To which of thine selves be true? Changes in Viscerosomatic Neural Activity with Mindfulness Meditation Training Reflect Improved Present-Moment Self-Awareness

by

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A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
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Abstract

Mindfulness training cultivates momentary awareness, a form of attention directed to non-evaluative, immediate sensation. This form of attention stands in contrast to a more temporally extended awareness, which allows for the evaluative organization of experience into a personal narrative. The neural mechanisms underlying such awareness, and their role in regulating emotions, are poorly understood. Thus, in three functional magnetic resonance imaging (fMRI) experiments, I explored the thesis that momentary and extended awareness represent dissociable modes of self-reference, with momentary self-reference reducing ruminative elaboration of events by biasing attention towards interoceptive signals from the body. I compared individuals who were randomly-assigned to either an 8-week Mindfulness-Based Stress Reduction (MBSR) training course against a waitlisted group (Controls). Three distinct studies examined the impact of Mindfulness on: 1) the contrast between explicitly directed momentary and extended self referential processing; 2) reactions to an induced sadness challenge; and 3) the contrast between interoceptive (breath-monitoring) and exteroceptive (visual) attention. In all three studies MBSR led to a shift in neural activity away from cortical midline structures, such as the medial prefrontal and posterior cingulate cortices, to predominantly right-lateralized viscerosomatic structures, and specifically the insular cortex. Cortical midline activity is thought to support habitual patterns of evaluation, and stands as the neural correlate of a narrated, extended self, while right-lateralized insula activity is thought to represent the recurrent integration of present moment context, the neural correlate of the
momentary self. These data revealed that MBSR may enhance the distinction between momentary and extended self-reference, reducing cortical midline responses and recruiting a novel, right-lateralized viscerosomatic network. Additionally, MBSR graduates demonstrated reduced emotional reactivity to a film-based sadness mood induction, reducing cortical midline activity and inhibition of the right insula. Moreover, the MBSR group demonstrated enhanced right middle insula recruitment during the monitoring of sensory experience associated with breath monitoring, a core mindfulness practice. The data from this final study also suggest that MBSR promoted an integration of posterior insular sensory representations with anterior insular subjective representations of present moment status. Preserved viscerosomatic activity in the face of emotional challenge may be a predictor of enhanced well-being following mindfulness training.
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Chapter 1

1 General Introduction

In an oft-quoted pearl of parental wisdom, Shakespeare’s Polonius cautions his son Laertes to “above all: to thine own self be true, and it must follow, as the night the day, thou canst not then be false to any man” (Hamlet, 1, 3, 78-81). Polonius worries that his son may be led astray by concerns of wealth or sensual pleasure, but beneath paternal concern the Bard points to an interesting psychological problem of self consistency: after all, aren’t all of Laertes’ actions reflections of Laertes’ true self? How can a self exist towards which one may act falsely? Is not the self the explanatory cause of one’s actions, such that every individual action is necessarily a ‘true’ indicator of that person’s self? This platitude of aiming for concordance between one’s actions and self points to a fundamental dichotomy in human psychology: the abstract or ideal self is something different from the self expressed from moment to moment. It seems as though there are two forms of self at play: the ideal self, a source of unity and consistency across time, and the momentary, agentic self, whose constituency is limited to the acts and sensations of the present moment.

While researchers agree that there are many different aspects to personality, the scientific investigation of selfhood has largely focused on a unitary, temporally extended and constant self. The present thesis will challenge the conventional description of an extended, unitary self. Fundamentally, it will explore the idea that I are all composed of two different types of selves: first, the conceptual self that is a source of conceptual constancy across time; but additionally, the self will be explored as it manifests from moment to moment, the agent in the field of action, defined by its present-centered sensations and expressions. This distinction between two selves has broad implications for our current conceptions of the neuroscientific and psychological basis of self-reference, emotion, and attention.

1.1 A Selfish History

We all have an awareness of who we are in the world. At each moment, we filter idiosyncratic information from a universe of stimulation: recollected attributes and histories, anticipated hopes and obligations, and immediate sensations all naturally cohere into a sort of reference point from which experience can be interpreted and understood. The convergence of
these disparate sources of information seems to outline a central entity, a self. And yet while the
momentary convergence of sensation provides a rich ground for the experience of selfhood in the
world (Merleau-Ponty, 1945), for many people the self is something that extends beyond our
momentary experience, representing a constant core that transcends momentary sensation. In
other words, there exists a ‘true’ self that momentary experience can affirm or betray. Indeed, the
history of psychology is full of appeals to just such a temporally-extended and relatively constant
self. For the sake of simplicity, I will distinguish between these two concepts as the **extended**
and **momentary** selves.

William James used the pronouns of first person speech to illustrate the
extended/momentary distinction, elaborating on an agentic ‘I’ who acts in the world, and the
objective ‘Me’ who is the integrated collection of inferences regarding the agent’s activities
(James, 1890). James conceded that while direct access to the ‘I’ was a potentially insolvable
problem, the objective self (i.e., the self as object) was richly accessible through reflection upon
the agent’s perceived activity, and thus formed a tractable basis for research. Since then, the
objective ‘Me’ has been a recurrent construct in psychological investigation, bearing the load of
research scrutiny, while the agentic ‘I’ is often reserved as the latent explanatory cause of self
organization rather than an empirically accessible component of the self (Table 1.1).

As James predicted, while the extended self may seem more abstract (and thus less
empirically accessible) than the momentary self, its greater constancy has made it more
experimentally tractable in psychological research. There is a rich history of behavioural data
demonstrating that cognition on the self holds privileged status: verbal descriptions are better
recalled when evaluated for self-relevance (“does the word describe you?”) than for lexical (“is
the word in capital letters?”) or semantic content (“is this a positive word?”) (Rogers et al., 1977;
Craik and Tulving, 1975). This oft-replicated finding known as the ‘self-reference effect’. The
self-reference effect suggests that individuals possess rich and powerful methods of self-
description which bias information processing towards self-consistent information: for example,
Kuiper & Derry (1982) found that while healthy participants showed a greater self-reference
effect for positive than negative trait words, depressed participants showed equivalent
enhancement for both categories, in accordance with their dysphoric self concepts. In nonverbal
paradigms, identification of images of oneself or close others evokes a similar processing
advantage over images of celebrities or more casual acquaintances (Keenan et al., 2000),
suggesting that the self-reference effect is not modality-specific; instead, the self-reference effect suggests the presence of a rich set of conceptual relations describing the self, automatically biasing processing resources towards self-relevant information (Kihlstrom & Klein, 1994; Klein & Loftus, 1988).

Self-referential bias may be an integral aspect of human development, in which the elaborated and extended self serves to prioritize and integrate information (Damon & Hart, 1988; Klein & Loftus, 1988). Cognition on the self develops across childhood and adolescence (Rochat, 1995), with the effect emerging at approximately 8 years of age (Halpin et al., 1984) and increasing in strength into adolescence, reaching adult levels by approximately 10 years of age (Ray et al., 2009). From this early age, it is hypothesized that the linguistically extended self provides a critical organizing concept for the prioritization and integration of information, allowing a progression from “low order inferences about simple perceptions to high-order inferences about complex cognitions” (Sarbin, 1952, p.12). It is theorized that the self-reference effect is a marker of a conceptual, extended self. This self may be conceptual in the sense that the self is defined by the individual’s own representations, but extended in that it is continuously reinforced and updated through experience (Damon & Hart, 1988). Yet for all the empirical rigor of the emergent self-reference effect, many authors have argued (e.g. Damon & Hart, 1988; Alston, 1977) that the intriguing question is not why a conceptual self exists at all, but rather, what are the processes of self-awareness that describe how self-referential information is awarded its privileged status?

1.2 The extended self through narrative generation

In attempting to determine the mechanisms underlying the self-reference effect, researchers and theorists alike have turned to the idea of personal narrative to describe the rehearsal and integration of self-relevant information (e.g. Carr, 1986; Taylor, 1989; Bruner, 1991, Peterson, 1999). In doing so, scholars have attempted to account for how a consistent set of self-relations can be maintained among disparate behaviours and sensations. The extended self can thereby be understood as a common set of self-referential processes across individuals rather than simply being an idiosyncratic taxonomy of traits that vary from person to person.

Given substantial evidence for a ubiquitous self-reference effect, why settle on narrative generation as the candidate process? Philosophers such as Daniel Dennett have convincingly
argued for the need of an objective self to codify, integrate and co-ordinate the many processes required of the agent to fulfill biological imperatives over time (Dennet, 1992). This self as a ‘locus of narrative gravity’ serves as an appealing construct in its simplicity and explanatory consistency with phenomenal experience. Since the more physical, sensory and embodied aspects of our awareness are not readily communicable to ourself and others, the construction of a communicable, objective self constituted by narrative, evaluation, and abstract representation seems appropriate. Indeed, following an infant’s understanding of their body in space (Sensorimotor period; Piaget, 1952) childhood developmental hallmarks are mainly of this abstract, conceptual sort. From observation we think of ourselves as possessing stable traits, reinforced by explanations of our histories and upbringings, and assign the same criteria for our understanding of others. Similarly, the need for a narrative in mature adults can be seen through our modes of self-description in the forms of autobiography, resumé, or anecdote, which occur predominantly in verbal, narrated formats.

By determining the grounds for self-relevance, narratives generate and maintain the extended self. Narratives filter attention, selecting in each moment the information relevant to the narrative at hand (Carr, 1986; Bruner, 1991). These filters powerfully shape behaviour, allowing only a selected few elements of our environment to influence us at any time: when crossing the street with a destination in mind, one rarely stops, mid-intersection, to consider the state of the clouds above. Indeed, it is argued that the narrative forms the basis for understanding our own action and the actions of others, that “narrative is that mode of mental life in which we understand the actions of people (protagonists) who pursue goals by means of plans that meet vicissitudes” (pg. 39, Oatley, 2002). From this perspective, narratives are continuously generated to explain others’ actions, as well as to keep our own behaviours in line with narrated intentions: well-rehearsed narratives provide basic archetypal forms through which observed events are rendered meaningful (Peterson, 1999). The extended self can thereby be understood as a process by which novel information is prioritized through its integration with latent narratives. By attributing intention and motivation to observed behaviour, we can pass moral judgment on such behaviour to determine an appropriate attitude and reaction to our observations; such moral inference is hypothesized to lie at the heart of human motivation to understand and react to social behaviour (Taylor, 1989). Thus, the extended self can be characterized as the habitual elaboration of experience into narrative arcs, combining sensory impressions with normative
evaluations and attributions. The importance of such narration is evident in appreciating why one may feel the need to react to a perceived event, as the meanings imparted by current narratives to the extended self provide normative cues to action in addition to enriching contextual descriptions of the event.

1.3 The extended self in the brain

Recent progress has been made in characterizing the neural bases of the extended self through narrative (Gallagher, 2004), highlighting the role of the medial prefrontal cortex (mPFC) in supporting self-awareness by linking subjective experiences across time (Neisser, 1997; Northoff & Bermpohl, 2004). Indeed, the mPFC has been shown to support an array of self-related capacities, including memory for self-traits (Craik et al., 1999; Fossati et al., 2003; Kelley et al., 2002; Macrae et al., 2004), traits of similar others (Mitchell, Macrae, & Banaji, 2006), reflected self-knowledge (Lieberman, Jarcho, & Satpute, 2004; Ochsner et al., 2005), and aspirations for the future (Johnson et al., 2006). Many of these studies have also demonstrated posterior cingulate cortical recruitment in these self-reference tasks (e.g. Craik et al., 1999; Johnson et al., 2002; Fossati et al., 2003; Johnson et al., 2006). Together, these medial cortical regions, operating along an anterior-posterior axis, suggest a broader network of self-reference at work along the cortical midline of the brain. These midline processes may therefore be characterized as supporting a form of narrative self-reference that maintains continuity of identity across time: the extended self (Gallagher, 2004; Neisser, 1997; Watkins & Teasdale, 2001).

While the mPFC is reliably recruited by self-evaluative judgements (e.g. ‘does the word describe me or not?’), it is unknown whether the mPFC and related cortical midline activity are reliably recruited by the less constrained act of narrating experience. It will be of special interest to demonstrate this recruitment during voluntary, unconstrained narration to establish this network’s prevalence, rather than simply replicating the findings of more tightly controlled but less externally valid paradigms of me/not me trait judgments. On the other hand, cortical midline activity has been robustly associated with automatic narrative generation: mind wandering from an active task condition during fMRI imaging results in cortical midline recruitment (Mason et al., 2007; Christoff et al., 2009), which is consistent with the idea that this narrating process occurs as a habitually reinforced cognitive act. The idea that that narration is in some ways a
‘default mode’ of operation in the brain is strongly supported by independent research on the brain at rest (see Buckner, 2008, for a review): relative to active cognitive task conditions, a ‘default’ or ‘resting state’ mode of neural activity has been well-characterized over the past decade, associated with widespread recruitment of cortical midline structures such as the mPFC and posterior cingulate (Gusnard et al., 2001; Raichle et al., 2001). The convergence between the neural activity associated with the narrated self and resting state has led researchers to postulate that the ‘resting state’ is actually one of great activity, in which participants engage freely in self-directed narrative generation.

The default network’s reliable activation in the absence of experimental tasks and its recruitment in extended self-reference make for a tempting inference that default network activity is synonymous with self-referential processing. From this perspective, the default network is a fundamental source of self-identity, with other patterns of neural activity indicating a departure from the experience of selfhood. However, a recent review of the neuroimaging literature makes the important point that while default network activity is found in evaluative self-referential tasks, this is only one of many paradigms recruiting the default network (Legrand & Ruby, 2009). Rather than being limited strictly to cognition on the self, this cortical midline network appears to be involved in many different cognitive processes involving memory and reasoning. For this reason, the authors argue that the default network has more to do with evaluation than some sort of self-specific process. By corollary, if the default network is better characterized by evaluative processes than selfhood in general, then the self-related activation of the default network may represent only a specific, evaluative form of self-reference. Other forms of self-reference that do not depend upon evaluation may therefore recruit other neural regions, providing they fulfill a basic requirement of representing the characteristics of the agent as an object of attention. We must not mistake the prevalence of the default network’s activity as indicating that it represents the totality of self-referential processing.

Even if the default network’s indication of extended self-reference is but one of many forms of self-identification, making such distinction presents a challenge to investigation. If extended self-reference is a core function of the mind at rest, extended self-reference occurs relatively automatically. It follows that other forms of self-reference which do not employ the narrative generation / evaluative elaboration process may not be as easily or automatically recruited, and may in fact be difficult to observe, given participants’ prepotent tendencies to
engage in extended self-reference. If self-referential processing is habitually biased through the ‘default’ recruitment of cortical midline structures associated with cognitive elaboration and appraisal, such as the mPFC, it may be necessary to study individuals with specific training in monitoring moment-to-moment experience to overcome such a default state and to demonstrate reliable dissociation in modes of self-reference.

1.4 The momentary self as experiential perception

Extended self-reference stands in stark contrast to the notion of momentary experience as an expression of selfhood (Gallagher, 2004). Most examinations of self-reference ignore mechanisms of momentary consciousness, which may represent core aspects of self-experience achieved earlier in development (Damasio, 1999; Gallagher, 2004; Zelazo & Frye, 1998) and may have evolved in nonhuman animal species (Panksepp, 2005). Self-reference can thus denote a more basic minimal identity constituted by immediate experience: the momentary self. However, little is known about whether the neural substrates underlying momentary self-reference are distinct from the cortical midline structures supporting narrative experience. One hypothesis suggests that awareness of momentary self-reference is derived from somatic markers that integrate information related to transient bodily states (Craig, 2004; Critchley et al., 2004; Damasio, 1999), constituting a more basic form of awareness that represents evolutionarily older substrates and origins of selfhood.

Based on this research we may question whether access to the momentary self is even possible. If the narrative network can be thought of as linking cues from the present moment into a historical context that is constrained by past experiences and future expectations, then this second, experiential network can be defined as an integration of the full complement of present-moment experiences into a sense of the self in the immediate world (Figure 1.1). This experiential network would still require the integration of sensory experience into a self-determining network for representation, but without requiring that these immediate sensations be further qualified through verbal labeling or historical autobiographical interpretation.

Theoretically, investigation of the experiential network represents a return to the forgotten side of James’ agent vs. object dichotomy: the agent. While it may be difficult for most people to directly experience the causal relations generating the experience of identity (i.e., pure subjectivity or agenthood), this does not mean that there is no integration of the huge influx of
sensory information from the agent (i.e., the body) from moment to moment. A major hypothesis of this thesis is that this ‘core’ awareness in humans constitutes its own self-determining network for the integration of present-centered sensation, without obligatory cognitive description and elaboration.

Critically, the representation of one’s physical embodiment in the world is required in situations that also contraindicate recruitment of more abstract and conceptual forms of self-reference. For instance, the risk of falling in elderly population is greatly increased if attention is divided by abstract spatial activities during the act of walking (Woollacott & Shumway-Cook, 2002), and embodied representations are often demanded in the performance of physical activity such as sports. Idiomatically, such appeals towards increased embodiment can be found through pleas to ‘get your head in the game’, tacitly asserting that one’s attention was focused on non-momentary representations and demanding that such attention be shifted to an embodied, present-centered state.

Momentary self-reference seems to be of a fundamentally different kind than extended self-reference, in that it eschews the well-rehearsed practice of prioritizing narration of experience in favour of continually-updating sensory representations. And yet, momentary self-reference does perform a self-referential function, integrating disparate sensory information from the body and environment to represent the self in the present moment. Thus the immediate, constant updating of sensory signals may represent a second mode of self-referential processing that is qualitatively different from extended self-evaluation. Given the pervasiveness of the momentary self in discussions of selfhood (Table 1) it is a reasonable starting point to formally characterize neural substrates not only the extended self’s process of narrative generation, but also to distinguish it from a proposed alternate mode of self-referential processing: the experiential awareness of the momentary self.

1.5 Mindfulness and the momentary self

The popularity of research on temporally-extended, narrative self-reference is founded in part on the ease in which participants are able to engage in extended self-related processes. On the other hand, for many people the transitory nature of momentary thoughts and sensations may contradict the idea of a ‘stable’ momentary self. In this way, pitting the extended self against the momentary self seems to be an uneven contest, in that participants have a wealth of experience
and practice with the extended self but little experience in attending to the momentary self. To allow for reliable distinctions between two modes of self-reference, it seems appropriate to include some training in the lesser practiced, momentary mode. Fortunately, training in this state of momentary awareness has been richly translated into western culture from Buddhist monastic traditions in the form of mindfulness meditation training (MT), which trains individuals to deploy their attention to focus on present moment experience (Kabat-Zinn et al., 1992).

In its most popular secular western application, mindfulness training takes the form of mindfulness-based stress reduction (MBSR; Kabat-Zinn, 1982), a manualised, 8-week program in meditation training, focusing on the cultivation of experiential awareness through the interoceptive practices such as body scanning, breath monitoring, and basic yoga postures. MBSR has been linked to increased indicators of well-being (Brown & Ryan, 2003), and shows special promise for emotion regulation in reducing the risk of depressive relapse (Segal et al., 2006). MBSR is predominantly offered in clinical settings rather than religious institutions, and this secular nature serves to limit the confounding influence of religiosity. Critically, the MBSR procedure has been replicated across numerous sites with comparable efficacies (see Hoffman et al., 2010; Grossman et al., 2004, for reviews) and thereby represents a relatively unique and reliable source of experiential attention training.

An important limitation of operationalizing mindfulness through the MBSR program is that it looks at only one specific type form of mindfulness. The term ‘mindfulness’ is ubiquitous in Buddhist scholarship, but can mean very different things depending upon its context. There is no single Buddhist tradition, but rather a great variety of practices and theories commensurate with Buddhism’s multiple geographical and historical origins (Dreyfus, in press; Dunne, in press). It is important therefore to recognize that the current conception of mindfulness as a state of non-evaluative, present-moment awareness is but one definition of the term, stemming from relatively newer Buddhist traditions that allow for the possibility of bare attention that is not directed towards any particular object of attention (Dunne, in press). Older, more mainstream Buddhist traditions have instead designated this bare experiential awareness as only a precursor to full or ‘wise’ mindfulness, in which experiential awareness becomes a first step to identifying objects for analysis (Dreyfus, in press). It has been suggested that such differences in definition are fundamentally dependent upon whether one believes that people have innate capacities for improvement that merely require bare, unbiased attention to be activated, or whether awareness
is only the first step in constructing a project of self improvement (Dunne, in press). In MBSR, the benefits of momentary self-reference ostensibly occur without any formal goal of analyzing present-moment experience, but one must bear in mind that even without formal instructions towards such goals, participants voluntarily engaging in mindfulness techniques may have such personal intentions in mind. Whether formal intentions and practices relating the contents of momentary awareness back into an analytic framework promote a fuller set of practice benefits is still an unresolved research question; yet addressing such a question would require a comparison of multiple traditions and practices that is however beyond the scope of the current inquiry on the cultivation of momentary self-reference.

Shelving then the theoretical distinctions between longitudinal goals and advanced stages of mindfulness training, we can make some basic distinctions to better characterize mindfulness in the MBSR setting, which is aimed at introducing non-meditators to the earliest phases of mindfulness training. Fortunately, in instructing beginning meditators, many of the traditions are united: mindfulness practice begins with cultivating access to the momentary rather than extended self. Classic Buddhist scholars have made this distinction, in which mindfulness is “identified with the direct or experiential knowledge bestowed by meditation, as distinguished from the inferential knowledge obtained by study and reflection” (Nyanaponika, 1972, p.60). By entering into this mode of direct or momentary experience, a person may witness impulses and inclinations to act as they arise; with this moment of awareness before action, it is possible to postpone conditioned, automatic reactions and allowing for selection between different possible responses (Austin, 1998; Schwartz & Begley, 2002).

