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Impact of short- and long-term mindfulness meditation training on amygdala reactivity to emotional stimuli

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A B S T R A C T

Meditation training can improve mood and emotion regulation, yet the neural mechanisms of these affective changes have yet to be fully elucidated. We evaluated the impact of long- and short-term mindfulness meditation training on the amygdala response to emotional pictures in a healthy, non-clinical population of adults using blood-oxygen level dependent functional magnetic resonance imaging. Long-term meditators (N = 30, 16 female) had 9081 h of lifetime practice on average, primarily in mindfulness meditation. Short-term training consisted of an 8-week Mindfulness- Based Stress Reduction course (N = 32, 22 female), which was compared to an active control condition (N = 35, 19 female) in a randomized controlled trial. Meditation training was associated with less amygdala reactivity to positive pictures relative to controls, but there were no group differences in response to negative pictures. Reductions in reactivity to negative stimuli may require more practice experience or concentrated practice, as hours of retreat practice in long-term meditators was associated with lower amygdala reactivity to negative pictures – yet we did not see this relationship for practice time with MBSR. Short-term training, compared to the control intervention, also led to increased functional connectivity between the amygdala and a region implicated in emotion regulation – ventromedial prefrontal cortex (VMPFC) – during affective pictures. Thus, meditation training may improve affective responding through reduced amygdala reactivity, and heightened amygdala–VMPFC connectivity during affective stimuli may reflect a potential mechanism by which MBSR exerts salutary effects on emotion regulation ability.

1. Introduction

Mindfulness meditation practices, which aim to cultivate an accepting awareness of the present moment (Bishop et al., 2004; Brown and Ryan, 2003; Kabat-Zinn, 1990) can improve emotion regulation, ameliorate symptoms underlying anxiety and depression and boost positive mood (Goyal et al., 2014; Hofmann et al., 2010; Jain et al., 2007). Mindfulness-Based Stress Reduction (MBSR) is a widely used form of meditation practice taught by a trained professional that involves didactics, individual and group practices including: breath awareness meditation, body scans, walking meditation and yoga. Each of the practices involves focusing attention on present-moment experience (Kabat-Zinn, 1990). MBSR has been shown to lead to reduced negative experience (Goldin and Gross, 2010; Kaviani et al., 2011) and quicker recovery from a negative challenge (Britton et al., 2012; Raes et al., 2009). Improvements in affective responses following mindfulness meditation training have also been shown in non-clinical populations, including reductions in emotional interference (Ortner et al., 2007) and decreased negative mood (Jha et al., 2010). Research on the neural mechanisms underlying these affective changes that utilizes active control conditions is sparse, and systematic examination of the impact of mindfulness meditation training on functional connectivity in emotion regulation networks has not been investigated.

Allen et al. provide initial evidence that mindfulness meditation alters neural processing to affective stimuli following a short-term intervention – participants who practiced longer had more insula activation during

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negative pictures in a whole-brain analysis (Allen et al., 2012). The current study investigated a greater range of practice by including long- and short-term practitioners and expands upon prior work by probing the neural response to positive pictures – in addition to negative pictures – in an important emotion regulation circuit using *a-priori* amygdala and ventromedial prefrontal cortex (VMPFC) regions of interest (ROIs). Research using a similar approach demonstrated decreased amygdala activation during positive affective pictures following short-term mindfulness meditation training, however it was limited to 12 participants per group (Desbordes et al., 2012). Precisely how mindfulness-based meditation impacts the neural circuitry of emotion regulation remains unclear.

The amygdala is central to emotion generation (Phelps and LeDoux, 2005) and regulation (Buhle et al., 2014), and VMPFC is implicated in automatic emotion regulation (Phelps et al., 2004; Urry et al., 2006), possibly through functional coupling with the amygdala (Banks et al., 2007; Lee et al., 2012). Automatic, or implicit emotion regulation consists of processes that alter the course of affective experience outside explicit, conscious attempts to do so. Affect labeling is a process which may engage automatic emotion regulation even absent an intention to volitionally regulate emotion, as affect labeling has been shown to dampen the amygdala response (Lieberman et al., 2007). Extinction learning is another example of an automatic emotion regulation process and involves both amygdala and VMPFC (Phelps et al., 2004). Non-human primate research reveals a specific mechanism for these effects whereby monosynaptic input to basolateral amygdala from MPFC inhibits activity from the central nucleus of the amygdala (Kim et al., 2011). Moreover, research in non-human primates indicates functional specificity of VMPFC for value updating (Rudebeck et al., 2013), providing evidence that VMPFC automatically processes information regarding the changing salience of stimuli. Recent studies in humans have also found converging support for the role of VMPFC in value updating (Levy and Glimcher, 2012).

