Mindfulness training modulates value signals in ventromedial prefrontal cortex through input from insular cortex

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ABSTRACT

Neuroimaging research has demonstrated that ventromedial prefrontal cortex (vmPFC) encodes value signals that can be modulated by top-down cognitive input such as semantic knowledge, price incentives, and monetary favors suggesting that such biases may have an identified biological basis. It has been hypothesized that mindfulness training (MT) provides one path for gaining control over such top-down influences; yet, there have been no direct tests of this hypothesis. Here, we probe the behavioral and neural effects of MT on value signals in vmPFC in a randomized longitudinal design of 8 weeks of MT on an initially naïve subject cohort. The impact of this within-subject training was assessed using two paradigms: one that employed primary rewards (fruit juice) in a simple conditioning task and another that used a well-validated art-viewing paradigm to test bias of monetary favors on preference. We show that MT behaviorally censors the top-down bias of monetary favors through a measurable influence on value signals in vmPFC. MT also modulates value signals in vmPFC to primary reward delivery. Using a separate cohort of subjects we show that 8 weeks of active control training (ACT) generates the same behavioral impact also through an effect on signals in the vmPFC. Importantly, functional connectivity analyses show that value signals in vmPFC are coupled with bilateral posterior insula in the MT groups in both paradigms, but not in the ACT groups. These results suggest that MT integrates interoceptive input from insular cortex in the context of value computations of both primary and secondary rewards.

Introduction

One hypothesis is central to the emerging field of decision neuroscience: that the ventromedial prefrontal cortex (vmPFC) encodes value signals at the time of choice in a range of decision-making tasks involving both primary and secondary rewards (Hampton et al., 2006; Lebreton et al., 2009; Padoa-Schioppa and Assad, 2006; Philiastides et al., 2010). In support of this hypothesis, recent neuroimaging work shows that value signals in vmPFC can be modulated by top-down cognitive input such as knowledge of price, monetary favors, brand and semantic knowledge (De Araujo et al., 2005; Harvey et al., 2010; Kirk et al., 2009, 2011a; McClure et al., 2004; Plassmann et al., 2008). Collectively, these studies have expanded the role of the vmPFC in value-based decision-making suggesting that biases may have a biological basis that subverts cognitive control. Building on this work, this study examines whether mindfulness training (MT) enables subjects to protect against top-down bias and

whether simpler components of such training may be responsible for beneficial effects. Despite extensive work on the neural underpinnings and behavioral dynamics of value-based decision-making, it remains unknown whether value signals can be modulated by MT, and what neural networks provide input for these computations.

The current study addresses both questions using functional magnetic resonance imaging (fMRI) in the context of 1) a primary reward paradigm by probing value-related regions at the time of reward (fruit juice) delivery, and 2) a secondary reward paradigm, namely a previously deployed version of the art-viewing paradigm, which uses monetary favors to examine the effect of bias on subjective decision-making (Harvey et al., 2010).

Mindfulness research has demonstrated that MT seems to act through interoceptive mechanisms (Allen et al., 2012; Farb et al., 2007, 2010, 2013; Kirk et al., 2011b; Lutz et al., 2008; Zeidan et al., 2011). As the insular cortex mediates subjective awareness of internal bodily processes, it has been argued that a sense of 'self-as-witness' is grounded in homeostatic bodily responses (Craig, 2002, 2003, 2009; Damasio, 2010; Gu et al., 2013). Indeed, MT enables practitioners to experience "space between one´s perception and response" (Shapiro et al., 2006), and recent

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work has suggested the neural implications for the psychological construct of such decentering abilities. For example, even a short training course of MT is effective in decoupling the activity of the insula from the activity of other regions involved in valuation and decision-making, such as the vmPFC (Falk, 2014; Farb et al., 2007; Tang et al., 2009). Other studies have observed increases in insular cortex coupled with decreases in posterior parietal cortex and vmPFC (Creswell et al., 2007; Farb et al., 2010; Holzel et al., 2007). Given the link between interoceptive processes in the insular cortex and MT, the current study tested the hypothesis that in the context of MT, value computation acquires input from areas involved in interoception such as the insular cortex, by modulating value signals in the vmPFC. As several types of top-down inputs are integrated in value signals computed in the vmPFC at the time of choice (or reward delivery), we speculated that MT leads to an altered weighing of different value signals. Specifically, we predicted that value signals computed in vmPFC in the group assigned to MT relative to the group assigned to active control training (ACT) in both the primary and the secondary reward paradigms, would integrate inputs from the insular cortex based on this region's role in interoceptive processing (Craig, 2002, 2003, 2009; Critchley et al., 2004). To investigate these aims we employed an experimental setup consisting of a fully randomized longitudinal design including 8 weeks of either MT or ACT.

