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Jennifer Mascaro Date

A Longitudinal Investigation of Empathic Behavior and Neural Activity and Their Modulation by Compassion Meditation

By
Jennifer Streiffer Mascaro

Doctor of Philosophy

Anthropology

____
Charles Raison
Advisor

____
James K. Rilling
Advisor

____
Todd Preuss
Committee Member

____
Carol Worthman
Committee Member

Accepted:

____
Lisa A. Tedesco, Ph.D.
Dean of the Graduate School

____
Date

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By

Jennifer Streiffer Mascaro
B.A., University of Notre Dame, 2000

Advisor: Charles Raison, MD; James K. Rilling, Ph.D

An abstract of
a dissertation submitted to the Faculty of the James T. Laney School of Graduate Studies
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Abstract

A Longitudinal Investigation of Empathic Behavior and Neural Activity and Their Modulation by Compassion Meditation

By Jennifer Streiffer Mascaro

While meditation is increasingly incorporated into clinical treatments for a variety of ailments and is offered to the public with claims of increasing overall health and well-being, there are sizeable gaps in our understanding of the outcomes related to its practice. First, very little is known about how meditation affects social cognition and related neural processes. Second, much of the current research on meditation is fraught with flawed experimental designs and incomplete assessments of practitioners, such that many have called into question *any* conclusions regarding the effects of meditation practices. Third, research on meditation has primarily been conducted under the assumption that all practitioners meditate for a common reason and with common goals, and that meditation acts the same way in all practitioners. This dissertation was designed to address the aforementioned gaps. More specifically, we aimed to assess **(1) the social cognitive, neurobiological and behavioral changes related to compassion meditation, (2) the mechanisms by which neurobiological change is translated into outcomes in practitioners, and (3) the nuanced ways in which *particular* individuals adopt the meditation practice and attain effects**. We used a randomized, controlled and longitudinal investigation of a secularized compassion meditation program adapted from the 11th century Tibetan Buddhist *lojong* tradition, and employed a battery of social cognitive, neurobiological, personality and behavioral assessments in order to explore the ways in which the practice of compassion meditation led to outcomes. Despite the fact that no study participants reported goals related to enhancing empathy, meditation enhanced empathic accuracy as well as the brain activity related to it, and it was meditation-related enhancement of neural activity in putative mirror neuron regions that partially accounted for enhanced empathic accuracy. However, other aspects of empathy remained unchanged, including self-reported levels of empathy, compassionate behavior, and the neural activity related to viewing another in pain. In addition, baseline brain activity predicted engagement with the practice, and baseline levels of anxiety and spiritual meaning moderated the effects of meditation. These findings highlight the importance of more holistic and rigorous meditation research, and suggest that compassion meditation may represent a unique behavioral intervention for enhancing empathy.

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Chapter 1
Introduction

Homo sapiens is a species defined in large part by the cognitive traits that support complex social experiences. And while much debate surrounds the question of whether cognitive features such as 'theory of mind' and 'empathy' are uniquely human, the extent to which humans have elaborated on and depend on these cognitive features makes them, at the least, *particularly* human. For example, while there exist moving anecdotal accounts of our closest living relatives engaging in what appears to be compassionate and "targeted helping,"(de Waal 2009 p. 92) humans routinely help kin, unrelated friends and acquaintances, as well as unknown others, sometimes at tremendous cost. What is more, it is increasingly clear that the human brain and body are organized to support prosocial emotions and behaviors. For example, the act of making anonymous donations to others recruits mesolimbic reward pathways (Moll et al. 2006), and a plethora of data show that compassionate behavior enhances immune function (McClelland and Kirshnit 1988) and ameliorates aspects of negative health such as depression (Musick and Wilson 2003; Thoits and Hewitt 2001) and chronic pain (Arnstein et al. 2002). Yet, while we know that humans have evolved complex neural systems for prosocial emotions, skills and behaviors, there is incredible variation in the extent to which we utilize them and in the contextual factors that help determine when and how we utilize them. The research described in this dissertation project was motivated, in part, by an interest in exploring the ways in which contextual factors and cultural behaviors modulate prosocial cognition and behavior.

