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# Altered anterior insula activation during anticipation and experience of painful stimuli in expert meditators

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ABSTRACT

Experientially opening oneself to pain rather than avoiding it is said to reduce the mind's tendency toward avoidance or anxiety which can further exacerbate the experience of pain. This is a central feature of mindfulness-based therapies. Little is known about the neural mechanisms of mindfulness on pain. During a meditation practice similar to mindfulness, functional magnetic resonance imaging was used in expert meditators (>10,000 h of practice) to dissociate neural activation patterns associated with pain, its anticipation, and habituation. Compared to novices, expert meditators reported equal pain intensity, but less unpleasantness. This difference was associated with enhanced activity in the dorsal anterior insula (aI), and the anterior mid-cingulate (aMCC) the so-called 'salience network', for experts during pain. This enhanced activity during pain was associated with reduced baseline activity before pain in these regions and the amygdala for experts only. The reduced baseline activation in left aI correlated with lifetime meditation experience. This pattern of low baseline activity coupled with high response in aIns and aMCC was associated with enhanced neural habituation in amygdala and pain-related regions before painful stimulation and in the pain-related regions during painful stimulation. These findings suggest that cultivating experiential openness down-regulates anticipatory representation of aversive events, and increases the recruitment of attentional resources during pain, which is associated with faster neural habituation.

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## Introduction

Many cognitive strategies regulate pain and distress by actively controlling the sensory, cognitive, or affective components of pain. These states include strategies which involve orienting attention away from the pain, such as listening to music to relieve distress, and those which involve altering the context of the experience, such as expressive suppression, cognitive reappraisal, hypnosis, or placebo (Rainville et al., 1997; Tracey, 2010; Wager et al., 2004; Wiech et al., 2008b). Recently developing bodies of clinical theory on acceptance and mindfulness suggest that a state or disposition that instead cultivates a quality of openness and experiential acceptance, that does not strive to ignore, reject or avoid pain through cognitive control should be more adaptive. This is especially true in circumstances where pain is unavoidable but known to be safe, because of these states' capacity to regulate the mind's conditioned tendency toward avoidance or anxiety, which overall could exacerbate the experience (Cioffi and Holloway, 1993; Gross and Levenson, 1997; Grossman et al., 2007; Hayes, 2004; Kabat-Zinn, 1982; McCracken, 1998; Wetherell et al., 2011). A growing body of evidence is beginning to provide support for this framework (Cioffi and Holloway, 1993; Gross and Levenson, 1997; Grossman et al., 2007; Hayes, 2004; Kabat-Zinn, 1982; McCracken, 1998; Wetherell et al., 2011). Actively suppressing the experience of pain produces a slower recovery from pain than merely monitoring the sensation of pain and strengthens the interpretation of a subsequent noxious sensation as being aversive (Cioffi and Holloway, 1993). Actively suppressing negative emotion also increases the intensity and frequency of sympathetic and cardiovascular activities (Gross and Levenson, 1997), which can have detrimental health consequences (Chambers et al., 2009; Gross and Levenson, 1997). Clinical interventions that cultivate experiential openness and acceptance, such as mindfulness-based stress reduction (MBSR) (Kabat-Zinn, 1982; Kabat-Zinn et al., 1985, 1986) or acceptance and commitment therapy (ACT) (Hayes, 2004) can reduce pain unpleasantness (Brown and Jones, 2010; Grant et al., 2011; Perlman et al., 2010; Zeidan et al., 2011) and lead to a reduction of symptoms in chronic pain patients (Grossman et al., 2007; Kabat-Zinn, 1982; Morone et al., 2008; Wetherell et al., 2011). In this study we used neuroimaging

*Abbreviations:* (aI), anterior insula; (aMCC), anterior mid-cingulate; (FA), Focused Attention; (GLM), general linear model; (OP), Open Presence; (MBSR), mindfulness-based stress reduction; (ACT), acceptance and commitment therapy.

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to explore the effects of a state of acceptance and openness on pain anticipation and processing and also the effects of this state on avoidance and anxiety-related processes across time.

States of acceptance and openness central to MBSR and ACT interventions are at the core of meditation practices labeled here Open Monitoring (Bishop et al., 2006; Chambers et al., 2009; Dunne, 2011; Hayes, 2004; Lutz et al., 2006, 2008). Open Monitoring practices aim to cultivate an effortless, open, and accepting awareness of whatever is occurring in the present moment, without reacting or being absorbed in the contents of the experience. Open Monitoring is said to increase pain acceptance and decrease unpleasantness by training one to recognize experientially that all components of the experience of pain are merely mental events, and thus do not necessarily need to be acted upon. Thus, the aim of this training is not to explicitly change the content of experience, but rather to change one's relationship to it. In that sense, the sensation produced by the painful stimulus can be experienced during this state with equal or increased vividness in the moment it occurs, without fear. This is said to reduce emotional reactivity, enhance behavioral flexibility, and lessen automatic action patterns (Bishop et al., 2006; Chambers et al., 2009; Lutz et al., 2008). Within a cognitive framework, this could be understood as faster habituation and weaker conditioning to harmless but aversive events, and these processes are established as playing a role in pain perception and disability (McCracken et al., 1992). The neural mechanisms of this role are explored in the present study.

