Whale, K., & Gooberman-Hill, R. (2019). Why sleep matters to pain research. *Pain News*.

Peer reviewed version

Why sleep matters to pain research

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Word count = 1926

Sleep and health

We are in the midst of a sleep crisis. Our current work and lifestyle environments are normalising poor sleep with substantial negative impacts on our health. In recent years, surviving on minimal sleep has often been seen as something to be proud of or even touted as a badge of honour. Famous figures such as Margaret Thatcher, who purportedly only slept a few hours a night, are seen as role models for productivity and efficiency; never mind the impact this lifestyle may have had on their health. Paying attention to one's sleep routine or going to bed early is viewed as a defiant act of 'self-care'. Sleeping 8 or 9 hours a night is not viewed as a positive health behaviour or mandatory for the body and brain to function but is frequently stigmatised as laziness or indulgence.

Research on sleep has linked sleep deprivation to poorer mental health[1], obesity[2, 3], cancer[4, 5], diabetes[6], heart disease[7], and a myriad of other health conditions. In the UK an estimated £40bn is lost in revenue due to sleep deprivation each year[8]. Our poor relationship with sleep and disregard for its importance is now not only affecting our individual health but is having a substantial impact on our economy.

Growing recognition of the importance of sleep and its health benefits has led to a boom in the commercial sleep industry. Barely a week goes past without seeing a new advert for the latest mattress in a box which guarantees idyllic uninterrupted restful hours, a new smartphone app promising to enable a peaceful repose, pillow sprays, supplements, weighted blankets[9], even robots to teach breathing techniques[10]; the list goes on. There are more sleep products than ever before, and people are buying in. A 2017 McKinsey report estimated the sleep-health industry to be worth between $30-40 billion, with a yearly growth rate of 8%[11].

Sleep and pain

Most of us know that sleep is good for us, and many of us want to have more of it, but why should research into chronic pain pay particular attention? The issue is that sleep deprivation and interrupted sleep are substantial problems for people who live with chronic pain (pain

that lasts or recurs for more than three months). Between 67% and 88 % of individuals with chronic pain experience sleep disruption and insomnia [12, 13], and at least 50% of people with insomnia report chronic pain [14]. Hence, there is known to be a relationship between sleep and pain. Experimental, cohort, and longitudinal studies have all demonstrated that restricted sleep is linked to greater pain. Poor sleep therefore not only affects general health but has a direct impact on pain response and experience. Thus, improving sleep in people living with chronic pain has the potential to deliver great benefit to many.

The evidence base

Experimental studies focusing on short-term sleep restriction and acute pain have consistently reported that sleep deprivation in healthy subjects, in particular slow wave sleep restriction, is associated with increased acute algesic responses to nociceptive stimuli [12, 15]. However, experimental studies have been criticised for their lack of generalisability to people with chronic pain. Experimental methods often enforce temporary sleep restriction to reduce total sleep time by either keeping participants awake longer before sleep or waking them early, and acute pain tests, such as pressure, heat, or ice. These methods do not necessarily evoke the experiences of disturbed sleep of people living with pain, which include multi-nocturnal waking. Some studies have partially addressed this by using 'forced awakening' techniques. These forcibly awaken participants multiple times per night to mirror the sleep patterns more commonly experienced by people with pain. Smith and colleagues conducted a study in which otherwise healthy women were awakened at 8 intervals during the night over an 8-hour sleep period. This restricted their total sleep time to 280 minutes (just over 4.5 hours). Compared with a restricted sleep group (same total sleep time but uninterrupted) and a control group who slept for 8 hours, forced awakening resulted in greater next-day spontaneous pain reports and reduced conditioned pain modulation[16].

Prospective longitudinal studies focusing on the effect of sleep on future pain have reported similar results. Studies in people who experience headaches and migraines have shown that elevated insomnia symptoms increase the risk of exacerbating existing headache, and in developing new headache symptoms at long-term follow-up ranging from 1-12 years [17-19]. A population-based study in Norway found that insomnia symptoms at baseline significantly increased the risk of developing chronic musculoskeletal pain at 17-year follow-up[20]. Cohort studies in women undergoing caesarean have found that pre-operative sleep quality is

associated with more severe pain when moving and increased analgesic intake following surgery[21]. In addition, a history of sleep disturbance prior to injury in burns patients has been shown to be correlated with greater pain during the night, pain in the morning, and pain during debridement procedures[22].

In addition to the negative impact on physical pain symptoms, reduced sleep has detrimental effects on psychological wellbeing and coping. Experimental work has shown that reduced sleep over a period of 12 days reduces optimism, sociability, and psychosocial functioning, in particular at the beginning and end of the day[23]. Poor sleep also has clear links with depression and pain catastrophising, both of which have established associations with pain coping and contribute to an increased pain experience[24-26].