The second over-arching motivation for this research project is that, while there are theoretical accounts regarding the mechanisms that underlie our ability to empathize with others, questions remain regarding the neural systems by which lower-level perceptual processes are translated into the ability to feel and understand others' emotions, as well as those systems by which such an empathic response is translated into compassionate, altruistic behavior. Is emotion regulation necessary for an empathic response to motivate altruistic behavior? If an empathic response is augmented, for example, by meditation, is this modulation due to enhanced activity in bottom-up (e.g. perceptual processes) or top-down (e.g. perspective-taking) systems? These are some of the many questions that motivated this dissertation.

These two motivations are part of a larger impetus, which ultimately served as fuel throughout this research project. That is, all of the research presented here was done with the understanding that prosocial emotions such as empathy and compassion, and concomitant behaviors, benefit individuals (both the person who initiates them and their target) as well as society. This understanding arises with research that has emerged in the last twenty years showing that empathy is related to moral development in adolescents (Eisenberg and Carlo 1995), and reduces aggression and violence toward others (reviewed in Davis 1996; Hoffman 2001). Equally important, research has shown that empathy and compassion help cultivate other positive attributes, such as friendliness, conscientiousness and openness (del Barrio et al. 2004), and is a crucial piece in any successful social relationship (Davis 1996). This research project was carried out with hopes that it would contribute to and build upon this growing literature by exploring the ways in which a behavioral practice might enhance these prosocial emotions and behaviors.

Goals of the research project

This research project has four primary goals.

1. Explore individual variation in the neural systems supporting three types of prosociality: 1. empathy for another person in pain, 2. empathic accuracy, and 3. compassionate behavior.

2. Examine how the neural systems supporting empathy for pain are related to compassionate behavior.

3. Investigate the ways in which training in and practice of a secularized compassion meditation practice based on the 11th century Tibetan *lojong* tradition impacts self-reported empathy and the neural systems supporting: 1. empathy for another person in pain, 2. empathic accuracy and 3. compassionate behavior.

4. Explore the ways in which underlying personality features moderate the effects of compassion training, in order to more fully understand how a behavioral practice operates in individuals to affect cognitive and behavioral change.

Background

What is empathy?

In his review of the historical trends surrounding the study of empathy, Davis (1996) remarked that "the study of empathy, as much as any topic in psychology, has been marked by a failure to agree on the nature of and relations among its core constructs" (p. 11). This is due to shifting historical trends regarding the emphasis, cognitive or affective, that researchers brought to the study of empathy. In addition to these shifting historical trends, Batson (2009) recently points out that researchers use the term empathy to investigate two different types of questions. First, researchers have asked "How can one know what another person is thinking or feeling?" Secondly, others have asked "What leads one person to respond with sensitivity and care to the suffering of another?" (p. 3) He notes that these questions may be related, but that often the two questions are approached separately by disparate disciplines: the first question is primarily asked by philosophers, cognitive scientists and neuroscientists, primatologists and developmental psychologists, while the latter question is generally grounds for developmental and social psychologists. In other words, research related to empathy has been problematic due to both historical and paradigmatic forces, which have determined differential approaches and theoretical models surrounding the construct. For this reason, this dissertation will begin with an explication of what is meant by various terms that will be used throughout this text, as well as a working theoretical model under which the research project began.

Glossary of empathy-related terms used in this text

1. **Empathy**: an isomorphic affective response to another coupled with some level of understanding that the affective state is elicited by the other (de Vignemont and Singer 2006; Eisenberg and Eggum 2009). An empathic response has two crucial components:

   a. **Affective**: involves a shared affective experience (this may be synonymous with *emotional contagion* and related to *simulation* below)
   b. **Cognitive**: the ability to understand or have some degree of conscious awareness that the affective experience is evoked by another. This may include, at least mechanistically, a self-other distinction and perspective-taking (this may be synonymous with *cognitive empathy*, *emotional theory of mind* and related to *perspective taking* below).
2. **Sympathy**: a non-isomorphic affective response to another.
3. **Compassion**: the wish for another to be free from suffering (HHDL 2001); related to loving kindness, or the wish or desire for another to experience well-being or happiness; can be synonymous with *sympathy*
4. **Emotional contagion** (sometimes called affective empathy): an isomorphic affective response automatically and unintentionally elicited by perception of that affective state in another (Hatfield et al. 1993)
5. **Personal Distress:** an aversive affective state evoked by witnessing the distress of another. As Batson explains (2009), "This state does not involve feeling distressed *for* the other or distress *as* the other. It involves feeling distressed *by* the state of the other" (p. 8)
6. **Cognitive empathy** (a.k.a. Theory of Mind, perspective taking): to know (to some degree/with some accuracy) the contents of another person's internal mental state
7. **Simulation:** automatic activation of neurobiological or physiological processes that matches those of an observed other. Some social cognitive neuroscientists

have called this the “shared representations account of social interaction and intersubjectivity” and it is thought of as an integral mechanistic process in the neurobiological account of empathy (Singer and Lamm 2009 p. 82).

