

# Meditative and Mindfulness-Focused Interventions in Neurology: Principles, Science, and Patient Selection

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## Abstract

A growing body of research suggests that meditative- and mindfulness-focused interventions may improve neuropsychiatric symptoms that commonly occur in a range of neurological disorders. In this article, the principles of meditation and mindfulness are first defined, as well as briefly describing the neurobiological mechanisms implicated in these interventions. Thereafter, a range of meditative- and mindfulness-focused interventions are detailed, along with their supporting evidence to treat neuropsychiatric symptoms in neurological conditions (e.g., headache, movement disorders, chronic pain, etc.). Overall, these interventions warrant further investigation among individuals with neurological conditions. When recommending these interventions, health care professionals must consider a combination of structural (e.g., insurance reimbursement) and patient factors (e.g., ability to tolerate a group setting).

## Keywords

- ▶ meditation
- ▶ mindfulness
- ▶ mind–body
- ▶ neurology

Over the past several decades, there has been growing interest in the use of mind–body interventions (MBIs) among both healthy and clinical populations in the United States. MBIs encompass a group of therapies broadly focused on harnessing the interactions between brain, mind, body, and behaviors to improve health and well-being.<sup>1</sup> Some of the most common MBIs and techniques include meditation-based programs, promotion of mindful awareness, relaxation practices (e.g., guided imagery, progressive muscle relaxation), yoga, and tai chi. While these interventions are often rooted in ancient practices, many of them have been secularized and tailored for medical settings. Growing evidence suggests that these interventions are relatively safe<sup>2,3</sup> and may be effective for reducing physical and emotional symptoms commonly associated with neurological disorders.

MBIs are multimodal in nature and incorporate several mind and body strategies (e.g., breath awareness, movement, meditation, mindfulness). In this narrative review, we will focus primarily on MBIs with a meditative or mindfulness component. A comprehensive review of all meditative- and mindfulness-focused interventions is beyond the scope of this article; instead, we will focus on select therapies with promise in neurology. Specifically, we will (1) define meditation and mindfulness; (2) provide an overview of select therapies with meditative or mindfulness components; (3) review the evidence of these therapies for neurological disorders and common neuropsychiatric symptoms; and (4) highlight structural and patient factors relevant to patient selection for these therapies.

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## Definition and Principles of Meditation and Mindfulness

Meditation consists of a group of mental practices that involve the regulation of attention from moment to moment on an object of awareness to foster various states, including emotional balance and well-being.<sup>4</sup> The type of meditation depends on the specific object of awareness, which can include interoceptive sensations (e.g., the breath, parts of the body), mental images and phrases (e.g., mantra), or external objects (e.g., a flame). Practices can involve a sustained focus on one object (i.e., focused attention), shifting focus from one object to another, or attending to one's moment-to-moment experiences without an explicit focus (i.e., open monitoring). Further, these practices can be completed in a stationary position or with movement.

Specific forms of meditation (e.g., focused attention, open monitoring) are used to cultivate mindfulness. Mindfulness, which is a key component of many MBIs, is defined as the self-regulation of attention to present moment experiences with an attitude of openness, curiosity, and acceptance.<sup>5</sup> The self-regulation of attention refers to purposefully guiding attention to present moment internal (e.g., thoughts, emotions, body sensations) or external (e.g., environment) experiences. These experiences are greeted without mental elaboration or judgment, regardless of their valence or desirability.<sup>5</sup> Mindfulness is conceptualized as both a state (i.e., actively attending to present moment experiences)<sup>6</sup> and a trait (i.e., one's disposition to be mindful in daily life),<sup>7</sup> and higher levels of state and trait mindfulness are associated with lower levels of emotional and physical symptoms.<sup>8–10</sup> Several interventions and techniques have been shown to improve state and trait mindfulness, including mindfulness-based interventions, yoga, tai chi, and other psychological interventions with a mindfulness focus (e.g., acceptance and commitment therapy).<sup>11–13</sup> Mindfulness-based interventions utilize various meditation practices (e.g., focused attention, open monitoring) to cultivate mindfulness, all of which involve regulating attention to present moment experiences with openness, curiosity, and nonjudgment.<sup>5</sup>

Mindfulness is often contrasted with automaticity, or automatic responding without deliberate intention.<sup>14</sup> It is well known that automatic and habitual responding to uncomfortable internal experiences (e.g., thoughts, emotions, body sensations) can have negative consequences. Indeed, automatic reactions can lead to efforts to avoid, suppress, or change uncomfortable internal experiences, which paradoxically exacerbate or maintain these experiences and increase emotional or physical distress.<sup>15</sup> As such, mindfulness-focused interventions help individuals change their relationship with difficult internal experiences. Specifically, mindfulness promotes decentering from (i.e., taking a step back from), rather than over-identifying with, thoughts, emotions, and body sensations.<sup>16</sup> In turn, this decouples the relationship between internal experiences and behaviors (e.g., an urge to avoid and subsequent avoidance), allowing individuals to choose a more adaptive response.<sup>17</sup>

## Neurobiological Mechanisms of Mindfulness

Neurobiological models of mindfulness suggest that mindfulness practice may exert its effects through structural and functional changes in brain regions and networks implicated in attention regulation, emotion regulation, and self-perspective and self-awareness.<sup>18–20</sup> Indeed, mindfulness interventions have been shown to improve various aspects of attention (e.g., selective, executive)<sup>21</sup>; in this regard, MBIs can be powerful forms of brain retraining—underscoring that brain–behavior relationships are bidirectional. In neuroimaging studies, mindfulness meditation was associated with functional changes in the cognitive control network, particularly the anterior cingulate cortex (ACC), which supports attention and control through conflict monitoring and decision-making, and the dorsolateral prefrontal cortex (PFC), which is essential for executive function.<sup>19</sup> There may also be structural changes in the ACC with mindfulness practice.<sup>19</sup>