We systematically examined the impact of mindfulness meditation training on affective processing by assessing amygdala activation and amygdala-VMPFC functional connectivity during an automatic emotion regulation task in a non-clinical, healthy population of adults who were in a normal state, not explicitly practicing any form of meditation. Brain activation was assessed using blood-oxygen level dependent functional magnetic resonance imaging (BOLD fMRI). We employed a rigorous design combining cross-sectional analysis of long-term meditators (LTM) compared to meditation-naïve participants (MNP), and a randomized controlled trial (RCT) in which a subset of MNP completed either an 8-week intervention with MBSR or a validated, active control condition (the health enhancement program; HEP) that was matched for intervention effects non-specific to mindfulness meditation (MacCoon et al., 2012). The LTM had a daily sitting meditation practice of at least 30 min for at least three years, and the primary type of meditation practice was most similar to that taught in MBSR — Vipassana (i.e. open monitoring; OM). In this form of meditation, practitioners cultivate sustained awareness to experience without attempting to control the focus of attention, but rather maintaining openness to any feelings that arise in awareness (Lutz et al., 2015).

We hypothesized that mindfulness meditation training would decrease reactivity to affective stimuli, as assessed by amygdala activation to positive and negative pictures (relative to neutral). We further hypothesized that mindfulness meditation training would enhance automatic emotion regulation, as reflected by greater amygdala- VMPFC functional connectivity during affective pictures (negative, positive) relative to neutral. First, we tested for differences in LTM compared to MNP, and then we tested for a similar pattern of effects following training with MBSR compared to HEP, while controlling for pre-treatment baseline (i.e. data collected prior to randomization). Using RCT data to follow up on cross-sectional analyses allowed us to rigorously control for influential factors that may have systematically differed between LTM and MNP. Finally, we assessed the length and type of meditation practice to test how variations in practice predicted differences in the brain and behavior.

2. Methods

2.1. Participants

We recruited 158 healthy human subjects from a non-clinical population, comprised of 127 meditation-naïve participants (MNP) and 31 long-term meditators (LTM). The MNP (average age 48.1 ± 10.7 years, 81 female) comprised a much larger group as they participated in both the RCT and cross-sectional arms of the study, and were recruited within Madison, WI and the surrounding community using flyers, online advertisements, and advertisements in local media. Recruitment materials requested participation in a study of "health and well-being" or the "benefits of health wellness classes." Following baseline data collection, a sub-set of MNPs who participated in the cross-sectional arm of the study were randomly assigned to mindfulness meditation training or an active control intervention for the RCT: Mindfulness Based Stress Reduction (MBSR; $N = 43$, average age 48.2 ± 10.0 years, 27 female) or the Health Enhancement Program (HEP; $N = 43$, average age 48.0 ± 12.2 years, 27 female), which has been validated in a separate study (MacCoon et al., 2012). The intervention and randomization procedures were identical to that detailed by MacCoon et al. (2012) Four participants did not complete the fMRI task following the intervention, and an additional 15 participants left the study prior to post-intervention data collection due to logistical reasons, resulting in 32 participants who completed MBSR (average age 50.8 ± 8.8 years, 22 female) and 35 participants who completed HEP (average age 48.1 ± 12.6 years, 19 female).

The LTM (average age 50.7 ± 10.1 years, 17 female) were recruited at meditation centers and through related mailing lists throughout the United States, in addition to flyers and advertisements in newspapers similar to the recruitment strategy for MNP. The LTM did not differ from the MNP in terms of age, gender, motion during the fMRI task, level of education, or socio-economic status measured with the Hollingshead index (Hollingshead, 1975), nor were there statistically significant effects of any of these demographic factors on any of the outcome variables, except in 2 cases as described in the Results section. Meditation recruitment criteria included at least three years of daily practice (at least 30 min per day of sitting meditation), experience with Vipassana, concentration and compassion/loving-kindness meditations, and at least 3 intensive retreats lasting 5 or more days. LTM had an average of 9081 lifetime hours of meditation practice, ranging from 1439 to 32,612 total hours, and which primarily consisted of mindfulness-based practices (focused attention and OM; 86% of daily practice hours), in addition to some practice with compassion/loving kindness meditations (14% of daily practice hours). Lifetime hours of practice were calculated based on subjects reports of their average hours of formal meditation practice per week and their total years of practice. Participants in either group were excluded if they had used medication for anxiety, depression, or other psychological issues, or had a psychiatric diagnosis in the past year. Participants were also excluded if they had any history of bipolar or schizophrenic disorders, brain damage or seizures.

The automatic emotion regulation task was one of a number of tasks administered during a 24-h lab visit as part of a larger, multi-session study. Meditation-naïve participants completed one lab visit prior to randomization, and then following the 8-week MBSR or HEP intervention participants returned for a post-training visit during which the same measures were collected. Experimenters were blind to the group assignment of meditation-naïve participants during data collection for the RCT. Subjects also completed a series of questionnaires, including the Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006), which includes a sub-scale that was used as a self-report measure of non-reactivity. Example items from the non-reactivity scale include: "When I have distressing thoughts or images, I just notice them and let them go", and "I watch my feelings without getting lost in them". A panel