8. **Prosocial:** behavior that benefits another
9. **Prosocial emotions:** affective responses that lead to behavior that benefits another.
10. **Altruism:** behavior that benefits another at a cost to oneself.

See **figure 1-1** for a schematic of the ways in which these empathy-related terms are related to one another.

We agree with others (Singer and Lamm 2009), that, in general, simulation processes and emotion contagion are the first step in the empathic process. These combine with some cognitive feature to produce empathy, which in turn may lead to sympathy and/or compassion, and then to prosociality (see **figure 1-1**) (Eisenberg 2000). Each of these processes, as well as the neurobiology related to them, will be discussed in more detail in relevant chapters to follow.

Main Study Design

Study Overview: A schematic overview of the study is presented in **figure 1-2.** This project was part of a larger study (CALM) that investigated the effects of meditative practices on the physiological response to psychosocial stress. All aspects of this study design will be explained in greater detail in appropriate sections of the dissertation, and this overview is only meant to orient the reader to the general study methodology. In order to address each of the overall aims of the dissertation, 29 subjects (16 male) were randomized to 8 weeks of either compassion meditation training or to participation in an active control condition comprised of a twice-weekly health education discussion group. Prior to, and again upon completion of, these interventions all subjects received fMRI scans and completed questionnaires that measure behavioral/psychosocial factors relevant to empathy, well-being and meditation, including:

1. A qualitative questionnaire asking subjects about their motivations for entering the study and about their goals with respect to meditation.
2. The Interpersonal Reactivity Index (IRI) (Davis 1983)
3. The Psychopathic Personality Inventory (PPI) (Lilienfeld and Andrews 1996)
4. The Depression Anxiety Stress Scale (DASS) (Lovibond and Lovibond 1995)
5. The Kentucky Inventory of Mindfulness Skills (KIMS) (Baer et al. 2004)
6. The Spiritual Meaning Scale (SMS) (Mascaro et al. 2004)

The fMRI scan consisted of a task designed to evaluate the neural correlates of empathy for others (empathy-for-pain, referred to as EFP), as well as a task designed to assess empathic accuracy (reading the mind in the eyes, referred to as RtME). All scans were completed prior to other CALM assessments, except in one case in which a subject had to reschedule due to a snowstorm.

Upon completion of the 8-week behavioral intervention, subjects completed Time 2 assessments, again prior to all other CALM assessments. A total of 21 (12 male; 13 Compassion) subjects continued through the entirety of the study and received the full complement of assessments. At Time 2, subjects completed an abbreviated set of questionnaires, including the IRI, DASS and SMS. The Time 2 scanning session was identical to the Time 1 session with the addition of a 5 minute resting state scan after the

DTI scan. Upon completion of the scan, subjects were removed from the scanner and underwent a compassion induction paradigm in which they were led to believe that another study participant had been in a car accident and were given a chance to give an anonymous donation to that person.

In designing our study to investigate the effects of compassion mediation on empathy, we chose our three assessments (1. EFP task, 2. RtME task, 3. Compassion induction) for several reasons. These will be discussed in turn.

1. Tasks of Affective *and* Cognitive emotional empathy: As defined in the glossary of terms, empathy is distinguished from related concepts because it includes both an affective and cognitive component. Recall that the *affective* component includes sharing the affective experience of another, and may be synonymous with emotional contagion or personal distress if the cognitive component is not present. The *cognitive* component involves some level of conscious awareness that the affective experience is evoked by another. Thus far, the branch of social cognitive neuroscience concerned with investigating empathy has used paradigms that focus on the more affective component of the empathic response. In fact, many of the study designs utilized have made it difficult to distinguish whether the neurobiological response is related to empathy or to personal distress. For this reason, we wanted to utilize a task that targeted both affective and cognitive aspects of an empathic response: 1. Empathy for Pain task, and 2. RtME. It should be noted that there is no reason to believe that each task does not evoke *both* affective and cognitive empathy (although some have pointed out how these two components are observed independent of one another at a surprisingly frequent rate (Lombardo et al. 2010). Rather, it is our belief that the empathy for pain task evokes (at the least) the affective dimension and the RtME task evokes (at the least) the cognitive dimension. By administering both tasks to subjects we can not only compare brain activity during both tasks, but investigate whether compassion meditation differentially affects the brain activity observed during the two different tasks.

