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The Bidirectional Relationship Between Sleep Complaints and Pain: Analysis of Data from a Randomized Trial

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Abstract

Objective—The goal of this study was to examine the bidirectional relationship of sleep and pain to determine if changes in sleep complaints over the course of a chronic pain treatment trial predict pain outcomes and vice versa, controlling for changes in depression and anxiety.

Methods—Data were analyzed from a 12-month randomized controlled trial that tested the effectiveness of a collaborative care intervention for Veterans with chronic musculoskeletal pain. Participants were 250 Veterans from 5 primary care clinics in a Veteran Affairs (VA) medical center. Measures of pain, sleep, and depression/anxiety symptoms were collected at baseline, 3 months, and 12 months. Factor analysis was used to clarify the boundaries of these domains, and structural equation modeling was used to examine if changes in sleep complaints and depression/anxiety during the trial predicted pain at the end of the trial, controlling for covariates. An alternative model was also tested in which changes in pain predicted sleep complaints.

Results—Changes in sleep complaints at 3 months significantly predicted changes in pain at 12 months (standardized path coefficient of .29, $p < .001$). To a lesser extent, changes in pain

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predicted changes in sleep (standardized path coefficient of .15, $p < .05$). Changes in depression/anxiety did not significantly predict changes in pain or sleep. There was also evidence of differential relations of specific sleep complaints with pain.

Conclusions—This work helps to further disentangle the complex relationship between pain and sleep. This bidirectional relationship may need to be considered to improve pain outcomes.

Keywords

chronic pain; sleep; depression; anxiety

Chronic pain is a significant public health problem, representing great individual and societal cost. Painful chronic musculoskeletal disorders are three of the top five causes of disability in the United States (US Burden of Disease Collaborators, 2013). The co-occurrence of sleep disturbances and mental health symptoms with chronic pain represent an exponential increase in pain and suffering. Estimates suggest that up to 50% of individuals with chronic pain have depression, with chronic pain exacerbating depression and depression increasing pain severity and functional impairment (Banks & Kerns, 1996; Kroenke et al., 2011; Outcalt et al., 2014). Sleep difficulties are also common among patients with chronic pain, with up to 89% of patients reporting at least one sleep complaint and 53% of patients attending pain clinics presenting with clinically significant insomnia (McCracken & Iverson, 2002; Smith, Huang, & Manber, 2005; Tang, Wright, & Salkovskis, 2007).

Although there is some evidence that pain and sleep have a reciprocal relationship, impaired sleep is a more consistent predictor of pain than pain is of sleep (Affleck, Urrows, Tennen, Higgins, & Abeles, 1996; Bigatti, Hernandez, Cronan, & Rand, 2008; Finan, Goodin, & Smith, 2013; Tang, Goodchild, Sanborn, Howard, & Salkovskis, 2012). Based on these findings, conceptual models have been proposed by which biopsychosocial mechanisms, including dopamine and opioid systems and emotional dysregulation, explain how sleep disturbance augments pain (Finan et al., 2013; Smith, Quartana, Okonkwo, & Nasir, 2009).

Understanding the directional nature of the relationship of sleep and pain, as well as the dynamic relations of pain with depression and anxiety, can inform the development of effective, multi-modal treatment for patients with chronic pain (Campbell et al., 2013). For example, it is clear that improvements in pain do not necessarily result in improvements in secondary symptoms, particularly insomnia (Becker, Sjogren, Bech, Olsen, & Eriksen, 2000; Kroenke, Krebs et al, 2014; Tang, 2009). Conversely, some preliminary studies suggest that behavioral sleep treatments result in significant improvements in pain severity and function (Tang, 2009; Tang, Goodchild, & Salkovskis, 2012).

Although initial findings are promising regarding the role of sleep in the management of chronic pain, published studies have had two key limitations. First, many studies examine the relationship among mental health symptoms, pain, and sleep complaints without first establishing the boundaries of these domains. Because of the high co-occurrence of these symptoms in patients with chronic pain and moderate to high correlations among these measures, it is important to delineate boundaries of sleep relative to other mental health

symptoms to determine if sleep complaints are an independent construct or a proxy for general distress.

A second limitation is that many previous studies have used limited measures of sleep complaints. These limited assessments likely contribute to weak and inconsistent findings and limit understanding of the sleep and pain relationship over time. Moreover, sleep complaints are usually measured as a single higher order construct. Evidence suggests that sleep disturbances can be conceptualized as two related but independent lower order dimensions, insomnia (difficulties falling and staying asleep) and lassitude (fatigue and sleepiness) (Koffel & Watson, 2009). Reliance on measures of general sleep complaints may mask differential relations of specific sleep complaints with pain outcomes.