There is also robust evidence that mindfulness interventions improve various indices of emotion regulation.<sup>22</sup> Neuroimaging studies suggest that functional changes may differ by level of experience (see ►Fig. 1). In beginners, mindfulness practice may be linked to enhanced activation in PFC regions and reduced activation of the amygdala in response to affectively valenced cues, indicative of top-down regulatory processes.<sup>19,23</sup> Long-term practice, on the other hand, may be associated with bottom-up emotion regulation strategies, characterized by reduced emotional reactivity without activation in PFC regions.<sup>19,23</sup>

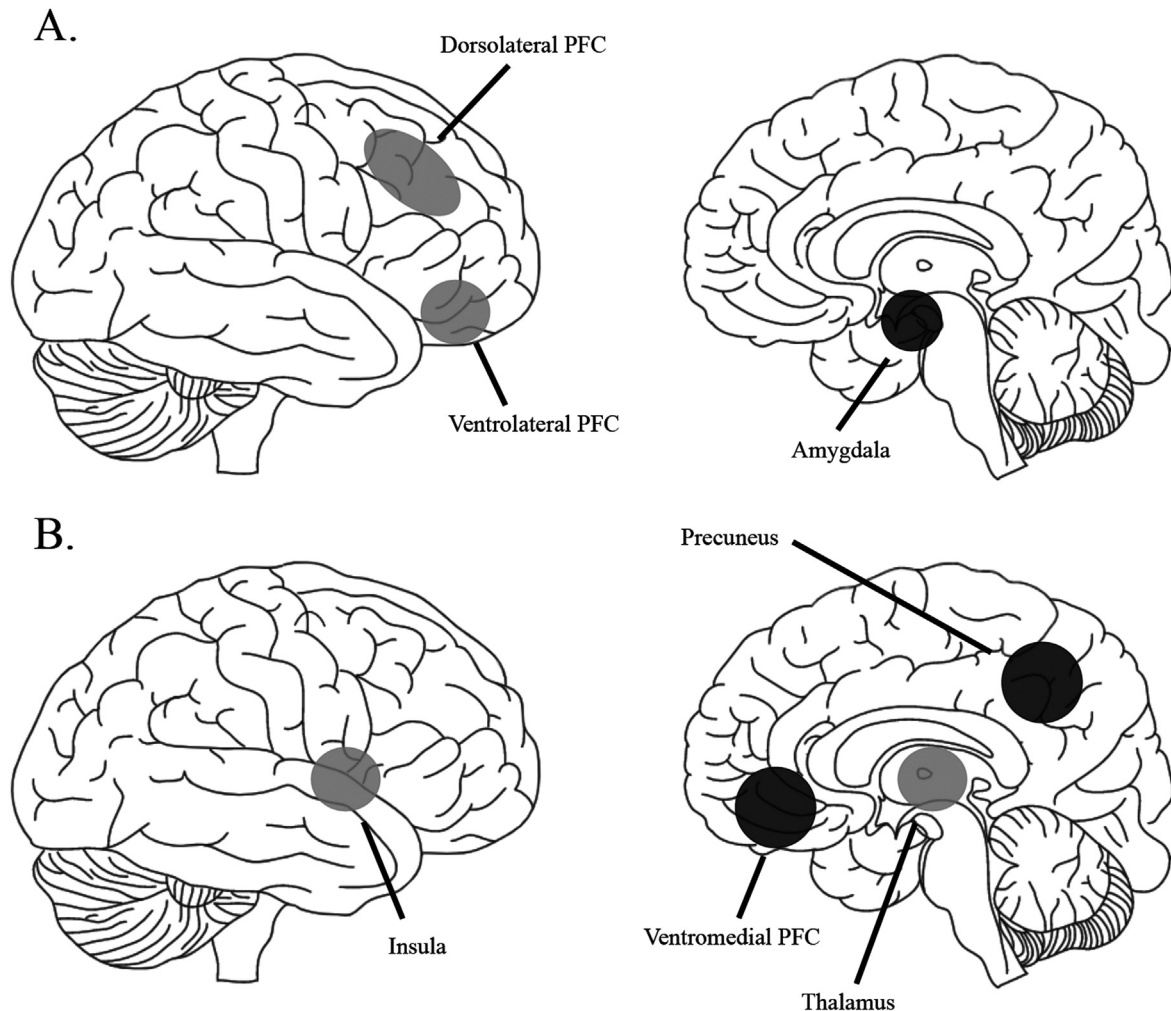
Mindfulness is also known to change various aspects of self-perspective (e.g., decentering, or taking a step back from thoughts)<sup>16</sup> and self-awareness (e.g., interoceptive awareness, or sensing and appraising internal physiological signals).<sup>24–26</sup> Neuroimaging studies have shown that activity and connectivity of the default mode network (cortical midline structures), which is thought to be involved in self-referential processing, is reduced in mindfulness meditators.<sup>19</sup> Examples of negative self-referential processing include rumination, worry, and self-criticism.<sup>27</sup> Studies have also demonstrated structural changes in regions associated with the experience of the self, such as the posterior cingulate cortex<sup>18</sup> and the insula.<sup>19</sup>

## Overview of Meditative- and Mindfulness-Focused Interventions

See ►Table 1 for an overview of the structure, components, and space requirements of select meditative- and mindfulness-focused interventions. See ►Table 2 for an example of a brief 5-minute mindfulness exercise.

