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The mindful migraine: does mindfulness-based stress reduction relieve episodic migraine?

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Migraine is a leading cause of disability worldwide, with episodic headaches, sensory sensitivity, nausea and vomiting imparting significant morbidity and even frequent bedrest during an attack [1; 13]. We also know that psychosocial factors can be important modifiers and even triggers of migraine attacks. For instance, perceived stress has been reported as the most common trigger of migraine headaches [22]. Hence, interventions that target stress should naturally be considered for the clinical management of migraine. Such interventions include integrative medicine therapies, which are used by about half of all patients suffering from migraines or severe headaches, and include mind-body therapies such as meditation training [26].

Mindfulness meditation training is a promising mind-body therapy for migraine [7; 27] and other chronic pain disorders [23]. Specifically, mindfulness meditation encourages non-judgmental awareness and acceptance towards inner experiences (thoughts, emotions) and physical sensations. In fact, this intervention encompasses various techniques, including focused awareness of sensory, emotional, and cognitive events, and open monitoring, in a non-evaluative manner [8; 10], likely relying on top-down brain-based mechanisms of action [11; 28]. As pain experience involves unpleasant sensory and emotional experiences, and is strongly influenced by negatively-valenced evaluative processes [4; 5], mindfulness meditation has significant potential to shape the chronic pain experience.

Perhaps the most common manualized mindfulness meditation training protocol is mindfulness-based stress reduction (MBSR), an 8-week empirically supported group education intervention demonstrated to enhance emotion regulation and reduce pain [6]. In fact, the first mindfulness meditation research trial was conducted specifically for chronic pain patients by Jon Kabat-Zinn, the founder of MBSR, in 1982 [12] and recent large N clinical trials have shown promise for clinical pain reduction [2; 3; 16; 17; 23]. However, the neural mechanisms supporting MBSR-mediated pain relief are poorly understood [29].

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With this in mind, Seminowicz et al. have now published the results of perhaps the largest MBSR study for migraine headache [24]. In this important study, episodic migraine patients experienced an enhanced form of mindfulness meditation training, while the control group experienced a series of stress management classes. Specifically, their MBSR intervention included an additional 8 weeks of biweekly visits, beyond the typical 8-week weekly format, hence dubbed MBSR+. The stress management control intervention included 12 didactic sessions over 4 months, and in contrast to MBSR+, did not include a retreat. The authors also assessed multiple MRI brain imaging outcomes - gray matter volume and fMRI resting brain connectivity metrics for dorsal lateral prefrontal cortex (DLPFC), a critical pain down-regulatory brain region [25], as well as block design fMRI for a cognitive (multi-source interference) task and thermal evoked-pain stimulation. Outcomes were collected at baseline and at 20 weeks (i.e. post-therapy). Long-term clinical outcomes were also assessed at 52 weeks.

The study demonstrated reduction in the primary clinical outcome, number of headache days per month, from baseline to 20 weeks for both MBSR+ and stress management control, with a significantly larger effect size for MBSR+. In fact, 52% of the MBSR+ group were classified as responders compared with 23% in the stress management control group. Migraine patients randomized to MBSR+ also reported greater reduction in headache-related disability (assess by the six-item Headache Impact Text) – a very important functional outcome. However, by 52 weeks, there were no differences between MBSR+ and stress management control groups in clinical outcomes. Importantly here, reduced headache frequency at 20 weeks for the MBSR+ group was still reduced at 52 weeks, while headache frequency for the control group showed a slower reduction, leading to a non-significant difference at 52 weeks.

Unfortunately, the *a priori* hypothesized primary structural and functional MRI outcomes did not show a significant group x time interaction, and imaging outcomes were not explicitly associated with clinical improvements, limiting our understanding of the brain-based mechanisms that may have contributed to the intriguing clinical improvements. The authors did note some secondary imaging outcomes with a group x time interaction. Compared to stress management control, migraineurs randomized to MBSR+ showed reduced post-therapy fMRI response to the cognitive task in the cuneus and parietal operculum. This result was interpreted as reflecting improved cognitive efficiency. Migraineurs also showed reduced post-MBSR+ resting fMRI connectivity between dorsal anterior insula and both cuneus and superior parietal lobule. The cuneus is an occipital cortical region important for visual processing, and perhaps future studies can explore if changes in such visual processing regions are linked to the existence or improvements in visual aura, a hallmark of cortical spreading depression and common prequel to migraine headache for many patients. Interestingly, the authors noted that these fMRI changes may reflect either the effects of MBSR training or result from reduced migraine attacks. Perhaps explicitly linking these imaging changes with changes in migraine attacks per month across different patients in this study could better tease apart these two scenarios.

However, DLPFC gray matter volume or resting connectivity did not demonstrate interesting longitudinal changes in this study on the whole brain level, while changes in brain

processing of heat pain were also not different between groups. The authors provocatively note that their primary imaging outcomes, developed following prior studies contrasting chronic pain patients with healthy adults, may not be the appropriate targets for longitudinal treatment studies. While this may indeed be true for the outcomes evaluated in this study, our group has demonstrated several outcomes, such as functional connectivity between default mode network regions and anterior/mid insula in fibromyalgia patients [9; 19; 20] and S1 neuroplasticity in carpal tunnel syndrome patients [14; 15; 18; 21], that both differed between chronic pain patients and healthy adults, and were altered toward the pattern found in healthy adults following successful non-pharmacological or even pharmacological therapy. Ultimately, as this study by Seminowicz et al. has generated a very rich dataset with clinical and imaging outcomes for episodic migraine, there is hope that future analyses may directly link these outcomes for responders versus non-responders, perhaps yielding a better understanding of the brain mechanisms supporting longitudinal improvements in migraine severity following MBSR. We should also not lose sight of the important conclusion that MBSR+ was indeed found to be an effective treatment option for episodic migraine, above and beyond an active control intervention.

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