This study addresses these limitations by clarifying the boundaries of sleep complaints, pain, and anxiety/depression in patients with chronic pain and investigating the dynamic relationship of these constructs over time. Data was analyzed from the Stepped Care to Optimize Pain Care Effectiveness (SCOPE) trial, a 12-month randomized controlled effectiveness trial of a collaborative care intervention for primary care patients with chronic musculoskeletal pain (Kroenke, Krebs et al., 2014), with measures collected at baseline, 6 months, and 12 months. The prospective, longitudinal nature of the data allowed us to test the two alternative conceptual models by which changes in sleep complaints predict pain and changes in pain complaints predict sleep, controlling for depression/anxiety. Based on previous initial research (Asih, Neblett, Mayer, Brede, & Gatchel, 2014; Koffel, Krebs, Arbisi, Erbes, & Polusny., in press; O'Brien et al., 2010), it was hypothesized that three relatively independent constructs of pain, sleep complaints, and depression/anxiety would be identified. It was also hypothesized that pain and sleep would demonstrate a bidirectional relationship, controlling for depression/anxiety, but that there would be stronger evidence for changes in sleep complaints predicting changes in pain. Because previous analyses have not examined how individual sleep complaints predict pain, there were not any specific hypotheses about differential relations.

Methods

Participants

Participants were 250 Veterans enrolled from June 2010 to May 2012 from 5 primary care clinics in a Midwestern Veteran Affairs medical center. The trial was approved by the Indiana University Institutional Review Board and the Roudebush Research Review Committee. Details of the study, including the medication algorithm, are provided in other publications (Kroenke et al., 2013; Kroenke, Krebs et al., 2014). Briefly, inclusion criteria were primary care patients aged 19 to 65 years who had musculoskeletal or more generalized pain of moderate severity and persistent pain lasting at least 3 months despite trying at least 1 analgesic medication. Exclusion criteria included severe mental illness, severe cognitive impairment, or a terminal illness. Of 940 potentially eligible participants contacted by letter, 690 were excluded, with the most common reason being unable to be contacted by telephone.

Eligible patients who were interested in participating provided informed consent during an initial study visit. Participants were randomized to either an intervention group (n = 124) or a usual care group (n = 126). The intervention consisted of automated symptom monitoring to inform pain management by a nurse care manager/physician pain specialist team, using an algorithm-guided stepped care approach to optimizing analgesics. The usual care group continued to receive care from their primary care physician. Sleep disturbances were not directly addressed by the intervention. As discussed in the primary report (Kroenke, Krebs et al., 2014), the intervention group had a clinically important decrease in pain scores compared to usual care. Patients in the intervention group also reported greater improvement in depression, anxiety, and sleep, with depression reaching the significance threshold for secondary outcomes.

The control and intervention groups were combined for these analyses and treatment condition was included as a covariate to provide more statistical precision than would be obtained by analyzing the groups separately. Assessments were collected at baseline, 3 months, and 12 months.

Sleep Measures

Patient Health Questionnaire-9 (PHQ-9) Sleep Complaints Items—The PHQ-9 is a self-administered version of the Primary Care Evaluation of Mental Disorders (PRIME-MD) measure developed to diagnose depression in clinical and research settings (Kroenke, Spitzer, Williams, & Lowe, 2010). The present study utilizes two items from the PHQ-9 measuring sleep disturbance and fatigue. The sleep disturbance item asks participant to rate how often over the past 2 weeks they have had “Trouble falling asleep, staying asleep, or sleeping too much.” Scores on this item range from 0 (“not at all”) to 3 (“Nearly every day”). The fatigue item asks the participant how often they were “Feeling tired or having little energy” along the same Likert scale range. Responses of 2 (more than half the days) or 3 (nearly every day) on these two items were combined to create one category of sleep complaints, with final scores ranging from 0 to 2. The PHQ-9 sleep disturbance item has been shown to effectively screen sleep disturbance in primary care settings (MacGregor, Funderburk, Pigeon, & Maisto, 2012).

36-Item Short-Form Health Survey (SF-36) Vitality Scale—The SF-36 was originally developed as a 20-item measure for use in the Medical Outcomes Study (MOS) to monitor patient outcomes in medical and research settings. The expanded 36- item measure includes scales for 8 core health outcomes: Physical functioning, Role-Physical, Bodily Pain, Mental Health, Role Emotional, Social Functioning, Vitality, and General Health Perceptions (Ware & Sherbourne, 1992). These scales have been shown to have adequate psychometric properties (McHorney, Ware, & Raczek, 1993).