2. Affective Empathy task: In choosing a task with which to study affective empathy, we decided to use the EFP task for two reasons. First, there have been a multitude of studies that have used some variant of this task, in which the participant receives stimuli (visual, auditory or a cue to imagine another person) related to empathy for another person in pain. The results from these studies are remarkably consistent and very well characterized (Lamm et al. 2011). Second, we wanted to employ a task that would allow us to make mechanistic hypotheses regarding the effects of meditation. With the EFP paradigm, we can more easily investigate whether meditation enhances neural activity in parts of the brain related to interoception (the anterior insula), autonomic arousal (anterior medial cingulate cortex), the evaluation of threat (amygdala), simulation processes in mirror neuron regions (e.g. inferior frontal gyrus), or mentalization (e.g. medial PFC). In contrast, if we choose to use more complex stimuli such as empathy-inducing stories or scenes (for example, as can be found in the International Affective Picture System) we would have a more difficult time definitively interpreting results.

3. A task of Empathic accuracy: Empathic accuracy is a measure of one's ability to *accurately* infer the emotions of another. While there have been a handful of neuroimaging studies investigating empathic accuracy (for example, Zaki et al. 2009 and the RtME studies referenced in chapter 2), the field of human social neuroscience that investigates empathy has thus far been more concerned with exploring the brain regions related to the more affective dimension of the empathic response. What is more, most of these studies use correlations of self-report levels of empathy with brain activity, and yet there is rich evidence that self-reported levels of trait empathy have little relation to empathic accuracy (Davis and Kraus 1997; Thomas and Fletcher 1997).

In addition to the fact that people are simply bad at estimating their own levels of trait empathy, it is crucial to investigate empathic accuracy because it is this cognitive skill that is likely most closely related to a final behavioral output or response. In fact, some have suggested that empathic accuracy measures far outperform self-report measures in predicting important life outcomes (Ickes 1997). For example, empathic accuracy in mothers (toward their children) is related to positive well-being in children (Crosby 2002), in males (toward their partner) is inversely related to levels of physical violence against their partners (Clements et al. 2007), and in adolescents (toward peers) is related to mental health and well-being (Gleason et al. 2009). Moreover, Levenson and Ruef (1997) report that, while emotional contagion is high in dissatisfied relationships, relationship distress is inversely related to levels of cognitive empathy that supports empathic accuracy.

Finally, important for this study, there are factors that modulate empathic accuracy. For example, Eisenberg and colleagues (1997) report that, in children, amount of social interaction and the extent to which one's culture promotes cooperation are related to the ability to accurately take the perspective of another. In other words, empathic accuracy not only appears to be most related to real outcomes, but it is affected by contextual factors and interactions among people, and thus may be subject to modulation by compassion meditation.

4. A task augmented by oxytocin: In order to test the effects of compassion meditation on empathic accuracy, an optimal task was one known to be affected by experimental manipulation of the neurobiological systems thought to be important for compassion and empathy. Given the importance of oxytocin for aspects of social perception such as eye gaze (Guastella et al. 2008), for positive affective dimensions of emotional interactions such as social reward (Insel and Young 2001) and feelings of romantic love (Gonzaga et al. 2006), and for prosocial behaviors such as generosity (Zak et al. 2007), trust (Heinrichs et al. 2003; Kosfeld et al. 2005), and empathy (Barraza and Zak 2009), it remains likely that, should compassion meditation enhance prosocial emotions, it does so at least in part by modulating the oxytocin system. Importantly, three studies suggest that oxytocin is related to performance on the RtME task. Domes et al. (2007) found that male volunteers who self-administered intranasal oxytocin performed more accurately on the RtME task compared to a placebo-controlled group. More specifically, this effect was only significant for the task items rated most difficult and the authors speculated that oxytocin may enhance perceptual networks related to face processing, perhaps by modulating emotional reactivity in the amygdala. More recently, Guastella and colleagues (2010) found that oxytocin administration improved task performance for adolescents (age 12-19) diagnosed with Autism or Asperger's syndrome. Another study by Rodrigues and colleagues (2009) found that genetic variation in a polymorphism of one oxytocin receptor gene (rs53576) explained variation in accuracy on the RtME task. Thus, we chose to use the RtME task of empathic accuracy in order to capitalize on the known modulatory properties of the oxytocin system on task performance.

