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Mindfulness Meditation for Fibromyalgia: Mechanistic and Clinical Considerations

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Abstract

Purpose of Review—Fibromyalgia is a disorder characterized by widespread pain and a spectrum of psychological comorbidities, rendering treatment difficult and often a financial burden. Fibromyalgia is a complicated chronic pain condition that requires a multimodal therapeutic approach to optimize treatment efficacy. Thus, it has been postulated that mind-body techniques may prove fruitful in treating fibromyalgia. Mindfulness meditation, a behavioral technique premised on non-reactive sensory awareness, attenuates pain and improves mental health outcomes. However, the impact of mindfulness meditation on fibromyalgia-related outcomes has not been comprehensively characterized. The present review delineates the existing evidence supporting the effectiveness and hypothesized mechanisms of mindfulness meditation in treating fibromyalgia-related outcomes.

Recent Findings—Mindfulness-based interventions premised on cultivating acceptance, non-attachment, and social engagement may be most effective in decreasing fibromyalgia-related pain and psychological symptoms. Mindfulness-based therapies may alleviate fibromyalgia-related outcomes through multiple neural, psychological, and physiological processes.

Summary—Mindfulness meditation may provide an effective complementary treatment approach for fibromyalgia patients, especially when combined with other reliable techniques (exercise; cognitive behavioral therapy). However, characterizing the specific analgesic mechanisms supporting mindfulness meditation is a critical step to fostering the clinical validity of this technique. Identification of the specific analgesic mechanisms supporting mindfulness-based pain relief could be utilized to better design behavioral interventions to specifically target fibromyalgia-related outcomes.

Keywords

Pain; Fibromyalgia; Mindfulness; Meditation; fMRI; Inflammation

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

Human and Animal Rights and Informed Consent All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Introduction

Musculoskeletal chronic pain affects over seven million Americans and is characterized by pain and loss of function in the joints, tendons, ligaments, bones, and/or muscles lasting for greater than or equal to 3 months [1]. To date, over 100 rheumatic disorders have been identified, with causes ranging from biochemical and biomechanical changes (osteoarthritis), inflammation (gout), infection (septic arthritis), and immune dysregulation (rheumatoid arthritis) to more complex origins (fibromyalgia).

Fibromyalgia is chronic pain condition characterized by widespread “aching” pain and is often accompanied by tenderness in 18 pre-specified bodily locations [2]. It is often accompanied by sleep disturbances and fatigue [3, 4]. Thus, effective treatment protocols should employ a multimodal approach to better improve pain, psychological comorbidities, and sleep [4]. Although there is growing evidence for the clinical utility of mindfulness meditation to treat fibromyalgia-related pain [5], the analgesic mechanisms supporting the use of this ancient technique remain poorly characterized. The present review will focus on identifying the efficacy and mechanisms supporting mindfulness-based therapies for fibromyalgia-related pain.

Recommended treatment guidelines for fibromyalgia include a combination of pharmacological and behavioral treatment approaches [6]. The two most commonly employed fibromyalgia drug treatments are antidepressants (tricyclics; serotonin/norepi-nephrine reuptake inhibitors) and GABAergic nerve pain medications (pregabalin) [6]. Exercise and cognitive behavioral therapy (CBT) have shown the most pronounced improvements in treating fibromyalgia-related pain in comparison to other behavioral interventions [6–8]. To date, CBT is the most effective psychological treatment for fibromyalgia [6, 8]. CBT helps patients identify and reduce maladaptive cognitions/behaviors and includes psycho-educational didactics relevant to fibromyalgia, “journaling,” relaxation techniques, and real-world desensitization applications [9]. CBT may reduce fibromyalgia-related outcomes by attenuating psychological factors involved in facilitating pain, including anxiety [10], depression [10, 11], and pain catastrophizing [12]. Pain catastrophizing is a cognitive and emotional state where patients magnify the threat value of a pain stimulus, report helplessness in the context of pain, and are unable to inhibit intrusive pain-related thoughts [13]. Exercise therapy is a supplementary treatment found to effectively decrease fibromyalgia-related disease burden by increasing physical strength, mobility, positive mood, and functional status [14, 15]. Unfortunately, the long-term effectiveness of these treatments is limited [16]. In fact, on average, only 10% of fibromyalgia patients report clinically significant improvements in disease symptomology over 10 years of treatment following current recommended treatment guidelines [16]. In contrast to pharmacologic therapies, we postulate that mindfulness-based treatments produce more stabilized improvements in pain and quality of life measures as a function of meditation training frequency and experience [17, 18]. Mindfulness-based therapies may uniquely reduce symptomology by engaging mechanisms involved in altering the evaluation of self-referential thought processes in a less reactive and present-centered fashion.