### Mindfulness-Based Interventions

Mindfulness principles and practices were adapted by Jon Kabat-Zinn from Buddhism and were secularized and packaged to improve accessibility for use in clinical practice.<sup>28</sup> “Mindfulness-based” interventions emphasize mindfulness meditation and incorporate mindfulness principles into a range of activities. The two most common mindfulness-based interventions are Mindfulness Based Stress Reduction



**Fig. 1** (A) Changes observed with mindfulness in early practitioners include increased dorsolateral and ventrolateral prefrontal cortex (PFC) activity in response to emotional stimuli (*gray*), and reduced amygdala activation (*black*). (B) Experienced meditators demonstrate reduced activation of precuneus and ventromedial PFC during meditation (*black*) and increased activation of ventral sensorimotor structures such as insula and thalamus in response to emotional or painful stimuli (*gray*).

(MBSR)<sup>29</sup> and Mindfulness Based Cognitive Therapy (MBCT).<sup>30</sup> MBSR was originally developed to treat patients with chronic pain who failed other treatment modalities.<sup>29</sup> MBSR has subsequently been shown in meta-analyses to improve depression and anxiety symptoms not only in chronic pain populations, but also in community samples.<sup>31</sup> MBCT was adapted from MBSR to prevent relapse of depression among individuals with recurrent depressive episodes.<sup>30</sup> Specifically, MBCT incorporates more attention to cognitive therapy elements as applied to ruminative depressive thinking. MBCT has subsequently been applied across a range of neuropsychiatric conditions (e.g., anxiety, chronic pain).

Various other mindfulness-based interventions have been developed for specific populations or conditions (e.g., Mindfulness-Oriented Recovery Enhancement for chronic pain),<sup>32</sup> most of which were adapted from MBSR or MBCT. In general, mindfulness interventions are completed in a group format and include eight weekly 1- to 2-hour sessions and daily

home practice (as well as a retreat day in some programs). Each session includes meditations, group discussion/inquiry, and didactics. Mindfulness interventions utilize both formal (e.g., meditation, yoga) and informal (e.g., mindful walking, eating) practices to build mindfulness skills to be applied in daily life.

### SMART Program

The Benson-Henry Institute for Mind Body Medicine has studied MBIs for over 40 years based on the pioneering work of Dr. Herbert Benson to define a “relaxation response,” which is thought to be the physiological inverse of the fight/flight response. The origins of this work began with meditative practices consisting of mental repetition of a word or short phrase in rhythm with the breath, and to passively attend to distracting thoughts, returning focus once again to the breath. This focused awareness practice has since been incorporated into a more diverse set of cognitive and physical practices that comprise the “SMART program,” or

**Table 1** Structure, components, and space requirements of select meditative- and mindfulness-focused interventions

Mind-body Intervention	Structure	Components	Space requirements
MBSR/MBCT	2 hours per week for 8 weeks + retreat day	Mindfulness principles, yoga, meditative practices, incorporating mindfulness into everyday life	Floor space for yoga mats; chairs for discussion
SMART	90 minutes per week for 8 weeks	Relaxation training, cognitive therapy, sleep hygiene, guided imagery, gentle yoga	Conference room with chairs
Yoga interventions	Vary: 6–12 weeks typical, group classes often 1 hour	Varies based on type, typically involves stretching postures held while attending to sensations of the breath and body	Dependent on type, usually floor space for yoga mats
Tai chi	Vary: 12 weeks, 1-hour classes, 2–3 days per week typical	Gentle physical movement performed while standing, attending to the breath and body movements	Open floor space or outdoor space
Mentalizing imagery therapy	4 weekly 2-hour sessions	Gentle chair yoga, mindfulness and guided imagery practices, group discussion	Conference room with chairs

Abbreviations: MBCT, mindfulness-based cognitive therapy; MBSR, mindfulness-based stress reduction; SMART, Stress Management and Resiliency Training.

**Table 2** Brief 5-minute mindfulness exercise instructions

Close your eyes and allow the muscles of your jaw and tongue to relax gently down. Bring your attention to your breathing. Notice how the breath feels as it enters the nose, flows into the head and down the throat. Pay attention to the natural movements of your body with the breath, the gentle expansion of the chest and abdomen with the inhalation, and their relaxation with the exhalation. If distracting thoughts arise, that is ok, simply acknowledge them, and return attention to your breathing.

Stress Management and Resiliency Training program, which includes relaxation response training, stress awareness, and cognitive approaches to stress management.<sup>33</sup> In addition, it provides training in a variety of other resilience enhancement approaches including positive psychology, acceptance, social support and pro-sociality, spiritual connectedness, and healthy lifestyle. SMART is a group program and involves 90- to 120-minute weekly sessions for 8 weeks. The program has been successfully implemented with patients who have a variety of symptoms, including chronic pain, fatigue, anxiety, and depression.<sup>34</sup>

### Mindful Movement-Based Therapies

Mindful movement-based therapies, such as tai chi and yoga, are perhaps the most widely implemented MBI in community settings. Tai chi is a multimodal intervention that includes movement, breath awareness, breathing exercises, postural and strength training, and mindful attention.<sup>35</sup> In tai chi, slow purposeful movements are coordinated with breathing or imagery to strengthen the mind and body and improve health.<sup>35</sup> Although the style and dose of tai chi varies in community settings, more standardized tai chi interventions have been developed for medical and research

settings. These interventions typically include 1-hour sessions, conducted two to three times per week for 12 weeks. While more systematic documentation of adverse events is needed, tai chi appears to be relatively safe, including for individuals with more chronic diseases (e.g., Parkinson's disease [PD]).<sup>36</sup>