Several neuroimaging studies of the impact of meditation on pain processing have recently appeared (Brown et al., 2008; Gard et al., 2011; Grant et al., 2011; Zeidan et al., 2011). Grant et al. found reduced pain ratings and reduced activity in areas including the amygdala, but increased activation in anterior cingulate cortex and insula during pain for experienced meditators compared to controls (Grant et al., 2011). Similarly, Zeidan et al. found a reduction in pain ratings and increased activity in the anterior cingulate cortex and anterior insula (aI) during pain after a brief mindfulness meditation training (Zeidan et al., 2011). Gard et al. also found a mindfulness-related reduction in unpleasantness, which was associated with decreased activation in the lateral prefrontal cortex (PFC) and increased activation in the right pIns during stimulation(Gard et al., 2011). Meditation also affects neural processes of pain anticipation. Brown et al. reported reduced pain unpleasantness ratings and less anticipatory neural activity prior to the pain stimulus as measured by EEG event-related potentials for experienced meditators compared to controls (Brown et al., 2008). Gard et al. reported increased rostral anterior cingulate cortex (rACC) activation during the anticipation of pain for mindfulness practitioners compared to controls (Gard et al., 2011). The effects of meditation on anticipation and habituation to pain have not yet been investigated with neuroimaging.

In the current study we focus on the amygdala and on the so-called 'salience network' (Seeley et al., 2007; Menon and Uddin, 2010; Legrain et al., 2011) that encompasses the anterior insula (aI) and anterior midcingulate cortex (aMCC) as well as subcortical areas important for emotion (e.g. amygdala), homeostatic regulation, and reward (e.g. VTA) (Ongür and Price, 2000; Seeley et al., 2007). As discussed above, Open Monitoring results in reduced pain ratings and increased activity in the salience network during pain. There is also increasing evidence from neuroimaging studies that activity in the salience network is associated with anticipatory processes about incoming pain and that this activity strongly influences pain experience (Atlas et al., 2010; Wiech et al., 2010). For instance, believing that upcoming pain stimuli are entirely safe reduces anticipatory activity in aI and its connectivity to MCC (Wiech et al., 2008a), and this anticipatory activity is linked to trial-to-trial variations in pain ratings (Atlas et al., 2010). More generally, aI and MCC are activated to varied forms of pain, including the emotional dimensions of pain (Peyron et al., 2000), subjective magnitude of pain (Baliki et al., 2009; Moayedi and Weissman-Fogel, 2009), empathy for pain (Singer et al., 2006), lack of perceived controllability (Salomons et al., 2004), uncertainty (Preuschoff et al., 2008), and social rejection (Eisenberger et al., 2003) (for review Friebel et al., 2011). Lesion studies also indicate that a subjectively available experience of pain can be instantiated by brain mechanisms that do not require the insular cortex (Starr et al., 2009). Abnormal processing in these regions also contributes to clinical conditions like anxiety and depression where pain perception and anticipation are subjectively amplified (Paulus and Stein, 2010). Importantly for understanding the value of acceptance, the magnitude of pain perception and anticipation processes influence the degree of conditioning and habituation toward future pain. Compared to controls, anxious patients showed less extinction-related activity in the amygdala during extinction in a fear-conditioning paradigm (Sehlmeyer et al., 2011). The expectation of increased pain intensity decreases the rate of pain habituation in the right operculum, amygdala, and insula (Rodriguez-Raecke et al., 2010). Overall this suggests that experiential acceptance and openness will decrease neural activity underlying avoidance and pain-related anxiety during anticipation and increase the rate of neural habituation in these regions to painful stimuli.

To investigate the impact of experiential acceptance and openness on pain we compared a group of long-term Buddhist practitioners with more than 10,000 h of formal meditation, who performed an advanced style of Open Monitoring meditation called Open Presence (OP; see Material and methods) during a neuroimaging pain paradigm to a control group with no meditation experience who were given matching meditation instructions. OP meditation consists, at least theoretically, of a state where the qualities of effortless openness and acceptance are vividly experienced with minimal control-oriented elaborative processes (Dunne, 2011; Lutz et al., 2006).

According to the framework described above, we examined the hypothesis that OP meditation will affect the subjective representations of pain throughout the task, including its immediate appraisal and its temporal representations of the future (anticipation) and past (habituation) painful trials and that these changes will be correlated to changes in neural activity in pain-related regions during the baseline preceding pain, during pain and across the experimental blocks. More specifically, our first hypothesis was that expert practitioners would show lower unpleasantness ratings and stronger BOLD activity in the salience network (aI, aMCC) during painful stimulation compared to novices, as a consequence of the enhanced acceptance and openness to pain during OP (Grant et al., 2011; Perlman et al., 2010; Zeidan et al., 2011). Our second hypothesis was that experts would display less anxiety-related anticipatory activity in the amygdala and salience network prior to pain compared to novices, as a result of the present-centered nature of this state (Bishop et al., 2006; Farb et al., 2007). Our third hypothesis was that experts compared to novices would show faster neural habituation to pain and its anticipation, here defined as a more negative temporal slope across experimental blocks of activity in amygdala and pain-related regions before pain and in pain-related regions during pain; and that this measure would be correlated with unpleasantness ratings.

## Material and methods

### *Participants*

Fourteen long-term meditation practitioners (45.2 ± 9.9 years old, 11 Caucasian, 3 Tibetan, 9 males and 5 females, stimulus temperature 48.1 ± 0.8 °C) and fourteen age-, sex-, and stimulus-temperature-matched controls (45.6 ± 11.5 years old, 13 Caucasian, 1 Hispanic, 9 males and 5 females, stimulus temperature 48.2 ± 0.8 °C) participated in the experimental procedure. Long-term meditation practitioners were selected based on a criterion of at least 10,000 h of formal meditation practice in the Nyingma and Kagyu traditions of Tibetan Buddhism, which have closely similar styles of practice (mean 27,000 h, SD 12,500). Based on this criterion, these practitioners are referred to as "experts" here for brevity. Fourteen control participants were recruited