Physiological Mechanisms of Fibromyalgia

Fibromyalgia patients exhibit a number of pain-related alterations in neural processing that support the role of central sensitization and cognitive/emotional processes in facilitating pain [12, 19•, 20–22]. Specifically, during noxious pressure stimulation, fibromyalgia patients reported greater pain and heightened activation in pain-related brain regions including the insula, anterior/posterior cingulate cortex, cerebellum, and primary (SI) and secondary (SII) somatosensory cortices when compared to healthy, age- and gender-matched controls [19•]. Furthermore, fibromyalgia patients, in comparison to healthy controls, exhibited heightened activation during noxious pressure stimuli in the medial prefrontal cortex (mPFC) [19•], a region associated with higher-order evaluation of nociceptive information [23]. Decreased activation during pain-inducing pressure in the dorsolateral PFC (dlPFC), a region associated with the cognitive/affective regulation of pain [24, 25], was also detected [19•]. Furthermore, Napadow and colleagues [22] revealed that fibromyalgia patients, while at rest (eyes closed), demonstrated greater connectivity between the default mode network (DMN), a neural network supporting self-referential [26, 27] and mind-wandering [28] processes, and the SII and insula when compared to healthy controls [22]. Heightened clinical pain was also associated with heightened connectivity between the right anterior and mid-insula and the DMN [22]. The anterior insula is involved in modulating the evaluation of noxious stimuli [29–31] and is associated with interoceptive awareness of bodily sensations [32]. Consequently, heightened connectivity between the DMN and the insula could reflect a mental state where patients are primed to observe and evaluate noxious stimuli due to pain “chronification.”

Other studies have shown that pain catastrophizing in fibromyalgia patients is positively associated with increased activation, during noxious stimulation, in brain regions associated with the anticipation (medial frontal cortex) [33], emotional evaluation (rostral anterior cingulate cortex (rACC)) [34–36], and sensory discrimination (SII) [37] of pain [21]. Fibromyalgia patients exhibiting high rates of pain catastrophizing demonstrated increased connectivity between SI and the anterior insula, suggesting greater sensitivity during the evaluation of nociceptive processes in patients classified as high pain catastrophizers [12]. Interestingly, subsequent CBT participation reduced pain catastrophizing, clinical pain, and SI/anterior insula connectivity [12]. Reduced pain catastrophizing was also associated with lower clinical pain and SI/anterior insula connectivity [12]. Psychological factors, such as pain catastrophizing, may be associated with fibromyalgia-related changes in neural network connectivity that subsequently heighten the experience of clinical pain. Thus, therapies focused on enhancing cognitive control and affective regulation may provide long-term relief for fibromyalgia patients.

Psychological stress also contributes to the enhancement of fibromyalgia-related symptoms by engaging processes that increase pain sensitivity. Fibromyalgia patients report high rates of stress [38] which is associated with increases in pro-inflammatory cytokines [39–41]. Specifically, fibromyalgia patients exhibit higher levels of the pro-inflammatory mole-cules interleukin-1 (IL-1) [42], IL-6 (IL-6) [43, 44], and IL-8 [45, 46]. Heightened inflammation exacerbates pain through activating and sensitizing peripheral nociceptors [47] and by increasing substance P [48], a nociceptive neuropeptide [49]. Interestingly, heightened ACC

and insula activation during social stress is associated with stress-induced increases in pro-inflammatory cytokines [50]. Increased ACC and insula activation is also associated with degree of inflammation in asthma patients showing asthma relevant emotional stimuli [51], suggesting that top-down processes may mediate the effects of stress on inflammation. Therefore, interventions aimed at attenuating stress-induced alterations in neural processing may impact fibromyalgia-related outcomes through decreasing inflammatory processes.

