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Improving pain and sleep in middle-aged and older adults: The promise of behavioral sleep interventions

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Insomnia and chronic pain are common comorbid conditions in middle-aged and older adults. Up to half of older adults with chronic pain have sleeping difficulties, which greatly increases pain-related distress and disability [46,47]. Natural age-related changes in sleep architecture and circadian rhythms further contribute to insomnia, including advanced sleep phase (falling asleep early and waking early) and reduced slow-wave sleep [33]. Unfortunately, insomnia medications can have adverse cognitive and behavioral effects, especially in combination with opioids, and are specifically contraindicated in older adults due to increased fall risk [3,18,31,35,56]. Off-label use of drugs such as antidepressants, antipsychotics, and anticonvulsants are used in practice to treat insomnia for older adults, but have not been extensively studied in this population and carry considerable risk of adverse effects [39].

Behavioral sleep interventions are a promising avenue for providing better and safer sleep and pain outcomes for middle-aged and older adults, while reducing the needs and hazards of excessive reliance on sedative hypnotics and opioids. The purpose of this review is to discuss evidence that sleep disturbance causes and exacerbates pain in middle-aged and older adults and that good sleep improves pain outcomes. We examine the efficacy of cognitive behavioral therapy for insomnia (CBT-I) on pain and sleep outcomes in middle-aged and older adults. Based on our review of the literature, we suggest an agenda for future research, including adaptation and additions to standard CBT-I to improve outcomes for middle-aged and older adults.

Worsening of Pain Following Sleep Disturbances: Observational Studies

Finan et al. [13] reported on five large prospective studies that established sleep disturbance as a risk factor for new incident and exacerbation of chronic pain over 1 to 17 years in population-based samples [5,22,28–30]. Conversely, good sleep quality controlling for psychosocial factors predicted a two-fold remission rate from widespread chronic pain [9]. McBeth et al. [23] found that self-reported nonrestorative sleep was the strongest independent predictor of new onset widespread pain among middle-aged and older adults (50) over 3 years. Finally, a recent systematic review including 16 longitudinal studies found that worsening sleep was associated with a two- to three-fold increase in risk of developing a pain condition, as well as worse physical functioning, whereas improvement in sleep was associated with better functioning [2]. The authors then conducted a meta-analysis with a subgroup of 5,902 older subjects (mean age 60) and found that onset and persistence of sleep problems was significantly related to worse physical health and pain across 2-5 years (effect sizes were small [8] and ranged from .33-.41).

Worsening of Pain Following Sleep Disturbances: Experimental Studies

Finan et al. [13] reviewed experimental studies that examined the effects of sleep deprivation on pain and concluded that experimental sleep deprivation has the potential to increase clinical pain and responses to quantitative sensory tests. Lautenbacher et al. [21] suggested that sleep deprivation interferes with the analgesic action of endogenous and exogenous opioids, as well as additional neurotransmitter systems including dopaminergic and serotonergic systems.

Importantly, some human evidence suggests that in females disrupted sleep continuity (i.e., wakefulness during the night) may contribute to the ongoing opioid epidemic through disruption of opioid circuits involved in the descending pain modulatory systems, possibly leading to reduced effectiveness of exogenous opioids [10,15,40]. For example, Smith et al. [40] found that forced awakenings in healthy females led to a loss of pain inhibition as measured using a diffuse noxious inhibitory control test with a cold pressor task; the authors suggest that one possible pathway from sleep disturbance to pain is an impairment in opioidergic descending systems. Similarly, Iacovides et al. [15] found that forced awakenings in healthy females led to increased pain sensitivity in superficial (pin prick thresholds) and deep tissues (forearm ischemia), possibly by impairing endogenous opioid systems. Eichhorn et al. [10] suggest a sex specific effect of total sleep deprivation on descending pain pathways as heat-pain thresholds significantly decreased in healthy females compared to males after one night of total sleep deprivation.

Most of this work has been preclinical, although preliminary studies with humans suggest that longer wake time at night measured by actigraphy predicts next day opioid use in burn patients [36] and that increased pre-surgery sleep duration reduced post-surgery pain and opioid use in older adults (mean age 61) undergoing knee- or hip-replacement surgery [38]. An hour more sleep in a group with extended time in bed compared to the control group corresponded to less average daily pain (4.4 vs. 5.6 on a 0-10 scale) and less daily morphine milligram equivalent intake (20.3 vs. 38.6 mg). This research suggests that increasing sleep

duration and decreasing wake time during the night are both important treatment targets. Definitive translational studies are needed to evaluate more clearly whether poor sleep is directly associated with increased opioid consumption and whether abuse of opioids to self-treat pain may be in part linked to poor management of sleep disturbances.