Many variations of yoga practice can be found. Overall, yoga aims to unite the mind and body and improve health through breathing exercises, movement (i.e., yoga postures), and meditation. Yoga practices range from gentle passive stretching (e.g., Hatha yoga) to active repetitions of yoga postures (e.g., Vinyāsa, Ashtanga) to intense sequences in environments heated to more than 100°F (e.g., hot yoga or power yoga). In a meta-analysis of randomized controlled trials (RCTs) employing a variety of yoga interventions, yoga appeared to be as safe as usual care and exercise but was associated with an increase in intervention-related and nonserious adverse events (but not serious adverse events) compared with psychological/educational interventions.<sup>2</sup> However, almost 70% of the located trials in this meta-analysis did not report safety data, pointing to the need for more comprehensive safety monitoring and reporting in yoga RCTs.

### Mentalizing Imagery Therapy

Mentalizing refers to the process of understanding the mental processes of self and others and their links to behaviors, including in the challenging interpersonal situations that often worsen or cause psychological symptoms. Caregivers of patients with chronic neuropsychiatric illness often struggle with the challenge of mentalizing those whose minds process information differently and evince less cognitive control. Mentalizing Imagery Therapy (MIT) is a newly developed intervention that seeks to incorporate fundamental principles of mentalizing into a set of mindfulness and guided imagery practices that caregivers can use to nonjudgmentally observe their experience and aid mentalization of the person whom they support.<sup>37</sup> MIT, which consists of four weekly 2-hour sessions, includes chair yoga, mindfulness, and imagery practices.

### Evidence for Common Neurological Disorders

In this section, we review the evidence of meditative- and mindfulness-focused interventions for headache, functional neurological disorder (FND), epilepsy, neurodegenerative disorders, movement disorders, stroke, mild cognitive impairment (MCI), and caregivers of individuals with neurological disorders.

#### Headache

Research examining mindfulness interventions for headache is growing. A 2019 meta-analysis ( $n = 5$  studies) found that MBSR did not improve headache frequency, duration, or intensity among individuals with tension type and migraine headaches.<sup>38</sup> Despite these negative results, two more recent RCTs demonstrated some potential benefits of MBSR. The first study compared MBSR to a control condition (headache education) among 89 adults with migraine.<sup>39</sup> While both groups showed improvements in migraine days, MBSR was associated with greater improvements in headache-related outcomes such as disability, catastrophizing, quality of life, and pain intensity and unpleasantness. In the second study among individuals with episodic migraine, compared with a stress management for headache program, enhanced MBSR (i.e., 12 sessions) was associated with greater reductions in headache days and headache-related disability at 20 weeks, but not 52 weeks.<sup>40</sup> Thus, the evidence for treating chronic headache with mindfulness meditation is somewhat mixed, but recent findings show some promise for migraine. Future research should address better targeting mindfulness therapies in this population.

In terms of medication use outcomes in headache, a nonrandomized study of a mindfulness-based intervention was conducted in 44 subjects with chronic migraine-medication overuse headache.<sup>41–44</sup> Participants who completed a medication withdrawal program chose a prophylactic medication regimen or a 6-week group-mindfulness training. Headache frequency and medication use decreased in both groups. However, there were no improvements in self-reported anxiety in either group, even though catecholamine

levels were reduced. Randomized trials are needed, but nevertheless this study suggests that mindfulness may have similar benefits to a standardized pharmacological treatment for refractory migraine-medication overuse headache among patients who select a nonpharmacological approach.

Findings from a recent meta-analysis ( $n = 5$  RCTs) suggested that yoga may improve headache frequency, headache duration, and pain intensity among individuals with tension headaches, but not migraines.<sup>45</sup> However, the quality of evidence was considered low due to methodological limitations, pointing to the need for more research in this area.

#### Functional Neurological Disorder

There has been increasing interest in employing mindfulness approaches to help patients with FND. In an uncontrolled study in a neurological population referred for evaluation ( $n = 98$ ) with a variety of diagnoses including FND, participation in a mindfulness-based intervention correlated with moderate decreases in anxiety and depression.<sup>46</sup> A subgroup analysis showed small size effects in FND subjects, medium size effects in those with nonprogressive neurological conditions, and large size effects in those with progressive conditions. All groups had improvements in stress coping. This may suggest that while mindfulness meditation is effective in reducing stress, there may be value added with efforts to enhance resilience through active coping using cognitive skills, positive psychology, and social support.

Treatment interventions for functional (psychogenic nonepileptic/dissociative) seizures (FSs) have become a focus of study, but few high-quality RCTs exist. In an uncontrolled study, Baslet and colleagues<sup>47</sup> examined a mindfulness-based intervention for individuals with FS. Despite high levels of dropout, individuals who completed the mindfulness intervention demonstrated improvements in FS frequency, intensity, and quality of life. This preliminary study, along with a case series with similar findings,<sup>48</sup> suggests that a mindfulness intervention may be feasible for individuals with FS and that more research is warranted.

#### Epilepsy

Thompson and colleagues<sup>49</sup> studied a distance-delivered MBCT group for preventing major depressive disorder (MDD) among individuals with both epilepsy and mild to moderate depressive symptoms. Results showed lower incidence of MDD episodes in the MBCT group (0%) compared with the treatment as usual group (10.7%). Greater decreases in depressive symptoms dimensionally were also found in the MBCT group. Similar effects occurred for web- and telephone-based MBCT. These findings suggest that there may be potential for MBCT in preventing depressive episodes among individuals with epilepsy.