Mindfulness Meditation-Based Pain Relief

There has been a significant surge in scientific evidence supporting the clinical efficacy of mindfulness meditation to attenuate pain [5, 52–58]. Although mindfulness interventions vary in didactic approaches, they are generally premised on (a) developing sustained attention to arising sensory, affective, and cognitive events, (b) recognizing such experiences as momentary and fleeting, and (c) attenuating reactions/judgments to said experiences [17]. Mindfulness training reliably improves catastrophizing [59], anxiety [60–63], depression [52, 64–66], mood [67], and stress [68, 69]. Thus, improvements in mood and cognitive flexibility could lead to greater pain relief by altering the way patients interpret/contextualize pain-related ruminations [70, 71]. Yet, it is not known if mindfulness attenuates clinical pain by targeting psychological comorbidities that exacerbate pain or vice versa.

Mindfulness Meditation and Fibromyalgia

The “standard” 8-week mindfulness-based stress reduction (MBSR) program is the most widely studied mindfulness treatment approach for fibromyalgia-related outcomes [5]. MBSR has been shown to be equally effective compared to other behavioral interventions (CBT; health education) in treating a wide spectrum of chronic pain-related outcomes [5, 56, 72]. MBSR educates individuals to respond more effectively to stress, pain, and illness through the use of multiple techniques, including meditation practice (focusing on the breath; walking meditation, eating meditation), yoga, daily homework, and a 1-day retreat [73].

There have been a number of studies that have shed light on the efficacy of MBSR in treating fibromyalgia. MBSR was found to be more effective than usual care in improving depression [54] and fibromyalgia-associated symptoms, such as fatigue, stress, sleep, pain, and global well-being [74, 75]. However, conflicting evidence exists as to whether MBSR is more effective than active control regimens in treating fibromyalgia-associated symptoms [76–78]. A recent review detected low quality of evidence for MBSR-induced quality of life and pain improvements in fibromyalgia patients when compared to usual care, health education training, and social support [5, 54, 55, 74, 76–78]. In one large and well-controlled study, 120 patients were randomized to 8 weeks of MBSR, a health education class, or a wait-listed control group [55]. Participants assigned to the MBSR intervention reported no significant pain reductions but rather improvements in quality of life when compared to the other groups. Yet, these benefits were not maintained at the 2-month follow-up, suggesting that MBSR does not produce stabilized improvements in quality of life for fibromyalgia patients. Other studies have shown more inconsistent findings across

fibromyalgia-based clinical trials [76–78]. These varying results are perplexing and highlight the perceived barriers associated with participating in an MBSR program, such as the non-trivial temporal and financial commitments. It may prove fruitful to implement shorter, more accessible and translatable interventions that are tailored to specifically target mechanisms found to improve fibromyalgia-associated outcomes.