This study utilized the Vitality scale, a 4-item measure assessing current energy level and fatigue. Participants choose from five response options ranging from 0 (“all of the time”) to 5 (“none of the time”). Scores are transformed into a scale ranging from 0 to 100, with lower scores indicating reduced levels of vitality. The scale has shown good criterion validity in

medical patients and is sensitive to the impact of both disease and treatment in the context of a variety of medical diagnoses (Bjorner et al., 2007).

Patient Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance and Fatigue scales—For this study, items from the PROMIS-29 profile were administered, including the 4-item Fatigue and Sleep Disturbance scales asking participants to rate their sleep-related symptoms over the past 7 days. The Fatigue scale contains items related to tiredness during the day (e.g., “I feel fatigued”), whereas the Sleep Disturbance scale contains items related to nighttime sleep complaints (e.g., “I had difficulty falling asleep”). Response options range from 0 (“Not at all”) to 5 (“Very much”), with the exception of the last question on the Sleep Disturbance scale regarding quality of sleep (responses can range from very poor to very good). Total scores range from 4 to 20, with higher scores indicating greater levels of sleep impairment and fatigue. The sleep-related PROMIS scales have been shown to have adequate psychometric properties (Buysse et al., 2010), including high convergent validity with well-established sleep measures (Yu et al., 2011).

Pain Measures

BPI—The BPI was originally designed to assess the impact of pain severity and interference in cancer patients (Cleeland & Ryan, 1994). The BPI total score includes items related to pain severity and pain interference in 7 areas (mood, physical activity, work, social activity, relations with others, sleep, and enjoyment of life). Scores range from 0 to 10, with higher scores indicating worse pain. The total score has been found to have strong construct validity, reliability, and sensitivity to changes over time in patients with chronic pain (Krebs et al., 2010).

SF-36 Bodily Pain scale—The SF-36 Bodily Pain scale consists of 2 items assessing pain severity and level of interference within the last 4 weeks (Ware & Sherbourne, 1992). The interference question asks patients how much their pain has interfered with normal work on a scale from 1 (“not at all”) to 5 (“extremely”), while the severity question asks patients how much pain they have had from 1 (“none”) to 6 (“very severe”). Total transformed scores range from 0 to 100, with higher scores indicating less severe pain. The scale has been found to be internally consistent, with strong test-retest reliability as well as convergent validity with other pain severity and disability measures (Von Korff, Jensen, & Karoly, 2000).

PROMIS Pain Interference Scale—The 4-item PROMIS Pain Interference scale consists of 4 items regarding level of pain interference with various activities in the last 7 days. Response options range from 1 (“not at all”) to 5 (“very much”), with total scores ranging from 4 to 20 and higher scores indicating greater pain interference. The PROMIS pain scales have been found to be highly reliable and have demonstrated concurrent validity (Amtmann et al., 2010; Revicki et al., 2009).

Depression/anxiety Measures

None of these measures contain items referring to sleep complaints, allowing an examination of the independence of sleep and depression/anxiety constructs without cross-contamination from similar items.

Generalized Anxiety Disorder 7 (GAD-7)—The GAD-7 is a brief self-report scale designed to assess GAD in clinical practice (Spitzer, Kroenke, Williams, & Lowe, 2006). It consists of 7 items that ask patients to rate their symptoms in the past two weeks. Scores range from 0 to 21, with higher scores indicating more severe anxiety symptoms. Individual item options range from 0 (“not at all”) to 3 (“nearly every day”). The GAD-7 has demonstrated strong internal consistency and test-retest reliability (Spitzer et al., 2006). It has also has shown to have strong construct and convergent validity and demonstrated good psychometric properties in primary care (Ruiz et al., 2011), psychiatric (Kertz, Bigda-Peyton, & Bjorgvinsson, 2013), and general population settings (Lowe et al., 2008).

SF-36 Mental Health Scale—The SF-36 Mental Health scale consists of 5 items assessing the four major mental health dimensions as outlined by the original Mental Health Inventory (MHI; anxiety, depression, loss of behavioral/emotional control, and psychological well-being) and confirmed via factor analysis of the full 38-item MHI (Ware & Sherbourne, 1992). Response options range from 1 (“none of the time”) to 5 (“all of the time”), with transformed total scores ranging from 0 to 100 and higher scores indicating greater levels of mental health. This scale has shown good convergent and criterion validity (McHorney et al., 1993).

