

Introduction to chronic pain and mindfulness

Chronic pain is pain in one or more areas lasting 3 months or longer (1). A recent systematic review and meta-analysis of population studies has estimated that chronic pain affects between one-third and one-half of the UK adult population, with a higher prevalence amongst older adults and 10.4% to 14.3% of cases being 'moderate-severely disabling chronic pain' (1). It is suggested that this figure is likely to increase as the population ages. The British Pain Society estimates the cost of back pain alone is likely to be in the region of £5billion per annum, putting chronic pain as an enormous burden on public healthcare spending (2). There is also an increasing demand for mental health services, due to the association between chronic pain, anxiety and depression (3).

In 1986, the World Health Organization (WHO) developed the analgesic stepladder for palliative cancer care, a model for the slow introduction and upward titration of analgesics (Figure 1.). This model was revolutionary in reversing the stigmatisation of opioid use, and ultimately resulted in less suffering during end of life treatment. This ladder is also extremely useful in the management of acute pain, for example postoperatively. However, the use of the WHO analgesic ladder in non-cancer chronic pain is frequently ineffective as there is no predictable trajectory and pain often becomes unresponsive to opioids. Further to poorly managed pain, addiction is becoming a growing concern. Between 1999 and 2010 the US saw a fourfold inflation in prescribing with a proportionate increase in opioid deaths and admission for misuse (4).

The approach to chronic pain in the UK is beginning to move toward a more holistic approach, with many patients being referred to group-based rehabilitative Pain Management Programmes (PMP). These programmes includes physiotherapy, clinical psychology, occupational therapy and specialist pain consultant sessions to improve patient understanding of chronic pain and provide tools to make positive changes in coping with and managing pain. Recently, there has been the incorporation of mindfulness meditation techniques in many PMPs around the country (5).

Meditation is a practice of Buddhist origin which dates back to the 12th century, but was initially brought into clinical healthcare in 1979 at the University of Massachusetts, where Professor Jon Kabat-Zinn developed the Mindfulness-Based Stress Reduction programme (6). He defines mindfulness as, "paying attention on purpose, in the present moment, and nonjudgmentally, to the unfolding of experience moment to moment." (6). The practice of mindfulness meditation focuses on separating awareness and experience from thoughts and feelings, and has since been implicated as a clinical intervention in numerous medical conditions including chronic pain, anxiety, depression, cancer, chronic disease, eating disturbances, cardiovascular disease and sleeplessness (6)(7).

The aim of this report is to explore some of the literature on hypothesised mechanisms of chronic pain, the efficacy of mindfulness-based pain management in chronic pain and the proposed mechanism of pain reduction in individuals practicing mindfulness meditation. Finally, some limitations will be discussed that practitioners and patients may face in recommending and adhering to mindfulness-based pain management programmes through published case-studies of chronic pain.

Mechanisms of chronic pain

In acute tissue injury, cytokines and other inflammatory mediators activate nociceptors in A δ and C fibres. These nerves synapse in the dorsal horn of the spinal column, the signal is then transmitted to the thalamus via the ascending pathway of the spinothalamic tract. The thalamus interacts with the cortex (where pain perception occurs), limbic system and brainstem. These areas modulate pain via descending pathways to the dorsal horn, in most cases decreasing the signal (8).

There are many identified chronic conditions which can cause long-term pain to patients. Chronic neuropathic pain is associated with damage to peripheral or central nerves, as seen in diabetic peripheral neuropathy and postherpetic neuralgia (9). Chronic nociceptive pain may be a result of continuing damage to somatic or visceral tissues due to trauma or inflammation, as seen in rheumatoid arthritis and osteoarthritis (10). Chronic inflammation may also result in peripheral sensitization through 'inflammatory soup' reducing the threshold of nociceptors, thus increasing their response (8). In the presence of chronic exposure to pain signals, increased excitability of central nerves results in abnormal pain modulation, which can amplify pain signals rather than decrease them. Several studies have shown frequent and prolonged activation of neural pathways can reinforce and amplify their effects, resulting in the positive feedback cycle of chronic pain. This can lead to allodynia (pain experienced in response to a non-painful stimulus) and hyperalgesia (increased perception of mildly painful stimuli) (3).

In many patients, investigations suggest absence of a peripheral pathology causing their chronic pain. This is indicative that the pathology lies within the aspects of the central nervous system involved in pain processing. There are many identified functional chronic pain conditions, including fibromyalgia, irritable bowel syndrome and chronic tension headache. Exacerbation of these conditions is strongly associated with emotional stress. It is hypothesised that excessive activity of the limbic system disrupts normal pain processing and results in abnormal amplification of pain signals, leading to the chronic pain cycle described above (11).