For instance, a recent 6-week, online mindfulness intervention compared the effects of a mindful socioemotional regulation regimen (MSER) to a “healthy lifestyle tips” (HLT) intervention [79]. Both regimens consisted of 12 online, 15-min presentations followed by weekly meditation homework for those assigned to the MSER group. MSER training promotes acceptance of affective experiences to improve quality of life and strengthen social networks [79]. The HLT intervention provided didactics on how to eat healthy, exercise, and sleep well. Neither intervention produced significant improvements in daily pain levels [79]. However, the MSER group reported significant improvements in stress and pain coping efficacy, positive affect, family stress, and loneliness when compared to the HLT group [79]. Further, depressed patients in the MSER group reported improvements in loneliness, family stress, and positive affect. This effect was not detected in the HLT group [79], suggesting that mindfulness techniques may uniquely exert increased effectiveness in patients diagnosed with concurrent depression. Interestingly, a separate study examined the efficacy of 7 weeks of mindfulness training in comparison to a wait-list control on depression, anger, and anxiety in fibromyalgia patients [80]. Mindfulness training incorporated aspects of MBSR but was similar to MSER in that it was modified to focus on acceptance of emotions, thoughts, and sensations. Mindfulness training effectively reduced state anxiety and depression and increased participant’s ability to control their anger [80]. These results were maintained at a 3-month follow-up. Thus, acceptance-based mindfulness practices may improve psychological comorbidities and physical symptomology associated with fibromyalgia.

A recent trial provides further support for the efficacy of tailoring mindfulness-based interventions to better target fibromyalgia [81•]. An 8-week meditation awareness training program was compared with cognitive behavioral therapy for groups, an intervention seemingly similar to CBT but performed in a group setting. This group-based CBT approach controlled for all the nonspecific aspects associated with meditation awareness training, including overall course length, facilitator, individual session duration and format, and inclusion of at-home practice [81•]. Meditation awareness training incorporated eight weekly, 2-h workshops, guided meditation “homework,” facilitated group discussions, and two one-on-one hour-long support sessions with the program instructor. The intervention differed from MBSR in that it educated practitioners on the principle of *non-attachment*, a concept based on the view that discomfort can arise from an individual’s attachment to experiences, ideas, and/or objects [81•]. Meditation awareness training was also modified to specifically address fibromyalgia-related symptomology, with mindfulness practices altered to incorporate (1) objectifying somatic pain, (2) compassion-empathy training, and (3) altruism promoting techniques.

The meditation awareness training group reported significant improvements over the control group in fibromyalgia-related symptomology, pain, sleep, psychological distress, and civic

engagement [81•]. Civic engagement partially mediated all treatment effects, whereas non-attachment almost *fully* mediated the effects of meditation awareness training on fibromyalgia-related symptomology and pain perception [81•]. Non-attachment-based coping strategies may decrease pain symptomology through didactics premised on detachments from the concept of "self" and one's relationship to pain, consequently decreasing the affective salience of noxious sensations. Taken together, these studies suggest that mindfulness-based techniques principled on developing (a) acceptance of pain, (b) nonjudgmental awareness of sensory experiences, and (c) non-attachment to concepts related to self, symptoms, or environment may be the most effective in improving fibromyalgia-related pain and psychological co-morbidities. Furthermore, interventions that help patients engage in social activities and relationships may further alleviate fibromyalgia-related symptomology, potentially through reducing stress [82] and depression [83].

Mindfulness-Based Analgesia Engages Unique Neural Mechanisms

Mindfulness meditation engages multiple mechanisms to reduce pain [84, 85•, 86–90]. However, the analgesic mechanisms supporting mindfulness-based analgesia are distinct across meditative training expertise and frequency [84, 85•, 86–90]. We have repeatedly demonstrated that mindfulness meditation, after brief mental training (four sessions; 20 min/session), significantly improves anxiety [61, 91, 92] and pain [84, 85•, 92, 93]. Mindfulness meditation-induced pain relief, after brief mental training, is associated with heightened activation in regions involved in the cognitive and emotional evaluation of pain such as the pregenual ACC (pgACC), the orbitofrontal cortex (OFC), and the right anterior insula [84, 85•]. Mindfulness meditation-induced analgesia after brief mental training is also associated with decreased activation in low-level sensory processing regions (i.e., thalamus) [84, 85•]. We proposed that the cognitive reappraisal mechanisms engaged by mindfulness meditation may alleviate pain through a cortico-thalamo-cortical gating mechanism [84, 85•, 93, 94].