PROMIS-29 Profile Anxiety and Depression scales—The PROMIS anxiety and depression scales each consist of 4-items assessing anxiety and mood symptoms over the past 7 days (Pilkonis et al., 2011). Response options range from 1 (“Never”) to 5 (“Always”). Overall scores range from 4 to 20, with higher scores indicating greater levels of anxiety/depression. These 4-item scales have demonstrated strong reliability and convergent validity, as well as the ability to discriminate between patients with chronic pain with and without anxiety diagnoses in primary care (Kroenke, Yu, Wu, Kean, & Monahan, 2014).

Statistical Analyses

Exploratory factor analysis was used to clarify the boundaries of sleep complaints, pain, and depression/anxiety symptoms, as well as to help define latent factors for the later structural equation modeling (SEM) analyses. The baseline measures described above were submitted to exploratory principal factor analysis with promax rotation using SAS (version 9.2). An oblique rotation was used to model the moderate to large correlations obtained among these measures in previous studies. The prior communality estimate was calculated using squared multiple correlations (SMCs). The goal in these analyses was to extract the greatest number of distinct and interpretable factors using the following guidelines. First, scales that loaded below .40 were considered weak markers of the dimension. Second, scales that loaded strongly onto more than one factor were considered to be multidimensional and thus

represented a threat to the discriminant validity of the dimensions. Finally, three scales were considered the minimum number of markers required for a well-defined factor.

Next, SEM in MPlus (version 7; Muthen & Muthen, 2012) was used to determine if changes in sleep complaints and depression/anxiety symptoms predict changes in pain and vice versa. Earlier analyses suggested that missing at random assumptions are satisfied for the variables of interest included in these analyses (Kroenke, Krebs et al., 2014). Following recommendations (Schafer & Graham, 2002), missing data was addressed with Full Information Maximum Likelihood (MLR) estimation. This procedure allowed us to use all available data from the 250 participants.

The SEM analyses involved several steps. First, a measurement model was developed in which latent variables were defined by observed indicators. Next, a latent variable or structural model was estimated. The latent variable model regressed changes in pain from baseline to end of treatment (12 months) on changes in depression/anxiety and sleep complaints at 3 months. An alternative conceptual model was estimated in which changes in sleep from baseline to end of treatment (12 months) was regressed on changes in depression/anxiety and pain at 3 months. Finally, to examine the influence of changes in specific sleep complaints on pain outcomes, a model that regressed changes in pain on changes in depression/anxiety and specific sleep complaints was tested, using the latent variables of insomnia (defined by scores on the PHQ-9 sleep disturbance item and PROMIS Sleep Disturbance scale) and lassitude (defined by scores on the PHQ-9 fatigue item, SF-36 Vitality scale, and PROMIS Fatigue scale).

Three different fit indices were used to evaluate these models, including the comparative fit index (CFI), the standardized root-mean-square residual (SRMR), and the root-mean-square error of approximation (RMSEA). In general, fit is considered acceptable if CFI is .90 or greater and SRMR and RMSEA are .10 or less (Finch & West, 1997; Hu & Bentler, 1998). However, more stringent cutoffs for these indices have been recommended, including values of .95 for CFI, .08 for SRMR, and .06 for RMSEA (Hu & Bentler, 1999). In these analyses, CFI values of .90 or greater are interpreted as reflecting an adequate fit and values of .95 or greater to reflect an excellent fit. Similarly, SRMR and RMSEA values of .10 or less are interpreted as representing an adequate fit and values of .06 or less represent an excellent fit.

Results

Descriptive Statistics

Table 1 presents demographic variables for the participants, as well as pain, sleep complaints, and depression/anxiety measures at baseline. The majority of participants (51.6%) reported pain for longer than 10 years. Participants had an average of two comorbid medical diseases and reported pain in multiple pain sites. In general, participants in both groups reported moderate levels of pain, sleep complaints, and depression/anxiety. The mean BPI total score was 5.2, indicating at least moderately severe pain. On average, participants were above the cut-score of 5 for having at least mild anxiety on the GAD-7. The majority of participants also reported having trouble with sleep and feeling fatigued on the PHQ-9 items. In the usual care group, 58% indicated feeling tired and 63% indicated trouble with

sleep more than half the days or nearly every day. In the intervention group, 60% indicated feeling tired and 57% indicated trouble with sleep more than half the days or nearly every day.