Sleep disturbance has also been linked to inflammatory mechanisms predictive of medical conditions commonly affecting older adults, including cardiovascular events, hypertension, and type 2 diabetes [16,17]. In a recent meta-analysis, Irwin et al. [17] found that sleep disturbance had modest but significant associations with increases in markers of systemic inflammation, including c-reactive protein and interleukin-6 (effect sizes were negligible to small [8] and ranged from .12-.20). Proinflammatory mediators, such as interleukin-6, are known to sensitize nociceptors and increase pain sensitivity [54]. Altogether, these data suggest the possibility that insomnia treatment may improve the functioning of endogenous descending pain inhibition and reduce markers of inflammatory risk in middle-aged and older adults at increased risk for age-related inflammatory disease, although few direct intervention studies have evaluated these possibilities. Preliminary work shows that CBT-I is associated with reduced risk of having high c-reactive protein levels in middle-aged and older adults (> 55 years) relative to a control group, with nearly a 50% decrease in the percentage of participants with high c-reactive protein in the CBT-I group at 16 month follow-up [16].

Rationale for Use of Behavioral Sleep Interventions in Middle-aged and Older Adults with Pain

The relationship between poor sleep and increased pain described above suggests that improving sleep might improve co-morbid pain in middle-aged and older adults. Indeed, behavioral sleep interventions have shown potential for improving both sleep and pain outcomes. In a widely accepted model of insomnia developed by Spielman and colleagues, maladaptive behaviors (napping, excessive time in bed) and cognitions (worry about sleep) perpetuate insomnia [42]. Emerging work with patients with chronic pain has identified pain specific cognitions (e.g., “I’ll never get good sleep because of pain”) and behaviors (e.g., napping, inactivity) that seem to enhance pain and insomnia, as well as higher levels of dysfunctional beliefs about sleep in general [1,37,48].

Figure 1 illustrates how behavioral sleep interventions, like CBT-I, target common mechanisms that worsen insomnia and pain in middle-aged and older adults. As shown at the top of the figure, middle-aged and older adults are vulnerable to both insomnia and pain due to age-related changes in sleep and increased prevalence of chronic medical conditions. Maladaptive beliefs and coping behaviors are hypothesized to enhance pain and insomnia. As shown on the left side of Figure 1, these cognitions and behaviors lead to further dysregulation of sleep processes (e.g., weakened circadian rhythm and sleep drive), which perpetuate insomnia symptoms and may lead to greater pain sensitivity and possibly increased risk of harm (e.g., use of opioid medication). As shown on the right side of Figure 1, CBT-I involves re-regulation of sleep processes, which leads to improvements in sleep and is hypothesized to improve pain. Improved sleep may also lead to opioid sparing, but most

work in this area is preclinical and additional evidence is needed. It is well established that CBT-I improves sleep among patients with chronic pain [43,45,57] and that this treatment is highly efficacious for improving sleep in older adults [26,33,35]. So, what is the impact of CBT-I on comorbid pain among middle-aged and older adults?

Improvement in Pain for Middle-aged and Older Adults Following Behavioral Sleep Interventions

Several recent reviews have highlighted improvement in pain symptoms following CBT-I. Tang et al. [45] reported the effect of CBT-I on pain across six randomized clinical trials (RCTs) involving 479 patients with long-term painful conditions (mean age 45-54 years). The overall effect size for improvement in pain at post-treatment was negligible but significant (.18) [8], leading the authors to conclude that there is a mild therapeutic impact on pain immediately after sleep treatments. Finan et al. [12] reviewed trials that tested both CBT-I and hybrid CBT for insomnia and pain (CBT-I/P), with the hypothesis that interventions targeting both sleep and pain may produce more favorable results on pain outcomes. Three hybrid trials were reviewed [34,44,51], one of which, the Lifestyles trial by Vitiello and colleagues, focused exclusively on older adults (≥ 60) [51]. The mean age of participants across all trials ranged from 49 to 73. All CBT-I/P interventions included standard CBT-I with the addition of pain education, pain-related cognitive therapy, behavioral activation and/or activity pacing. Table 1 provides a detailed description of these components. One trial demonstrated significant improvements in pain interference relative to the control group with a large effect size of 1.34 [8,44], but no improvements in pain severity were found for the hybrid interventions relative to the control groups.