There is more limited evidence for mindful exercise therapies in epilepsy. A Cochrane review identified only two studies of yoga among individuals with epilepsy, which demonstrated promising effects for seizure outcomes and quality of life.<sup>50–52</sup> Overall, more research is needed to better



understand mindful movement therapies for individuals with epilepsy.

### Neurodegenerative Disorders

There are a growing number of studies examining mindfulness interventions for multiple sclerosis (MS). In an RCT among individuals with MS, compared with treatment as usual, a mindfulness-based intervention was associated with small-to-medium reductions in anxiety, depression, and fatigue, as well as a large improvement in quality of life.<sup>53</sup> Effects were generally maintained at the 6-month follow-up and improvements were particularly pronounced in the more severely symptomatic subgroup (i.e., clinical levels of depression, anxiety, fatigue).

A 2019 meta-analysis of 12 RCTs examined the effects of mindfulness-based interventions on mental well-being in a total of 744 individuals with MS.<sup>54</sup> The authors found a moderate effect of mindfulness interventions on overall well-being. In terms of specific outcomes, there were small to medium effects for anxiety, depression, and stress reduction. Taken together, these results suggest that mindfulness-based interventions may be effective for improving common neuropsychiatric symptoms among individuals with MS.

Recognizing the disability associated with MS, studies have relied upon distance interventions being provided via telehealth.<sup>55</sup> A 2015 survey of over 2,800 individuals with MS found that there was considerable unmet psychological need.<sup>56</sup> This underscores the need to optimize the accessibility of psychological services and support.<sup>56</sup> Mindfulness-based interventions provided through distance telemedicine provide an opportunity for health promotion in patients with neurodegenerative diseases like MS.

### Movement Disorders

Among the movement disorders, PD has been most studied using mindfulness-based interventions. In a recent systematic review of MBSR for PD ( $n=3$  studies),<sup>57</sup> one study showed improvements for PD outcomes, depression, mindfulness, and quality of life, and a second found an increase in gray matter density on magnetic resonance imaging following MBSR compared with usual care. While these results are promising, the review authors concluded that there is limited evidence to support the use of MBSR for PD given the small number of studies, methodological limitations, and lack of adverse event reporting. Larger RCTs with longer follow-ups and systematic safety monitoring are warranted.

Motor symptoms, as well as neuropsychiatric symptoms such as anxiety and depression, are known to increase due to stress in PD. In a survey study (5,000 PD patients and 1,292 controls), Van der Heide and colleagues<sup>58</sup> found that individuals with PD perceived more stress than controls and stress was associated with increased rumination, lower quality of life, lower self-compassion, worsening motor symptoms, and lower dispositional mindfulness. Mindfulness was practiced by 38.7% of individuals with PD in the past 3 months, with varying amounts of practice across patients (e.g., 53.2% reported weekly practice and 21.5% reported practicing less than once per month). Individuals with PD

who practiced mindfulness endorsed improvements in both motor (e.g., gait, tremor) and nonmotor (e.g., anxiety, depression) symptoms, with the greatest effects for anxiety and depressive symptoms. These results suggest acceptability of mindfulness among a large proportion of patients with PD and support the further study of mindfulness-based interventions in PD.

A 2019 meta-analysis examined the effects of cognitive behavioral therapy (CBT) and mindfulness-based interventions among individuals with MS, PD, and Huntington's disease (HD).<sup>59</sup> Across 12 studies ( $n=8$  in MS and  $n=4$  in PD), these interventions demonstrated a medium decrease in psychological distress. In seven studies involving patients with MS, there were small reductions in distress. There were no studies identified in HD populations. Despite the positive effects among individuals with MS and PD, the overall quality of studies was considered low, pointing to the need for more rigorous research in this area.

Tai chi has also been studied among individuals with PD. In a large RCT ( $n=195$ ), tai chi outperformed resistance training and stretching in improving in postural stability.<sup>60</sup> Tai chi also demonstrated greater improvements in gait and strength when compared with stretching and greater improvements in stride length and functional reach compared with resistance training. Moreover, tai chi lowered the incidence of falls compared with stretching, but not resistance training. A 2017 meta-analysis suggested that tai chi was associated with improvements in motor outcomes, balance, timed walking, falls, depressive symptoms, and quality of life among individuals with PD.<sup>61</sup> Cognition did not improve. Tai chi shows promise as an intervention for PD.

### Poststroke Recovery

Mindfulness-based interventions may be helpful poststroke. Results from a 2013 systematic review involving four studies ( $n=160$ ) suggested that there were favorable trends for mindfulness-based interventions following a stroke with regard to biopsychosocial outcomes, including anxiety, depression, fatigue, blood pressure, perceived health, and quality of life.<sup>62</sup> Another study demonstrated that a 2-week home-based mindfulness intervention was feasible among chronic stroke survivors with spasticity ( $n=10$ ).<sup>63</sup> There were preliminary effects for decreasing spasticity and increasing quality of life. This is a very small study, but it is supportive of a short, low-risk, and low-cost mindfulness intervention that may potentially benefit both physical and mental symptoms poststroke. Prospective and controlled research with larger sample sizes will be required to confirm these findings.

There is also limited but promising evidence for mindful movement therapies in stroke. A meta-analysis of 19 RCTs suggested that tai chi may improve balance function and exercise capacity following stroke.<sup>64</sup> In a systematic review of eight studies, tai chi and yoga both showed promise for improving psychological stressors and quality of life among poststroke patients.<sup>65</sup> However, more rigorous and adequately powered RCTs are needed to better evaluate movement-based therapies in stroke.