There was strong convergent validity among instruments within the same domain for pain, sleep complaints, and depression/anxiety (correlations generally ranging from 0.6 to 0.8), with modest evidence for discriminant validity (correlations generally ranging from 0.3 to 0.5 across domains). These correlations are available as supplemental material online in Table S1. Among the sleep measures, scales and items referring to insomnia tended to be more highly correlated with each other than with lassitude measures and vice versa. This suggests that sleep complaint items, while moderately correlated with each other, represent two distinct lower order factors. Correlations of potential baseline covariates with pain outcomes were examined and significant but small correlations of pain at 12 months with education (−0.16, $p < .05$), income (0.20, $p < .01$), duration of pain (0.15, $p < .05$), pain sites (0.20, $p < .01$), and medical comorbidities (0.20, $p < .01$), as well as treatment group (0.23, $p < .01$) were found. These significant baseline covariates were controlled for in the SEM analyses.

Factor Structure of Pain, Sleep, and Depression/anxiety

The Kaiser-Meyer-Olkin (KMO) (.88) and Bartlett's test of sphericity ($\chi 2 = 2263.71$, $p < .0001$) showed that factor analysis was adequate for this data. Exploratory factor analyses initially revealed the presence of a large and relatively broad factor of sleep complaints, pain, and depression/anxiety symptoms that accounted for 77% of the total variance. In the next step, two factors representing depression/anxiety symptoms and pain/sleep complaints were extracted. These factors were moderately correlated at 0.61 and accounted for 91% of the common variance. When three factors were extracted, they represented depression/anxiety symptoms, sleep complaints, and pain and accounted for all of the common variance. When four factors were extracted, the third factor was defined by lassitude measures (PHQ Fatigue, SF Vitality, PROMIS Fatigue) and the fourth factor was defined by insomnia measures (PHQ Sleep Disturbance item and PROMIS Sleep Disturbance). The scree plot leveled off after the second factor, indicating that two factors are the minimum number to retain. Although both the three and four factor models resulted in distinct, interpretable factors, the four factor model was not well defined (2 to 3 variables for most factors). Therefore, results on the three-factor model are reported in supplementary Table S2. Depression/anxiety is defined by scales measuring symptoms of depression and anxiety. Sleep complaints is defined by scales measuring insomnia and lassitude. Pain is defined by scales measuring pain intensity and interference. The three-factor structure is clear and distinct, with limited cross-loadings. Correlations among factors ranged from .55 to .60.

Structural Equation Modeling

Two of the three fit indices for the measurement model ($\chi^2 = 245.02$, df = 51) suggest at least an adequate fit (CFI = .91, SRMR = .06), with RMSEA suggesting a less than adequate fit at .12. The standardized factor loadings and 95% confidence intervals were examined prior to interpreting the structural model to ensure that the latent variables of pain, sleep complaints, and depression/anxiety were adequately defined by the specified indicators. All

loadings were consistently high in the predicted direction and significant at p < .001, suggesting that the scales were good markers of their respective factors.

Prior to estimating structural equation models, we tested whether changes over time in the observed variables were accounted for by mean differences at the level of the latent factors. A formal factorial invariance model with strong invariance constraints (i.e., constrained loadings and intercepts) across the three time points for the latent sleep complaints, pain, and depression/anxiety factors fit adequately well (RMSEA = .11, CFI = .91, SRMR = .07), indicating that change in the indicators were accounted for by their respective factors. Supplemental Table S3 presents the standardized changes in factor means from baseline to 3 and 12 months. There were significant changes in the latent factors of pain and sleep at 3 months compared to baseline and at 12 months compared to baseline.

Figure 1 shows the model in which changes in sleep complaints and depression/anxiety symptoms from baseline to 3 months predict changes in pain at 12 months (χ^2 = 886.54, df = 370). Although not shown in the model, baseline covariates of education, income, pain sites, duration of pain, medical comorbidities, and treatment group were included, with treatment group and income as the only covariates with significant paths in this model. Standardized regression coefficients were .18, $p < .01$ and .11, $p < .05$, respectively, for these covariates. The significant treatment group covariate suggests that patients in the treatment group had greater improvement in pain than those in the control group, as would be expected. Overall, the majority of indicators suggested an adequate fit, with CFI at .90 and RMSEA below .10 (RMSEA = .08). SRMR was .11, which suggests a less than adequate fit.

Standardized parameter estimates and 95% confidence intervals for the estimated model are shown in Figure 1. The majority of regression coefficients were significant at p <.001, except the path from depression/anxiety at 3 months to pain at 12 months. As was hypothesized, changes in sleep complaints at 3 months significantly predicted changes in pain at 12 months. Unexpectedly, changes in depression/anxiety symptoms did not predict pain outcomes after controlling for covariates and changes in sleep.