Since the publication of these reviews, several additional papers have suggested that 1) middle-aged and older adults with higher levels of comorbid pain and insomnia may be most likely to experience improvement in pain following behavioral sleep interventions, and that 2) early improvements in sleep are related to sustained benefits for pain outcomes in middle-aged and older adults, with pain benefits accruing over time. Secondary data analyses from the Lifestyles trial revealed that older adults with elevated levels of baseline insomnia and pain (Insomnia Severity Index ≥ 11, subthreshold to severe insomnia [4]; Graded Chronic Pain Scale ≥ 5 [53]; 27% of overall sample) had significant reductions in pain severity at 18 months in the pain and sleep treatment arm compared to pain treatment alone [27], and across all treatment groups, patients with clinically significant improvement in insomnia post-treatment had significant improvement in pain severity and arthritis symptoms relative to non-improvers at 9- and 18-month follow-up (medium effect sizes ranging from .51-.63) [8,50]. Given that improvements in pain outcomes were not evident at post-treatment, the authors suggested that the benefits of improved sleep for pain outcomes accumulate over time [50]. Research suggests that some aspects of insomnia, including duration of total sleep time, continue to show improvement over time following completion of CBT-I [19]. As a result, responders to CBT-I may experience greater reductions in pain after they have experienced several months of a regularized sleep-wake cycle and obtained the full benefit of using CBT-I techniques.

Lami et al. [20] recently published similar results from a trial comparing CBT-I/P with usual care and CBT for pain in patients with fibromyalgia (mean age 50). There was a significant reduction in pain intensity in the CBT-I/P group relative to other treatment arms at 3-month follow-up, but not at post-treatment. Smith et al. [41] examined CBT-I for patients with knee osteoarthritis (mean age 59) and found that 33% of patients achieved a 30% reduction in pain over six months, mediated by post-treatment improvement in wake after sleep onset time (i.e., total time awake between sleep onset and final awakening). This effect increased across the follow-up assessment points and was greater for the CBT-I group relative to control.

In summary, the effect sizes for pain reduction following behavioral sleep interventions are modest and variable (effect sizes in reviewed studies ranged from negligible to large, -0.02 to 1.34 [8]) but comparable or even superior to those following psychological therapies for pain [6,52,55], suggesting that behavioral sleep interventions are a promising avenue for improving both pain and sleep in middle-aged and older adults.

Discussion

To ensure more middle-aged and older adults with chronic pain can benefit from behavioral sleep interventions, work is needed on several fronts. This research agenda is summarized in Table 2. First, we need clinical effectiveness trials of behavioral sleep interventions with middle-aged and older adults (including the oldest old, ≥ 85), with a focus on patient-centered outcomes and risk reduction outcomes relevant to this population [6,49]. Outcomes related to risk reduction will be particularly important to investigate in future trials. The link between sleep and opioid use is perhaps one of the most crucial yet underdeveloped area of research, especially in older adults, who are at increased risk for adverse events related to pain and sleep medication. Patients may misuse prescription opioids as a sleep aid [37] and it is possible that improved sleep would lead to a reduction in opioid use, but this needs to be systematically examined in clinical trials. Future trials should include long-term follow-up and reasons for treatment drop-out, objective measures of sleep, screening for comorbid sleep disorders which, if untreated, may diminish the effect of CBT-I, and an increased focus on mechanism-based trials. A wide-range of sleep disturbances are associated with pain; determining how specific sleep disturbances contribute to specific pain mechanisms will help develop mechanism-driven interventions.

Second, we need to continue testing alternative delivery approaches for behavioral sleep interventions in middle-aged and older adults. Alternative approaches have been developed to increase access, including briefer treatments, group treatment, and telephone-based interventions [7,11,19,25]. Self-management approaches using books, web-based programs, and mobile applications for smartphones and tablets also have potential to maximize convenience and access for patients; however, the comparative effectiveness of alternative delivery approaches is unknown, especially in regard to pain outcomes [32]. It is also unclear if alternative formats, such as mobile applications, are acceptable and feasible across age groups, particularly the oldest old (i.e., 85 years and older).