Anxiety and depression are common comorbidities in patients presenting with chronic pain. Frequent exposure to negative sensations such as pain increase incidence of low mood. Perception of pain may also be negatively affected by social factors via cognitive modulation. This may be the case when pain inhibits an individual's ability to carry out their daily activities or causes the breakdown of their relationships, which in turn can lead to feelings of isolation causing anxiety and low mood (3). Pain can also impact on sleep, which may feed into the cycle mentioned above to further exacerbate cognitive stress and alter the modulation of pain.

It is worth noting that the pathophysiology described in this section is only the tip of the iceberg in regards to the mechanisms of chronic pain, which remains a hotly contested and ever-expanding field of study.

The mechanisms outlined above highlight the importance of neuroplasticity and psychosocial factors in the pathophysiology of chronic pain. This would suggest that, depending on the pathophysiology of pain in the individual presenting patient, conventional drug therapy may prove ineffective. Furthermore, these factors are targets of mindfulness-based therapies (*see: Proposed Mechanisms of MBPB*), thus the mechanisms of chronic pain support the hypothesis that mindfulness meditation may be an appropriate therapy in patients presenting with chronic pain.

The Efficacy of Mindfulness-Based Pain Management

There are many studies which support the efficacy of mindfulness meditation in managing chronic pain. In a study investigating the effects of an 8-week mindfulness programme on chronic back pain, participants were randomised to an 8-week mindfulness-based meditation program or to a wait-list control group (12). The study found that chronic pain acceptance questionnaire scores significantly improved in the meditation group, while the control group worsened during the 8 weeks. Of the

participants who attended a 3-month follow-up, 76% were continuing mindfulness meditation techniques. The researchers concluded that mindfulness meditation may lead to increased pain acceptance and physical function in patients with chronic lower back pain. One limitation of this study, and others like it in the field, is a recruitment bias towards people willing to undertake an 8-week meditation programme. This means the results may not reflect the outcomes of a mindfulness programme in the general population, many of whom could be precontemplative.

A study by Jon Kabat-Zinn and colleagues (7) investigated the longitudinal effects of mindfulness meditation on chronic pain management. The study found that in the majority of patients the initial benefits of mindfulness meditation in management of their chronic pain were maintained at 4 years. The conclusion by the authors is that mindfulness meditation is effective in the long-term management of chronic pain. This study is useful as it included a large sample size, but was limited by some patient follow-up being shorter than the 48-month benchmark, which may have resulted in false reporting of positive outcomes.

A systematic review and meta-analysis of 11 studies investigated the effects of mindfulness meditation on chronic pain conditions including fibromyalgia, rheumatoid arthritis, chronic musculoskeletal pain, failed back surgery syndrome, and mixed aetiology (13). This meta-analysis found that mindfulness-based interventions may have positive effects on perceived pain control with a moderate impact size ($g = 0.58$), but there was no significant evidence of benefit in pain intensity or depression. The discussion of this study highlights the limitations of the review due to the inconsistent methodological quality of the studies used, including small sample sizes which may have been underpowered to detect effects in 7 of the 11 studies, and concludes that better quality studies in the field of mindfulness meditation as a clinical intervention for chronic pain are needed.

Most studies mentioned above have investigated the efficacy of mindfulness techniques, either individually or incorporated into a pain management programme, in the treatment of nociceptive pain. However, it should be noted that a study comparing physical and psychological function in neuropathic pain and nociceptive pain is indicative that pain management programmes may also be effective in individuals with neuropathic pain if adjusted appropriately to reflect the differences in their response to pain, beliefs about pain and the main issues associated with pain (14).

There are conflicting conclusions from the literature concerning the efficacy of mindfulness meditation in chronic pain management. Many individual studies suggest positive patient outcomes in the management of chronic pain in response to mindfulness-based intervention. Systematic reviews and meta-analysis do not support this hypothesis, but are limited by a lack of coherent, high-quality studies in the field. Thus, further research in the area is needed to determine the efficacy of mindfulness meditation as a therapy in patients presenting with chronic pain.

Proposed Mechanisms of Mindfulness-Based Pain Management

Neuroplasticity is hypothesised to play a role in the analgesic properties of mindfulness meditation, reducing activation in pain pathways and reversing the amplification process. One study using MRI to compare brain structure in meditators and non-meditators found that specific regions of the cortex, such as the prefrontal cortex and right anterior insula, were thicker in meditators than the non-meditator group (15). The researchers hypothesise this remodelling may reduce cognitive stress in response to emotional input, reversing the pain amplification cycle and resulting in a reduction in the perception of pain. One limitation of this study was that there was no positive control group receiving sham treatment in order to investigate the placebo effect.