Materials and methods

Subjects

Fifty-two subjects participated in the art-viewing paradigm. They were divided in two groups; both the ACT and the MT group consisted of 26 subjects. The ACT group included 15 women and 11 men (mean age 31.3; standard deviation (SD) 10.1), while the MT group included 14 women and 12 men (mean age 32.2; SD 10.4). The two groups did not differ in terms of mean age or gender distribution. A separate cohort of 33 subjects participated in the primary reward paradigm; 17 of these subjects were assigned to the MT group and 16 to the ACT group. The ACT group included 9 women and 8 men (mean age 32.4; SD 11.4), while the MT group included 10 women and 7 men (mean age 32.7; SD 11.1).

Recruitment procedures consisted of advertising for participants "who want to learn to deal with stress issues in everyday life"; the study was framed as a stress-management program lasting 8 weeks. This recruitment strategy was employed in order to reduce self-selection bias in order to gain volunteers from a broad demographic range. Subjects were recruited with the understanding that the study consisted of comparing two equally valid stress reduction interventions, which minimized motivation and placebo effects. In addition, subjects were notified that they would be assigned to a stress reduction intervention in a random manner, which eliminated any self-selection effects between the two intervention. The study was advertised for staff and students around Virginia Tech. This recruitment strategy resulted in 238 volunteers who signed up for the study. Of this initial number, 45 subjects were found to be ineligible (33 subjects were using psychiatric medication or had a medical history of psychiatric medication; 12 subjects were MRI ineligible due to either metal implants, claustrophobia or subjects who had previously suffered from concussions that included a loss of consciousness for more than 10 min). In addition an exclusion criterion for the study was prior experience (i.e. regular practice) with mindfulness meditation. The subjects included in the study were randomly selected from the eligible group, and the non-selected volunteers were put on a waitlist to participate in future studies involving stress-management training. The subjects who were included in the current study were subsequently randomly assigned to receive either MT or ACT. Subjects in the study received compensation for their participation according to the following payment scheme: Subjects were paid $20 for attendance in each of the 8 weekly group sessions independent of group modality (MT/ACT). In addition subjects were paid $20 for participation in the primary reward task, and $300 on each visit (pre and post) for

participation in the art-viewing paradigm. The subjects received compensation associated with the fMRI-tasks immediately after each scanning session. However, attendance compensation for the 8 weekly group sessions was paid in total upon study completion. All subjects across the two experiments had normal or corrected-to-normal vision, and none had a history of neurological or psychiatric disorders. All procedures were conducted in accordance with the institutional review board of Virginia Tech.

Procedure for MT

The MT consisted of 8 weeks of practice of mindfulness that mimic the canonical mindfulness program entitled Mindfulness Based Stress Reduction (MBSR) (Kabat-Zinn, 1990). The MT program was taught by a certified MBSR instructor. The program includes introducing participants to moment-to-moment awareness and non-judgmental awareness. A structured group format was applied whereby participants attended weekly group sessions that introduced them to formal meditation practices. Each group session lasted 2.5 hours. The MT program also included a full day of meditation between the sixth and seventh meeting sessions. Participants were required to attend at least seven of the eight group sessions and the full-day session to be considered compliant with the training protocol. In addition to group meetings, participants were asked to practice meditation on non-class days for 20 minutes a day with the assistance of guided meditation CDs. The formal meditation practices included breath monitoring, body scans, and attention to sounds, thoughts, feelings and bodily sensations. Participants were instructed to maintain a daily log of practice completion, which was collected by the course instructors at every weekly session. In addition to class attendance, participants were required to complete at least 50% of the recommended daily homework.

Procedure for ACT

For the ACT, a structured group format was applied whereby participants attended weekly group sessions introducing them to progressive muscle relaxation. The ACT program was taught by a certified and experienced instructor in progressive muscle relaxation. The weekly sessions were 2.5 hours in duration and included 30 minutes of stretching and exercise. These moves could be easily completed in comfortable clothing and some positions performed while seated. Then there would be group discussion for 30 minutes. Participants would share their experience on a particular topic and give updates from previous weeks. Sometimes a question was asked to the group to facilitate conversation and each person in the group would take a turn to answer the question. This time was then followed by the introduction of a new topic by the facilitator. Topics included: time management, physical activity, sleep, healthy eating, organization, communication, and future goal setting. The facilitator provided information gathered from online sources about each topic. During the week in between classes, participants were expected to complete their stretching/exercise moves daily and to reflect on the topic for the week. The ACT program also included a full day of physical relaxation exercises between the sixth and seventh meeting sessions. Participants were required to attend at least seven of the eight group sessions and the full-day session to be considered compliant with the training protocol. In addition to group meetings, on non-class days participants were asked to practice stretching and relaxation exercises for 20 minutes a day with the assistance of guided CDs. Participants were instructed to maintain a daily log of practice completion, which was collected by the course instructors at every weekly session. In addition to class attendance, participants were required to complete at least 50% of the recommended daily homework.