5. A behavioral measure of compassion: In order to test social psychological and neuroscientific models of empathy and altruism (see **figure 1-1** for relationship), we felt it was important to investigate the way in which prosocial emotions lead to compassionate, altruistic behavior. This required a behavioral metric of altruistic action, and we wanted to be able to relate that action to empathy-related neural activity. For this reason, we chose to employ deception in order to induce compassion for a person that the study participants had previously seen in the EFP video clips, so that we could relate brain activity during the EFP task to helping behavior. In coming up with the compassion induction, we also considered factors related to Tibetan Buddhist models of compassion. For example, we wanted to make sure that we were measuring an active, behavioral type of compassion (rather than just asking subjects to report on how compassionate they felt). This was particularly important given that the last stage of the compassion training is one in which the participant "is guided through a meditation designed to move from simply wishing others to be free of unhappiness to actively committing to assistance in their pursuit of happiness and freedom from suffering." Moreover, we wanted a situation in which the participants knew that they were not obligated to this person in need and would likely never see the person again, but that (1) the person was suffering, and (2) the participant had the means to help them (in the form of the cash they had just received for participating in the study).

For these reasons, we have chosen to employ the EFP task, the RtME task, and the compassion induction in our investigation of prosocial cognition and its modulation by compassion meditation.

What follows?

The second and third chapters present and discuss the investigation of cognitive and affective empathy in which we utilized the Reading the Mind in the Eyes and the Empathy for Pain task, respectively. The focus of these chapters is on the task itself, and thus, there is no discussion of changes related to meditation practice in either of these chapters. The fourth chapter presents results for the longitudinal investigation of compassion meditation with respect to changes in the RtME and EFP tasks and group differences in compassionate behavior. The fifth chapter presents and discusses a more in-depth exploration into the ways that underlying personality factors and attitudes were related to engagement with the meditation practice as well as the ways in which these factors moderated the effects of meditation practice.

Specific Aims of the dissertation

1. Construct an EFP task using dynamic video stimuli, and validate that this task activates neural regions thought to be important for empathy. In addition, we will investigate the relationship between neural activity during the task and self-reported levels of trait (IRI) and state (post-task probe) empathy.

2. Construct an empathic accuracy task based on the RtME task, and validate that this task activates neural regions thought to be important for accurately identifying others' emotions based on their facial expressions.

3. Investigate the effects of randomization to, and practice of, compassion meditation on
    a. State and Trait empathy levels

   b. Neural activity during the EFP and RtME tasks
   c. Compassionate behavior

4. Investigate whether meditation-related changes in neural activity are related to meditation-related changes in self-reported empathy (state and trait), empathic accuracy, or compassionate behavior

5. Investigate whether baseline personality features, meditation-related goals or brain activity during empathy tasks predicted engagement with meditation training.