To the extent that MBSR affords a window onto the distinction between narrative and experiential modes of self-reference, it will then be important to understand how this training effect also influences effects dependent upon self-reference, such as emotional processing. Self-reference has been powerfully linked to emotional state through appraisal theory, in which one’s self-appraisals of the situation influence the strength of the emotional response (e.g. Ellsworth & Scherer, 2003; Frijda, 1987; Lazarus, 1991; Ortony et al., 1988). For instance, the intensity of negative affect following stressful situations is predicted by the type of self-appraisals made, such as assuming personal responsibility for the situation and or attaching self-importance to performing positively (Siemer et al., 2007). Since the absence of such self-relating appraisals predicts a lower intensity of negative emotion, momentary self-reference with its emphasis on
the avoidance of such cognitive appraisal could result in profound changes in the ensuing emotional response. It is an interesting question whether momentary self-reference, already associated with long term increases in well-being (e.g. Frewen et al., 2007) affects the neural and behavioural short term responses to stress.

1.6 Mindfulness as a distinct emotion process

One of the most promising aspects to MBSR training is the promise of increased well-being through the cultivation of momentary self-awareness. Mindfulness training has been associated with increases in self-reported well-being, reliably increasing reported positive affect and increasing tolerance for pain and negative emotions (see Grossman et al, 2004 for a meta-analysis). Mindfulness strategies involve maintaining awareness of an aversive event rather than avoiding (distraction) or repeatedly analyzing (rumination) the experience (Broderick, 2005). Mindfulness techniques therefore do not seek to avoid challenging experiences, but rather reduce rumination upon negative events (Teasdale et al., 2002), with the latter thought to be a maladaptive effort to regulate one’s emotions (Nolen-Hoeksema, 2000). Experimentally, a mindfulness strategy reduces the effects of induced negative mood relative to both distraction and rumination strategies (Broderick, 2005).

While it is hard to dispute the ubiquitous positive effects of MBSR on subjective well-being, explaining how mindfulness alters emotions is still more a matter of theory than empirical research. And yet, the distinction between the extended and momentary self maps nicely on to classic theories of emotion that suggest that emotions arise out of discordance between expected and perceived states (e.g. Larsen, 2000). In this example the extended self is constituted by a set of consistent expected states, thereby promoting a sense of self-constancy, whereas the momentary self is constituted by the individual’s perceived state, fluctuating at each moment. Potent negative emotions are generated when an individual’s momentary self-perception fails to align with expectation derived from an extended form of self-reference (Frijda, 1983; Scherer, 2004; Siemer, 2007). One means by which one can reduce negative affect might be to limit appraisals, the comparisons of expectations to perceptions, to maintain awareness of the stimuli at hand rather than dwelling in the self-implications that stressors may bring (Teasdale, Segal & Williams, 1995). In our current parlance, such regulatory efforts would entail reducing extended self processing in favor of attention to the momentary self; in bypassing the process of extended...
self-reference, the frequency of appraisal processes can be limited, thus reducing opportunities for the generation of negative emotion.

One might question why reducing negative appraisals and ruminations require a fundamental change in self-reference. After all, why would an individual not simply ‘soldier on’ in the face of negative events? While stoic resilience in the face of stress may be an admirable ideal, in practice negative emotions such as sadness powerfully bias cognition, capturing attention (e.g. Ortner, Kilner & Zelazo, 2007), and reducing processing of local features (Gable & Harmon-Jones, 2010; Schmitz et al., 2009), effects which may, in turn, reduce the individual’s ability to effectively respond to environmental challenges. For example, an exam-writing student realizing that he cannot answer one of the questions would be better served by completing the rest of the test rather than obsessing over his local failure. Despite such sage advice, it is an all too common occurrence to observe students becoming entranced with difficult questions, often to the detriment of their overall performance. Momentary self-reference offers one opportunity to circumvent the biasing effects of negative emotion by preventing the generation of negative affect rather than attempting to regulate such affect once it arises.

By non-judgmentally attending to the experience of a stressor, enhancement of momentary awareness through MT represents a novel and distinct method for regulating negative emotions. The mindful approach is also very different from traditional accounts of another effective emotion regulation strategy known as reappraisal (e.g. Gross and Ochsner, 2002), in which participants attempt to maintain awareness of the aversive event, but focus on generating more positive interpretations of the event. Rather, mindfulness training advances the notion that a unified sense of self-reference can occur in the absence of interpretation and evaluation (Kabat-Zinn, 1982). By viewing even traditionally aversive sensory experiences with equanimity and without judgment, the appraisal process cued by the aversive stimulus can be disrupted, reducing the emotional intensity and self-relevance of aversive events (Segal et al., 2006). Negative and threatening events naturally imply a disconnection between ideal self states and the present perception of self status; by reducing the relationship between a given stressor and the extended self, the need for an emotional reaction is also reduced (Watkins & Teasdale; 2001).

Traditionally, extended self-reference is an adequate means by which to regulate emotion, the disconnection between the ideal self state and stressor galvanizing the individual to
react and correct the situation. Momentary self-reference in reaction to a stressor is however a novel approach to emotion regulation in that it may be applied in situations where positive reappraisal is difficult or impossible. Studies of emotion regulation have shown that initial reactions to negative affect can determine the intensity of subsequent distress, with important differences between the individual strategies evoked (Gross, 2002). In healthy populations reappraisal techniques often effectively reduce the intensity of fear and anxiety (Ochsner et al., 2004). Yet regulatory reactions to emotion may also be maladaptive, as in the cases of rumination or self-focused attention, in which elaborating on negative affect ironically perpetuates the very mood it is intended to reduce (Nolen-Hoeksema, 2000; Watkins, Moberly & Moulds, 2008). Thus alternatives to reappraisal strategies may be of paramount importance for individuals whose reappraisal abilities are compromised due to chronic illness or other long-term undesirable circumstances. Through repeated observation of affective states as ‘objects’ of attention (Creswell et al., 2007), participants learn that emotions have their own somatic signatures, whose fluctuations in intensity and duration provide continuous cues for re-focusing attention on momentary sensation (Jha et al., 2007; Brefczynski-Lewis et al., 2007), especially when allocation of scarce mental resources to maladaptive, ruminative processing has been the default (Slagter et al., 2007).

Neuroimaging investigations of emotion regulation have identified a constellation of prefrontal regions associated with active reappraisal of the emotional salience of events (see Ochsner & Gross, 2008, for a review), such as the medial prefrontal, orbital frontal, and subgenual cingulate cortices. Studies of sadness provocation in both clinically-depressed samples and in remitted patients who are at risk for relapse have demonstrated altered activation in these same regions (Liotti et al., 2002; Keightley et al., 2003). Specifically, dysphoria-linked changes in dorsal and ventral prefrontal engagement have been associated with compromised cognitive control over emotional responses (Johnstone et al., 2007; Ramel et al., 2007). Taken together, clinical and experimental data suggest that chronic depressed mood or clinical depression may originate in part from an impaired ability to regulate emotion rather than a lack of reappraisal effort per se (Segal et al. 2006).

Although mindfulness training has been associated with increases in self-reported well-being, it remains unclear whether and how such training influences the neural representations of emotional experience. Evidence of reduced extended self-referential activity in favour of
integrating information from the momentary self would suggest that through this training, practitioners acquire emotion regulation skills that reduce their affective reactivity to stressful or challenging experiences. In short, the momentary self may be a less emotionally reactive means by which to attend to challenging experiences insofar as momentary self-reference is readily available to the mindfulness-trained individual independent of the attentional demands posed by the stressor.

1.7 Momentary self-reference as a distinct attention process

Even if emotional reactivity can be limited through reliance upon the momentary self, the question remains as to how reactivity has been altered. For the nature of self-reference to be fundamentally altered through training, some change must occur in how one directs attention to the self. Traditionally, attention has been investigated by modulating the complexity and/or difficulty of experimental tasks, with more demanding experimental tasks associated with increased activation of a fronto-parietal cortical executive system (e.g. Duncan & Owen, 2000; Corbetta & Shulman, 2002; Wendelken et al., 2007). Critically, this network appears to be co-activated with the default network during mind-wandering (Christoff et al., 2009), suggesting an interplay between effortless resting state and effortful executive network activity. Together, these networks form the basis for integrating information into working memory and thus for the continuity of perception over time, the hypothesized process constituting the extended self.

While attention has traditionally been linked to a fronto-parietal cortical system, momentary self-reference suspends attempts to manipulate and sustain information in working memory. Instead, momentary self-reference employs attention to constantly re-orient awareness to immediate sensation, disengaging from habitual generation of extended self representations. As such, the momentary self may recruit a distinct attention system from the traditional executive network. Instead, since momentary self-reference focuses predominantly on the inclusion of interoceptive sensory afferents, it may be that the process of interoceptive monitoring recruits a distinct attention network dedicated towards the generation of bodily representation, which organizes information independently from attention towards more conceptual tasks.

If it is the case that both extended and momentary self-reference are recruited by a common attentional process, then explicit attention to interoceptive and exteroceptive sensory
afferents should not alter the frontoparietal cortical recruitment required for both referential modes, but instead involve a differentiation of afferent sensory regions and their appropriate primary representation areas. For instance, attention to the visceral pain of a stubbed toe versus the social pain of group exclusion may both activate attention processes in the anterior cingulate cortex, despite possessing sensory representations in different areas, such as the thalamus for physical pain and superior temporal sulcus for social evaluation (Eisenberger et al., 2003; Wager et al., 2004). However, if momentary self-reference relies on a fundamentally different attentional process than extended self-reference, then one might expect to find that training oneself to focus on momentary self-reference, i.e. interoceptive sensory afferents from respiration and body sensation, might recruit brain regions outside of the frontoparietal cortical system typically attributed to selective attention.

Reflecting upon the extended and momentary self from an attentional perspective, an intriguing difference emerges between the intended targets of attention. Simply put, the momentary self includes attention to the body and internal sensations as part of one’s awareness of the world, whereas the extended self refers primarily to external objects in their relation with a constant self concept. To elaborate: if the extended self is one which imparts a feeling of constancy, then the role of attention with respect to the extended self may be seen as exteroceptive, integrating sensations from the external world with respect to a fixed and constant reference point (the extended self). Thus for the extended self the world is perceived as a set of experiences interpreted by how they correspond with one’s historical self; memories bias the types of new information that are encoded and stored, reducing broad encoding across experiences to maintain consistency of memory organization over time (Conway, 2005). On the other hand, mindfulness’ momentary self purports to maintain awareness of the transitory stream of experience without a fixed origin of perception. i.e., the perceiver is not assumed to be constant and unchanging. In this way, the bias for encoding information consistent with past memories is reduced in favour of greater correspondence between new encoding and immediate experience. Thus, mindful attention requires extending information processes beyond exteroceptive sensation to also include the myriad interoceptive fluctuations in the body and mind from moment to moment. In this way, recognition of the ever changing nature of the material self is brought to attention, providing direct evidence of the momentary self, and
disrupting the perception of a causal connection between momentary sensations and a fixed self object.

Interoception is important to the cultivation of momentary self-awareness in several ways. The conceptualization of mindfulness as a strengthening of interoceptive attention can be found both practically, through the core practice of breath monitoring as the foundation for mindful states (e.g. Kabat-Zinn, 1982) and also conceptually in many classical Buddhist texts, particularly around instructions to avoid ‘floating away’ from one’s body awareness (e.g. Buddhaghosa, 1999, Visuddhimagga XIV 141). Interoception represents a critical conceptual distinction in discussions of mindfulness, as it provides a positive account of directed attention towards a new category of representation rather than just providing a negative account of how mindfulness turns attention away from perceptions of constant identity, appraisal, and narrative.

1.8 The Current Research

In the next three chapters, I will present three studies investigating the effects of MBSR through a series of fMRI experiments. Chapter 2 will present an experiment seeking to determine whether participants can voluntarily engage in extended and momentary modes of self-reference. This experiment was designed to test my initial hypotheses surrounding the automatic nature of extended self-reference, and to what extent mindfulness training could help individuals to overcome such automatic biases in their self-representations. Chapter 3 extends the question of training effects to examine why MBSR is associated with such reliable increases in reported well-being. By exposing participants to a sad mood challenge, the study identifies how the neural response to sadness may be altered by mindfulness training despite similar subjective reports of induced sadness. Critically, it is these neural responses rather than immediate feelings of sadness that are better predictors of broader well-being, implying a neural mechanism by which MBSR may moderate the long term effects of negative emotional stress. Chapter 4 delves deeper into the question of mechanism, examining a core practice in mindfulness training: the monitoring of one’s own breath. This focus on interoceptive attention is contrasted against more familiar exteroceptive visual tasks before and after mindfulness training, to determine how access to the body’s internal states are affected by the daily practice. This final study offers insights into a lesser known attention system responsible for awareness of the body’s internal state, and also links mindfulness training to changes in the interplay between internal and external attention.
systems. Together, these three studies should present a consistent theme of mindfulness training as reducing the obligatory recruitment of powerful and well-rehearsed neural processes in favour of balancing such processes with the inclusion of lesser-known sources of self-relevant information, particularly in the form of momentary bodily feedback. These findings will be discussed as they relate to the central hypothesis of dissociable extended and momentary selves in Chapter 5.
Chapter 2

2 Distinguishing between the extended and momentary selves


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2.1 Rationale

It has long been theorized that there are two temporally distinct forms of self-reference: extended self-reference linking experiences across time, and momentary self-reference centered on the present. Despite considerable advances implicating cortical midline structures in supporting temporally extended self-reference, little is known about the neural mechanisms underlying momentary self-experience. While it is true that most individuals engage in both momentary and extended self-reference each day, it is important to demonstrate that this distinction can occur volitionally; in other words, a first step in distinguishing between modes of self-reference will require demonstrating neural distinctions commensurate with participant self-referential intentions. If contrasting between these two modes of self-reference generates a reliable neural distinction, we may begin to characterize the neural activity associated with both the extended and momentary selves.

To characterize the brain regions supporting the hypothesized dual-modes of self-reference, participants were instructed to assume distinct modes of self-focus (Watkins & Teasdale, 2001) in response to reading trait-related adjectives: 1) a “narrative” mode, where individuals reflected on what the adjective meant about them as a person, and 2) an “experiential” mode, where individuals monitored their moment-to-moment reactions to the adjectives’ meaning. To increase the probability of self-referential processing in this study, and to control for the potential confounding influence of differing attentional foci between the two modes, in both modes of self-reference participants will view matched trait descriptive words while being asked to either create a self-referential narrative about themselves and the trait (extended self-reference) or to notice all the broad aspects of their experience at once in reaction to the adjectives.
to reading the words without focusing on any single thought or sensation (momentary self-reference). Narrative generation may be so ubiquitous and obligatory that it resists voluntary disengagement, so it will also be important to examine the narrative / experiential distinction in an MBSR group, whose members should have greater access to distinct modes of self-reference as a consequence of their 8-weeks of experiential practice. This first study has the potential to demonstrate a fundamental neural dissociation between the two selves: moment-to-moment experience may be associated with decreased engagement of cortical midline structures traditionally associated with cognitive-affective representations of the self and increased access to right lateralized neural representations of the “bodily” self.

2.2 Study 1 Hypotheses

2.2.1 Narrative relative to experiential focus will recruit cortical midline activity and left-lateralized language regions.

2.2.2 Experiential relative to narrative focus will reduce cortical midline processing.

2.2.3 Experiential relative to narrative focus will recruit a right-lateralized insula pathway.

2.2.4 Recruitment of the right-lateralized experiential network will be conditional upon MBSR training; untrained participants may demonstrate a reduced/absent pattern of dissociation between the two modes of self-reference.

2.3 Abstract

It has long been theorized that there are two temporally distinct forms of self-reference: extended self-reference linking experiences across time, and momentary self-reference centered on the present. To characterize these two aspects of awareness, I used fMRI to examine monitoring of enduring traits (“narrative” focus, NF) or momentary experience (“experiential” focus, EF) in both novice participants and those having attended an 8-week course in mindfulness meditation, a program that trains individuals to develop focused attention on the present. In novices, EF yielded focal reductions in self-referential cortical midline regions (medial prefrontal cortex, mPFC) associated with NF. In trained participants, EF resulted in more marked and pervasive reductions in the mPFC, and increased engagement of a right lateralized network, comprising the lateral PFC and viscero-somatic areas such as the insula, secondary somatosensory cortex and inferior parietal lobule. Functional connectivity analyses further demonstrated a strong coupling between the right insula and the mPFC in novices that was uncoupled in the mindfulness group. These results suggest a fundamental neural dissociation
between two distinct forms of self-awareness that are habitually integrated but can be dissociated through attentional training: the self across time and in the present moment.

2.4 Introduction

Since William James’ early conceptualization, the “self” has been characterized as a source of permanence beneath the constantly shifting set of experiences that constitute conscious life. This permanence is often related to the construction of narratives that weave together the threads of temporally disparate experiences into a cohesive fabric. To account for this continuity, William James posited an explanatory “me” to make sense of the “I” acting in the present moment (James, 1890). Recently progress has been made in characterizing the neural bases of the processes supporting William James’ “me” in the form of “narrative” self-reference (Gallagher, 2004), highlighting the role of the medial prefrontal cortices (mPFC) in supporting self awareness by linking subjective experiences across time (Neisser, 1997; Northoff & Bermpohl, 2004). The mPFC has been shown to support an array of self-related capacities, including memory for self-traits (Craik et al., 1999; Fossati et al., 2003; Kelley et al., 2002; Macrae et al., 2004), traits of similar others (Mitchell, Macrae, & Banaji, 2006), reflected self-knowledge (Lieberman, Jarcho, & Satpute, 2004; Ochsner et al., 2005), and aspirations for the future (Johnson et al., 2006). As such, cortical midline processes may be characterized as supporting narrative self-reference that maintains continuity of identity across time (Gallagher, 2004).

Narrative self-reference stands in stark contrast to the immediate, agentic “I” supporting the notion of momentary experience as an expression of selfhood. Most examinations of self-reference ignore mechanisms of momentary consciousness, which may represent core aspects of self experience achieved earlier in development (Damasio, 1999; Gallagher, 2004; Zelazo & Frye, 1998) and may have evolved in earlier animal species (Panksepp, 2005). Indeed, little is known about whether the neural substrates underlying momentary self-reference are one and the same, or distinct from, cortical midline structures supporting narrative experience. One hypothesis suggests that awareness of momentary self-reference is neurally distinct from narrative self-reference and is derived from neural markers of transient bodily states, in particular, right lateralized exteroceptive somatic and interoceptive insular cortices (Craig, 2004; Critchley et al., 2004; Damasio, 1999). In the present study, I examined this thesis.
I investigated these hypothesised dual modes of self-reference by employing functional magnetic resonance imaging (fMRI) during attention to two temporally distinct foci of attention: the self as experienced across time and in the immediate moment. One obstacle to investigating present-centred awareness is the well-established tendency for the mind to wander and become distracted from the present moment in favour of temporally distant, stimulus-independent thought (Smallwood & Schooler, 2006). Stimulus-independent thought (SIT) consists of automatically-generated verbal or visual experiences (Teasdale et al., 2003; McGuire, Paulesu, Frackowiak & Frith, 1996) akin to William James’ notion of a running ‘stream of consciousness’ (James, 1890), the basis of the narrative form of self-reference described above. SIT-related neural activation has been shown to reflect an automatic tendency to engage in narrative processes in the absence of a strong requirement to respond to external stimuli (McKiernan, Angelo, Kaufman & Binder, 2006).

The theory of narrative generation as a default state of self-reference is increasingly supported by neural evidence: the cortical midline activity which underlies narrative-generating mind-wandering (Mason et al., 2006) is very similar to activity associated with the ‘default mode’ of resting attention (Gusnard et al., 2001; Raichle et al., 2001). This default mode suggests an endemic reliance upon the networks supporting temporally-extended narrative processing, potentially obscuring recruitment of distinct networks for more immediate self-reflection. It may, therefore, be important to study individuals with specific training in monitoring moment-to-moment experience to more reliably recruit the brain regions supporting momentary self-focus in the face of a narrative generation bias. Mindfulness meditation is a form of attentional control training by which individuals develop the ability to direct and maintain attention towards the present moment (Segal et al, 2002; Kabat-Zinn et al., 1992). The current study examined individuals with mindfulness meditation training (MT) in addition to a novice group without such training, in an effort to determine whether the MT group would show an increased capacity to disengage from narrative generation and reveal the neural networks supporting present-centred self-awareness.

To characterize the brain regions supporting the hypothesized dual-modes of self-reference, participants were instructed to assume distinct modes of self-focus. Narrative focus calls for cognitive elaboration of mental events, thereby reducing attention towards other temporally proximal sensory objects. By contrast, experiential focus calls for the inhibition of
cognitive elaboration on any one mental event in favour of broadly attending to more temporally proximal sensory objects, canvassing thoughts, feelings, and physical sensations without selecting any one sensory object. As such, narrative focus has been associated with increased ruminative thoughts about the self, while experiential focus avoids rumination by disengaging attentional processes of self-referential elaboration (Watkins & Teasdale, 2001). In response to reading trait-related adjectives participants in the present study were asked to engage either: 1) a “narrative” mode, reflecting on what the adjective meant about them as a person, or 2) an “experiential” mode, monitoring their moment-to-moment experience in response to the adjectives. Trait-related adjectives were chosen for their ability to promote self-reflection as evidenced by previous research (e.g., Fossati et al, 2003).

