. Okifuji A, Turk DC, Sherman JJ. Evaluation of the relationship between depression and fibromyalgia syndrome: Why aren’t all patients depressed? *J Rheumatol* 2000; 27: 212-219.

90. Berber JSS, Kupek E, Berber SC. Prevalence of depression and its relationship with quality of life in patients with fibromyalgia syndrome. *The Brazilian Journal of Rheumatology* 2005; 45: 47-54.

91. Börsbo B, Peols mossen M, Gerdl B. The complex interplay between pain intensity, depression, anxiety and catastrophising with respect to quality of life and disability. *Disabil Rehabil* 2009; 31: 1605-1613.

92. Leplée JP, Briley M. The epidemiology of pain in depression. *Hum Psychopharmacol* 2004; 19: 3-7.

93. Aalto TJ, Malmivaa ra A, Kovacs F, Herno A, Alen M, Salmi L. et al. Preoperative predictors for postoperative clinical outcome in lumbar spinal stenosis: systematic review. *Spine* 2006; 31: E648-E663.

94. Trief PM, Grant W, Fredrickson B. A prospective study of psychological predictors of lumbar surgery outcome. *Spine* 2006; 25: 2616-2621.

95. Walker MP, Harvey AG. Obligate symbiosis: sleep and affect. *Sleep Med Rev* 2010; 14: 215-217.

96. Prather AA, Bogdan R, Hariri AR. Impact of sleep quality on amygdala reactivity, negative affect, and perceived stress. *Sleep Med Rev* 2010; 14: 215-217.

97. Davis MC, Zautra AJ, Reich JW. Vulnerability to stress and pain: a case-control study. *Eur Spine J* 2008; 17: 839-844.

98. Harrison L, Wilson S, Heron J, Stannard C, Munafò MR. Exploring the associations shared by mood, pain-related attention and pain outcomes related to sleep disturbance in a chronic pain sample. *Psychol Health* 2016; 446: 1-13.

99. Hall M, Buyssse DJ, Nowell PD, Nofzinger EA, Houck P, Reynolds CF et al. Symptoms of stress and depression ascorrelates of sleep in primary insomnia. *Psychosom Med* 2000; 62: 227-230.

100. Morin CM, Gibson D, Wade J. Self-reported sleep and mood disorder in chronic pain patients. *Clin J Pain* 1998; 14: 311-314.

101. Morin CM, Gibson D, Wade J. Self-reported sleep and mood disturbance in chronic pain patients. *Clin J Pain* 1998; 14: 311-314.

102. Rutledge DN, Jones K, Jones CJ. Predicting high physical function in people with fibromyalgia. *J Nurs Scholarsh* 2007; 39: 319-324.

103. Vitello MV, Moe KE, Larsen LH, Strinz PN. Age related sleep disturbance in chronic pain patients. *Clin J Pain* 2004; 20: 131-137.