6. Explore whether baseline personality features or meditation-related goals moderate the effects of meditation.

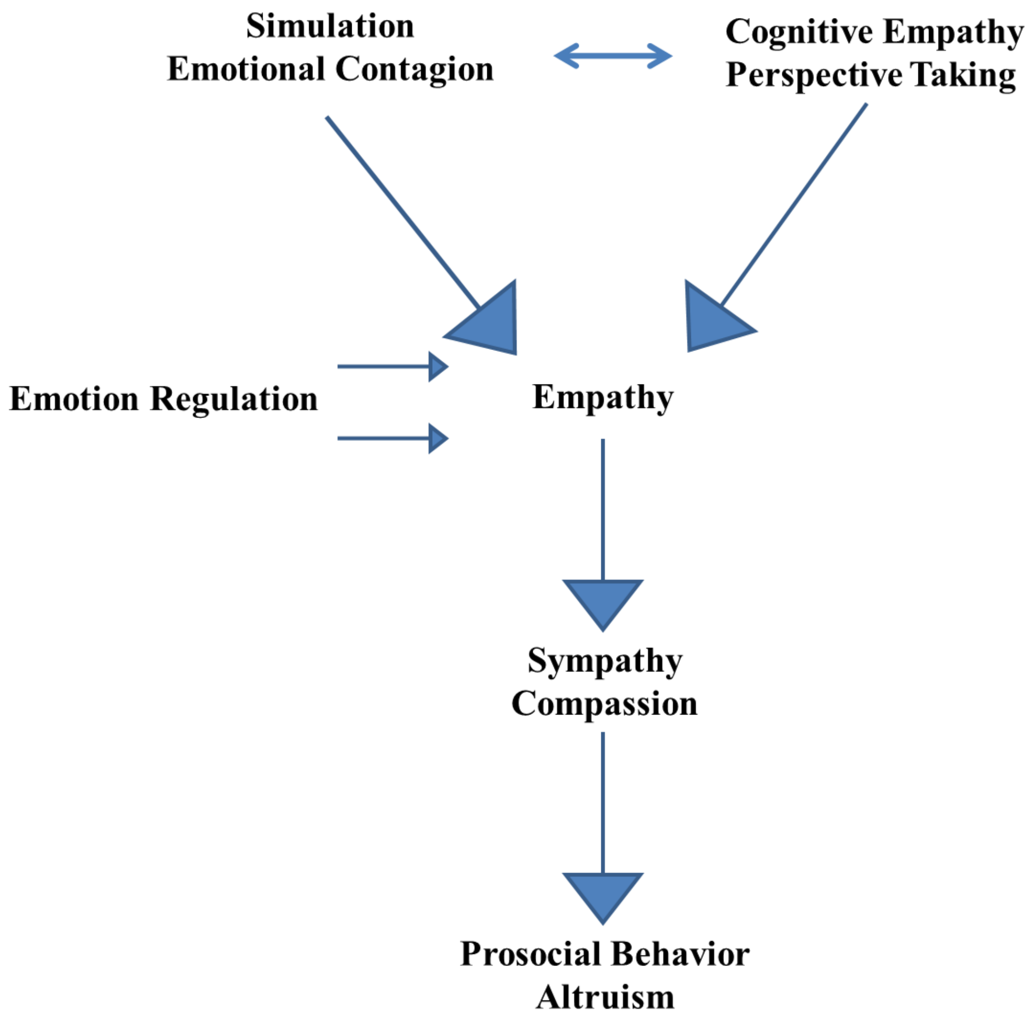

Figure 1-1: Schematic of theoretical orientation of various components of prosocial emotions, cognitions and behaviors and how they relate to one another.