A randomised-control trial investigating the effects of a mindfulness-based pain management program on mental health in patients with musculoskeletal pain found increased perceived control over pain in the mindfulness group compared to the control (16). Electroencephalography showed increased activity in cognitive control regions of the brain, indicative of improved mental health, during pain anticipation. The authors of this study suggest that this greater perceived control over pain is therefore a result of improved regulation of the emotional response to pain. Whilst much of the methodology of this study is sound and a good outline of the mindfulness programme is provided, there is no positive control group present.

The placebo effect was investigated by a randomised-control trial comparing mindfulness meditation with sham meditation and placebo conditioning (patients in this group believed they were participating in “an experimental trial of a new formulation of a topical, local anaesthetic being tested for its pain reducing effects over time.”)(17). Using functional magnetic resonance imaging (fMRI) researchers found significant differences in regions of activation in the brain between the mindfulness-meditation group and the placebo conditioning group, suggesting differing mechanisms of action. The mindfulness meditation group showed increased activity in areas associated with cognitive modulation of pain (including the subgenual anterior cingulate and anterior insular cortex), whereas analgesia in placebo conditioning group was associated with deactivation of the secondary somatosensory cortex (sensory processing regions). Furthermore, there was significantly higher pain reduction in the mindfulness-meditation group than the sham-meditation group. This study has well-described methodology with no evident bias, thus if results were replicated a meta-analysis would be very strong evidence to support increased activation of cognitive pain modulation as a mechanism of action in mindfulness meditation as an analgesic.

This section has thus far focussed on individual trials, whilst important in forming hypotheses around mindfulness practice in pain management these are not the gold standard of evidence supporting clinical practice. A systematic review of fMRI studies into the effectiveness of mindfulness in chronic pain management found that mindfulness meditation consistently reduced the affective experience of experimentally-induced pain, but lowered pain intensity ratings were less consistent. The review concluded that “the neural mechanisms behind this pain alteration appear to be linked to upregulation of brain regions that are key nodes of the SN [salience network] and downregulation in nodes of the CEN [central executive network]” (18). This review highlights in its discussion discrepancies between existing reviews of the literature due to varying definitions of mindfulness practice, for example some studies may include yoga and other forms of meditation, thus differing criteria of inclusion. This particular review is limited by the small number of studies included (n=5). However, it is important to note that broader inclusion criteria resulting in an abundance of studies being included in a review of a practice with fluid definitions, such as mindfulness meditation, may also be unreliable.

A literature review by Epel et al. (2009) contextualizes the significance of stress reduction on a cellular level (19). This paper suggests that cognitive states and skills acquired in those practicing mindfulness lead to a reduction in the stress response. In the literature reviewed, mindful meditation lowers cortisol and decreases oxidative stress. The data presented in the paper implies a link between cognitive stress and telomere shortening (a marker of cellular aging) via oxidative stress. However as there was no standardized selection criteria for this review presented, there is a strong possibility of selection bias in the evidence presented. A systematic review investigating the effects of cognitive state on telomere length is absent from literature searches, but would provide greater insight into the effects of reducing stress on a cellular level and may further our understanding of the mechanisms of mindfulness practice in reducing pain.

The mechanisms proposed above demonstrate modulation of chronic pain through alternative pathways to those targeted by conventional drug therapies, mainly involving neuroplastic structural changes in response to an altered cognitive state. This would imply that mindfulness-based pain management could be an appropriate therapy in targeting pain with central pathophysiology.

Behavioural Changes and Case Studies in Mindfulness-Based Pain Management

Qualitative analysis of individual cases reveals improvement in pain and quality of life in many patients practising mindfulness meditation (20). However, such studies also suggest that the practice is ineffective in some patients who don't have confidence in their diagnosis or the analgesic properties of the intervention. They highlight a misunderstanding in some individuals about chronic pain, particularly in patients without a peripheral pathology. A recurring theme in such case studies indicates that many patients view a recommendation of mindfulness-based pain management, or the diagnosis of a functional pain disorder, as disbelief on the part of the physician of the patient's suffering (20)(21).

Figure 2. (appendix) highlights the various stages of behavioural change as proposed by Transtheoretical model (22). The decision to practice mindfulness meditation and/or reduce ineffective drug therapy as a means of pain management involves behavioural change. This model is a useful tool in assessing the suitability of mindfulness for individual patients as it not only allows identification of patients who are ready to undertake such a behavioural change, but also indicates how the physician may assist progression to contemplative stage in precontemplative patients. Communicating the mechanisms of chronic pain, particularly how pain can arise in the absence of peripheral pathology, is essential in promoting awareness and reassurance in patients. Furthermore, education on the evidence supporting mindfulness-based therapies encourages contemplation and adherence to mindfulness-based pain management programmes, and ultimately more positive patient outcomes (22).

Case studies highlight the benefits and limitations for patients of mindfulness-based pain management programmes in practice, whilst the Transtheoretical model provides a template which can be used to address these limitations on a case-by-case basis. Thus, individual cases support mindfulness-based pain management as an appropriate therapy in certain patient groups presenting with chronic pain.