### Mild Cognitive Impairment

A 2019 meta-analysis of 40 randomized controlled studies including 3,551 older adult participants addressed the question of whether mind–body interventions affected cognition in older adults.<sup>66</sup> MBIs were classified as meditation (which included mindfulness as well as other styles), yoga, tai chi, and other mindful movement therapies (e.g., Qigong). Small to moderate effects across cognitive domains were found with low risk of bias. Further analysis suggested a higher effect size for patients with MCI. These results demonstrated that effects were more robust for longer term interventions (i.e., >12 weeks) with session practice frequency of at least three times per week and longer session duration (i.e., at least 45 minutes of practice time). Such interventions are longer than those offered in the usual clinical setting (such as MBSR or MBCT). Recent mindfulness studies have focused on molecular pathways thought to be mechanistically related to MCI and found sex-specific reductions in C-reactive protein in females but not in males with MCI,<sup>67</sup> but no effect on circulating amyloid- $\beta$  42 levels.<sup>68</sup> Mindfulness interventions may more likely modify immune activity related to MCI than amyloid level.

### Caregivers

Meditative- and mindfulness-focused interventions have also shown promise for caregivers of individuals with neurological disorders. For example, a recent review found low-quality evidence that MBSR may lead to short-term reductions in depressive and anxiety symptoms in caregivers of those with dementia.<sup>69</sup> Lavretsky and colleagues<sup>70</sup> demonstrated that Kirtan Kriya yoga, which involves approximately 20 minutes of repeated chanting of a mantra with guided imagery, resulted in improvements in depression and executive function in family dementia caregivers. MIT has also shown feasibility and acceptance. In a small trial of MIT compared with a waitlist control augmented by optional relaxation exercises, family dementia caregivers who received the MIT intervention exhibited greater improvements in depression and anxiety symptoms.<sup>71</sup> Neuroimaging findings revealed increased dorsolateral PFC connectivity with an emotion regulation network in the MIT group, but not waitlist. Qualitative findings suggested improvements in well-being, mood, anxiety, and sleep, as well as in perceiving themselves more objectively within challenging relationship situations.<sup>72</sup> Clearly, larger randomized, controlled trials of these interventions are needed.

### Evidence for Common Neuropsychiatric Symptoms

In this section, we review the evidence of meditative- and mindfulness-focused interventions for neuropsychiatric symptoms, including depression, anxiety, chronic pain, and sleep difficulty.

#### Depression

Research suggests that mindfulness-based interventions are effective for reducing depressive symptoms and preventing

relapse of depression. In one of the most recent meta-analyses of RCTs, mindfulness-based interventions (e.g., MBCT, MBSR) were found to be superior to no treatment and other active therapies, and equivalent to existing evidence-based therapies (e.g., CBT) for individuals with a depression diagnosis or elevated symptoms.<sup>73</sup> In a meta-analysis exclusively among individuals with a current depressive or anxiety disorder, mindfulness interventions demonstrated a medium-to-large effect on depressive symptom severity, and overall effects on primary symptom severity were particularly pronounced for MBCT.<sup>74</sup>

MBCT has also been shown to effectively reduce the risk of depressive relapse within a 60-week follow-up period among individuals with recurrent depression in full or partial remission, particularly among individuals with higher residual symptoms at baseline.<sup>75</sup> Further, MBCT was found to be comparable to active treatments, including antidepressant medication.<sup>75</sup> MBCT may reduce the risk of depression relapse through improvements in trait mindfulness, rumination, decentering, worry, and self-compassion.<sup>76</sup>

The SMART program has demonstrated promise for reducing depressive symptoms in a variety of populations. For example, in a small open-label study among individuals with MDD, SMART was associated with improvements in resilience and reductions in depressive symptoms and perceived stress.<sup>77</sup>

Yoga and tai chi have also shown potential for reducing depressive symptoms.<sup>78</sup> In a 2013 meta-analysis, yoga reduced the severity of depression among individuals with a depressive disorder or elevated symptoms compared with usual care, with more limited evidence of reductions compared with relaxation and aerobic exercise.<sup>79</sup> Tai chi may also reduce depressive symptoms, although more high-quality studies are needed.<sup>80</sup>

#### Anxiety

There is evidence that mindfulness-based interventions may effectively reduce anxiety symptoms among individuals with a range of conditions. In a meta-analysis among individuals with various conditions (e.g., cancer, other medical conditions, depression), mindfulness-based interventions demonstrated a medium effect on anxiety symptoms.<sup>81</sup> Subsequent meta-analyses have shown that mindfulness-based interventions reduce anxiety symptoms among healthy adults<sup>82</sup> and individuals with chronic pain conditions (e.g., fibromyalgia).<sup>83</sup>

The evidence for mindfulness-based interventions among individuals with anxiety disorders is somewhat less consistent. Vøllestad and colleagues<sup>84</sup> found that in controlled studies, mindfulness interventions moderately improved anxiety symptoms among individuals with anxiety disorders. However, results from a recent meta-analysis suggested that mindfulness-based interventions (e.g., MBCT, MBSR) were superior to no treatment controls, but equivalent to other active therapies and evidence-based treatments for individuals with anxiety disorders or elevated symptoms.<sup>73</sup> Moreover, in a meta-analysis among individuals with current anxiety disorders, there was no significant effect of mindfulness-based interventions on symptom severity.<sup>74</sup>