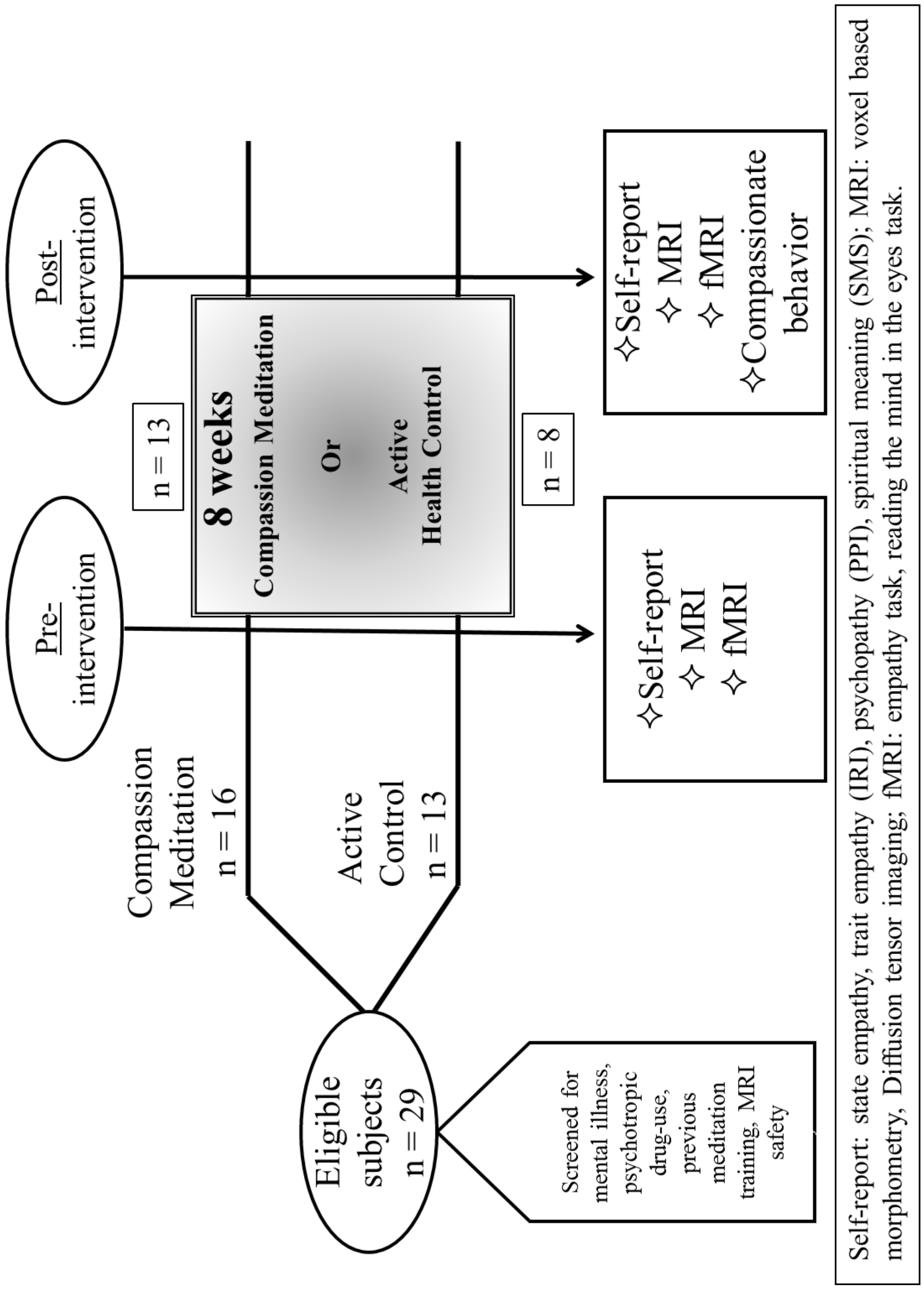

Figure 1-2: Overview of the complete study design.

Chapter 2

Empathic Accuracy

Introduction

Understanding the neural mechanisms of face-to-face interactions is a dominant goal within social cognitive neuroscience. In particular, a plethora of research has sought to identify the neurobiology underlying the ability to accurately identify and understand another person's emotional mental states. This might be considered one aspect of a broader cognitive feature which is often referred to as Theory of Mind (ToM) or mentalization, defined as the ability to represent and attribute beliefs, desires, intentions and emotions to oneself and to others. It is this ability that underpins successful human social functioning, and which many have argued distinguishes humans from other species (Premack and Woodruff 1978; Povinelli and Vonk 2003; Saxe 2006).

Over the last two decades, the use of functional neuroimaging has made possible an exploration of the neural underpinnings of our ability to mentalize. While there remains debate regarding which neural regions are unique to the process of mentalization, it is clear from a host of studies employing a wide variety of ToM tasks that the act of mentalizing engages a network of regions, including the medial prefrontal cortex (dmPFC) and anterior paracingulate cortex, the temporal poles, posterior superior temporal sulcus (pSTS) and temporo-parietal junction (TPJ) (Gallese et al. 2004; Saxe 2006; Siegal and Varley 2002; Singer 2006).

In addition to the aforementioned regions that are active regardless of ToM task, it has become clear that the ability to infer others' mental states based on biological motion (e.g. bodily movements, facial expressions) recruits brain activity thought to make up the mirror neuron system. More specifically, when reasoning about others' actions, humans automatically and unconsciously simulate aspects of that action, providing them a first-person experience of the action that the observed individual is performing (Gallese et al. 2004; Keysers and Gazzola 2007). This simulation perspective is related to ideas that emerge from the study of embodiment, which suggest that bodily states arise and change during social interactions and play a crucial role in social information processing (Barsalou et al. 2003). With regards to emotion understanding, these simulation and embodiment processes appear to be crucial. When subjects are asked to judge the facial expression of another person, not only do subjects subtly and covertly mimic the facial expression, but their accuracy is related to the extent to which they mimic the facial expression. When mimicking is blocked (for example, when subjects are told to hold a pen in their mouth), subjects are much slower in categorizing facial expressions (Barsalou et al. 2003).