The alternative conceptual model was tested in which early changes in pain and depression/anxiety predicted changes in sleep from baseline to 12 months (χ^2 = 852.55, df = 370), as shown in Figure 2. As in the previous model, the majority of indicators suggested an adequate fit, with CFI at .90 and RMSEA below .10 (RMSEA = .07). SRMR was .11, which suggests a less than adequate fit. Standardized parameter estimates and 95% confidence intervals for the estimated model are shown in Figure 2. As in the previous model, the majority of regression coefficients were significant at $p < .001$. The path from pain at 3 months to sleep at 12 months was significant at $p < .05$ and the path from depression/anxiety at 3 months to pain at 12 months was nonsignificant.

As an exploratory analysis, the sleep complaints factor was divided into the two lower order factors of lassitude and insomnia to determine if these dimensions have differential relations with changes in pain over 12 months (χ^2 = 834.55, df = 365). Loadings for the latent variables of insomnia, lassitude, pain, and depression/anxiety were consistently high and significant at $p < .001$. Fit indices were comparable to the first model (CFI = .90, SRMR = .

11, RMSEA = .07). The standardized parameter estimates and 95% confidence intervals are reported in supplemental Figure S1. Changes in insomnia predicted changes in pain at $p <$ .05. The remaining regression coefficients were significant at $p <$.001, with the exception of pain regressed onto depression/anxiety and lassitude. The finding that depression/anxiety was not a significant predictor of pain parallels the earlier analysis, whereas the finding that lassitude was not a significant predictor of pain has not been previously reported in the literature.

Discussion

The findings from this study suggest that pain, depression/anxiety, and sleep complaints represent distinct constructs that are moderately correlated in patients with chronic pain. In accordance with previous research, regression coefficients suggest that changes in sleep were a stronger predictor of changes in pain (.29, $p < .001$) than changes in pain predicting changes in sleep (.15, $p < .05$). In the current study, sleep was not targeted in the intervention or control group, but early improvements (i.e., within 3 months) in sleep based on self-report measures predicted improvements in pain over the course of a year; conversely, worsening sleep predicted worsening pain over time.

The finding of three distinct symptom domains supports the theory that sleep disturbance and depression/anxiety symptoms may be precipitated by pain, but eventually develop into independent conditions requiring direct treatment (Smith et al., 2005). This appears to be particularly relevant for insomnia. Evidence for improvement in mood following pain treatment is more robust than that for improvement in sleep (Becker et al., 2000; Flor, Fydrich, & Turk, 1992; Kroenke, Krebs et al., 2014; Scascighini et al., 2008; Tang, 2009). More research is clearly needed for how to address these secondary symptoms in the context of chronic pain treatment, as patients rate improvement in sleep as an important outcome of pain therapy (Turk et al., 2008).

We found that changes in sleep from baseline to 3 months were related to changes in pain at 12 months, controlling for baseline covariates and depression/anxiety symptoms. In the second model, changes in pain from baseline to 3 months were related to changes in sleep at 12 months, although this path was not as large as the path from sleep to pain in the previous model. Together, these SEM analyses support a bidirectional relationship between sleep and pain and agree with prior research suggesting that changes in sleep complaints are more strongly related to changes in pain than vice versa. Contrary to our hypotheses, improvements in depression/anxiety symptoms did not predict improvements in pain, despite that pain and depression/anxiety have shown to have a reciprocal relationship (Kroenke et al., 2011). Although the non-significant findings may be partially explained by range restriction given less overall change in depression/anxiety relative to sleep and pain (see Table S3), sleep does appear to be a particularly important condition to target in treating patients with chronic pain.

Exploratory analyses suggest that the lower order factors of lassitude and insomnia can be identified in patients with chronic pain and that insomnia has a marginally stronger relationship with pain, such that improvements in insomnia are predictive of improvements

in pain. Although this research is preliminary, it suggests the utility of examining lower order sleep dimensions in the context of pain.

Limitations and Conclusions

This study addresses limitations of previous research by delineating the boundaries of pain, sleep complaints, and depression/anxiety symptoms in patients with chronic pain prior to examining the longitudinal relationship of these variables. However, there are limitations to this secondary analysis that should be noted. Given that the majority of fit indices were adequate, the latent variable models will need to be replicated in additional larger samples; it is possible that the relatively small sample used in these analyses contributed to adequate rather than excellent fit for these models (MacCallum, Browne, & Sugawara, 1996; Tanaka, 1987).