Conclusion

In conclusion, a holistic approach is essential in effective chronic pain management. The proposed mechanisms of chronic pain, particularly neuroplasticity and dysregulation of the pain modulatory system due to psychosocial factors, highlight inefficiencies in a drug-only approach to management. There is evidence to support the efficiency of mindfulness-based management of chronic pain in many patients contemplating non-drug therapies. The proposed mechanisms of mindfulness meditation intervention in chronic pain differ from those targeted by the WHO analgesic ladder, thus reinforcing the argument for the appropriateness of mindfulness meditation therapy in certain groups of patients where conventional drug therapy is ineffective. However, case studies indicate mindfulness-based pain management is often ineffective in the precontemplation stage, and in such cases alternative drug and other non-drug therapies may be more appropriate, adjunct to reassurance of diagnosis and patient education. There are conflicts and discrepancies between the existing literature and reviews due to the mixed methodological quality and the ambiguous nature of defining mindfulness meditation interventions, thus more studies with consistent methodologies and systematic reviews with clear inclusion criteria are needed in the field.

The Analgesic Ladder for Pain Control

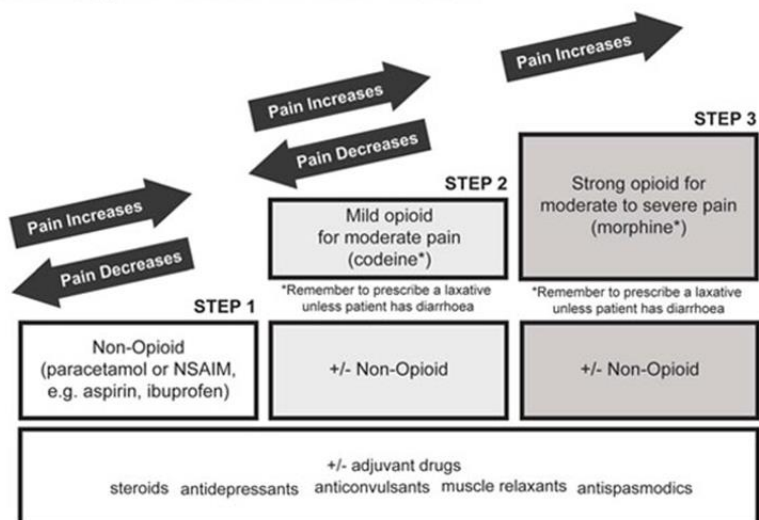


Figure 1. The WHO analgesic ladder for pain control using pharmaceutical interventions (4). Image from: ‘Essential Pain Management Lite’ (8).

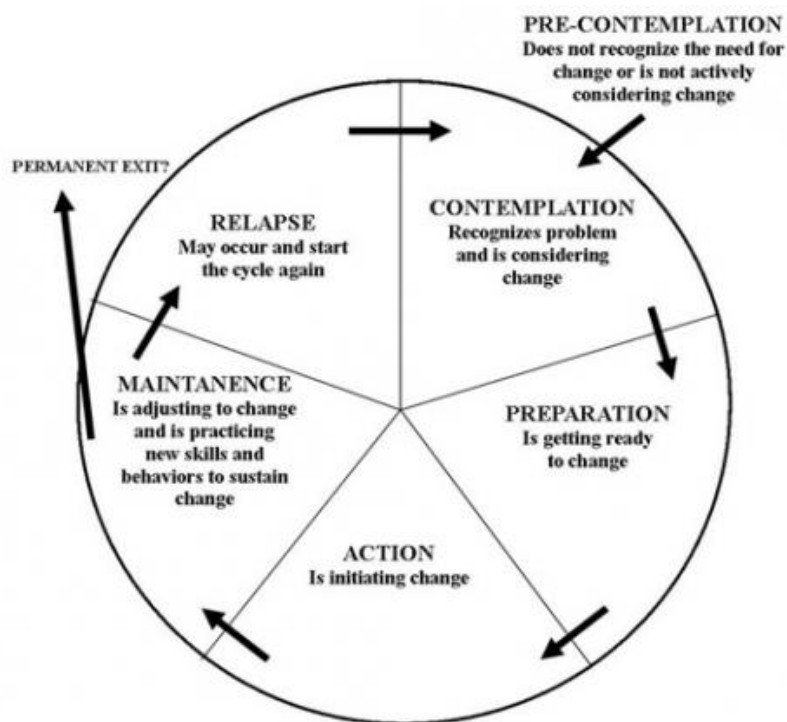


Figure 2. Cycle of behavioural change, outlining the different stages of behaviour modification, from Proschka and DiClemente’s Transtheoretical model (22).

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