The cognitive state of mindfulness meditation reduces acute pain by maintaining/sustaining attention on a meditative object (i.e., breath) and nonjudgmentally acknowledging innocuous and noxious sensory events as they arise. Thus, shifts in executive attention (engaging breath > disengaging breath > engaging distraction non-judgmentally > reengaging breath) are likely mediated by rostral aspects of the ACC and OFC [84, 85•, 95]. Thalamic deactivation is then driven by prefrontal cortices to reduce the elaboration of nociceptive information throughout the cortex (i.e., primary somatosensory cortex) [84, 85•, 93–95], thereby decreasing the subjective experience of pain. Furthermore, brief, yet intensive meditation training increases resting state functional connectivity between the DMN and the dlPFC, a region involved in top-down executive control [96]. Increased connectivity between these regions was associated with decreased IL-6 in highly stressed, unemployed individuals [96], suggesting that reappraisal mechanisms engaged by short term mindfulness meditation may also alleviate inflammatory processes associated with fibromyalgia-related outcomes [43, 44]. However, greater frequency of meditative training may render long-term, stabilized reductions in the subjective experience of pain and likely employs distinct mechanisms from those exhibited by novice practitioners.

Davidson and colleagues examined the effects of 8 weeks of MBSR training in healthy participants on brain electrical activity [electroencephalography (EEG)] and immune function [97]. MBSR training produced stabilized increases in left-lateralized, alpha-band activity corresponding to the anterior temporal region immediately following positive mood induction. Furthermore, MBSR training was associated with increases in antibody titers in response to an influenza vaccine, and MBSR-associated increases in alpha-band activity in the central electrodes corresponding to the sensory/motor cortices were associated with increased immune responses [97]. Additional trials have found that MBSR training reduces pro-inflammatory nuclear factor kappa B (NF-κB) gene expression, associated with stress responses, in older adults [98] and increases the rate of resolution of psoriatic lesions [99], further suggesting that 8 weeks of mindfulness training directly impacts inflammatory-associated conditions.

Multiple studies reveal that adept meditators (>1000 h of meditation practice) report lower levels of pain sensitivity [86–90] and higher pain tolerance [88]. Neuroimaging findings show that experienced meditators exhibit heightened activation in sensory processing regions (thalamus; SI; SII) [89, 90] but deactivation of prefrontal cortices [89, 90], reflecting a unique ability to fully attend to salient sensory processes without engaging higher-order appraisals and judgments of said sensory events. These mechanisms are remarkably consistent with the principles of mindfulness (i.e., non-judgmental awareness of arising sensations, feelings, and emotions).

Additional studies focused on adept meditators report reduced anticipation and/or expectations of impending sensory events [86, 87]. During mindfulness meditation, expert meditators demonstrated decreased pre-stimulus activity in the anterior insula when compared to novices, indicating that long-term practitioners may maintain focus on present moment experiences and reduce expectations of impending pain [87]. Brown and Jones used EEG and noxious laser stimulation to examine the impact of long-term mindfulness on pain and pain anticipation while practitioners were instructed not to practice meditation [86]. Greater meditation experience was associated with smaller anticipatory-related evoked potentials in regions associated with the expectation of a stimulus, such as the right inferior parietal cortex and mid-cingulate cortex. Reduced mid-cingulate cortex activation during the anticipation of pain predicted lower pain unpleasantness ratings in the meditation but not the control group [86], suggesting that changes in expectations regarding a noxious stimulus may particularly facilitate lower pain ratings in experienced meditators. Additionally, heightened activation in the ACC and ventromedial PFC during the anticipation of pain was positively correlated with pain ratings in control subjects but negatively correlated with pain for meditators [86]. Thus, cognitive reappraisal mechanisms engaged immediately prior to the experience of a noxious stimulus may play an important role in mediating the pain-relieving effects of long-term meditation training. Taken together, greater bouts of meditation training may target the emotional augmentation of chronic pain through decreasing the anticipation and negative appraisal of clinical symptoms while increasing cognitive and emotional control immediately prior to a known noxious stimulus.