2.5 Methods

Participants. Participants were recruited upon enrolment in the Mindfulness-Based Stress Reduction (MBSR) program at St. Joseph’s Hospital in Toronto, an 8-week intensive course (Kabat-Zinn et al., 1992) that involves daily exercises in focusing attention on the present moment, as described in Kabat-Zinn et al. (1992). The MBSR program featured weekly in-class sessions in which participants were trained in several exercises, consisting chiefly of practicing the continuous focus of attention on one’s breathing and other sensations, as well as attentional body scans and some basic hatha yoga postures. On each of the six days between classroom sessions, participants were asked to practice the attentional exercises on their own for at least 45 minutes (Kabat-Zinn, 1982). Participants were randomly assigned to either a pre-training waitlist group (twelve women and four men, mean age 42.00 ± 9.24); or a post mindfulness training (MT) group (fifteen women and five men, mean age 45.55 ± 13.38). A cross-sectional design was chosen to limit the effects of repeated exposure to the task and scanner environment. No group differences were found for age, gender, prior meditation experience, pre-training anxiety (BAI; Beck & Steer, 1990; Novices 13.38 ± 8.49, MT 16.35 ± 12.59), depression (BDI-II; Beck, Steer & Brown, 1996; Novices 20.56 ± 13.10, MT 23.35 ± 14.22), or other psychological symptoms (SCL-90-R; Derogatis, 1984; Novices 79.88 ± 50.41, MT 108.25 ± 64.68). All were right handed volunteers that gave informed consent to procedures that were approved by the Sunnybrook and Women’s College Health Sciences Clinical Ethics Committee. Subjects were reimbursed for their participation.
Materials and procedure.

**Verbal Stimuli.** Eight sets of six personality-trait adjectives were constructed from a well-established list of personality-trait words (Anderson, 1968). Each of the 8 lists words contained 3 mildly positive traits and 3 negative traits (e.g., confident, melancholy), selected from the top and bottom 20% of Anderson’s sample (Fossati et al., 2003), as these traits would lend themselves naturally towards self-reference. Word lists were randomly assigned to each condition.

**Training procedure.** Participants were first trained on the distinction between experiential and narrative forms of self-focus, derived from Watkins & Teasdale (2001). Experiential focus was characterized as engaging present-centered self-reference, sensing what is occurring in one’s thoughts, feelings and body state, without purpose or goal, other than noticing how things are from one moment to the next; if a participant noticed themselves getting distracted by a particular thought or memory, they were asked to calmly return their attention to their current experiences whenever they noticed such distraction. Narrative focus was characterized as judging what is occurring, trying to figure out what that trait word means to the participant, whether it describes the participant, and allowing oneself to become caught up in a given train of thought. Participants were given multiple examples of each mental-state and were invited to ask questions and generate examples about the distinction. Once participants could competently describe the experiential/narrative distinction in their own words, they were then trained in these conditions as well as additional baseline tasks (1-back working memory, arrow key-press, monitor breathing, and thought suppression), which were not analyzed for the present report. Training required approximately 20-25 minutes in total. During the experiment each condition lasted for 36 seconds and was preceded immediately by a 10 second instruction screen with a condition cue to inform and prepare participants for the next task. The instruction screen consisted of a cue word and icon to inform the participant of which type of self-focus to perform; the instruction screen was presented for a 10 s duration to allow participants adequate time to disengage from one focus and reorient themselves for the next task. One run in the scanner consisted of two repetitions of each condition and each participant completed two runs. The condition order was randomized for each participant.
**Self-focus task.** To enable comparison of these hypothesized distinct modes of self-reference, narrative and experiential self-focus were separately applied while reading intermixed mildly positive (e.g., charming) and negative (e.g., greedy) trait descriptive words. Trait-adjectives appeared on the screen singly every 6 seconds for 4 seconds in duration. To aid in accessing momentary experiential focus, no overt responses were collected during scanning.

**Post-scanning ratings.** To acquire a subjective index of task effort and compliance, following exiting the scanner participants rated the ease they found employing each self-focus mode. A two-way mixed ANOVA, with group (novice vs mindfulness trained, MT) and self-focus (narrative vs. experiential), revealed that narrative focus was easier to employ than experiential focus, $F(1, 34) = 8.59, p < .007$. Additionally, the MT group found both forms of self-focus easier to engage than the pre-group, $F(1, 34) = 5.54, p < .03$, with no differential effect of training on ease of engaging a particular self-focus mode, $F(1,34) < 1$. A further examination of whether the groups differed in a tendency to mind wander during scanning revealed no group differences, $F(1, 34) < 1$.

**Data acquisition.** Imaging was performed at Sunnybrook and Women’s College Health Sciences Centre (S & W) using a 3-T Signa MRI system (CV/i hardware, LX8.3 software; General Electric Medical Systems, Waukesha, Wis.) with a standard quadrate birdcage head coil. Functional MRI (fMRI) was conducted using T2*-weighted single-shot spiral in-out k-space trajectories optimized for sensitivity to the blood-oxygenation-level-dependent (BOLD) effect (TE/TR/flip angle = 30 ms/2000 ms/70 degrees, 20 cm field-of-view (FOV), 5 mm slice thickness, 64 by 64 matrix, 26 slices in axial oblique orientation. Spiral in-out technique provided improved capability to acquire fMRI signals in regions of high magnetic susceptibility (Glover & Law, 2001). The first 15 TRs of each run were discarded due to scanner equilibration effects. Structural imaging was conducted with 3D inversion recovery-prepped fast spoiled gradient echo imaging (IR-prep FSPGR; 300 ms prep time, TE/flip angle=min. full/15 degrees, 24 cm FOV with 0.75 phase FOV right-to-left, 256 by 192 matrix, 124 slices 1.3 mm thick). Stimulus presentation was controlled by Presentation software (Neurobehavioural Systems, Inc., Albany, Calif.) viewed via a back-projection screen.

**Data pre-processing and analysis.** Statistical Parametric Mapping (SPM; version 2) was used to extract time series functional data, which was spatially co-registered and re-aligned to
correct for small head motions within and between functional scans. Data were then normalized into a common stereotactic reference space (MNI) and spatially smoothed (FWHM=8mm). FMRI responses to the presentation of each event type were modeled by a canonical hemodynamic response function scaled relative to the block duration, with the entire 36 second word presentation period modelled as a single block. For each individual, contrast images were calculated by applying appropriate weights to the parameter estimates for each event type. Group analyses were then performed on these individual subject contrast images, which were submitted to paired t-tests, with subject entered as a random effect. Cluster thresholding was applied to increase power in identifying heavily recruited neural areas while maintaining a reasonably low Type-I error rate (Forman et al., 1995). Two criteria were employed in evaluating activations: i) only regions with peak voxels of p < .001 were considered; ii) only clusters of activation including k >= 6 voxels in which all voxels met an uncorrected threshold of p < .005 were considered, yielding a functional threshold equivalent of p < .001 according to cluster size significance level corrections (Forman et al., 1995). The cluster volume threshold was based on voxels resampled into an isotropic 4x4x4 mm space. Group contrast images were overlaid on an average high-resolution FSPGR T1 image for viewing.

Region of interest analyses. As a follow up to the voxel-wise analyses, functionally defined regions from the MT group were used to interrogate whether these activations reflected subthreshold contrasts between modes of self-focus in the novice group. ROIs were recruited from the MT group since only this group showed major differentiation of narrative and experiential focus through the recruitment of a priori regions of interest. The ROI analyses were therefore designed to support the qualitative observation of an increased distinction between focus conditions by showing that the neural distinctions made in the MT group analysis were significantly more reliable than activation differences in the novice group. Weighted parameter estimates from the peak voxel in each ROI were extracted and submitted to an additional ANOVA to confirm an increased neural distinction between focus conditions in the MT relative to the novice group. The 5mm spherical ROIs were derived from peak voxels in each cluster allowing independent examination of contiguous activated regions.

Functional connectivity analyses. Linearly detrended whole-brain time series activation patterns were compared to activation in a volume of interest (spherical, 5mm radius) defined in the narrative vs. experiential contrast in the MT group. Seed voxels were used in a physio-
physiological interaction (PPI; Friston et al., 1997) to test for significant correlations with activity in the rest of the brain voxels across the observed time series. Functional connectivity regions of interest were defined by selecting areas that demonstrated significant connectivity differences with the seed ROIs in a comparison between novice and MT groups (p < .001). These areas were then subjected to more detailed linear regression analysis. Any activation outliers greater than 3 standard deviations within a given region were excluded from the time series data.

2.6 Results

**Narrative self-focus.** To characterize the narrative self-focus state, participants from both the novice and MT groups were collapsed into a single analysis of narrative self-focus compared to the baseline conditions. Consistent with narrative focus reflecting a higher-order and linguistically mediated mode of self-reference and replicating prior studies of self-reference (Craik et al., 1999; Fossati et al., 2003; Johnson et al., 2002; Kelley et al., 2002; Northoff & Bermpohl, 2004; Ochsner et al., 2005), narrative self-focus resulted in pronounced recruitment of midline cortical structures, including the rostral and dorsal extent of the mPFC (BA 8/9/10/32; at peak height: x, -16; y, 52; z, 36; Z = 6.75, p < 0.001), and the posterior cingulate (BA 23/31, -8 – 56 24; Z =3.91, p < 0.001; Figure 2.1), left hemisphere language areas, including the inferolateral PFC (BA 44/45, -56 20 12; Z = 5.94, p < 0.001) and middle temporal gyrus (BA 21, -64 -40 -4; Z =5.45, p < 0.001), right inferior frontal gyrus (BA 47, 56 32 -8; Z = 3.58, p < 0.001), right precentral gyrus (BA 4, 28 -20 72; Z = 3.38, p < 0.001), cuneus (BA19, 0 -96 32; Z = 4.12, p < 0.001), and left head of caudate (-12 12 4; Z = 3.36, p < 0.001), and cerebellum (32, -80, -48, Z = 6.53, p < 0.001).

**Experiential Focus: Novice participants.** I was specifically interested in examining how experiential focus differed from narrative focus in each of the novice and MT groups. Beginning with the novice group, directly contrasting these conditions revealed several focal differences in activation (Figure 2.2ab). Relative to narrative self-focus, experiential self-focus was associated with relative reductions in several discrete regions along the cortical midline: gyrus rectus of the subgenual cingulate (BA 25; 27 voxels, 16 16 -12; Z = 3.29, p < 0.001), posterior cingulate (BA 23/31; 41 voxels, –8 -52 28; Z = 3.29, p < 0.001), and with a lower cluster threshold, a relatively restricted reduction in the rostral mPFC (BA 10; 4 voxels, -4 64 16; Z = 3.16, p < 0.001). Experiential self-focus was associated with a relative increase in left lateralized regions, yielding
significantly greater activations in the dorsolateral PFC (BA 45/46; 23 voxels, -36 32 24; Z = 3.60, p < 0.001), ventrolateral PFC (BA 47; 11 voxels, -36 40 4; Z = 3.13, p < 0.001) and posterior parietal cortices (BA 39, 23 voxels, -48 –48 56; BA 40; 9 voxels, -32 -52 28; Z = 3.06, p < 0.001).

**Experiential Focus: Mindfulness-Trained participants.** Increased left sided dorsolateral and posterior parietal recruitment may reflect greater task related executive control and attentional allocation (Gusnard et al., 2001) or at the very least an attempt to resist narrative mind wandering (Mason et al., 2006), rather than the neural correlates of present-centered experiential focus. As such, the above results suggest that moment-by-moment self-experience may rely simply on task-related suppression of midline cortical representations very similar to those supporting narrative self-focus. Another possibility is that dissociable neural markers of self-reference may be more evident following extensive training in present-centered self-focus in the MT group, where engaging distinct modes of self-reference may be more effortless.

In the MT group, experiential self-focus did result in pervasive deactivations along the anterior cortical midline relative to narrative focus, including the rostral subregions of the dorsal mPFC (BA 9/10/32; 87 voxels, -12 56 40; Z = 3.77, p < 0.001) and ventral mPFC (BA 10; 86 voxels, 8 68 8; Z = 3.98, p < 0.001; Figure 2.3a), as well as reduced activity in the left dorsal amygdala (BA 34; 9 voxels, -24 -8 -8; Z = 3.20, p < 0.001), suggesting that moment-by-moment self-experience may rely on suppression of mPFC cortical representations supporting narrative self-focus. In addition to the mPFC reductions, experiential focus resulted in increased recruitment of a right lateralized cortical network, including the dorsal and inferolateral PFC (BA 46/45; 77 voxels, 48 56 -8; Z = 3.50, p < 0.001), insular cortex (BA 48; 6 voxels, 40 -8 16; Z = 3.24, p < 0.001), a region along the supramarginal gyrus consistent with the secondary somatosensory cortex (SII, BA 40; 24 voxels, 40 -40 20; Z = 3.61, p < 0.001) extending posteriorly and dorsally into the angular gyrus of the inferior parietal lobule (BA 39; 7 voxels, -36 -76 48; Z = 3.11, p < 0.001; Figure 2.3bcd). This pattern is consistent with the MT group demonstrating a marked shift from midline mPFC-centered recruitment during experiential focus towards right lateralized prefrontal cortical and paralimbic structures, in particular demonstrating recruitment of hypothesized posterior viscero-somatic representations.
To examine whether the distinct experiential focus regions revealed in the MT group were novel areas of recruitment compared to novices rather than the product of subthreshold but similar patterns of activation, I further performed ROI analyses of activation patterns from each participant in both the MT and Novice groups (Figure 2.3, right panel). Experiential relative to narrative self-focus was associated with significant reductions in the ventral (F = 11.88, p < 0.003) and dorsal mPFC (F = 19.09, p < 0.001), in the MT but not the novice group (p’s > .3). By contrast, experiential self-focus resulted in significantly greater recruitment of the right lateral PFC (F = 14.75, p < .001), right insula (F = 14.41, p < .001), and SII/inferior parietal lobule (F’s > 10.28, p’s < .003) in the MT but not the novice group (p’s > .3).

Functional connectivity analyses. One reason that novices may have difficulty separately attending to distinct modes of self awareness is the habitual coupling of posterior-lateral and mPFC representations. To examine this more directly, I assessed functional connectivity between the viscero-somatic cortices and the mPFC across the entire time series (Figure 2.4). Out of the potential posterolateral seed regions, the right insula was chosen as being the best documented in supporting viscero-somatic awareness (Craig, 2004; Critchley et al., 2004; Adolphs, 2002; Damasio, 1999). An analysis of right insular functional connectivity revealed that novices demonstrated strong coupling with midline cortical regions, including the orbital sectors of the vmPFC (BA 11; 6 voxels, -4 56 -24; Z = 3.68, p < 0.001) (R = .609, p < .001), suggesting viscero-somatic signals are by default associated with activation in the ventral medial prefrontal cortices. Such a strong correlation may preclude dissociation of these modes of self-focus in novice participants. Successfully maintaining present-moment awareness may require MT individuals to decouple the automatic responsiveness of the vmPFC to insular activation. Supporting this hypothesis, the right insular and vmPFC cortices were rendered uncorrelated in the MT group (R = .056, Fisher’s r to Z = 13.36, p < .001). This decoupling was replaced by an increased coupling of the right insula with the dorsolateral prefrontal cortices (BA 9/44; 17 voxels, -56 20 32; Z = 3.18, p < 0.001), as seen in the change from a modest correlation in the novice group (R = .283) to a very strong correlation (R = .783, Fisher’s r to Z = 12.09, p < .001) in the MT group. This pattern of results suggests MT may afford greater access to distinct modes of self-focus by promoting a shift away from viewing viscero-somatic activity through the lens of the mPFC towards a distinct mode of sensory awareness supported by the lateral PFC.
2.7 Discussion

Consistent with a theory of self-reference as mentalizing (Zelazo & Frye, 1998), linguistically mediated (Rochat, 1995) and of higher order executive origin (Amodio & Frith, 2004; Craik et al., 1999; Fossati et al., 2003; Johnson et al., 2002; Kelley et al., 2002; Macrae et al., 2004; Northoff & Heinzel, 2006; Ochsner et al., 2005), participants engaged midline prefrontal cortices (ventral and dorsal mPFC) and a left lateralized linguistic-semantic network (inferior lateral PFC, middle temporal and angular gyri) while processing events with a narrative focus. Demonstrating a default bias towards narrative self-focus as previously revealed in “resting” mind wandering states (Mason et al., 2006), relatively restricted reductions in the cortical midline network were found when attention was explicitly directed towards a moment-to-moment experiential focus in novice participants with little training in this form of self-reflection. These individuals revealed increased left lateralized prefrontal-parietal activations likely reflecting greater task related linguistic processing that has been shown to be associated with decreased medial prefrontal recruitment (Gusnard et al., 2001).

Participant inexperience with different forms of self-focus might limit the ability to accurately reveal functionally and neurally distinct forms of self-awareness. I also examined individuals with more extensive training in present moment centered self-awareness. Following an intensive 8 week course in mindfulness meditation, during which individuals learn to develop the capacity to monitor moment-to-moment experience, experiential focus resulted in a pronounced shift away from midline cortices towards a right lateralized network comprised of the ventral and dorsolateral PFC, as well as right insula, secondary somatosensory (SII), and inferior parietal lobule. Consistent with a dual-mode hypothesis of self-awareness, these results suggest a fundamental neural dissociation in modes of self-representation that support distinct, but habitually integrated, aspects of self-reference: 1) higher order self-reference characterized by neural processes supporting awareness of a self that extends across time and 2) more basic momentary self-reference characterized by neural changes supporting awareness of the psychological present. The latter, represented by evolutionary older neural regions, may represent a return to the neural origins of identity, in which self-awareness in each moment arises from the integration of basic interoceptive and exteroceptive bodily sensory processes (Craig, 2004; Critchley et al., 2004; Damasio, 1999; Panksepp, 2005). By contrast, the narrative mode of self-reference may represent an overlearned mode of information processing that has become
automatic through practice, consistent with established findings on training-induced automaticity (e.g. MacLeod & Dunbar, 1988).

Altered cortical midline activation, particularly in the vmPFC, has been associated with judgments of self-relevance (Phan et al., 2004), as well as appreciation of emotional valence, ranging from simple sensory to more complex and abstract events (Anderson et al., 2003; Cunningham, Raye, & Johnson, 2004; O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). As this region receives connections from all exteroceptive (Barbas, 2000) and interoceptive modalities (Carmichael & Price, 1996), it has been viewed as a polymodal convergence zone (Rolls, 2000), supporting the integration of external and internal stimuli with judgments about their affective relevance to the self (Ochsner & Gross, 2005). Following MT, experiential focus resulted in a shift away from both the vmPFC and the amygdala, toward more lateral prefrontal regions supporting a more self-detached and objective analysis of interoceptive (insula) and exteroceptive (somatosensory cortex) sensory events, rather than their affective or subjective self-referential value. This pattern mirrors neural dissociations between the affective and sensory components of pain sensation, with the former supported by anterior midline structures, and latter supported by posterior lateral sensory cortices (Rainville et al., 1997). This detached or objective mode of self-focus may be aided by the recruitment of the right angular gyrus of the inferior parietal lobule. In addition to studies showing that this region is involved in switching between first and third person perspectives (Ruby & Decety, 2004), stimulation of this region has been associated with “out of body experiences” (Blanke et al., 2002) where an individual experiences stepping outside of themselves, affording a detached perspective on their corporeal self. Altered access to these posterolateral body schema representations may underlie neurological conditions such as anosognosia or de-personalization syndrome (Berlucchi & Aglioti, 1997), where there is loss of body ownership, with the body no longer being perceived as belonging to the “self.”

The shift toward dorsal lateral PFC regions following MT may reflect an enhanced capacity to represent a non-linguistic based awareness of the psychological present in working memory (Gray, Braver, & Raichle, 2002; Miller & Cohen, 2001); whereas increased activity in the ventrolateral PFC may represent augmented inhibitory control (Bunge et al., 2001; Gusnard et al., 2001) necessary to curtail a default tendency toward narrative self-reference. The right posterior paralimbic and neocortical regions, including the insula, SII, and inferior parietal lobule
likely represent the contents of this present-focused awareness, with these regions associated with feedback regarding the interoceptive physiologic, exteroceptive somatic condition of the body, and overall corporeal awareness. Indeed, prior structural and functional imaging research has linked right insular volume and activity with increased sensitivity to interoceptive signals and global visceral awareness (Critchley et al., 2004) and thus has been hypothesized to reflect a global representation of interoceptive activity (Craig, 2004). In conjunction with the secondary somatosensory cortex, these regions have been argued to serve as somatic markers (Adolphs, 2002; Damasio, 1999), enabling a cortical representation of the overall somatic and physiologic state of the body (Craig, 2004; Damasio, 1999).

It is important to underscore that although a present-centered focus may involve aspects of monitoring one’s body state, meditation practice is associated with developing moment-to-moment awareness of all available stimuli. Accordingly, during experiential focus participants were not instructed to narrowly attend to the body, rather they were encouraged to maintain a temporally narrow but experientially broad attentional focus centered on momentary experience, including internal thoughts, emotions, and physical sensations as well as external sensory events. The insula, somatosensory cortices, and inferior parietal lobule may then have a special role to play in the representation of transitory experience in all its forms (Craig, 2004). While these areas have been associated with a default or resting state in which self-narration and momentary awareness co-mingle (Mason et al., 2006), training in maintaining momentary awareness suggests viscerosomatic cortical areas support an immediate information processing network of identity, distinct from abstract and narrative representations of the self. Indeed, converging with the present results, meditation practice is associated with cortical thickening in the right insular, somatosensory and inferior parietal lobule cortices (Lazar et al., 2005), suggesting these regions may be altered with extended daily focused attention to moment-to-moment experience, and thus may represent the neural underpinnings of self-reference in the psychological present.