Finally, novel treatment development research is needed to optimize and maximize the effects of behavioral sleep interventions for middle-aged and older adults with chronic pain. This includes investigating adaptations for older adults, such as adjusting instructions and materials to accommodate visual and cognitive impairments and minimize fall risk when up during the night, as well as focusing on care-giver assisted behavioral techniques to improve sleep in patients with dementia (e.g., daily walking, increased light exposure) [14,24]. Trials have also generally lacked a mechanism-based focus targeting improvement of specific sleep parameters believed to alter specific mechanisms driving chronic pain. Work is needed to determine how specific sleep disturbances contribute to specific pain mechanisms to inform necessary modifications to standard CBT-I. This work will also inform the next generation of hybrid sleep-pain interventions by identifying empirically based CBT-I and CBT for pain components that address key underlying sleep-pain mechanisms.

Behavioral sleep interventions hold great promise for improving pain outcomes while reducing the harms and hazards of sedative-hypnotics and opioids for middle-aged and older adults. It is our hope that continued research in this area will help providers deliver safe and effective care for their aging patients.

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Figure 1.

CBT-I disrupts the negative cycle of chronic pain and insomnia, improving both pain and sleep functioning [1,37,52]

Table 1.

Components of Cognitive Behavioral Therapy for Insomnia (CBT-I) and hybrid Cognitive Behavioral Therapy for Insomnia and Pain (CBT-I/P) [34,44,51]

CBT-I	
Sleep restriction	Limiting time in bed to consolidate sleep and increase the sleep drive
Stimulus control	Restricting the behaviors that occur in the bed/bedroom to sleep and sex and ensuring that protracted periods of wakefulness do not occur in the bed/bedroom to promote a strong association between sleep and sleep-related stimuli
Sleep-related cognitive therapy	Identifying and challenging unhelpful thoughts and beliefs about sleep to decrease sleep-related anxiety
Sleep education/sleep hygiene	Increasing understanding of factors affecting sleep and encouraging healthy sleep behaviors
Relaxation training	Training in techniques to reduce physiological hyperarousal (e.g., progressive muscle relaxation, guided imagery, and paced breathing)
Additional components in CBT-I/P	
Pain education	Increasing understanding of acute vs. chronic pain and connection between interpretation of and response to pain
Pain-related cognitive therapy	Identifying and challenging unhelpful thoughts and beliefs about pain to reduce pain catastrophizing and encourage psychological and behavioral flexibility
Behavioral activation/activity pacing	Increasing engagement in valued and pleasurable activities and learning to balance activity and rest

Table 2.

High priority research needs for improving pain and sleep in middle-aged and older adults

Research Focus	Research Needs
Effectiveness trials	<ul style="list-style-type: none"> • Inclusion of clinically relevant outcomes (e.g., pain interference) and harm reduction outcomes relevant to middle-aged and older adults (e.g., discontinuation of sedative-hypnotics and opioids, fall reduction, improvement in cognitive functioning, reduction in hospitalizations) • Inclusion of older adults and the oldest old (i.e., 85 years and older) • Long-term follow-up and reasons for treatment drop-out • Objective measures of sleep (e.g., actigraphy) • Screening for comorbid sleep disorders • Focus on mechanism-based trials
Testing alternative delivery formats and tools	<ul style="list-style-type: none"> • Examine comparative effectiveness of alternative formats/tools relative to standard in-person behavioral sleep interventions on sleep and pain outcomes (e.g., brief behavioral treatment, group treatment, telephone-based interventions, self-management) • Examine acceptability and feasibility of alternative delivery formats/tools across age groups, particularly the oldest old (i.e., 85 years and older)
Developing and testing adaptation to standard CBT-I	<ul style="list-style-type: none"> • Examine age-specific adaptations to standard behavioral sleep interventions (e.g., adjust instructions and materials to accommodate visual and cognitive impairments, minimize fall risk during nighttime awakenings, focus on care-giver assisted behavioral techniques to improve sleep in patients with dementia) • Developing mechanism driven adaptations to standard CBT-I to improve pain and functional outcomes by targeting specific dimensions of sleep that drive specific mechanisms of chronic pain • Develop and test hybrid sleep-pain interventions, identifying specific, empirically based CBT-I sleep components that combine with CBT for pain components to synergize pain-related outcomes