Although the current study uses a comprehensive assessment battery relative to previous research, the lower order dimensions of sleep disturbances were not well defined and the analyses conducted with these lower order dimensions should be considered preliminary. In addition, the data in this study were based on self-report obtained from questionnaire measures. It is well established that discrepancies exist between self-reported and objectively measured sleep with polysomnography. Next steps include replicating the conceptual models using a multi-method approach, including interview and objective sleep measures. As this secondary data analysis necessitated the use of some non-traditional measures of depression and sleep (e.g., PHQ-9, SF-36), findings will need to be replicated with more widely-used symptoms measures.

It is also important to note that we were unable to control for medication in the SEM models given the complexity of the intervention. The parent trial was designed to test a treatment approach for pain guided by an algorithm and there was considerable variability in the number and types of analgesics used by each patient, as well as duration of use and dosages. Given the numerous medication changes over the 12-month pragmatic trial at varying time points in individual patients, it was impossible to isolate medication effects. Although the relations between sleep, pain, and mood may be partially moderated by medication, it is unlikely that improvements in sleep represented a proxy for medication. The effect of analgesic medication on sleep is modest at best and sedation does not directly translate into good sleep quality (Mystakidou et al., 2011).

Finally, these data were limited to Veterans enrolled in a clinical trial of treatment for musculoskeletal pain, so demonstrating that findings replicate across patient populations and medical conditions is an important area for future research. As a related limitation, the clinical trial data did not allow conclusions to be drawn regarding what factors instigated changes in symptoms. For example, it is unclear why sleep improved over time across all patients, as it was not a target of the intervention. Moreover, these analyses reported changes in symptoms from baseline on continuous measures and do not necessarily reflect clinical levels of improvement, such as minimally important differences or clinical cut-offs.

Chronic pain treatment studies represent an important avenue for continuing to untangle the complicated interplay of pain, depression/anxiety, and sleep complaints. Comprehensively

assessing these symptoms over the course of treatment can help identify modifiable treatment targets to maximize improvements in pain outcomes. Several clinical trials have begun to modify pain interventions to include components that directly address sleep disturbances (McCurry et al., 2014; Pigeon et al., 2012; Tang, Goodchild, & Salkovskis, 2012). These treatments appear promising, particularly in patients with severe pain and insomnia (McCurry et al., 2014). It will be important to continue investigating the effect of targeted sleep treatments on both sleep and pain outcomes to achieve a better understanding of the generalizability, replicability, and long-term effects of these treatments in improving pain functioning.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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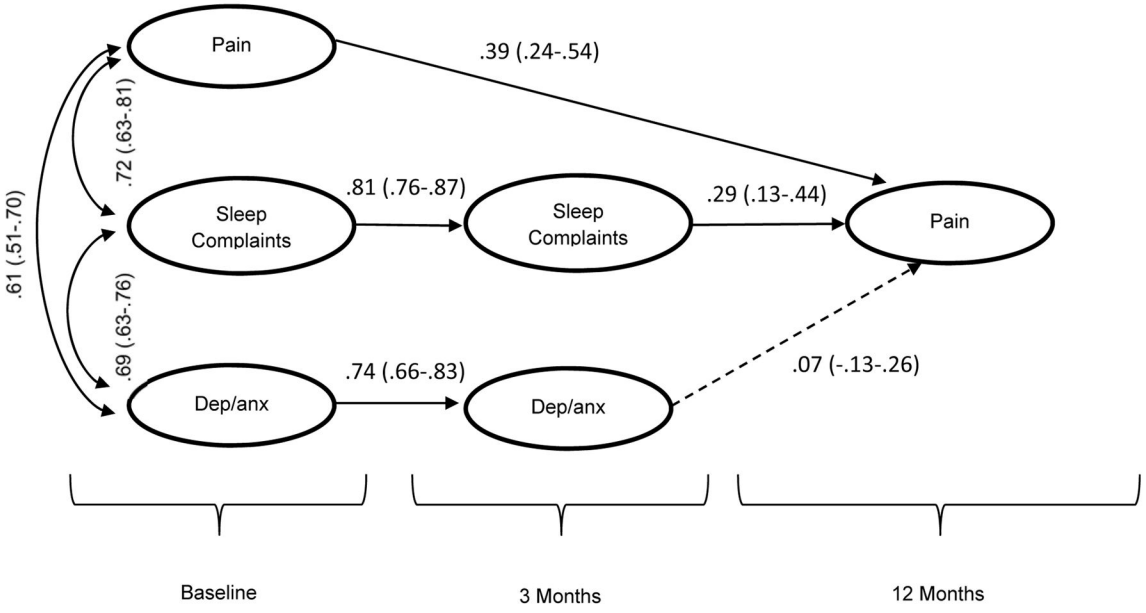

Figure 1.