One important limitation of the present study is the lack of a true pre/post intervention design; as such, the evidence does not support a claim that mindfulness training per se allowed for the increased differentiation between narrative and experiential attentional networks, but rather that those with MT show qualitatively different distinctions between self-referential focus modes than those only anticipating MT (the novice group). It can be reasonably inferred from these results that expertise in developing momentary awareness is associated with the ability to
disengage from these default mPFC centered networks, even when subjective effort and perceived task-efficacy is equated. Testing participants before and after MT would allow us to investigate whether our observation of neural decentering is a pervasive, trait-like training effect resulting in chronic suppression of the mPFC-centered network, or whether instead MT results in greater voluntary, but state-like, suppression of an otherwise undiminished mPFC-centered network, thereby illustrating the mechanisms underlying the enhanced recruitment of viscerosomatic representations of the momentary self.

The functional connectivity results suggest that a default mode of self-awareness may depend upon habitual coupling between mPFC regions supporting cognitive-affective representations of the self and more lateral viscero-somatic neural images of body state. This dual-mode of self-reference is better revealed following MT, where these modes become uncoupled through attentional training. This hypothesized cortical reorganization following MT is consistent with the notion that mindfulness training allows for a distinct experiential mode in which thoughts, feelings and bodily sensations are viewed less as being good or bad or integral to the “self” and treated more as transient mental events that can be simply observed (Williams et al. 2007). As such, the capacity to disengage temporally extended narrative and engage more momentary neural modes of self-focus has important implications for mood and anxiety disorders, with the former having been shown to increase illness vulnerability (Segal et al., 2006). Conversely, a growing body of evidence suggests approaching self-experience through a more basic present-centered focus may represent a critical aspect of human well-being (Davidson, 2004).
Chapter 3

3 Mindfulness and Emotion


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3.1 Rationale

Recovery from emotional challenge and increased tolerance of negative affect are both hallmarks of mental health. Restoring balance between affective and sensory neural networks-supporting conceptual and body based representations of emotion- could be one path through which mindfulness reduces vulnerability to dysphoric reactivity. Mindfulness training (MT) has been shown to facilitate positive emotional outcomes, yet little is known about its mechanisms of action. This second study therefore investigated the effects of mindfulness training (MT) on emotional experience and its neural expression. To examine the neural effects of mindfulness training on emotional reactivity, I employed functional magnetic resonance imaging (fMRI) to compare neural responses to sadness provocation in participants who completed a Mindfulness-Based Stress Reduction Program and waitlisted Controls.

While it would be easy enough to conclude this thesis with a demonstration of distinct modes of self-referential processing, such a distinction holds little practical merit if it cannot be related to pertinent outcome variables such as individual health and well-being. Mindfulness training has however been linked to improvements in reported well-being (Garland et al., 2007). While a term such as well-being represents a broad mental health category, this broad category must itself be predicated on the individual’s reaction to specific stressful events. Indeed, emotional reactivity to short-term negative mood challenge has predicted depressive relapse risk (Segal et al., 2006), suggesting that it is how an individual assigns self-relevance to negative events and feelings that determines the long term impact of these stressors.
If MBSR can be demonstrated to strengthen momentary self-representation to trait words in study 1, then it should also predict changes in the response to emotional stressors in terms of neural recruitment. Critically, the neural changes to emotional stress should occur in the absence of specific instructions toward self-referential modes, as some change in self-referential habits ought to accompany the long term prophylactic effects of mindfulness training that extend well beyond the 8-week training period. The tendency to respond to stressors with negative, self-directed narratives is known as rumination, the tendency towards which has been repeatedly identified as a risk factor in depression (Nolen-Hoeksema, 2000). Thus, it would be reasonable to hypothesize that part of the prophylactic effects of MBSR are tied to the ability for individuals to resist such negative self-narration following emotional stressors. As this paradigm was novel in its use of experiential processing as an alternative to narrative reactions to stressors, I looked for such a distinction in a community sample rather than a clinical population. Again, a waitlisted control design was used to match the groups. In order to perform an emotional challenge in the scanner, sadness-inducing film clips were shown to participants during fMRI data acquisition, with neutral film clips serving as the within-participant baseline condition. The comparison of sad – neutral film clip activity served as the primary neural index of emotional reactivity, while established self-report measures of depression, anxiety and mental-health served as broader indices of well-being.

### 3.2 Study 2 Hypotheses

3.2.1 Emotional reactivity will recruit a cortical midline and left-lateralized neural network consistent with narrative self-reference.

3.2.2 Emotional reactivity will reduce recruitment of the right-lateralized experiential network

3.2.3 Mindfulness training will reduce the strength of narrative network response to emotional stressors, improving experiential network recruitment

3.2.4 While elevated sadness ratings following emotional challenges will predict narrative network activity, long term well-being will be more related to experiential network activation (or the lack thereof)

### 3.3 Abstract

Recovery from emotional challenge and increased tolerance of negative affect are both hallmarks of mental health. Mindfulness training (MT) has been shown to facilitate these
outcomes, yet little is known about its mechanisms of action. The present study employed functional magnetic resonance imaging (fMRI) to compare neural reactivity to sadness provocation in participants completing 8 weeks of MT and waitlisted Controls. Sadness resulted in widespread recruitment of regions associated with self-referential processes along the cortical midline. Despite equivalent self-reported sadness, MT participants demonstrated a distinct neural response, with greater right-lateralized recruitment, including visceral and somatosensory areas associated with body sensation. The greater somatic recruitment observed in the MT group during evoked sadness was associated with decreased depression scores. Restoring balance between affective and sensory neural networks—supporting conceptual and body based representations of emotion—could be one path through which mindfulness reduces vulnerability to dysphoric reactivity.

3.4 Introduction

In Shakespeare’s Macbeth, a noble chastises a fearful messenger to “give sorrow words: the grief that does not speak; whispers the o'er-fraught heart and bids it break.” It seems a common wisdom that to deal with a negative emotion one must ‘give it voice’, to articulate emotional experience in a way that can temper its impact. Indeed, studies of emotion regulation have shown that initial reactions to negative affect can determine the intensity of subsequent distress, with important differences between the individual strategies evoked (Gross, 2002). For example, reappraisal, in which a negative feeling is recast more optimistically or viewed from a third person perspective, has been shown to effectively reduce the intensity of fear and anxiety (Ochsner et al., 2004). Yet regulatory reactions to emotion may also be maladaptive, as in the cases of rumination or self-focused attention, in which elaborating on negative affect ironically perpetuates the very mood it is intended to reduce (Nolen-Hoeksema, 2000; Watkins, Moberly & Moulds, 2008). When one’s best regulatory efforts only exacerbate the stress of an emotional challenge, how does one break the dysphoric cycle?

Neuroimaging investigations of emotion regulation have identified a constellation of prefrontal regions associated with active reappraisal of the emotional salience of events (see Ochsner & Gross, 2008, for a review). Studies of sadness provocation in both clinical and at-risk samples show altered activation in these same regions, notably the medial prefrontal, orbital frontal and subgenual cingulate cortices (Liotti et al., 2002; Keightley et al., 2003). Critically,
dysphoria-linked changes in the configurations of prefrontal engagement may signal compromised cognitive control over emotion (Johnstone et al., 2007; Ramel et al., 2007), suggesting perseverative efforts to regulate negative emotion without commensurate relief. Taken together, clinical and experimental data suggest that chronic depressed mood or clinical depression may stem in part from an impaired ability to regulate emotion rather than a lack of reappraisal effort per se (Segal et al. 2006).

If dysphoric reactions following reappraisal failure explain why some individuals become overwhelmed by negative emotion, one approach to reducing dysphoric reactivity is to develop metacognitive skills for tolerating and approaching negative affect from a wider attentional frame (Teasdale et al., 2002). Supportive evidence comes from studies in which increased metacognitive awareness of emotions was associated with reduced endorsement of dysfunctional cognitions following sadness challenge (Fresco et al., 2007), reduced cognitive processing of negative material in present moment awareness (Frewen et al., 2007), and an increased willingness to tolerate negative affect (Arch & Craske, 2006). Increases in metacognitive awareness have been reliably linked to the practice of mindfulness meditation, which is now taught through a number of clinical protocols for the treatment of depressive, anxiety and chronic pain disorders (Segal et al., 2002; Kabat-Zinn, 1990).

Critically, mindfulness training purports to regulate affect without altering the momentary subjective experience of emotion. Mindfulness may differ from traditional reappraisals, which are based on the view that affective distress is problematic and requires cognitive alteration. The distinction between the mindful and reappraisal approaches may be better understood with reference to pain research, where distinct neural systems subserve the affective and sensory components of pain appraisal (e.g. Singer et al., 2004). While the somatosensory cortices, thalamus and the posterior insula provide discriminative information about nociceptive stimulus sensation, cortical midline structures such as the anterior cingulate support affective appraisals related to perceived unpleasantness (Craig, 2002). Applying this model, reappraisal processes focus on altering affective judgments and evaluation, whereas mindfulness practice may focus attention on emotions as transitory sensory responses. Following mindfulness meditation, negative emotions may be experienced more as fluctuations in body state sensations and less as affective mental states reflecting what is good or bad for the self. Thus, mindfulness training may reduce chronic reactivity by shifting attention away from
subjective appraisals of affect, towards the incorporation of more sensory-based representations of emotions.

Supporting this altered process of self-reflection, Farb et al. (2007) used fMRI to study how mindfulness trainees and waitlisted controls differed in their capacities for self-representation. While freely engaging in self-referential thought, individuals exhibited distinct engagement of cortical midline structures, including the pregenual dorsomedial prefrontal (dmPFC) and posterior cingulate cortices, regions associated with the affective appraisal of events as good or bad for the self (e.g. Northoff & Bermpohl, 2004; Ochsner et al., 2004). By contrast, mindfulness practitioners engaging in a metacognitive focus exhibited a pronounced shift away from midline cortical activation towards a right-lateralized network comprised of the ventral and dorsolateral PFC, as well as sensory representations in the insula and secondary somatosensory cortices. These regions may support more detached, objective interoceptive and somatic awareness (Craig, 2002) that may serve as the primitive sensory representations of the “self”. Through repeated observation of affective states as ‘objects’ of attention (Creswell et al., 2007), participants learn that emotions have their own somatic signatures, whose fluctuations in intensity and duration, provide a continuous cue for re-focusing attention (Jha et al., 2007; Brefczynski-Lewis et al., 2007), especially when allocation of scarce mental resources to maladaptive, ruminative processing has been the default (Slagter et al., 2007).

The present study investigated the effects of mindfulness training (MT) on emotional experience and its neural expression. Although mindfulness training has been associated with increases in self-reported well-being (see Grossman et al, 2004 for a meta-analysis), it remains unclear whether and how such training influences the neural representations of emotional experience. Evidence of reduced self-referential activity in favour of integrating information from viscerosomatic cortices would suggest that through this training, practitioners acquire emotion regulation skills that reduce their affective reactivity to stressful or challenging experiences. To examine the neural effects of mindfulness training on emotional reactivity, I employed fMRI to compare neural responses to sadness provocation in participants who completed a Mindfulness-Based Stress Reduction Program and waitlisted Controls.
3.5 Methods

Participants

Participants were recruited upon enrolment in the Mindfulness-Based Stress Reduction program (MBSR; Kabat-Zinn, 1990) at St. Joseph’s Health Centre in Toronto. All participants were right-handed volunteers that gave informed consent to procedures that were approved by the St. Joseph’s Health Centre and Sunnybrook and Women’s College Health Sciences Clinical Ethics Committees. There were 36 participants in total, of which 16 participants were randomly assigned to the waitlisted Control group (Controls) and were scanned before they attended MBSR, while 20 participants were randomly assigned to the mindfulness training group (MT) and were scanned after they completed MBSR. Participants were predominantly self-referred and were enrolled in the MBSR program following self-initiated registration with the Stress Reduction Clinic at St. Joseph’s Health Centre.

Measures

Beck Depression Inventory- Second Edition (BDI-II, Beck et al., 1996). The BDI-II is a 21-item, 4-point Likert scale style questionnaire measuring depressive affect and associated behavioural symptoms, with high validity and reliability. Scores range from 0-63, with clinical cutoff of 17-20, with an internal reliability of $\alpha > .9$ across both psychiatric and non-psychiatric samples. Beck Anxiety Inventory (BAI, Beck & Steer, 1990). The BAI is a 21 item, 4-point Likert scale designed to assess multiple behavioural and cognitive aspects of anxiety; scoring, validity and reliability are all similar to the BDI. Symptom Checklist 90 Revised (SCL-90-R, Derogatis, 1994). The SCL-90-R is a 90-item, 5-point Likert scale used to broadly canvass participant psychopathology across multiple positive symptom dimensions, with high ($\alpha > .8$) internal reliability in most samples.

Training Protocol

Mindfulness-Based Stress Reduction is delivered by an instructor in eight weekly two-hour group sessions involving up to 25 participants. Mindfulness is taught through lying, sitting, walking or eating meditations and yoga. The program includes daily homework of CD-guided and self-guided mindfulness practices, designed to increase moment-by-moment non-judgmental awareness of bodily sensations, thoughts and feelings, together with the application of awareness
skills into daily life. Participants learn to cultivate an acceptant mode of response to experience, in which they intentionally face difficulties and discomfort, and to develop a metacognitive perspective on thoughts and feelings, in which these are viewed as passing events in the mind.

**Sadness Provocation**

Participants viewed four sets of film clips, with audio. Each set of clips came from a different source; neutral clips from television programs on gardening and woodworking, and sad clips from the films ‘The Champ’, and ‘Terms of Endearment’. Sets of clips were 3 minutes long and were edited into four 45 second clips. Clips were shown in their original order from each film with an interspersed 30 s reflection period between clips. At the end of each reflection period participants had 6 s to rate their level of sadness on a 5 point Likert scale. Sets of film clips were always shown in the order neutral/sad/neutral/sad to limit the amount of emotional contagion between blocks.

**Procedure**

The experiment was conducted in two runs, with one set of neutral and sad films (composed of 4 clips each) presented in each run. A sample run would involve presentation of the four neutral film clips (45 sec each) interleaved with rest periods between each clip (30 sec each), followed by a resting state period for 36 seconds, then followed by 4 sad film clips interleaved with rest periods. Prior to each set of film clips a 10 second instruction screen appeared to orient the participant to the viewing task. The resting periods at the beginning, middle, and end of each run constituted the basis for the implicit baseline used to investigate the independent effects of sad and neutral films. Questionnaire data was collected in separate interviews at St. Joseph’s Health Centre.

**Image Acquisition**

Images were collected on a 3-T Signa MRI system (CV/i hardwarne, LX8.3 software; General Electric Medical Systems, Waukesha, Wis.) with a standard quadrate birdcage head coil. *Functional MRI (fMRI)* was conducted using T2*-weighted single-shot spiral in-out k-space trajectories optimized for sensitivity to the blood-oxygenation-level-dependent (BOLD) effect (TE/TR/flip angle = 30 ms/2000 ms/70 degrees, 20 cm field-of-view (FOV), 5 mm slice thickness, 64 by 64 matrix, 26 slices in axial oblique orientation.
Image analysis

Data pre-processing and analysis were performed using Statistical Parametric Mapping (SPM5). Time series functional data was spatially co-registered and motion-corrected, and then normalized into a common stereotactic reference space (MNI) and spatially smoothed (FWHM=6mm). FMRI responses to each event were modeled by a canonical hemodynamic response function scaled to film clip duration. At the first level of analysis (within-subject), contrast images were calculated between sad and neutral film conditions; the ensuing contrast maps were then entered in a separate second-level random effects analysis for each group to investigate neural response to emotion challenge. Follow-up comparisons of each condition to a common baseline were made by comparing sad and neutral film clip activity to SPM’s implicit baseline, which includes all unmodelled time points, i.e. task unrelated activity between film viewing periods. For the between group differences in emotional challenge reactivity, participant sad vs. neutral difference maps generated at the first level of analysis were subjected to a two-way mixed ANOVA between the Control and MT groups and the Neutral and Sad film viewing conditions. Cluster thresholding was applied to increase power in identifying heavily recruited neural areas while maintaining a reasonably low Type-I error rate. Only clusters of activation yielding k >= 10 voxels at the uncorrected activation thresholds of p < .001 were considered, yielding a functional threshold equivalent of p < .0001 (Forman et al., 1995).

To further characterize between-group differences in emotional reactivity, functionally defined ROI clusters were identified from the between-group independent samples t-test. ROIs were constructed using a 6mm radius sphere around the peak voxels from the ROI-identifying contrast, and extracting the mean signal from this sphere from both the sad and neutral film conditions. To relate altered neural activity to patient with patient symptom measures, task-related signal from each of these ROIs was tested for correlation with the Beck Depression Inventory, Beck Anxiety Inventory, and the Symptom Checklist-90.

3.6 Results

Emotion ratings

Mood ratings were collected over four time points for both neutral and sad films. Data was subjected to a 2 (Control vs. MT) X 2 (sad vs. neutral film) X 4 (time point) mixed model
ANOVA. Main effects of sadness, F(1,34) = 206.73, \( p < .001 \), suggested that the sad films induced a reliably greater dysphoric mood than the neutral films. A main effect of time point was also found, F(3,102) = 28.67, \( p < .001 \), which was qualified by an interaction between film type and time point, F(3,102) = 33.36, \( p < .001 \); simple effect analyses suggested that sadness increased upon viewing consecutive sad, but not neutral, film clips. Sadness ratings did not differ between the Control and MT groups, F(1,34) = .714, \( p = .403 \).

Clinical effects of mindfulness training

Control and MT participants did not differ in age or gender distribution. All participants showed moderate levels of depression and anxiety, according to the clinical cut-offs on the Beck Depression Inventory (BDI; Beck & Steer, 1987), Beck Anxiety Inventory (BAI; Beck & Steer, 1990) and Symptom Checklist-90-Revised (SCL-90; Derogatis, 1997), with no significant differences between the groups prior to mindfulness training. The MT group showed substantial reductions in depression, anxiety and somatic distress following training (see Table 1). Thus, while both groups demonstrated equivalent and moderately high pre-training levels of self-reported psychopathology, the MT group showed significant training-related improvements on all three scales.

Neural Correlates of Sadness Provocation

I first examined the neural correlates of sadness in the Control group (Figure 3.1A). Sadness provocation revealed a midline network of activation associated with ruminative and self-reflective processing (Supplementary Table 3.1); including the ventral medial prefrontal cortex (vmPFC, BA 11) dorsal medial prefrontal cortex (dmPFC, BA 9/32) and a wide expanse of the posterior cingulate extending from the retrosplenial cortex (BA 29) dorsally through to the precuneus (BA 23). Induced sadness was also associated with predominantly left-sided activations, including the left dorsolateral prefrontal cortex extending into the left operculum including Broca’s area (BA 9/10/46/47), left mid-temporal gyrus (BA 21), and in bilateral caudate, as well as on the right hippocampus, cerebellum, and temporal parietal junction (BA 41/42).

Mood provocation also led to robust cortical deactivations (reductions relative to the neutral film condition) in the right viscerosomatic cortices, peaking in the right insula and
extending rostrally into the anterior right amygdala and subgenual anterior cingulate cortical (subgenual ACC) regions (BA 25), and caudally into the right superior temporal gyrus (BA 22) (Figure 3.1B). Deactivations were also found bilaterally in superior parietal regions (BA 7/40), extending rostrally and medially into the mid-cingulate (BA 24) and somatosensory cortices (BA 3/4/5). Several other deactivated clusters were detected, including the dorsal and ventral extents of the right lateral prefrontal cortex (BA 45-47), left dorsolateral prefrontal cortex (BA 46), the bilateral parahippocampal gyrus (BA 36/37) extending on the left side through the fusiform gyrus (BA27), and in the right superior temporal gyrus (BA 21). Several deactivations in bilateral motor and supplementary motor regions were also observed (BAs 4 & 6).

Effects of Mindfulness Training on the Neural Correlates of Sadness Provocation

To examine the effects of MT on induced sadness, the sad film vs. neutral film viewing differences were contrasted between the Control and MT groups (see Supplementary Table 3.2 for areas significantly related to sadness in the MT group). These analyses revealed areas reliably linked to sadness provocation whose reactivity was also sensitive to mindfulness training (Table 3.2, Figure 3.2). Primarily two classes of between group difference were observed, both of which indicated reduced reactivity to the sadness challenge: i) areas deactivating with sadness provocation (deactivating regions) in Controls, but not in the MT group and ii) areas activating with sadness provocation (activating regions) in Controls, but not in the MT group.

Deactivating Regions. The MT group showed greater signal intensity relative to Controls in the right basal ganglia extending dorsolaterally into the right insula and claustrum, the right subgenual ACC (BA 25) and gyrus rectus (BA 11) extending into the ventromedial prefrontal cortex, the right ventrolateral prefrontal cortex (BA 45), and the right superior frontal gyrus (BA 9). Follow up ROI analyses revealed that in areas where sadness evoked deactivations in Controls, there was little neural reactivity in the MT group, i.e. there were few areas with distinct levels of activation during sad relative to neutral film clip viewing. This indicated that regions of relatively increased activity in MT represent a recovery from the deactivations related to sadness found in Controls (Figure 3.2).