A reciprocal relationship between sleep and pain

The dominant view of the relationship between sleep and pain is that they are reciprocally related, i.e. reduced sleep increases pain, and increased pain reduces sleep. However, studies exploring the reciprocal, bidirectional relationship between sleep and pain suggest that there is temporal precedence for sleep over pain. Studies of adolescents with a range of chronic pain complaints have found that total sleep time and wake after sleep onset were associated with next-day pain reports. However, pain was not prospectively associated with any sleep measure within the study [27]. In contrast a prospective UK-based study and a longitudinal Norway-based study both found that widespread chronic pain predicted the incidence of disturbed sleep and insomnia over a 3-year period[28, 29]. These findings show that whilst the evidence for pain disrupting sleep is less clear-cut than the evidence for poor sleep increasing pain, there is still a case for a bidirectional relationship, albeit a potentially unbalanced one.

A possible reason for the conflicting findings about the reciprocal relationship between pain and sleep is the variation in pain pathways and treatment for nociceptive pain and neuropathic pain. Nociceptive pain is caused by actual or potential damage to tissues, such as a cut, burn, or damage to joints such as osteoarthritis[30]. Neuropathic pain is caused by changes or damage to the nerves themselves and affects the way that pain signals are sent back to the brain[30]. Neuropathic pain can result from prolonged nociceptive pain, such as chronic pain conditions, or a result of damage during surgical procedures such as joint replacement.

Chronic pain is commonly treated with traditional painkillers and anti-inflammatory medications[31]; these medications lessen the nociceptive pain experience but have little impact on neuropathic pain symptoms.

A recent study exploring the bidirectional relationship between pain and sleep in joint replacement patients found that neuropathic pain symptoms were a stronger predictor of sleep disturbance than nociceptive joint pain. Predictive analysis of pain and sleep demonstrated that the impact of joint pain on sleep was moderated by medication use, but neuropathic pain scores were associated with the development of sleep disturbance even after adjustment for joint pain[32]. These data suggest that for individuals who experience nociceptive pain only, medications used to treat this are likely to mediate the impact that their pain has on their sleep. However, for individuals who experience both nociceptive and neuropathic pain, such as some chronic pain populations, these medications will only mediate for one of these pain responses. These findings demonstrate that there is a strong likelihood of sleep disturbance due to neuropathic pain.

Interventions to improve sleep

Findings from research to date highlight why interventions to improve sleep could be of such great benefit to people with pain. Although there are many medicines that can help with management of nociceptive pain—such as pain relief and anti-inflammatory medicines and steroids—neuropathic pain is harder to manage with medication. Medicines for neuropathic pain include antidepressants and anticonvulsants, both of which can come with unwelcome side effects, and opioids about which there are growing concerns. Sleep interventions offer a complementary approach by targeting the other side of the relationship: improving sleep to decrease pain, rather than focusing on the pain symptoms as the first target for management.

Current treatment approaches for insomnia may offer a starting point. Alternative interventions to pharmacotherapy such as psychological interventions, complementary therapies, social and physical activity, and sleep aids are gaining increasing traction as a cost-effective sustainable approach. The most common of these is cognitive behavioural therapy for insomnia (CBT-I) which has been shown to be equally effective or even superior to pharmacotherapy[33]. CBT-I can be done on an individual basis or in a group and is applied through a course of sessions commonly consisting of psychoeducation and sleep hygiene information, sleep restriction, relaxation, stimulus control, and cognitive therapy. The

evidence for the effectiveness of CBT-I for improving sleep for people with chronic pain is promising[34]. CBT has been shown to be effective in the treatment of back pain, in particular for reduced fear of movement and pain and improved pain management[35]. A recent systematic review and meta-analysis of sleep interventions in patients with osteoarthritis and spinal pain also found CBT to be of the most effective interventions for improving sleep[36].

Despite increasing knowledge, the development and application of sleep interventions for improving chronic pain still has some way to go. Given the evidence base for the link between sleep and pain it might be tempting to move straight to implementation. However, one of the driving forces behind the sheer range of commercial sleep products is that the multiple dimensions of sleep and variation in individual sleep problems means that there is no 'one size fits all' approach for improving sleep. In order to be effective, robust intervention development must first explore the factors that are associated with poor sleep and identify which of those have the greatest scope for change, within particular patient populations[37]. There are a number of different chronic pain populations, including people experiencing back pain, migraine, fibromyalgia, arthritis, sickle cell disease, chronic post-surgical pain, and multiple sclerosis, all of which come with different profiles of pain and sleep experience. It is crucial that we understand the specific issues affecting each group in order to develop targeted interventions tailored to patients' needs. Targeted and carefully designed inventions have a better chance of patient acceptability, engagement, and effectiveness. Researchers can work together to conduct robust studies that include multiple approaches, such as qualitative work, wearable sleep monitors, and sleep diaries, in order to identify the key issues that affect sleep and pain.

Conclusions

Given the strong relationship between sleep and pain, it is evident that poor sleep, and in particular multi-nocturnal waking, makes pain worse. Moreover, chronic pain populations commonly experience poor sleep, and that chronic pain in turn can disrupt sleep. The message is clear: people with chronic pain would benefit from better sleep. This provides an exciting and potentially impactful avenue of exploration for developing health interventions that form part of multi-modal approaches to pain management. Sleep need no longer be a

secondary factor to take note of or a symptom of pain disruption, but front and centre in pain research.

Funding

This study was supported by the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

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