Standardized path coefficients for the conceptual model in which early changes in sleep and depression/anxiety predict changes in pain. 95% confidence intervals are given in parentheses. $n = 250$. Significant paths and estimates have solid lines ($p < .001$). Dep/anx = Depression/anxiety.

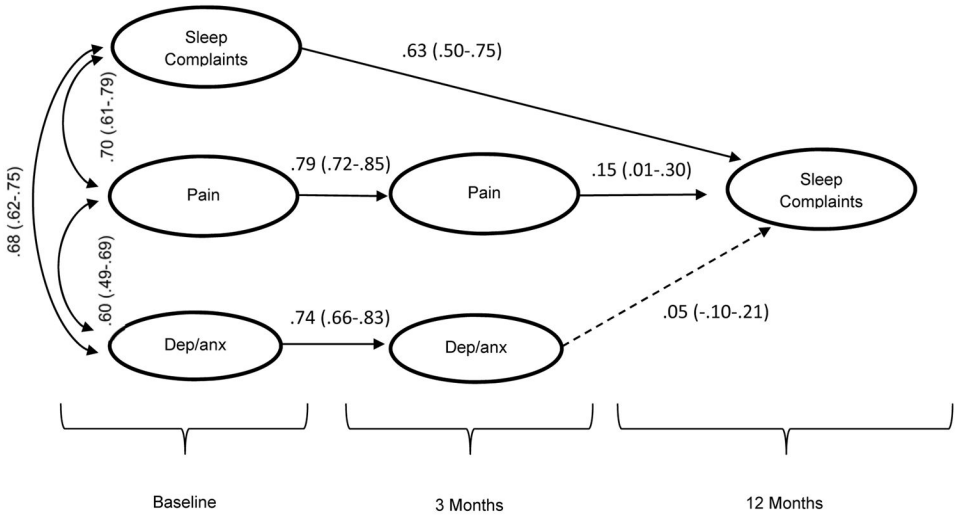

Figure 2.

Standardized path coefficients for the conceptual model in which early changes in pain and depression/anxiety predict changes in sleep. 95% confidence intervals are given in parentheses. $n = 250$. Significant paths and estimates have solid lines ($p < .05$). Dep/anx = Depression/anxiety.

Table 1

Baseline Characteristics of Participants Enrolled in the Stepped Care to Optimize Pain Care Effectiveness (SCOPE) Study

	Intervention (n = 124)	Usual Care (n = 126)
Demographics, No (%)		
Age, mean (SD), y	55.0 (9.0)	55.3 (7.9)
Men	109 (87.9)	98 (77.8)
Caucasian	89 (71.8)	103 (81.8)
Married	98 (79.0)	87 (69.1)
Education > high school	94 (75.8)	91 (72.2)
Employed	76 (61.3)	84 (66.7)
Income adequate by self-report	107 (86.3)	118 (93.7)
Comorbid medical diseases, mean (SD), No.	2.0 (1.2)	2.1 (1.4)
Number of pain sites, mean (SD), No.	5.3 (3.0)	4.6 (3.0)
Duration of pain, No. (%), y		
≤5	37 (29.8)	36 (28.6)
6–10	24 (19.4)	24 (19.1)
>10	63 (50.8)	66 (52.4)
Sleep Complaints, mean (SD)		
PHQ-9 sleep disturbance item (range, 0–2 [worst])	1.3 (.83)	1.5 (.77)
PHQ-9 fatigue item (range, 0–2 [worst])	1.4 (.79)	1.4 (.78)
SF-36 Vitality (range, 0–100 [best])	40.5 (22.5)	40.7 (22.8)
PROMIS Fatigue (range, 4–20 [worst])	12.7 (4.4)	12.2 (4.2)
PROMIS Sleep Disturbance (range, 4–20 [worst])	12.6 (4.3)	12.8 (4.3)
Pain, mean (SD)		
BPI total (range, 0–10 [worst])	5.3 (1.8)	5.1 (1.8)
SF-36 Bodily Pain (range, 0–100 [best])	34.6 (16.8)	35.1 (16.4)
PROMIS Pain Interference (range, 4–20 [worst])	11.3 (4.3)	11.4 (4.2)
Depression/anxiety, mean (SD)		
GAD-7 (range, 0–21 [worst])	6.1 (5.6)	5.7 (5.7)
SF-36 Mental Health (range, 0–100 [best])	70.9 (21.8)	69.1 (21.7)
PROMIS Anxiety (range, 4–20 [worst])	7.1 (3.6)	7.2 (3.8)
PROMIS Depression (range, 4–20 [worst])	6.9 (3.8)	7.0 (4.3)