Subsequent analyses of deactivating regions using the implicit baseline (composed of resting state activity between film clips) demonstrated that variance from the resting state in areas such as the right insula was much greater in the Control group than in the MT group, with
both reliable activations and deactivations from the global mean during sad film clip viewing in the Control group, \( t(15) > 2.19, p < .05 \), but with no reliable changes in the MT group (Figure 3.1, Panel C). Similar profiles of higher neutral film activation and sad film deactivation versus the global mean were also observed in the subgenual and ventrolateral cortices. These results support the notion that the deactivating regions observed were driven by generalized greater reactivity in the Control group, as the source of this reactivity seems to stem from both elevated activation in the neutral film clip condition, and deactivations in the sad film clip condition.

**Activating Regions.** The MT group also showed reductions relative to Controls in posterior cortical midline areas such as the right precuneus/posterior cingulate (BA 7/31), and left-lateralized reductions in the prefrontal cortex (BA 45) and frontal operculum / Broca’s area (BA 47), superior temporal Sulcus / Wernicke’s area (BA 42/22) and inferior temporal gyrus (BA 21). ROI analyses revealed that the deactivations in MT represent a reduction of activations related to sadness (Figure 3.2). Subsequent analyses of activating regions using the global mean revealed that while neutral films led to equivalent deactivation relative to the resting state between the two groups, \( t(34) = .2, \text{n.s.} \), sad films reliably activated areas such as the precuneus and mPFC, and the degree of activation was reliably greater in the Control than the MT group, \( t(34) = 3.40, p < .002 \), suggesting that it is primarily the sad film condition driving the reactivity scores (Figure 3.1, Panel C for the Control group).

**Post-Hoc Comparisons**

To more sensitively assess training-related changes, a more liberal post-hoc analysis (\( p < .05 \)) was conducted restricted to the reliable regions of reactivity in the Control group (Control ROIs; Supplementary Table 3.1) to determine whether these established regions of emotional reactivity were differentially recruited in the MT group. In addition to the areas described in the between-groups analysis above (Table 2), several other left-lateralized activating Control ROIs demonstrated reduced activity in the MT group, including the Broca’s area (BA 47/48), the left ventromedial prefrontal cortex (BA 11), right temporal junction (BA 41/42), and right cerebellum. Of the deactivating Control ROIs, the somatosensory/middle cingulate clusters (BA 3/4/5/40) bilaterally demonstrated reduced deactivations, as well as some additional right-lateralized clusters such as the supplementary motor area (BA 6), and superior temporal (BA 21)
clusters. By contrast, none of the motor or parahippocampal clusters showed between-group differences in reactivity.

To assess the presence of novel reactivity following mindfulness training, the same ROI-based between-group comparison was performed on clusters of reactivity in the MT group (MT ROIs; Supplementary Table 3.2). Relatively few of the MT ROIs demonstrated altered activity between groups compared to the number of Control ROIs. Only the left hippocampus and right inferior orbitofrontal (BA 47) clusters demonstrated reliably greater reactivity in the MT group, and only the left inferior frontal gyrus (BA 9) and right cerebellum demonstrated greater deactivations in the MT group.

Effects of Mindfulness Training on Neural Reactivity and Clinical Symptoms

Correlation analyses was run using each participant’s mean signal scores from the reactivity ROIs and their BDI, BAI and SCL-90 scores, thus capturing between-group variance in clinical outcome. One participant was excluded from the MT group for not providing post-training outcome scores. Of the three scales, only the BDI was reliably correlated with the ROIs, demonstrating a negative correlation with the right insula ROI, $r(34) = -.465$, $p < .005$, and the right LPFC, $r(34) = -.406$, $p < .02$, such that higher BDI scores were related to greater deactivations in these regions (Figure 3.3). A positive correlation was also detected between BDI scores and left superior temporal sulcus, $r(34) = .542$, $p < .001$, in an area corresponding to Wernicke’s area. Notably, the right insula and right LPFC ROIs, both sadness-deactivating regions, were negatively correlated with activity in the Wernicke’s ROI, a sadness-activating region, $r(34) > -.501$, $p < .001$, suggesting an opponent relationship between left-sided language and right-sided interoceptive areas. No ROIs demonstrated correlations with symptom change scores in the MT group, nor with pre-training scale scores.

3.7 Discussion

This study represents the first neuroimaging investigation of changes in emotion regulation associated with mindfulness training. Sadness provocation was associated with elevated self-reported ratings of sadness, accompanied by activation along the posterior and anterior regions of the cortical midline, as well as in left-lateralized language and conceptual processing centers. These cortical areas are characteristic of cognitive elaboration, increased self-
focus, and ruminative problem solving that would be typical of reappraisal processes (Ray et al., 2008; Ochsner & Gross, 2008). Sadness provocation was also associated with widespread deactivations in posterior parietal attentional regions, somatosensory cortex, right insula and right ventral and dorsolateral prefrontal regions, as well as the subgenual anterior cingulate (ACC), areas that may contribute information important to the primary appraisal of emotion (Craig, 2002). In the context of work on different forms of self-focus (Farb et al., 2007), such findings are consistent with the notion of a cognitively evaluative neural network responding to emotion challenge, accompanied by the simultaneous deactivation of a viscerosomatic-centered experiential network (Figure 3.1).

Examining the effects of mindfulness training, I found that despite similar levels of self-reported dysphoria, the MT group demonstrated less neural reactivity to sadness provocation than the Control group. While both groups showed some recruitment of sadness-related activation along midline cortical areas associated with self-referential processing, the MT group demonstrated reduced reactivity both medial and lateral regions. In particular, the MT group demonstrated reduced activation in the cortical midline regions associated with autobiographical memory retrieval and self-referential processing (Cavanna & Trimble, 2006), and in classical language areas like the left posterior superior temporal gyrus (Wernicke’s area) and the left frontal operculum (Broca’s area). The MT group also demonstrated reduced deactivations, in that the lower BOLD response during sad relative to neutral films was significant in the Control group, but not in the MT group. The presence of deactivating regions suggests that part of the neural response to emotional challenge may involve the down-regulation of these regions. Specifically, the reduced deactivation in the insula during dysphoric challenge may therefore be associated with increased interoceptive awareness (Critchley, 2004), while altered subgenual ACC activity, a region of strong anatomical connections with the insular cortex (Barbas et al., 2003), has also been observed in the recovery of patients with mood disorders (Goldapple et al., 2004; Figure 3.2). While there are several plausible accounts for reduced neural reactivity in the MT group, similar self-reports of sadness across both groups makes it unlikely that these effects are simply due to a blunting of emotional experience or impairment in affective processing, but instead suggests a more fundamental change in regulatory response. The equivalence of sadness ratings between groups also undermines the suggestion of demand characteristics at play, implying that the change in regulatory response is not simply a product of participant
expectations. Recent research has associated mindfulness training with reductions in emotional interference following the viewing of affective pictures (Ortner, Kilner & Zelazo, 2007). The neural patterns observed in the present study suggest that the reduced emotional interference associated with mindfulness may stem from the objectification of emotion as innocuous sensory information rather than as an affect-laden threat to self requiring a regulatory response. A plausible mechanism of action for mindfulness effects may include the development of metacognitive skills for detached viewing of emotions, rather than the elaboration of emotional content through cognitive reappraisal.

Volitional emotion regulation is traditionally predicated on cognitive strategies for reappraising aversive events in unemotional terms, or behavioural strategies for suppression of emotion-expressive behaviour (Goldin et al., 2008; Schmitz & Johnson, 2007). However, a number of studies now point to compromised medial frontal modulation of limbic circuitry as underlying ineffective regulation of negative emotion (Johnstone et al., 2007; Ressler et al., 2007). Compared to controls, effortful down regulation of sadness via reappraisal is rated as more difficult by mood disorder patients (Keightley et al., 2003) and is shown to be less successful in decreasing limbic activation (Craig, 2002). In the presence of these disrupted neural circuits, especially in at-risk populations, strategies for generating positive affective appraisals may paradoxically reactivate existing negative appraisals. The use of mindfulness training to shift regulation strategies from medial and left-lateralized cortical regions supporting cognitive-affective representations of the self to more lateral viscerosomatic representations of body state may be one such example. In the present study, left-lateralized language areas were activated during mood challenge in Controls, and such activation was negatively correlated with right insula recruitment. The MT group by contrast, showed reduced reactivity in both regions, resulting in an attenuation of the negative relationship between the two regions. Disengaging reappraisal of negative affective content, in favour of engaging attention towards sensory integration, would allow for the generation of novel affective appraisals rather than attempting to manipulate an existing negative cognitive set (Garland, 2007).

The idea that interoceptive recovery is important for successful emotion regulation is strongly supported by the negative correlation observed between BDI scores and right insula activation: this finding suggests that the participants experiencing the least dysphoria actually possessed the highest interoceptive activation in context of a dysphoric emotional challenge.
(Figure 3.3). Furthermore, right insula and right LPFC activity was negatively correlated with activity in Wernicke’s area, suggesting that there may be some tradeoff between language and interoception-based reactions to mood challenge, with more language-laden regulatory efforts predicting higher BDI scores. Mindfulness training may reduce reliance on secondary appraisal systems in response to dysphoric challenge, an imbalance which predicts depressive symptoms.

Several limitations are apparent in the interpretation of the present data. While the present findings are based on comparisons among randomly assigned pre- and post-treatment participant groups, testing the same individuals before and after treatment would have warranted stronger conclusions regarding the temporal effects of mindfulness training, but at the expense of controlling for carryover effects. In addition, gauging the frequency of mindfulness practice over the 8-week program would have permitted testing the relationship between mindfulness practice and the establishment of neural balance in response to affective challenge. The variance in participant practice over an 8-week period was, however, not large enough to be used as a predictor of training outcomes as most participants reported similar levels of practice during the course, approximately 75% adherence to assigned homework hours each week. While the present results help to explain the effects of mindfulness on affective reactivity in a mixed community sample, recruiting a carefully diagnosed clinical sample would have enabled us to answer specific questions about emotion regulation in clinical depression or other disorders. Similarly, comparisons against an active control group would be needed to tease apart alternative explanations of enhanced emotion regulation, such as group support and destigmatization, which are unrelated to MT. Nevertheless, this study is the first of its kind to implicate specific neural mechanisms of emotion regulation as potentially underlying the effects of mindfulness training, and can inform these future efforts.

Affective reactivity, seen in the combination of cortical midline and language area recruitment and viscerosomatic suppression, characterized participants undergoing dysphoric mood provocation. By balancing participants’ regulatory responses to sadness with co-ordinated monitoring of less valenced and more sensory visceral information, mindfulness may represent one neural path for reducing affective reactivity and disorder vulnerability.
Chapter 4

4 Interoceptive and Exteroceptive Attention

4.1 Rationale

Numerous studies have examined the neural basis of attending to the exteroceptive senses, advancing our understanding of how the brain senses the external world. However, there have been few accounts of how attention modulates interoception, sensation of the world inside our bodies. Critically, interoception may represent an oft-ignored mechanism for self-reference, as it appears to be strongly associated with the momentary rather than extended self. In this third and final thesis study, I therefore examined how focal attention influenced primary and secondary interoceptive cortical activity during breath monitoring, and functional plasticity in these representations following 8 weeks of daily interoceptive training associated with the MBSR course.

Using mindfulness training to improve access to the momentary self, the first two studies investigated how such expertise impacts self-reference and emotion regulation respectively. However, even if the hypotheses in these studies are validated, the mechanisms by which mindfulness training impacts self-reference will only have been assessed in terms of their consequences on self-reference and emotion. Presumably, mindfulness training more directly impacts attention systems in the brain which are recruited during self-reference and emotional challenge. However, the right-lateralized network hypothesized to support experiential self-reference is not conventionally recruited by neuroimaging studies of attention, which tend to activate frontal and parietal cortices instead (e.g. Corbetta & Shulman, 2002; Wendelken et al., 2007). Since MBSR focuses predominantly on interoceptive sensory afferents, this disparity in implicated attention networks may be a consequence of different targets of attention rather than a separate attention network. On the other hand, it may be that the process of interoceptive monitoring recruits a distinct attention network dedicated towards the generation of experiential representation, which organizes information independently from attention towards objects outside of the body.
In this third study I therefore undertook to examine: 1) what networks support attention to interoceptive versus exteroceptive events; 2) whether the voluntary deployment of attention modulates primary and secondary interoceptive cortical representations; and 3) if these cortical representations are amenable to functional plasticity with increased interoceptive monitoring practice.

4.2 Study 3 Hypotheses

4.2.1 EA (relative to IA) will recruit a ‘traditional’ attention network involving the cortical midline, dorsolateral prefrontal cortices, and inferior parietal cortices, as well as the visual cortices serving as sensory afferents in the EA tasks.

4.2.2 IA (relative to EA) will recruit a novel network consistent with the experiential network, including the right insula and somatosensory association cortices, as well as primary interoceptive cortex in the posterior insula and primary somatosensory cortex in the post-central gyrus.

4.2.3 Mindfulness training will selectively improve recruitment during IA relative to EA, increasing cortical representation of IA, especially in the right insula.

4.3 Abstract

Numerous studies have examined the neural basis of attending to the exteroceptive senses, advancing our understanding of how the brain senses the external world. However, there have been few accounts of how attention modulates interoception, sensation of the body’s internal state. I examined how focal attention influenced primary and secondary interoceptive cortical activity when directed towards the interoceptive stimulation associated with breathing, and found functional plasticity in these representations following 8 weeks of daily interoceptive training via a mindfulness meditation course. Moreover, I controlled for the attentional demands of interoception with exteroceptive visual tasks requiring cognitive maintenance and suppression. In both untrained and mindfulness trained groups, exteroceptive attention (EA) was associated with modulation of striate and extrastriate visual cortices as well as recruitment of the dorsolateral prefrontal, superior parietal, and frontal opercular cortices, including the agranular insula. By contrast, interoceptive attention (IA) was associated with modulation of bilateral
granular and dysgranular regions of the insula, consistent with primary and secondary interoceptive cortices, as well as the hippocampus, mid-cingulate cortex and the precuneus. Region of interest analyses of the insula revealed a gradient of IA to EA recruitment along its posterior-anterior axis, consistent with increasing multisensory integration. Mindfulness training altered this gradient, resulting in increased recruitment of the right anterior dysgranular insula during IA. These findings dissociate attention networks for monitoring exteroceptive and interoceptive signals, and suggest that interoceptive attention modulates primary interoceptive cortical representations. Furthermore, the anterior dysgranular insular cortex demonstrates neural plasticity in its modulation by interoception attention.

4.4 Introduction

Attention allows for the selection and maintenance of behaviourally relevant signals, while suppressing contextually irrelevant information. Attending towards a particular sense selectively enhances domain-specific cortical representations, in vision (Brefczynski & Yoe, 1999), hearing (Hall et al., 2000), touch (Bauer et al., 2006), taste (Veldhuizen et al., 2007), and olfaction (Zelano et al., 2005), suggesting that attentional modulation of sensory representation is a fundamental principle of the human nervous system. In contrast to this rich history of studying the exteroceptive senses, little is known about interoception, attention to the body’s internal state, proposed by William James in 1890 to be the basis for the experience of emotions.

While the exteroceptive senses have well-defined sensory cortical regions, it was once argued that interoceptive afferents were too diffuse to allow for a primary sensory interoceptive region and associated awareness (Cannon, 1927). However, a lamina I spinothalamocortical pathway was recently proposed to carry sympathetic afferents that signal the physiological condition of all tissues of the body (Craig, 2002); these inputs project to the posterior granular and mid dysgranular regions of the insular cortex, serving as primary interoceptive cortex (Flynn, 1999). Further propagation of interoceptive signals to the anterior insula has been argued to reflect the integration of afferent physiological signals with higher-order contextual information (Craig, 2009; Critchley, 2005), consistent with an account of the anterior insula serving as an interoceptive association cortex.
However, despite arguments for its role in interoception, anterior insular activity is also commonly associated with exteroceptive tasks requiring cognitive control (Derfuss et al., 2005; Duncan & Owen, 2000), such as the suppression of irrelevant information (Aron et al., 2004). Since suppression of salient external stimuli may be required to detect weaker interoceptive signals, anterior insula activity during interoception is confounded with suppression, especially since most visceromotor activity, such as the heartbeat, is poorly detected (Khalsa et al, 2008). To maximize the potential for detecting interoception-related neural modulation, the present study considered a more powerful generator of viscerosensory signals: respiration. Respiration is unique among interoceptive sources as it is generally amenable to direct voluntary control and conscious inspection. Consequently, respiratory attention may powerfully engage cortical viscerosensory regions in addition to regions supporting attentional suppression and maintenance.

Extending beyond transient attention effects, attention training has been associated with domain-specific enhanced perceptual and cortical recruitment (Sasaki et al., 2010; Yotsumoto & Watanabe, 2008). Accordingly, in the present study I examined the potential for attentional modulation of the viscerosensory representation in the insula. Mindfulness meditation promotes interoception through daily practice in monitoring one’s breathing (Kabat-Zinn, 1982). Morphometric studies have associated greater insula grey matter volume with long term meditation practice (Holzel et al., 2007; Lazar et al, 2005), but the plasticity of interoceptive insular recruitment is still unproven. To address these questions, I used functional magnetic resonance imaging (fMRI) to contrast interoception against exteroception conditions. The manipulation was performed in an untrained group waitlisted to receive mindfulness meditation training and a second group with 2 months of mindfulness meditation training.

4.5 Methods

The present study contrasts interoceptive attention (IA) to the internal sensations of the breath against exteroceptive attention (EA) to visually-presented word stimuli. Exteroceptive attention was operationalized through a combination of two tasks that involved processing of an external stimulus that were selected to control for different potential executive function demands related to interoceptive attention: 1) 1-back: maintaining a stimulus representation online in working memory, and 2) cognitive suppression: suppressing internal responses to external stimulus representations. Maintenance may be necessary for observing changes in stimulation
from one moment to the next. Suppression may be necessary for inhibiting competing sources of external stimulation to focus attention on interoceptive signals. Both maintenance and suppression have been shown to recruit common neural networks that include regions such as the lateral prefrontal and posterior parietal cortices (Bunge et al, 2001; Wendelken et al., 2007), and together allow for discrimination of interoception-specific neural activity while controlling for attentional demands.

**Procedures**

*Participants.* Participants were recruited through the Mindfulness-Based Stress Reduction (MBSR) program at St. Joseph’s Hospital in Toronto, and were randomly assigned to being tested before training began (untrained group), or following completion of the 8 week course (trained group). The untrained group included twelve women and four men (N = 16; mean age 42.00 ± 9.24), while the trained group included fifteen women and five men (N = 20; mean age 45.55 ± 13.38). All participants were right-handed, healthy volunteers that gave informed consent to procedures that were approved by the Sunnybrook and Women’s College Health Sciences Clinical Ethics Committee. Participants were financially compensated for their participation and time.

*Training Procedure.* Participants were trained on the distinction between the three experimental tasks, breath monitoring (“Breathe”), cognitive suppression (“Suppress”), and working memory maintenance (“Maintain”) prior to fMRI data acquisition. For the Breathe task, participants were instructed to fix their gaze upon a fixation cross presented in the center of their visual field, and to attend to the sensory aspects of their breath, i.e., in the nose, throat, chest and diaphragm, without intentionally altering their respiratory rhythm. In the event of mind-wandering, participants were asked to calmly return their attention to the breath. For the Suppress task, participants were instructed to read foveally-presented words, but to inhibit any sort of subsequent cognitive or emotional response, to keep their minds blank while attending to the visually-presented word stimulus. For the Maintain task, participants were asked to make a key press whenever the same word was repeated (a ‘1-back’ task). Each task was preceded by an instruction screen consisting of a visual cue picture and above the task name.

*Experimental Task.* The block design experiment was composed of alternating blocks of interoceptive (Breathe) and exteroceptive (Maintain or Suppress) attention tasks. Each condition
had a 36 second duration and was immediately preceded by a 10 second instruction screen with a condition cue to inform and prepare participants for the next task. One run in the scanner consisted of two repetitions of each condition and each participant completed two runs. The condition order was randomized for each participant.

In the Suppress and Maintain tasks, a single word appeared on the screen for 4 seconds in duration, followed by a 2 second interstimulus interval during which a blank screen was presented, a 6 sec total duration which approximates the average respiration rate in humans (Sherwood, 2006), thereby matching the durations of word and breath stimuli. In the Maintain task, only one word in each block was repeated in a randomized position in the word list. Before scanning, participants received approximately 45 minutes of instructions and training on the fMRI environment and a variety of experimental tasks.

Verbal Stimuli. To approximate the self-focus demands of the breath monitoring task, personality trait adjectives were chosen as word stimuli for the Maintain and Suppress tasks. Eight sets of word lists were constructed from a well-established list of personality-trait words (Anderson, 1968), which lend themselves to deep levels of processing (e.g., Craik & Lockhart, 1972). Word lists were randomly assigned to each condition.

Imaging Setup. Imaging data was collected with a Signa 3-T MRI system (CV/i hardware, LX8.3 software; General Electric Medical Systems, Waukesha, Wis.) with a standard quadrate birdcage head coil. Stimulus presentation was controlled by the Presentation software package (version 9.81; Neurobehavioural Systems, Inc., Albany, Calif.). Low-amplitude transistor-transistor logic pulses were monitored via a parallel port cable to synchronize slice acquisition and stimulus delivery with millisecond accuracy. Stimuli were presented on a rear-mounted projection screen, set at a (native) 1024x768 resolution.

Structural imaging. For each participant, a three-dimensional magnetization-prepared rapid acquisition gradient echo pulse sequence was used to obtain a high-resolution T1-weighted structural volume. The imaging parameters were as follows: repetition time (TR) = 2000 ms; echo time (TE) = 2.63 ms; matrix = 256 X 192; FOV = 256 X 256; slice thickness = 1.3 mm thick; 192 oblique axial slices; total acquisition time = 6.5 min.