In pilot trials, the SMART program has been shown to improve anxiety symptoms in several populations, including parents of children with learning and attentional disabilities, breast cancer survivors, and patients with other medical conditions such as hypertension and neurofibromatosis.<sup>85–88</sup>

In terms of mindful movement-based therapies, Cramer and colleagues<sup>89</sup> found that yoga reduced anxiety symptom severity when compared with no treatment and active controls for individuals with elevated anxiety symptoms, but not individuals with a Diagnostic and Statistical Manual of Mental Disorders (DSM)-diagnosed anxiety disorder. Further, a recent meta-analysis found that yoga was superior to nonmindful forms of exercise for reducing anxiety symptoms.<sup>90</sup> While more rigorous RCTs are needed, there is emerging evidence that tai chi may be helpful for anxiety symptoms.<sup>80</sup>

### Chronic Pain

There is growing evidence for the efficacy of mindfulness-based interventions for chronic pain-related outcomes. Among individuals with a variety of chronic pain conditions (e.g., headache, back pain, fibromyalgia), meta-analytic results ( $n = 30$  RCTs) suggested that mindfulness-based interventions significantly improved pain symptoms compared with treatment as usual, passive controls, and education/support groups.<sup>91</sup> However, the quality of evidence was considered low due to heterogeneity of the included studies and possible publication bias. In this review, only four studies included analgesic use outcomes and results were mixed. One specific mindfulness intervention, Mindfulness-Oriented Recovery Enhancement, has shown promise for improving opioid-related outcomes (e.g., misuse risk).<sup>92</sup> In a meta-analysis of mindfulness interventions for individuals with chronic pain conditions ( $n = 25$  RCTs), these therapies had a small effect on pain intensity and disability, and a moderate effect on pain interference when compared with waitlist, treatment as usual, and education/support groups.<sup>93</sup> Interestingly, neural mechanisms of mindfulness-based pain reduction appear to vary by level of training. While brief training is associated with reappraisal mechanisms (e.g., activation of the subgenual ACC, orbitofrontal cortex, and right anterior insula), longer training is associated with nonappraisal, or the ability to separate the physical sensations of pain from the affective and evaluative reactions commonly associated with pain (e.g., activation of somatosensory regions and deactivation of prefrontal regions).<sup>94</sup>

Garland and colleagues<sup>95</sup> conducted a meta-analysis on a broad array of MBIs among individuals using opioids for pain. Across 60 RCTs, MBIs (e.g., meditation, hypnosis, relaxation) were associated with reductions in pain symptoms and opioid dose. Of the included MBIs, meditation demonstrated the largest effect size for pain reduction. In addition, four out of five meditation studies reported improvements in opioid-related outcomes (e.g., opioid misuse, cravings).

Yoga and tai chi may also be helpful for specific chronic pain conditions. Meta-analyses have shown that yoga is associated with short-term improvements in neck pain-related outcomes (e.g., pain intensity, disability;  $n = 3$

RCTs)<sup>96</sup> and both short- and long-term improvements in back pain-related outcomes (e.g., pain, disability, global improvement;  $n = 10$  RCTs).<sup>97</sup> Tai chi may produce short-term improvements in pain and disability among individuals with musculoskeletal pain conditions.<sup>98</sup> Importantly, American College of Physician guidelines recommend MBSR, yoga, and tai chi for chronic low back pain.<sup>99</sup>

### Sleep Difficulty

According to proposed theoretical frameworks, mindfulness-based interventions may be helpful for sleep problems through reductions in rumination, arousal, sleep monitoring and effort, and distorted perceptions.<sup>100</sup> In a meta-analysis of 18 RCTs, mindfulness-based interventions (e.g., MBSR, MBCT) improved sleep quality among various patient populations with clinically significant sleep problems when compared with active controls, but not evidence-based sleep treatments.<sup>101</sup> Mindfulness-based interventions may also reduce insomnia symptoms compared with placebos and waitlist controls.<sup>102</sup> Overall, more rigorous research is needed to compare mindfulness-based interventions to evidence-based sleep treatments.<sup>100</sup>

Mindful movement-based therapies have shown potential for sleep problems. Results from a recent meta-analysis indicated that yoga modestly improved sleep quality in women.<sup>103</sup> In a meta-analysis of 22 RCTs, tai chi was shown to have a moderate effect on sleep quality among individuals with various conditions and sleep complaints when compared with both inactive and active controls (e.g., exercise, health education).<sup>104</sup>

### Approach to Patient Selection

In this section, we highlight several structural and patient factors to consider when referring to or recommending meditative- or mindfulness-focused interventions (see ►Fig. 2).

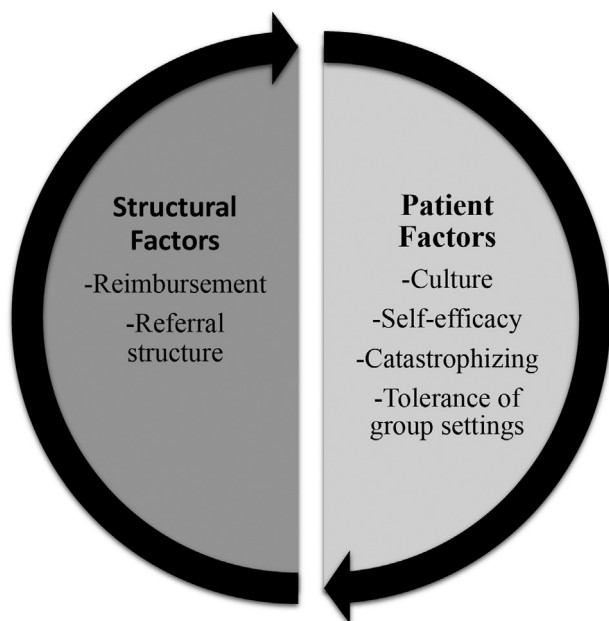
#### Structural Factors

From a provider perspective, there may be structural barriers when referring to or recommending MBIs in clinical practice.<sup>105</sup>