Conclusion

Mindfulness meditation attenuates pain by enhancing cognitive flexibility and the ability to regulate emotional reactions with a nonjudgmental and nonreactive focus. MBSR may effectively improve outcomes such as stress, quality of life, pain, and symptom severity in fibromyalgia patients when compared to a wait-list control [74, 75]. However, mindfulness interventions that specifically focus on the principles of acceptance, non-attachment, and social engagement in addition to nonjudgmental awareness appear to be most effective in improving fibromyalgia-related outcomes [79, 80, 81•]. This subset of mindfulness-based interventions produces improvements in depression, anxiety, anger, pain, fibromyalgia-related symptomology, stress, coping efficacy, and positive affect in comparison to wait-list and active control regimens [79, 80, 81•]. Future studies should examine the impact of mindfulness-based interventions on fibromyalgia-associated inflammatory and neural processes in order to better identify biological mechanisms associated with meditation-based pain relief.

Preliminary evidence suggests that the concept of non-attachment to self, experiences, and environment may be a key mediator of the effects of mindfulness on fibromyalgia-related pain [81•]. Consequently, an individual's ability to detach from the personal salience and affective value of a stimulus may be an important factor in facilitating fibromyalgia-related symptom improvement. Interestingly, expert meditators have been shown to demonstrate greater reductions in pain unpleasantness, but not pain intensity, when compared to novice meditators [87], further suggesting that meditation practices may improve outcomes through modifying an individual's evaluation of painful experiences without impacting the strength of the stimulus.

Yet, mindfulness meditation is a cognitively demanding task that may not be appropriate for all fibromyalgia patients. Up to 65% of rheumatic patients report severe fatigue [100], and mindfulness meditation requires constant and sustained attention on a meditative object while also recognizing and reappraising discursive sensory events as they arise. This can be very demanding on fibromyalgia patients. Thus, non-pharmacologic approaches that are less cognitively engaging may prove more useful for some subsets of patients (CBT; relaxation; acupuncture; yoga). Interestingly, preliminary evidence suggests that acceptance and commitment therapy (ACT), a type of CBT, may effectively improve pain-related and psychological outcomes in fibromyalgia patients [101]. ACT educates patients on principles of acceptance and mindfulness through helping participants notice interfering thoughts and sensations while refraining from acting on them. ACT is aimed at increasing cognitive flexibility, enabling patients to engage in goal-oriented behaviors even in the presence of negative experiences. Consequently, mindfulness-based therapies may exert increased effectiveness when combined with ACT.

Other prominent mind-body interventions such as yoga [102], massage therapy [103], and heart rate variability (HRV) biofeedback [104] are effective at reducing fibromyal-gia pain. Relaxation-based regimens may improve such outcomes by decreasing stress and/or anxiety [105–107]. Yoga may impact fibromyalgia-associated outcomes through a number of mechanisms due to the combination of exercise, mindfulness techniques, and social support.

Similar to exercise, yoga may improve balance [108], strength [109], and mobility [110] and thus improve functional status. Additionally, instructors teach practitioners to observe thoughts and sensations associated with the practice of yoga without reaction or judgment. The ability to nonjudgmentally observe uncomfortable mental and physical experiences during yoga may enable patients to engage mindfulness-related skills more effectively during the experience of clinically relevant stimuli. Yoga is often taught within group settings and may provide social support that could alleviate stress and depression-induced augmentation of pain [105]. Taken together, yoga may alleviate current clinical pain and buffer against future symptoms through combining multiple techniques that may reduce the physical and psychological symptoms of fibromyalgia. It may also prove fruitful to incorporate mindfulness-based physical exercises (yoga; walking meditation) in a group setting to better attenuate pain and comorbid symptomology. Nevertheless, a more comprehensive understanding of the specific mechanisms of action supporting mind-body approaches will significantly inform our understanding of fibromyalgia epidemiology. Although behavioral treatments may not fully alleviate fibromyalgia-related pain, mindfulness techniques could be optimized to help patients detach from the reflexive personalization and negative evaluation of such an experience.

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