Functional Imaging. Functional MRI (fMRI) was conducted using T2*-weighted single-shot
spiral in-out k-space trajectories optimized for sensitivity to the blood-oxygenation-level-dependent (BOLD) effect (TE/TR/flip angle = 30 ms/2000 ms/70 degrees, 20 cm field-of-view (FOV), 5 mm slice thickness, 64 by 64 matrix, 26 slices in oblique axial orientation, improving the capability to acquire fMRI signals in regions of high magnetic susceptibility (Glover, 2001). The first 10 images in each run were discarded to remove scanner equilibration effects.

Data Analysis

Respiration Analysis. In the interoceptive condition, participants were directed to attend to the internal sensations associated with breathing. However, while meditation training may alter awareness of the breath, many accounts of meditative practice have also documented respiratory slowing effects (e.g. Jevning, Wallace & Beidebach, 1992), which in turn can influence the BOLD response (Birn et al., 2006). To control for any interaction effects of respiratory change between interoceptive and exteroceptive conditions and between trained and untrained participants, respiration phase, rate and volume for each TR of scanning were derived from a respiration belt worn by participants during the scanning session. Respiratory phase (the cycle of inspiration and expiration) is linked to motion-related noise in fMRI data and was used as a nuisance regressor in the first level of analysis. Since changes in respiratory pattern could also confound activation differences between task blocks, respiratory rate and respiratory volume per time (RVT) were also included at the second (between subjects) level of analysis as nuisance covariates. RVT is used as an index of respiratory efficiency, and has been linked to respiration-related fMRI effects (Birn et al., 2006).

The respiratory belt signal was sampled at 40 Hz and analyzed for each participant in Matlab (R2009b). Respiratory signal was linearly detrended, and a low-pass butterworth filter was applied to remove respiratory frequency greater than .5 Hz (patterns of breathing faster than 1 breath per 2 seconds), based on the absence of high power peaks above this frequency across participants. Respiratory peaks and troughs were then estimated using a counting method, which was corroborated with visual inspection of peak and trough placement, and whose primary frequency estimates correlated highly with a fast fourier transform of the data (r > .8 for all participants). Respiratory phase was modeled by coding TRs containing peaks as ‘1’, troughs as ‘-1’, and TRs containing either both peaks and troughs or neither as ‘0’. To assess respiratory rate, that mean time between respiration signal troughs was calculated for each TR using a 5 TR
sliding window centered on the TR in question. To assess respiratory volume per time (RVT), respiratory signal change from peak to the average of the two surrounding troughs was computed and divided by the time between the two troughs.

**Preprocessing.** Functional activation was determined from the BOLD signal using Statistical Parametric Mapping (SPM5, University College London, London, UK; http://www.fil.ion.ucl.ac.uk/spm/software/spm5). Following reconstruction (SPM5 DICOM import utility), the time series functional data were spatially co-registered and re-aligned to correct for motion within and between functional scans (translational motion parameters were less than 1.5 mm for all participants) and co-registered with their T1-weighted structural image. The T1 image was bias corrected and segmented using template (International Consortium for Brain Mapping) tissue probability maps for gray-white matter and CSF. Warping parameters were obtained from the tissue segmentation procedure and subsequently applied to the time series data (resampling to 3 mm³ voxels). Warping parameters were used to normalize the data into a common stereotactic reference space (MNI); the time series data was then spatially smoothed to a 6mm³ full-width half maximum Gaussian kernel. Finally, to control for changes in the global BOLD response across the time series, a global mean detrending procedure was applied (Macey et al., 2004).

**First-level statistical models.** Following preprocessing, single subject time series were submitted to a first-level general linear statistical model (Friston et al., 1994). Using the SPM5 design specification, task-specific boxcar stimulus functions were convolved with the canonical hemodynamic response function (HRF), modeling the onsets of the Breathe, Suppress, or Maintain tasks. Each model included within-session global scaling and the AR1 method of estimating temporal autocorrelation, as well as corrections for respiratory phase (detailed above). Due to technical difficulties, only 7 of the 16 participants in the untrained group had complete respiration data; all results discussed below therefore have been tested with the full cohort of untrained participants as well as with the reduced sample with respiration data. Result values are reported for the full cohort, but are only reported where both models achieved statistical significance.

**Second-level statistical models: whole brain analysis.** To examine differential effects of attentional focus (interoceptive vs. exteroceptive) and training (untrained vs. trained), positive
effect $t$ contrasts for each experimental condition (Breathe, Suppress & Maintain) were examined at the second level using a full-factorial mixed-model ANOVA. Within this model, the Breathe condition was weighted against the Suppress and Maintain conditions to form the Attention contrast. Group level $t$ contrasts for Attention effects used a false-discovery rate threshold of $P_{FDR} < .05$ and voxel extent of $K > 10$ as base thresholds. To more closely examine potential breathing rate-related confounds and to perform exploratory analyses, I applied a reduced height threshold of $P_{unc} < .005$, but an increased voxel extent threshold of $K > 30$. Respiratory rate and RVT were included as nuisance covariates in the model for each participant in each of their three attention tasks.

**Second-level statistical models: Region of Interest Analysis.** Eight gray matter regions of interest (ROIs) were selected according to the anatomical divisions of the insular gyri as defined on a high-resolution T1-weighted template anatomical volume, based on well-characterized cytoarchitectonic divisions (Mesulam & Mufson, 1982; Chikama et al., 1997). Insular gyri ranged from the anterior accessory gyrus, through the short and long gyri of the middle insula, and into the short and long gyri of the posterior insula (Craig, 2009). Since the cellular layer divisions of the insula do not neatly segregate by gyrus in anterior insula zones, the accessory and short gyri were also partitioned into dorsal and ventral zones to characterize the anterior insula distinction between dysgranular and agranular cellular layers (Chikama et al., 1997). The dorsal zone encompassed the anterior long, posterior short, middle short, and dorsal aspects of the anterior short, and accessory gyri. The ventral zone encompassed the posterior long and ventral aspects of the anterior short and accessory gyri. Insular ROIs were hand drawn on each anatomical slice using the MRIcron software package (http://www.sph.sc.edu/comd/rorden/mricron/), selecting only gray matter aspects of the gyri, and were exclusively masked to ensure that no overlapping voxels were selected (Figure 4.1). All ROIs covered a functional imaging volume of at least 27 voxels, comparable to 6mm spherical ROIs but mapped along the cortical surface.

In the ROI analyses, mean time courses were extracted from each ROI using the MarsBar toolbox for SPM (http://marsbar.sourceforge.net). Percent signal change estimates of task-related block activity were obtained using the same general linear model of interoceptive and exteroceptive attention conditions used in the whole-brain analyses. The signal peaks for interoceptive and exteroceptive attention were entered into separate statistical analyses using
MarsBar to determine percent signal change for each participant in each attention condition for each ROI. Mean percent signal changes from these seed regions were extracted for both the interoceptive and exteroceptive attention conditions. Difference scores between attention conditions (interoceptive – exteroceptive) were calculated within-subject for each region to represent the attentional tuning of that region.

4.6 Results

Respiration Analyses

Overall, participants breathed at a frequency of .21 Hz, or 12.5 breaths per minute, which is consistent with the population average observed respiration rate (Sherwood, 2006). Participant respiratory frequency distributions differed between interoceptive and exteroceptive attention conditions, with slower respiration during IA than EA (Figure 4.2, Panel A). To formally test for this difference, mean respiratory signals were analyzed as a function of attention condition, with 1) respiration rate, 2) volume, and 3) respiration volume / time (RVT; a measure of respiratory efficiency), each analyzed separately in 2 (group) X 2 (attention) mixed model ANOVAs.

For respiratory rate, a significant main effect of attention was found ($F_{(1,25)} = 9.607, p = .005$), with slower respiration for interoception than exteroception. However this main effect was driven by an interaction between attention and group ($F_{(1,25)} = 6.620, p = .016$) with interoceptive slowing in the trained group relative to the untrained group: trained participants’ respiratory frequency slowed by approximately .05 Hz or 3 breaths per minute during interoception, while untrained participants did not slow their breathing (Figure 4.2, Panel B). Respiratory volume showed a complimentary pattern of results, with a main effect of attention demonstrating greater volume during interoception ($F_{(1,25)} = 10.265, p = .004$). The attention x group interaction for volume was also significant ($F_{(1,25)} = 8.330, p = .008$), with reliably greater volume for the trained group interoception condition than the other experimental conditions (Figure 4.2, Panel C). Despite the slower and deeper breathing uniquely associated with interoception in the trained group, respiratory efficiency (RVT) was equivalent across groups, with no significant main effects or interaction. RVT has been shown to be a confounding predictor of gray matter activity independent of activation associated with respiratory motion (Birn et al., 2006) and thus, is most
essential to control in investigating a task that may alter both the mechanics and perception of the respiratory signal. Critically, our two groups did not differ on RVT.

To confirm that respiration differences were limited to rate and volume but not efficiency (RVT), the relationship between rate and volume was examined in a correlation analysis, using rate and volume estimates from each participant task block (Figure 4.2, Panel D). Respiratory rate was strongly negatively correlated with respiratory tidal volume ($r_{(214)} = - .85, p < .001$), such that faster breaths were shallower; however, this rate/volume relationship was equivalent between interoceptive and exteroceptive tasks ($r_{\text{interoception}} = -.82, r_{\text{exteroception}} = -.80, z_{\text{fischer's}}(106,106) = .36, n.s.$) and participant groups ($r_{\text{untrained}} = -.83, r_{\text{trained}} = -.85, z_{\text{fischer's}}(54,158) = -.40, n.s.$). Thus any BOLD differences between interoceptive and exteroceptive conditions or between untrained and trained groups are more likely to reflect changes due to attention, since RVT is the better estimator of global neural activity than rate or volume changes alone (Birn et al., 2006). These considerations notwithstanding, I corrected for respiratory rate in the group level task analyses because of the presence of an attention-related respiratory rate and volume changes in the trained group.

In addition to first level correction for TR by TR respiratory rate at the first-level, condition-averaged respiratory rates for each participant were entered as a covariate in second level factorial analyses of group and attention condition. Thus for each participant in each attention condition (Breathe, Suppress and Maintain) a covariate of average respiratory rate in that condition was included in the factorial model. I collapsed across groups to visualize regions associated with interoceptive respiratory inputs to demonstrate regions of primary interoceptive representation. A cluster of activity in the right short (middle) gyri of the insula extending into the posterior putamen was positively associated with respiratory rate ($t_{(1,101)} = 3.26, p = .001$; Table 1, top panel), such that faster breathing was linked to greater activation (Figure 4.3, Panel A). A post-hoc analysis of the correlation between these regions as a function of attention condition revealed that the associations between breathing rate and neural activity were driven by the exteroceptive condition when breathing was unattended ($r_{\text{insula(25)}} = .66, p < .005$), rather than the interoceptive condition, when breathing was unattended ($r_{\text{insula(25)}} = -.17, n.s.$; Figure 4.3, Panel B). It should be noted that this stronger coupling during EA was consistent in both the untrained ($r_{\text{extero(5)}} = .60, r_{\text{intero}} (5) = .06$) and the trained ($r_{\text{extero(18)}} = .71, r_{\text{intero(18)}} = -.10$) groups. This suggests that right insular cortical activity is broadly associated with respiratory rate, with
reduced coupling with respiratory rate during interoceptive attention, where top-down influences may decouple insular response from stimulus driven inputs. Several areas were negatively correlated with respiratory rate as well, primarily throughout the ventral cerebellum (Table 1, bottom panel).

**Interoceptive versus Exteroceptive Attention: Insula ROI Analysis.**

Mean percent signal changes from anatomically defined seed regions were extracted for both the interoceptive and exteroceptive attention conditions in the untrained participants. Difference scores between attention conditions (interoceptive – exteroceptive) were calculated within-subject for each region to represent the attentional tuning of that region. Attentional tuning scores were divided into a 5-seed dorsal zone and a 3-seed ventral zone for trend analysis (see methods for greater detail). The dorsal zone ROIs were subjected to a 2 (left vs. right hemisphere) x 5 (seed location) repeated-measures ANOVA. A main effect of seed location was observed (F(4,60) = 36.20, p < 1x10^{-14}), with IA recruitment of posterior regions giving way to EA recruitment in anterior regions (Figure 4.4). A similar anterior to posterior axis was found for the 3 ventral zone ROIs (F(2,30) = 36.20, p < 1x10^{-14}).

**Effect of Mindfulness Training.** The same ROI analyses conducted on the untrained group were also performed on the trained group. In both the dorsal and ventral zones, similar effects of location were observed, (F(4,76) = 9.90, p < 1x10^{-5}) and (F(2,38) = 25.45, p < 1x10^{-6}), with IA recruitment of posterior regions giving way to EA recruitment in anterior regions (Figure 4.5).

**Between group differences.** Each ROI was compared for tuning differences (IA – EA) between the two groups (Figure 4.6). At the omnibus level, ROIs were compared using a 2 (group) x 2 (left vs. right hemisphere) x 8 (anterior to posterior seed location) mixed-model ANOVA. A main effect of seed location was found (F(7,238) = 23.21, p < 1x10^{-23}), recapitulating the progression of interoceptive to exteroceptive tuning along the posterior to anterior axis. Additionally, an interaction was found between location and group (F(7,238) = 3.02, p < .005), such that interoceptive tuning was greater in the anterior regions for the trained than untrained group. In follow-up tests of each ROI, only the dorsal anterior insular cortices suggested reliable between group differences. The right anterior short gyrus demonstrated significantly greater interoceptive tuning in the trained group in the right hemisphere (t(1,34) = 2.72, p = .01). Follow-up analyses of the right anterior short gyrus revealed that a significant difference between groups
in interoceptive percent signal change ($t_{(1,34)} = 2.21, p = .03$), but not in exteroceptive signal change ($t_{(1,34)} = .48, n.s.$), indicating that the between groups effect was driven primarily by the differences in the interoceptive attention condition. At trend levels, interoceptive bias was greater for the trained than untrained group in the most anterior dorsal insular region (accessory gyrus) in both the left ($t_{(1,34)} = 1.89, p = .07$) and right hemispheres ($t_{(1,34)} = 1.86, p = .07$); furthermore, a marginally greater IA response for the trained group was observed in the left anterior short gyrus ($t_{(1,34)} = 1.82, p = .08$).

**Interoceptive versus Exteroceptive Attention: Whole Brain Analysis.**

To characterize the attentional networks implicated in interoceptive and exteroceptive attention, IA and EA contrast images from each untrained participant were combined in a repeated-measures ANOVA. F tests for the main effect of attention were conducted at FDR corrected thresholds, and subsequent t-tests distinguished these regions into interoceptive and exteroceptive activation areas. Exteroceptive attention was associated with activity in putative primary and secondary visual cortices, dorsomedial prefrontal cortex (dmPFC), bilateral dorsolateral prefrontal cortex (dlPFC), inferior and superior parietal cortex, bilateral frontal opercula extending into the left head of the caudate, and the cerebellum (Figure 4.7; Panels C & D; Table 2). Interoceptive attention was associated with bilateral activity along the posterior to mid insula, as well as hippocampus, caudate, posterior and middle cingulate, and medial somatosensory cortices (Figure 4.7; Panels A & B; red, Table 2).

**Effect of Mindfulness Training.** Similar to the untrained group, IA and EA contrast images from each trained participant were combined in a repeated-measures ANOVA. A similar pattern of exteroceptive and interoceptive network activity to that reported in the untrained group was found in the trained group (Figure 4.8; Table 3). Exteroceptive attention recruited occipital, dorsal prefrontal, opercular, and parietal regions, while interoceptive attention was associated with bilateral activity along the posterior to mid insula, as well as hippocampus, caudate, posterior and middle cingulate, and medial somatosensory cortices.

Between Group Differences. At FDR corrected levels, no interactions were found between group (trained vs. untrained) and attention (IA vs. EA). However, at an exploratory threshold, ($p < .005, k > 30$), the dorsomedial prefrontal cortex (BA 8, at peak $p < 1x10^{-5}$, $x = -3$; $y = 27$; $x = 51$, $k = 79$) demonstrated a reliable interaction between group and attention. Follow up signal
extraction revealed a consistent pattern of DMPFC activation during EA and IA in the untrained group, but a unique deactivation during IA in the trained group.

4.7 Discussion

The present study offers four significant findings. First, attention modulated primary and secondary visual cortical regions during exteroception, but also modulated primary and secondary interoceptive representations bilaterally in the posterior granular and middle dysgranular insular cortices during interoception. Second, exteroception and interoception appear to rely on dissociable attention networks. Exteroception was associated with a well-characterized fronto-parietal network (e.g., Corbetta & Shulman, 2002). By contrast, interoception was characterized by limbic and paralimbic recruitment, including hippocampus and mid-cingulate cortex (BA 23), extending into the precuneus (BA 7) and paracentral gyrus (BA 5). Third, there was a graded insular response to the attention manipulation, with interoceptive responses in the posterior insula shifting towards exteroceptive responses in more anterior agranular gyri. This pattern implicates the insula as a region of multisensory integration between interoceptive and exteroceptive attention, consistent with prior work demonstrating the region’s importance for the integration of multidimensional signals in present moment awareness (Craig, 2009, Critchley et al., 2004). Finally, two months of mindfulness training, characterized by daily interoceptive practice, revealed interoception-specific functional plasticity in the right dorsal middle and anterior insula.

Right Insula Representation and Respiratory Signal

Consistent with its anatomical innervations by afferent viscerosensory pathways, insula activity correlated directly with respiratory rate. However, this coupling was dependent upon attentional framing: task-averaged respiratory rate predicted right insula and putamen activity when respiration was unattended during exteroception, but this correlation was absent during interoception. Interoceptive attention appears to alter insula representation of stimulus-driven interoceptive signals via a top-down modulation of the region, such that its activity is less driven by mechanical signals from the body. Interoceptive attention, therefore, appears to increase the complexity and integration of viscerosomatic information rather than simply increasing the strength of viscerosensory coupling with neural representation.
The decoupling of insula activity and respiratory signal during interoception may be indicative of the insula’s broader role in integrating interoceptive and exteroceptive information to constitute the individual’s sense of self in the present moment (e.g., Farb et al. 2007; Craig, 2009). Function across insular gyri may also be heterogeneous, commensurate with variations in connectivity along the insular posterior-anterior axis. Posterior regions of the insula receive inputs from somatosensory association cortices (Mufson & Mesulam, 1982; Friedman et al., 1986), and have been linked to multiple forms of interoceptive representation, including cutaneous stimulation (Schneider et al., 1993), pain and temperature sensation (Casey et al., 1994) and body representation (Preuss & Goldman-Rakic, 1989). These interoceptive representations are somatotopically organized in posterior insula regions (e.g., Brooks et al., 2005), implicating the posterior insula as a primary viscerosomatic cortex. Connectivity however shifts from somatosensory cortices in the posterior insula to the striatum in the middle insula (Menon & Levitin, 2005), and finally to the anterior cingulate and orbitofrontal cortices in anterior insular nuclei (Critchley et al., 2003). The anterior and middle insula may therefore integrate viscerosomatic signals into a motivational space that no longer directly represents bodily sensation (Critchley, 2002). For example, while the physical temperature of thermal stimulation is represented in the posterior and middle insula, subjective ratings of thermal intensity recruit the anterior insula and orbitofrontal cortices (Craig et al., 2000). It is thus understandable that while interoceptive stimuli generally predict activity in the caudal aspects of the insula, interoceptive attention may bind visceral signals with exteroceptive representations represented in rostral insular regions, disrupting the direct relationship between viscerosensation and posterior insula activity.

**Exteroceptive vs. Interoceptive Networks**

Interoceptive attention recruited a limbic and para-limbic network, irrespective of training condition. By contrast, a fronto-parietal network was recruited during exteroception, regardless of whether exteroception was defined as attention towards external visual stimuli (maintenance) or away from internal signals (suppression). Voluntary attention effectively selected between these two sensory networks. The neural distinction was not however limited to sensory regions, as would be observed when comparing two exteroceptive foci such as hearing and vision (e.g. Johnson & Zatorre, 2005); instead, interoception-related activity extended beyond primary interoceptive and somatosensory regions to include the anatomically-connected
posterior cingulate and hippocampus (Eckert et al., 2008), which may be critical for the
representation of broader contextual information (Vogt et al., 2006). The present findings also
differentiate interoception from notions of internally-generated and stimulus-independent
thought, in which participants are asked to visualize objects or mind-wander relative to
exteroceptive tasks (e.g., Christoff et al., 2003; Gilbert et al., 2005), which recruit dorsolateral
prefrontal cortical circuits rather than the interoceptive network demonstrated here.

The present study suggests that the fronto-parietal network broadly associated with
attention may only be specific to tasks requiring exteroceptive maintenance and suppression,
which constitute the majority of published attention paradigms. The ability to regulate processing
of exteroceptive signals has been associated with the frontal operculum (see Aron, Robbins &
Poldrack, 2004 for a review), whereas working-memory maintenance tasks commonly recruit the
dorsal lateral prefrontal (DLPFC) and superior parietal (SP) cortices (Wendelken, Bunge &
Carter, 2008) as well as caudate (McNab & Klingberg, 2007) and cerebellum (Desmond et al.,
1997). All of these regions were more active during exteroception than interoception, supporting
their exteroception-specific role.