#### Reimbursement

MBIs take time to deliver. Given the current reimbursement structure for most providers, it is important to recognize that patients might have to self-pay and that the cost for a course is often several hundred dollars. This is due to a lack of clear-cut mechanisms for reimbursement, especially for providers who are not from mental health care fields. Centers that offer MBIs often make them out of pocket expenses that are not billed to insurance. Especially among underserved, and often underrepresented populations of lower socioeconomic status, access to MBIs becomes an inherent barrier. Some mindfulness-based interventions are offered by mental health providers and are subject to standard referral procedures and insurance reimbursement. There has also been an increased focus on developing insurance reimbursable mindfulness programs to be delivered in primary care settings.<sup>106</sup>





**Fig. 2** Structural and patient factors to consider when recommending and referring to meditative- and mindfulness-focused interventions.

### Referral

MBIs require an administrative and referral structure. There must be administrative assistance that supports patient navigation and agency around clinical services. This is especially true in chronic neurological conditions, which historically have relied upon pharmacologic and procedural management of care. As MBIs are behavioral modalities, there may be more questions asked by patients—creating greater potential administrative burden.

### Patient Factors

Although not an exhaustive list, below we review several patient-specific factors that should be considered when referring to MBIs.

### Culture

The MBIs reviewed here were derived from Eastern meditative and spiritual disciplines, which may not be agreeable to some patients based on their religious beliefs. While in practice we have found most patients to be open to “anything that works,” a careful discussion is merited regarding the practices that participants might expect within the MBI, and whether it is expected that any culture-specific elements might be presented (e.g., from Buddhism, Hinduism, or Taoism).

### Self-Efficacy

One cognitive process that may be related to the success of MBIs is self-efficacy. Self-efficacy refers to the ease or difficulty in performing a behavior. This is semantically different from controllability, which refers to the belief about the extent to which performing the behavior is up to the individual.<sup>107</sup> Self-efficacy has been found to act as a

mediator of change in health behaviors and in use of the health care system. In addition, self-efficacy has also been related to increased energy, better sleep, and decreased pain and discomfort, as well as with overall satisfaction with life.<sup>108</sup> As such, when there are neurobehavioral and physical symptoms that pose direct challenges to self-efficacy, the resulting low levels of self-efficacy may present a barrier to the adherence, and inevitably the success of the MBI—thereby creating a perpetual negative feedback loop. Therefore, providers referring to or delivering MBIs may benefit from assessing and understanding a patient’s self-efficacy as this may help participation and engagement with the MBI.

### Catastrophizing

Cognitive psychological processes may also be important to consider in the context of MBIs. One specific process, catastrophizing, is often studied in the context of pain and has been shown to be associated with poor pain-related outcomes.<sup>109</sup> Pain catastrophizing refers to the tendency to magnify the threat of pain, ruminate on pain, and feel helpless in regard to pain.<sup>110</sup> Patients with high degrees of catastrophizing may engage in maladaptive behaviors (e.g., avoidance of activity) and experience psychological distress (e.g., depression, anxiety).<sup>110</sup> Overall, this may magnify symptom intensity and disability, thereby affecting the patient’s willingness to participate in an MBI and implement positive health behavior change. Therefore, it may be helpful for providers to assess for levels of catastrophizing, particularly for patients with chronic pain, to better facilitate participation and engagement with a MBI.

### Ability to Tolerate Group Setting

Because many MBIs occur in groups, it is necessary to assess the patient’s level of ability to function in a setting that involves physical proximity to others and its attendant distractions (e.g., visual stimulation from movements by other group members, errant noises). Moderate to severe disturbances in memory or attention, or behavioral symptoms resulting from loss of inhibition, paranoia, and hallucinations, might become exacerbated in a group setting.

### Freely Available Online Resources

While delivery of MBIs has largely been scientifically studied in person in the group setting, several of the programs reviewed in this article have high-quality, free online resources to which highly motivated and technologically sophisticated patients can be directed. Palouse Mindfulness (<https://palousemindfulness.com/>) provides a free online MBSR course for self-study with peer support available through a Facebook group. MIT audio recordings are freely available on the Fern Hill Center Web site (<https://www.fernhillcenter.org/>). The Massachusetts General Hospital Department of Psychiatry has placed curated online stress reduction resources and links to MBI trainings (for both patients and providers) that can be accessed here: <https://www.massgeneral.org/psychiatry/guide-to-mental-health-resources>.

## Conclusions

Meditative- and mindfulness-focused interventions may improve neuropsychiatric symptoms commonly comorbid with neurological disorders. Mindfulness-based interventions (i.e., MBSR, MBCT) have the strongest evidence, particularly for preventing relapse to depression and reducing depressive, anxiety, and chronic pain symptoms. Although mindful movement-based interventions (i.e., yoga, tai chi) show promise for common neuropsychiatric symptoms, higher quality studies that systematically track adverse events are needed. Overall, more research is warranted examining meditative- and mindfulness-focused interventions in neurological populations, specifically. Health care providers should consider structural (e.g., insurance reimbursement) and patient factors (e.g., ability to tolerate group formats) when referring to these mind-body therapies.

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