While not all attention recruits the fronto-parietal network, the data also suggest that not
all insula recruitment is interoceptive: the anterior insula, particularly in its ventral divisions, was
primarily tuned towards exteroception rather than acting as a marker of somatic awareness (e.g.,
Damasio, 2000). The idea of greater anterior insula activity during exteroception is again
consistent with the notion of increased contextualization of internal representations to meet
external contexts and task demands as signal propagates rostrally along the insular gyri (Craig,
2009). On the other hand, interoceptive attention still dominated recruitment of posterior regions
of the insula near the parietal operculum, which are not typically activated in exteroception
(Wager & Barrett, 2004). Thus the breath monitoring paradigm represents a novel attention
manipulation for voluntarily recruiting posterior insula regions classically associated with
involuntary visceral sensation (e.g., Dupont et al., 2003; Aziz, 2000), but challenges the notion
that the insula is exclusively dedicated towards interoceptive processing.

Practicing Interoceptive Attention

While attending to one’s breath activated the posterior insula bilaterally across all
participants, interoceptive tuning in the right middle and anterior insula was unique to the trained
group. Specifically, maximal group differences in interoceptive bias were found in the right dorsal anterior short insular gyrus, part of the dysgranular layer of the insula. The predominantly dorsal effects of mindfulness training on interoceptive recruitment are consistent with our understanding of anatomical divisions in the anterior insula: the striatum underlying the anterior insula has been functionally divided into a dorsal ‘sensorimotor’ region and a ventral ‘limbic’ region based on cortical projection analysis (Chikama et al., 1997). The dorsal dysgranular layer of the insula includes dense interconnections with supplementary motor and sensorimotor association cortices, whereas the ventral ‘limbic’ region is more densely connected with orbitofrontal cortex, amygdala and entorhinal cortex (Mufson & Mesulam, 1982; Carmichael & Price, 1996). This anatomical distinction suggests a functional distinction between a dorsal body-integration pathway and a ventral homeostatic pathway, consistent with current neuroimaging studies of emotion (e.g. Jabbi et al., 2007; Harrison et al., 2010). Such a distinction is also consistent with the intention of the mindfulness training intervention, to cultivate interoceptive but non-judgmental awareness, recruiting dorsal viscerosomatic insular cortex distinct from valence-laden orbitofrontal connectivity of the ventral insula. This theory of non-evaluative awareness is further supported by the observation of a unique, training-specific decrease in dmPFC activity during interoception in the trained group, consistent with an account of expertise helping to reduce the coupling of viscerosomatic with evaluative networks found along the cortical midline of the brain (Farb et al 2007; Farb et al 2010).

Concluding Remarks

Taken together, the results of the present study suggest that like exteroceptive sensory systems, interoceptive cortices are modulated by top down attention, with pronounced modulation of primary interoceptive cortex in the posterior granular and dysgranular insular cortices. Differences in neural recruitment between interoceptive and exteroceptive attention suggest a fundamental division in attention networks as well as primary representation areas. Furthermore, this study suggests state related functional plasticity in interoceptive sensory representations following 2 months of breath monitoring practice.

The present work was has several important limitations. Between-group training effects were far less robust than the main effects of attention focus, suggesting 2 months of training may only begin to yield functional plasticity. It is known that gray matter volume correlates with
years, rather than weeks, of mindfulness practice (Holzel et al., 2007; Lazar et al., 2005), so examinations of a group possessing more extensive training may also yield more powerful functional changes. It is also still unclear what consequences attention-related increases in insula activity have for interoceptive awareness, which could be addressed by linking training related increases to objective performance measures such as the heartbeat detection task. Future work will need to better operationalize the quality of representation accompanying interoceptive insula recruitment, to determine how signals from the body are integrated into a broader motivational context.
Chapter 5

5 General Discussion

5.1 A New Look at an Old Self

The idea of the momentary self is a deep-rooted one, derived from descriptions of ancient Buddhist mindfulness practices with mechanisms largely unexamined by modern western science. Acknowledging this oversight, this dissertation eschewed promoting a single description of mindfulness, particularly given the lack of consensus on the term after millennia of discussion and debate by classical academics. Hence, I generated a functional, neuroscientific account of mindfulness by examining the effects of manualized mindfulness practices on traditional psychological distinctions of selfhood, emotion, and attention.

The chief contribution of this research is in demonstrating that momentary self-reference recruited a reliable network of neural regions distinct from those found in conventional self-reference tasks, challenging descriptions of the self as an extended, unitary, and language-laden construct. Specifically, momentary self-reference was associated with a right-lateralized, viscerosomatic pathway, extending rostrally from the temporal parietal junction along the dorsal right insula towards the frontal operculum. Consequently, it is argued that human beings have access to at least two different modes of self-reference: the conventional, extended self that is a source of conceptual constancy across time, and a newly described, momentary self that is a source of immediate sensory feedback, based upon constantly updated integration of immediate sensation and expression.

While the extended self was considered to be easily accessible as a default mode of self-reference, access to the momentary self was manipulated through the use of an 8-week course known as Mindfulness-Based Stress Reduction (MBSR; Kabat-Zinn, 1982), in which a randomly assigned community sample of participants completing the MBSR program were compared to their waitlisted counterparts to serve as the Control group. MBSR training in momentary self-reference was evidenced in: increased ability to engage in viscerosomatic processing in response to trait words, maintenance of viscerosomatic processing following a sadness challenge, and increased interoceptive activity in middle and anterior portions of the right insula. Taken together, these findings provide converging evidence for the existence of a substantive mode of
self-representation that appears to be independent of conventional linguistic and evaluative pathways.

5.2 The Dominant Narrative Network

A major hypothesis in the generation of these research paradigms was the ubiquitous and, to some degree, obligatory nature of extended self-reference as indexed by narrative network processing. Consistent with this theory of self-reference as one mediated by linguistic and conceptual self-description, participants in all three studies engaged midline prefrontal cortices while processing events using narratives (chapter 2), in response to emotional challenge (chapter 3), and when attending to exteroceptive stimuli (chapter 4). In addition to relating the extended self’s narrative processing to cortical midline activity, a strong bias towards narrative processing over more momentary, experiential modes was demonstrated across multiple studies. In the first study, supporting the hypothesis of a ‘default’ bias towards narrative self-focus (e.g., Gusnard et al., 2001), only restricted reductions in the mPFC centered cortical midline network were found when attention was explicitly directed towards a momentary, experiential focus in novice participants with little training in this form of self-reflection. In other words, untrained efforts to shift self-referential processing away from the extended self’s cortical midline regions of activity were largely unsuccessful, consistent with a theory of a habitually reinforced bias towards narrative processing.

Turning to the realm of emotion, the extended self appears to be a dominant and habitual mode of processing with respect to emotional challenges as well. In this second study, the sadness provocation was associated with elevated self-reported ratings of sadness, accompanied by activation along the posterior and anterior regions of the cortical midline, as well as in left-lateralized language and conceptual processing centers. These cortical areas are characteristic of cognitive elaboration, increased self-focus, and ruminative problem solving that would be typical of reappraisal processes (Ray et al., 2008; Ochsner & Gross, 2008). Sadness provocation was also associated with widespread suppression of right viscerosomatic cortices, including the right insula, areas that may contribute information important to the primary appraisal of emotion (Craig, 2002). Such findings are consistent with the notion of a cognitively evaluative neural network responding to emotion challenge by monopolizing information processing resources, prioritizing conceptual cortical midline activity to the detriment of the momentary viscerosomatic network.
The third study focused on a contrast between interoceptive and exteroceptive attention rather than contrasting the two modes of self-reference directly. Nevertheless, relative to interoception, exteroceptive attention was associated with a previously well-characterized fronto-parietal attention network (e.g., Corbetta & Shulman, 2002), whose regions of activation strongly overlap with the extended self network, including dorsomedial prefrontal cortices and the angular gyri. By contrast, regions responding more to interoceptive attention were not associated with this pattern of narrative network activity, relating more to the viscerosomatic cortices consistent with momentary self processes. Such findings point to the strong connection between processes of exteroceptive attention and the extended self, consistent with an account of the extended self as a fixed frame of reference, relative to which external stimuli may be oriented and appraised. Consistent with the finding of insula suppression following sadness stressors in the second study, exteroceptive network recruitment came at the cost of interoceptive network activity, suppressing the shifting, viscerosomatic representations of the momentary self, particularly in the posterior cingulate cortex, insula, and somewhat surprisingly, the hippocampus.

5.3 Mindfulness as both extended self inhibition and momentary self recruitment

Given the potentially antagonistic relationship between extended and momentary self processes in the brain, it would seem that mindful processes in untrained participants can be characterised by their inhibitory effects on the narrative network. Indeed, a common misconception of mindfulness practice is that its effects are primarily inhibitory: curious folk have often asked me if meditation simply means ‘not thinking’. It seems that lay conceptions of meditation often involve the suppression of narrative, of evaluation, and perhaps thought itself. Clearly mindfulness techniques do aim to reduce some cognitive processes, such as rumination, the critical self-referential evaluation of experience. On the other hand, such inhibitory effects should not overshadow the compelling evidence that mindfulness training, operationalised here through MBSR, also involves the active recruitment of other forms of self-representation through the activation of viscerosomatic cortical representations of the body in the present moment. Thus the momentary self is not some vacuous concept defined by the absence of the extended self, but rather represents a substantive mode of self-reference in its own right.
The discovery of reliable neural correlates of momentary self-reference along a right-lateralized, viscerosomatic pathway begs the question of what function this pathway serves. I observed this visceromatic recruitment across three distinct experimental paradigms, in conjunction with reduced processing in cortical midline and fronto-parietal executive cortical regions. In order to understand that connection between mindfulness training and neural activity, it may be useful to consider both these positive (new recruitment) and negative (reduced recruitment) findings in turn.

5.3.1 Positive Findings

In the first study, dealing with self-referential processing, an experiential focus designed to promote access to the momentary self resulted in novel recruitment of a right lateralized network comprised of the ventral and dorsolateral PFC, as well as right insula, secondary somatosensory (SII) cortex, and the inferior parietal lobule. This right lateralized network contains anterior components in the frontal lobe associated with the flexible allocation of attention (Cunningham & Zelazo, 2007), the dorsolateral PFC for working memory maintenance (e.g. Gray, et al., 2002; Miller & Cohen, 2001); and ventrolateral PFC for inhibitory control of unwanted processing (e.g. Bunge et al., 2001; Gusnard et al., 2001). Together, these right frontal regions might be employed to alter the habitual mode of information processing in the brain. In addition, posterior paralimbic and cortical regions such as the insula, secondary somatosensory cortex, and the inferior parietal lobule likely represent the contents of this present-focused awareness, such as interoceptive physiologic, exteroceptive somatic condition of the body, and overall corporeal awareness (Berlucchi & Aglioti, 1997; Craig, 2004; Critchley et al., 2004). These evolutionary older neural regions, may represent the neural origins of identity, in which self-awareness in each moment arises from the integration of basic interoceptive and exteroceptive sensory processes (Craig, 2004; Critchley et al., 2004; Damasio, 1999; Panksepp, 2005).

In the second study, which dealt with emotional processing following a sad mood challenge, the MBSR group demonstrated reduced deactivations in right viscerosomatic cortices, in that the Control group demonstrated reliable viscerosomatic deactivation following sadness challenge, but the MT group did not. The presence of deactivating regions following sadness challenge suggests that part of the neural response to aversive emotions may involve the down-regulation of viscerosomatic regions. By reducing such inhibitory tendencies, the MBSR group
may be better able to maintain interoceptive awareness in the face of such a stressor. Recent research has associated mindfulness training with reductions in emotional interference following the viewing of affective pictures (Ortner, Kilner & Zelazo, 2007), and the present findings suggest that this reduced interference may stem from the objectification of emotion as innocuous sensations rather than as a threat requiring a regulatory response. A plausible mechanism of action for mindfulness effects may include the development of meta-cognitive skills for detached viewing of experience.

The third study attempted to uncover neural mechanisms associated with mindfulness training by studying a mindfulness practice in action. Breath monitoring, a core mindfulness practice, was associated with recruitment of a diffuse network of brain regions, ranging from the somatosensory cortices, ventrally through the parietal lobe and into the posterior insula and basal ganglia. While breath monitoring activated bilateral posterior insula across all participants, interoceptive tuning (i.e., greater activation for interoceptive attention than exteroceptive attention) in the right middle and anterior insula was unique to the MT group. While the posterior insula may represent a primary viscerosomatic cortex, the more anterior aspects of the insula may be critical for the integration of visceral information with behavioural and emotional events (Saper, 1982; Craig, 2009). One mechanism for the training of mindful attention may therefore be increasing the integration of present moment visceral sensation represented in posterior insular cortices into present-moment context representation regions located in the anterior insula and operculum.

5.3.2 Negative Findings

Despite earlier qualifications that momentary self-reference is more than just thought suppression, there are important inhibitory components to present-moment awareness. In the self-reference study, experiential focus following MBSR training resulted in a shift away from medial cortical structures such as the vmPFC and posterior cingulate toward more lateral prefrontal regions supporting a more self-detached and objective analysis of interoceptive (insula) and exteroceptive (somatosensory cortex) sensory events, rather than their affective or subjective self-referential value. This pattern mirrors neural dissociations between the subjective affective objective sensory qualities of pain stimuli, with the former supported by anterior midline structures, and latter supported by posterior lateral sensory cortices (Rainville et al., 1997).
With respect to the emotional effects of mindfulness training, I found that despite similar levels of self-reported dysphoria, the MT group demonstrated less neural reactivity to sadness provocation than the Control group. While both groups showed some recruitment of sadness-related activation along midline cortical areas associated with self-referential processing, the MBSR group demonstrated reduced reactivity both medial and lateral regions. In particular, the MBSR group demonstrated reduced activation in the cortical midline regions associated with autobiographical memory retrieval and self-referential processing (Cavanna & Trimble, 2006), and in classical language areas like the left posterior superior temporal gyrus (Wernicke’s area) and the left frontal operculum (Broca’s area).

The third study investigated mechanisms of attention associated with training in momentary self-reference. While the results of this study demonstrated broad recruitment of a viscerosomatic network, it is important to note that mindfulness training was also associated with a unique, training-specific decrease in dmPFC activity during interoceptive attention; this dmPFC region is a primary node in the cortical midline network constituting the neural basis of extended self-reference and exteroceptive attention. Thus, from a mechanistic standpoint, expertise in momentary self-reference appears to help to reduce the coupling of viscerosomatic states with external events and their associated evaluations.

Taken together, these three studies provide strong convergent evidence for the prevalence of cortical midline activity during the voluntary evaluation of self, emotion, and even sensations from the body. For participants naive to mindfulness training (Controls), these cortical midline activations were found even under momentary self-reference conditions, such as the experiential focus condition in study 1, and in the interoceptive attention condition in study 3, as well as in the non-directed evaluation of sad film clips in study 2. MBSR training however seems to disrupt the seemingly obligatory recruitment of cortical midline structures, particularly in the dorsal forebrain and posterior midline (e.g., precuneus and posterior cingulated cortex). While these studies cannot hope to define dmPFC activity in terms of specific function, the recruitment of the dmPFC in study 3 in exteroception in both the MT and Control groups suggests that this region may hold an important role in the orienting of attention towards external stimuli; the proximity of this region to the pain-alerting (e.g. Rainville et al., 1997) and homeostatic-integrating (Critchley, 2005) anterior cingulate cortex suggests that the dmPFC may represent a reactionary response co-ordination to detected environmental stressors. Based upon these results, it is plausible that momentary self-reference may disrupt the formation of these reactionary responses
in favour of a richer allocation of attention resources towards viscerosomatic perceptual representations. The negative findings discussed above are an important part of this story, explaining how response-generating neural mechanisms are down-regulated to free perceptual resources.

5.3.3 Altered relationship between the two networks

An intriguing finding of the first study is the alterations in connectivity between cortical midline structures and viscerosomatic cortices. Indeed, functional connectivity analyses suggested a default mode of self-awareness that may depend upon habitual coupling between mPFC regions supporting cognitive-affective representations of the self and more lateral viscerosomatic neural images of body state. I show this dual-mode of self-reference is best revealed following MT, where these modes become uncoupled through attentional training. This cortical reorganization following MT is consistent with the notion that mindfulness training allows for a distinct experiential mode in which thoughts, feelings and bodily sensations are viewed less as being good or bad or integral to the “self” and treated more as transient mental events that can be simply observed (Kabat-Zinn et al., 1992). As such, the capacity to disengage from evaluative narration and to engage in more nonjudgmental, momentary self-focus has important implications for mood and anxiety disorders, with the former having been shown to increase illness vulnerability (Segal et al., 2006). Conversely, a growing body of evidence suggests approaching self-experience through a more basic present-centered focus may represent a critical aspect of human well-being (Davidson, 2004).

5.4 The boon and bane of first person neuroscience

One goal of the present work was to develop methods in first person neuroscience, in which research participants’ own experiences are considered an experimental variable of interest (Table 5.1). The neuroimaging paradigms discussed in this dissertation together represent a departure from traditional experimental tasks in that they entrust the participants to voluntarily manipulate their attentional state, which does not readily produce a behavioural dependent variable, rather than focusing on behavioural task performance. While most research paradigms attempt to treat participants’ internal states as noise while manipulating external task requirements, the present studies held task requirements relatively constant while manipulating participant internal states.
In many ways, asking participants to manipulate their internal states was essential for the measurement of momentary self-reference: requiring veridical responses from participants would constrain attention away from the construct of interest. For instance, it would be difficult to maintain interoceptive awareness if one had to monitor and respond to cues on an external monitor. On the other hand, while the participant-facilitated approach to studying momentary awareness holds strong external validity with mindfulness practices, it necessarily lacks the empirical method of behavioural paradigms, in which participant action can be described in terms of reaction time and accuracy. Thus the reliance on participants’ voluntary direction of attention can be seen as both a strength and weakness of the present research: great external validity is gained in asking participants to regulate and direct their own attention systems, yet at the cost of tightly controlling for how such regulation occurs. And yet, fMRI seems to be an ideal investigative technique for such an open-ended experimental manipulation, as one would not expect to see reliable differences in neural recruitment across individuals unless some common cognitive mechanism was being employed by these individuals. A major challenge for the development of these first-person neuroscience methods will be to provide behavioural evidence that can serve as manipulation checks on participant compliance to experimental instructions, perhaps by requiring more detailed feedback from participants on their experiences during the experimental process. Nevertheless, the present work represents an interesting first foray into what promises to become an exciting extension of the field of cognitive neuroscience.

5.5 Recommendations for future research

Several limitations are apparent in the interpretation of the present data. While the present findings are based on comparisons among randomly assigned pre- and post-treatment participant groups, testing the same individuals before and after treatment would have warranted stronger conclusions regarding the temporal effects of mindfulness training, but at the expense of controlling for carryover effects. Given appropriate resources, a more ideal study would control for both practice effects by using a pre and post testing design, and also for group effects by including a control group. To this end, active control designs in which similar expectations for improved well-being but without mindfulness training content will be critical in establishing mechanistic differences between mindfulness and the placebo effect. For example, while the present results help to explain the effects of mindfulness on affective reactivity in a mixed community sample, recruiting a carefully diagnosed clinical sample would have enabled us to
answer specific questions about emotion regulation in clinical depression or other disorders. Similarly, comparisons against an active control group would be needed to tease apart alternative explanations of enhanced emotion regulation, such as group support and destigmatization, which are unrelated to mindfulness training. Our current work is progressing in these directions, in one study comparing the effects of MBSR to an active control group trained in progressive relaxation, and in another study examining the effects of mindfulness-based cognitive therapy on a carefully recruited group of clinically depressed patients. Furthermore, we are attempting to integrate simple behavioural tasks into the imaging paradigms to verify participant compliance and establish quantifiable metrics of efficiency in the deployment of attention.

In addition, while I assume that the 8 week MBSR course represents an equivalent training period across participants, homework compliance was somewhat variable between participants. Gauging the frequency of mindfulness practice over the 8-week program would have permitted testing the relationship between mindfulness practice and the establishment of neural balance in response to affective challenge. The variance in participant practice over an 8-week period was, however, not large enough to be used as a predictor of training outcomes as most participants reported similar levels of practice during the course, approximately 75% adherence to assigned homework hours each week. A further issue is that there is no guarantee that 8 weeks of compliant practice is sufficient to characterize the full effects of a long term practice. While as an initial manipulation of momentary self access the 8 week training period served its purpose, future research should attempt to vary the training duration to better understand the development of viscerosomatic network representation. However, it may be necessary to develop different length versions of the MBSR training to maintain consistency across training instructions and the experimental design. Another possibility lies in efforts to find participants with mindfulness practices and varying levels of experience, but such an approach reduces explanatory power as it would shift the research from a true experimental to a cross-sectional design.

5.6 Concluding Remarks

Access to the momentary self is associated with a right lateralized, viscerosomatic pathway chiefly constituted by the right insula. This pathway is engaged specifically during attention to present-centered experience, and is distinct from the constellations of neural activity associated with conventional self-referencing tasks. The present research provides the first substantive evidence for the neuroscience of the momentary self, both in demonstrating the
recruitment of the right viscerosomatic pathway during momentary self-reference, but also in demonstrating the importance of attentional practice for maintaining viscerosomatic activity amidst competing cognitive habits such as evaluation, rumination and exteroception.

While the right insula is clearly implicated in the cultivation of momentary self-reference, the specific functional correlates of insula subregions and its cortical and subcortical connections are still unknown. A major question posed by the present results lies in the functional distinction between dorsal (dysgranular) and ventral (agranular) insular regions; it is yet unknown whether it is specifically the ventral agranular insula which whose dysfunction is linked to emotional disorders (e.g. Dupont et al., 2003) and addiction (Naqvi & Bechara, 2009), whereas the dorsal dysgranular regions may represent a less affectively-laden representation of present-moment context as intended in mental training such as mindfulness meditation (Kabat-Zinn, 1982). Future work will need to better specify the quality of representation accompanying increased right insula recruitment, as well as to more tightly delineate the experiential consequences of the altered activity, as the sensory consequences of enhanced insular recruitment during interoceptive attention and following prolonged interoceptive training remain unproven (e.g., Khalsa et al., 2008).

The present dissertation has evidenced the existence of neural correlates of momentary self-reference, corroborating subjective accounts of present-centered experience. Using MBSR training to strengthen access to the momentary self, this research has laid the foundations for a first person neuroscience, providing relatively normal individuals with the expertise to voluntarily manipulate their foci of attention, with dramatic consequences in terms of neural activity, reported experience, and participants’ broader sense of well-being. Broadly, the question of momentary self-reference has begun to be addressed in terms of a right viscerosomatic pathway associated with the cultivation of interoceptive attention. However, this research has only begun to crack open the door to the neuroscientific investigation of momentary self-consciousness; hopefully these efforts will help to inspire a new field of neuroscience research to ultimately help us to understand the rich mental world we inhabit in this life.
Figure Captions

Figure 1.1. A visual schematic of the potential range of attention across sensory modalities and time. Given a limited scope of attention, temporally-extended narratives necessarily require a narrowing of present-moment attentional scope, whereas a temporally-narrow scope can include a greater range of immediate sensations to the exclusion of temporally-extended elaboration.

Figure 2.1. Narrative self-focus condition in the collapsed Novice (pre mindfulness training) and MT (following 8 weeks of mindfulness training) groups. Cortical midline areas associated with narrative focus (Narrative > times series baseline). VMPFC = ventromedial prefrontal cortex; DMPFC = dorsomedial prefrontal cortex; PCC = posterior cingulate cortex.

Figure 2.2. Experiential and Narrative self-focus conditions in the Novice (pre mindfulness training) group. a) Areas of greater association with the Narrative condition (Narrative > Experiential) are in blue, and b) areas of showing greater association with the experiential condition (Experiential > Narrative focus) are in red. VMPFC = ventromedial prefrontal cortex; DMPFC = dorsomedial prefrontal cortex; PCC = posterior cingulate cortex; LPFC = lateral prefrontal cortex; PP = posterior parietal cortex.

Figure 2.3. Experiential versus Narrative focus conditions following 8 weeks of mindfulness training (MT). Areas of activation showing a greater association with the experiential condition (Experiential > Narrative focus) are in red, and narrative-associated areas (Narrative > Experiential) are in blue: a) rostral and dorsal MPFC b) right LPFC c) right Insula; d) right secondary somatosensory cortex (SII). Bar graphs indicate region of interest analyses of the magnitude of activation associated with the Narrative vs. Experiential contrast in the MT (post) and novices (pre) groups. Left panel green region represents y coordinate of each ROI. NF = narrative focus; EF = experiential focus; VMPFC = ventromedial prefrontal cortex; DMPFC = dorsomedial prefrontal cortex; LPFC = lateral prefrontal cortex; Insula = insula; IPL = inferior parietal lobule; SII = secondary somatosensory area.

Figure 2.4. Functional connectivity in the Novice and MT groups. Areas showing increased connectivity with the right insula (MT > Novice) are in red, and areas showing reduced connectivity (Novice > MT) are in blue. a) ventromedial prefrontal cortex; and b) dorsolateral prefrontal cortex. The right panel demonstrates rank ordered inter-regional correlations with the
right insular ROI in both the Novice and MT groups. VMPFC = ventromedial prefrontal; PCC = posterior cingulate; LPFC = lateral prefrontal cortex.

**Figure 3.1:** Regional activation (a) and deactivation (b) in response to sadness provocation in the Waitlisted Control group (sad vs. neutral within-group contrast). Red clusters = sad > neutral. Blue clusters = neutral > sad. Pcn = precuneus; Opc = operculum; vmPFC = ventral medial prefrontal cortex; STS = superior temporal sulcus; mPFC = medial prefrontal cortex; rLPFC = right lateral prefrontal cortex; Som = primary and secondary somatosensory cortices; Subgen = subgenual anterior cingulate cortex; mCing = middle cingulate gyrus; sPar = Superior Parietal Lobule. Panel (c) provides some examples of both activation (Precuneus and mPFC) and deactivation (right insula) in the control group relative to a resting state baseline; activation/deactivation is computed as the difference score between sad and neutral film clip activity.

**Figure 3.2:** Differences in regional activation and deactivation between Control and MT groups in response to sadness provocation (the interaction between-groups and sad vs. neutral within group-contrasts). Top panel: sadness-related deactivations in the Control group with non-significant activity in the MT group (red clusters = MT > Control); bottom panel: sadness-related activations in the Control group with non-significant activity in the MT group (blue clusters = Control > MT). Error bars are 95% confidence intervals. LPFC = lateral prefrontal cortex; STS = superior temporal sulcus / Wernicke’s Area.

**Figure 3.3:** Correlation plot between the right insula % signal change from all participants (Control and MT) and their raw Beck Depression Inventory (BDI) scores. Greater BDI scores at time of fMRI scan predict greater reductions of activity in the right insula ROI.

**Figure 4.1:** Region of interest (ROI) locations along the insula cortex. ROIs were drawn to fit each visible gyrus of the template brain, yielding 8 anatomically defined regions. These regions conform to the anatomical divisions outlined in Craig (2009), and illustrated in Mesulam & Mufson (1982) and Chikama et al., (1997), representing the posterior, anterior, and accessory gyri, and further subdividing these regions into dorsal and ventral subregions to capture the three major divisions in insular cellular layers, the granular, dysgranular, and agranular regions.
**Figure 4.2:** Respiration signal analyses. Panel A: average power and frequency of respiration as a function of attention condition, as derived from a fast fourier transform of the respiration data across all participants. Panel B: mean respiratory frequency (Hz) as a function of group and attention condition, as derived from a breath counting algorithm. Greater differentiation between attention conditions was found in the trained group. Panel C: mean respiratory volume (arbitrary respiration belt units) as a function of group and attention condition, as derived from a breath counting algorithm. Again, greater differentiation between attention conditions was found in the trained group. Panel D: rate/volume tradeoffs for respiration as a function of attention condition. The slopes for the two conditions did not significantly differ.

**Figure 4.3:** Neural correlates of respiratory rate and interactions with experimental tasks. Panel A: neural correlates of respiratory rate modeled at the second level; the only positive correlate is shown in the right middle insula /putamen. Panel B: the positive correlation between the right middle insula and respiratory rate is driven more by the exteroceptive condition (right) than interoceptive condition (left).

**Figure 4.4:** Insula attention tuning by anatomical partitions in untrained participants. A significant effect of insula location was found, such that interoceptive bias shifts to exteroceptive bias from posterior to anterior insula. Panels A/D: left dorsal/ventral insula percent signal change plots for interoceptive and exteroceptive recruitment as a function of location. Panels B/E: seed locations shown bilaterally across the dorsal/ventral insula. Panels C/F: right dorsal/ventral insula attention tuning plots. Error bars represent standard errors. Asterisks represent areas of areas of significant difference between interoceptive and exteroceptive attention. AC = accessory gyrus; AS = anterior short gyrus; MS = middle short gyrus; PS = posterior short gyrus; AL = anterior long gyrus; PL = posterior long gyrus.

**Figure 4.5:** Insula attention tuning by anatomical partitions after mindfulness training. A significant effect of insula location was found, such that interoceptive bias shifts to exteroceptive bias from posterior to anterior insula. Panels A/C: left dorsal/ventral insula percent signal change plots for interoceptive and exteroceptive recruitment as a function of location. Panels B/D: right dorsal/ventral insula attention tuning plots. Error bars represent standard errors. Asterisks represent areas of areas of significant difference between interoceptive and exteroceptive
attention. AC = accessory gyrus; AS = anterior short gyrus; MS = middle short gyrus; PS = posterior short gyrus; AL = anterior long gyrus; PL = posterior long gyrus.

**Figure 4.6:** Between-groups comparison of insula attention tuning signal by anatomical partitions. A significant effect of insula location was found, such that interoceptive bias declines from posterior to anterior insula. A marginal interaction between location and group was also found, suggesting that there is preserved interoceptive bias in anterior regions of the insula in trained relative to untrained participants. Panels A/C: left dorsal/ventral insula tuning plots for Interoceptive – Exteroceptive recruitment as a function of location. Panels B/D: right dorsal/ventral insula attention tuning plots. Error bars are standard errors. Asterisks (*) denote significant (p < .01) between-group comparisons at a specific location, whereas circles (•) denote marginally significant (p < .1) between-group comparisons. AC = accessory gyrus; AS = anterior short gyrus; MS = middle short gyrus; PS = posterior short gyrus; AL = anterior long gyrus; PL = posterior long gyrus.

**Figure 4.7:** Untrained participants: main effects of attention (Interoception vs. Exteroception). Panels A & B summarize the interoceptive network regions while panels C & D summarize exteroceptive network regions. Panel A: right insula. Panel B: paracentral gyrus. Panel C: inferior occipital / primary visual cortex. Panel D: frontal operculum.

**Figure 4.8:** Trained Group: main effects of attention (Interoception vs. Exteroception). Panels A & B summarize the interoceptive network regions while panels C & D summarize exteroceptive network regions. Panel A: right insula. Panel B: paracentral gyrus. Panel C: inferior occipital / primary visual cortex. Panel D: frontal operculum.
Figures

Figure 1.1
Figure 2.1

Figure 2.2
Figure 2.3
Figure 2.4
Figure 3.1
Figure 3.2

Figure 3.3
Figure 4.1
Figure 4.2
Figure 4.3

**a** Neural Correlates of Respiratory Rate

**b** Rate / Insula Correlation by Condition

- **Interoception (r = -0.17)**
  - Condition-Averaged Respiratory Rate (Hz)
  - Insula % Signal Change

- **Exteroception (r = 0.66)**
  - Condition-Averaged Respiratory Rate (Hz)
  - Insula % Signal Change
Figure 4.4
Figure 4.5
Figure 4.6
Figure 4.8
### Table 1.1. Some well known investigators’ nomenclature for the Agent vs. Object distinction.

<table>
<thead>
<tr>
<th>Momentary Self</th>
<th>Extended Self</th>
<th>Investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Me</td>
<td>(James, 1980)</td>
</tr>
<tr>
<td>Minimal Self</td>
<td>Narrative Self</td>
<td>(Gallagher, 2000)</td>
</tr>
<tr>
<td>Noetic</td>
<td>Autonoetic</td>
<td>(Tulving, 2001)</td>
</tr>
<tr>
<td>Core</td>
<td>Extended</td>
<td>(Damasio, 1999)</td>
</tr>
<tr>
<td>Experiential</td>
<td>Analytic</td>
<td>(Teasdale, 2001)</td>
</tr>
<tr>
<td>Core Self / SELF</td>
<td>Higher Order</td>
<td>(Northoff &amp; Panksepp, 2008)</td>
</tr>
<tr>
<td>Self-as-subject</td>
<td>Self-as-object</td>
<td>(Legrand &amp; Ruby, 2009)</td>
</tr>
</tbody>
</table>

### Table 2.1. Locations of Activation Differences between Narrative and Experiential Focus in the Novice Group

<table>
<thead>
<tr>
<th>Region</th>
<th>BA</th>
<th>Side</th>
<th>Narrative Focus</th>
<th>Co-Ordinates, X/Y/Z</th>
<th>Voxels in Cluster, No.</th>
<th>Z Score §</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrative &gt; Experiential</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gyrus Rectus</td>
<td>25</td>
<td>R</td>
<td></td>
<td>16 16  -12</td>
<td>27</td>
<td>3.29</td>
</tr>
<tr>
<td>Posterior Cingulate</td>
<td>23</td>
<td>L</td>
<td></td>
<td>-8  -52  28</td>
<td>41</td>
<td>3.77</td>
</tr>
<tr>
<td>Temporal Pole</td>
<td>38</td>
<td>R</td>
<td></td>
<td>44   8   -36</td>
<td>30</td>
<td>3.73</td>
</tr>
<tr>
<td>Inferior Temporal</td>
<td>20</td>
<td>R</td>
<td></td>
<td>24  -4   -40</td>
<td>5</td>
<td>3.85</td>
</tr>
</tbody>
</table>

| Experiential > Narrative|    |      |                 |                      |                        |           |
| Posterior Parietal      | 40 | L    |                 | -32  -52  28         | 9                      | 3.06      |
| Dorsolateral PFC        | 45 | L    |                 | -36  32   24         | 23                     | 3.60      |
| Mid Cingulate           | 24 | R    |                 | 8    4    32         | 5                      | 3.16      |
| OFC                    | 47 | L    |                 | -36  40   4          | 11                     | 3.13      |
| Angular                | 39 | L    |                 | -48  -48  56         | 23                     | 3.06      |

§ z Scores greater than 2.6 correspond to a P < .01; z scores greater than 3.09 correspond to P < .001 (2-tailed).
### Table 3.1
**Levels of Depression and Anxiety in Control and MT Patients**

<table>
<thead>
<tr>
<th></th>
<th>Age (±SD)</th>
<th>Gender (M/F)</th>
<th>BDI-II (±SD)</th>
<th>BAI (±SD)</th>
<th>SCL-90R (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Both Groups at Pre-training (N=36)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls (N=16)</td>
<td>42.00</td>
<td>4/12</td>
<td>20.56 (13.10)</td>
<td>13.38 (8.49)</td>
<td>79.88 (50.41)</td>
</tr>
<tr>
<td>MT (N=20)</td>
<td>45.55</td>
<td>5/15</td>
<td>23.35 (13.92)</td>
<td>16.35 (12.66)</td>
<td>108.25 (66.52)</td>
</tr>
<tr>
<td>t-test (df=34)</td>
<td>0.94</td>
<td>n.s.</td>
<td>0.62</td>
<td>n.s.</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>MT Group Training Effects (Pre vs. Post Mindfulness Training)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-Training</td>
<td>6.58 (5.67)</td>
<td></td>
<td>9.79 (9.82)</td>
<td>55.63 (50.13)</td>
<td></td>
</tr>
<tr>
<td>Difference Score</td>
<td>-15.84 (11.04)</td>
<td></td>
<td>-5.32 (6.64)</td>
<td>-47.00 (39.44)</td>
<td></td>
</tr>
<tr>
<td>t-test (df=19)</td>
<td>6.25</td>
<td>p&lt;.001</td>
<td>3.49</td>
<td>p&lt;.003</td>
<td>5.19</td>
</tr>
</tbody>
</table>

### Table 3.2
**Differences in regional activation and deactivation between Control and MT groups in response to sadness provocation**

<table>
<thead>
<tr>
<th>Anatomical Region</th>
<th>BA</th>
<th>Side</th>
<th>Cluster Size</th>
<th>Peak Z</th>
<th>x, y, z (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MT &gt; Control (training-related increases)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insula</td>
<td>48</td>
<td>R</td>
<td>43</td>
<td>4.07</td>
<td>33</td>
</tr>
<tr>
<td>Lateral Prefrontal Cortex</td>
<td>46</td>
<td>R</td>
<td>13</td>
<td>3.90</td>
<td>42</td>
</tr>
<tr>
<td>Subgenual ACC / Gyrus Rectus</td>
<td>11</td>
<td>R</td>
<td>11</td>
<td>3.87</td>
<td>6</td>
</tr>
<tr>
<td>Subgenual ACC / Gyrus Rectus</td>
<td>25</td>
<td>R</td>
<td>13</td>
<td>3.57</td>
<td>3</td>
</tr>
<tr>
<td>Thalamus (Pulvinar)</td>
<td></td>
<td>L</td>
<td>11</td>
<td>3.35</td>
<td>-12</td>
</tr>
<tr>
<td><strong>Control &gt; MT (training-related decreases)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Temporal Sulcus</td>
<td>22</td>
<td>L</td>
<td>32</td>
<td>4.26</td>
<td>-54</td>
</tr>
<tr>
<td>Lateral Prefrontal Cortex</td>
<td>10</td>
<td>L</td>
<td>13</td>
<td>3.87</td>
<td>-30</td>
</tr>
<tr>
<td>Middle Temporal Gyrus</td>
<td>21</td>
<td>L</td>
<td>18</td>
<td>3.65</td>
<td>-45</td>
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<tr>
<td>Precuneus</td>
<td>7</td>
<td>R</td>
<td>15</td>
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Table 4.1

Neural correlates of task-block-averaged respiratory rate

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<th>Anatomic region</th>
<th>BA</th>
<th>Side</th>
<th>Cluster size</th>
<th>Peak Z</th>
<th>x</th>
<th>y</th>
<th>z (mm)</th>
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<td>Insula</td>
<td>48</td>
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<td>33</td>
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<td>-72</td>
<td>-36</td>
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<td>-39</td>
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<td>53</td>
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<td>33</td>
<td>-21</td>
<td>-21</td>
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*Note. R = right; L = left; B = Bilateral; in the case of bilateral activations, the peak listed is for the side with the greater peak activation.*
### Table 4.2

*Differences in Regional Brain Activity Between Interoceptive and Exteroceptive Attention in Controls*

<table>
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<th>Anatomic region</th>
<th>BA</th>
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<th>x</th>
<th>y</th>
<th>z (mm)</th>
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<td>27</td>
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<td>12</td>
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<tr>
<td>Mid Cingulate</td>
<td>6/23/24</td>
<td>B</td>
<td></td>
<td>5.57</td>
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<td>-12</td>
<td>51</td>
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<td>45</td>
<td>-24</td>
<td>24</td>
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<tr>
<td>Extrastriate</td>
<td>17</td>
<td>B</td>
<td></td>
<td>5.29</td>
<td>-24</td>
<td>-51</td>
<td>6</td>
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<td>Pulvinar of Thalamus</td>
<td>-</td>
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<td>5.15</td>
<td>-9</td>
<td>-24</td>
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<td>-60</td>
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<td>Cerebellum (Area 9, Vermis 10)</td>
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<td>B</td>
<td>302</td>
<td>4.54</td>
<td>-9</td>
<td>-48</td>
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<td>Cerebellum / V1 / Extrastriate</td>
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<tr>
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<td>7</td>
<td>L</td>
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<td>-54</td>
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<td>Head of Caudate</td>
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<td>R</td>
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<td>3.63</td>
<td>12</td>
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<td>-3</td>
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<td>36</td>
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</table>

*Note.* R = right; L = left; B = Bilateral; in the case of bilateral activations, the peak listed is for the side with the greater peak activation.
### Table 4.3

*Differences in Regional Brain Activity Between Interoceptive and Exteroceptive Attention in the MT Group*

<table>
<thead>
<tr>
<th>Anatomic region</th>
<th>BA</th>
<th>Side</th>
<th>Size</th>
<th>Peak Z</th>
<th>x</th>
<th>y</th>
<th>z (mm)</th>
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<td><strong>Interoception &gt; Exteroception</strong></td>
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<td>15</td>
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<tr>
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<td>6/23/24</td>
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<td>5.95</td>
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<td>51</td>
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<td>Pulvinar of Thalamus</td>
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<td>18</td>
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<td>Posterior Cingulate</td>
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<td>51</td>
<td>-21</td>
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<td>Retrosplenial Cortex</td>
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<td>-3</td>
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<td>27</td>
<td>51</td>
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<tr>
<td>DLPFC, Operculum, Head of Caudate</td>
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<td>111</td>
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<td>57</td>
<td>0</td>
<td>-39</td>
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</table>

*Note.* R = right; L = left; B = Bilateral; in the case of bilateral activations, the peak listed is for the side with the greater peak activation.
Table 5.1  Summary of Experimental Task Manipulations

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<tr>
<th>Experiment</th>
<th>Stimuli</th>
<th>Attentional Task</th>
<th>Manipulation</th>
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<td>1)</td>
<td>Trait words</td>
<td>“Control the way you react to the words”</td>
<td>Narrative vs. Experiential Focus</td>
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<td>2)</td>
<td>Film clips</td>
<td>“Watch and reflect upon the film clips”</td>
<td>Controls vs. MBSR</td>
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<td>3)</td>
<td>Words/Fixation ‘+’</td>
<td>“Keep the target in mind”</td>
<td>Exteroceptive vs. Interoceptive target</td>
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</tbody>
</table>
References


prefrontal cortex of macaque monkeys. *Journal of Comparative Neurology, 371*(2), 179-207.


Critchley, H.D., Mathias, C.J., Josephs, O., O’Doherty, Zanini, J.S., Dewar, B., Cipolotti, L.,...


Wager, T.D., Rilling, J.K., Smith, E.E., Sokolik, A., Casey, K.L., Davidson, R.J., Kosslyn, S.M.,


Yotsumoto, Y. & Watanabe, T. (2008). Defining a Link between Perceptual Learning and Attention. PLOS Biology, 6(8), e221.


### Supplementary Table 2.1 Trait words used from Anderson (1968).

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<th>Word</th>
<th>Lik</th>
<th>Var</th>
<th>Mean</th>
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<td>468</td>
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<td>362</td>
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<td>360</td>
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Lik = likability rating; Var = Variance of likability ratings; Mean = meaningfulness.
### Supplementary Table 3.1

**Emotion challenge regions in the Control Group**

<table>
<thead>
<tr>
<th>Anatomical Region</th>
<th>BA</th>
<th>Side</th>
<th>Cluster Size</th>
<th>Peak Z</th>
<th>x, y, z (mm)</th>
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<tbody>
<tr>
<td><strong>Sad &gt; Neutral Film Viewing (Activations with sadness)</strong></td>
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### Supplementary Table 3.2

**Emotion challenge response in the MT Group**

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