The mirror neuron circuit thought to support the simulation of facial expressions includes two mirror neuron regions, one located in pars opercularis of the inferior frontal gyrus (IFG) and the other in the inferior lateral parietal cortex, along with a region in the superior temporal sulcus related to higher-order visual processing (Iacoboni and Dapretto 2006). Some have advanced the idea that the STS provides a visual description of the action, while the frontal mirror region is related to understanding the goal of the observed action (Iacoboni and Dapretto 2006). A recent study used functional connectivity analyses to show that, when viewing an emotional facial expression, activity in the IFG had an earlier and causal relationship with limbic activity in the anterior insula (AI) and fronto-orbital regions (FO) (Jabbi and Keysers 2008). This region of the insula and frontal cortex is known to be crucial for interoceptive awareness, and others have suggested that it is this activity in the anterior insula that serves as a link between lower-level sensory aspects of simulation and the higher-level structures involved in mentalizing (Keysers and Gazzola 2007). Taken together, we see a plausible series of neural events that culminate to support mentalizing: lower level perceptual processing of the facial expression in the temporal cortex (pSTS) feeds into mirror neuron regions related to understanding the goal or meaning behind the expression (IFG). This mirror simulation leads to activity in limbic regions (AI and FO), which in turn feed into higher order regions thought to subserve inference and reasoning about the facial expression (dmPFC, temporal poles and TPJ). (See **figure 2-1** for a schematic of the proposed mechanism)

The Reading the Mind in the Eyes Task

The Reading the Mind in the Eyes' (RtME) task was developed as an adult test of what the creator Simon Baron-Cohen and colleagues called an 'advanced theory of mind'. By "advanced" the authors mean that the task is more difficult than one that assesses an individual's ability to infer the thoughts of others (first order ToM) or to reason about what one person thinks about another person's thoughts (second order ToM). Rather, accuracy on this task involves extracting social information from a subtle source and using this information to infer the mental states of another (Baron-Cohen et al. 2001).

The authors give the following mechanistic account of what is involved in accurately performing the task:

> "The subject needs to have a mental state lexicon and know the semantics of these terms. The Eyes Test then involves mapping these terms to fragments of facial expressions of mental states – just the part of the face around the eyes. At a reportedly unconscious, rapid and automatic level, subjects must match the eyes in each picture to examples of eye-region expressions stored in memory and seen in the context of particular mental states to arrive at a judgment of which word the eyes most closely match." (Baron-Cohen et al. 2001 p. 241)

The authors note that while the RtME is an advanced test of theory of mind, it only involves the first aspect of mentalization: processing social stimuli in such a way that allows one to infer the mental state of another individual (e.g. distressed). It does not include the next stage of mentalization, which involves inferring aspects of the context of the emotion state (e.g. distressed because he is late for work.) (Baron-Cohen et al. 1997).

The RtME task was developed in order to identify specific deficits in autistic adults, and in fact, investigations using the task reveal a consistent inverse relationship between performance on the RtME and scores on the Autism Spectrum Quotient (AQ) (Baron-Cohen et al. 1997). Since then, it has become a useful instrument for testing mechanistic models of various psychiatric disorders that are characterized in part by social deficits. For example, psychopathic individuals (defined by the Hare Psychopathy Checklist-Revised, 1991) show no impairment in the task (Richell et al. 2003), while schizophrenic patients perform significantly worse than controls (Russell et al. 2000). More recent studies have shown that individuals with eating disorders (Harrison et al. 2010) perform worse on the task, as do women with unipolar clinical depression. Interestingly, both of these results remain significant even when controlling for anxiety. However, a second study found that college students who scored high on the dysphoria subscale of the Beck Depression Inventory (BDI) performed better on the task (Lee et al. 2005). Moreover, a follow-up study further suggests that dysphoria may be *the* causal - rather than an associated - feature, as positive mood induction in previously depressed subjects led to poorer task performance (Harkness et al. 2010). Similarly, a study by Fertuck and colleagues (2009) showed that a population with borderline personality disorder (BPD) performed better than a control group; however, many other studies have found that patients with BPD are *less* accurate in judging facial expressions (Bland et al. 2004), so the reported results using the RtME may not be entirely consistent with other research, or may reflect differing levels of empathic accuracy in those with BPD depending on the valence of the emotional facial expression that they are asked to identify.

Non-clinical populations consistently exhibit a sex difference in performance on the RtME task, with females performing more accurately (Baron-Cohen et al. 1997; Baron-Cohen et al. 2001). More recently, the task has been extended to explore differences in empathic accuracy in healthy populations. Domes et al. (2007) found that intranasal administration of oxytocin, compared to a placebo, increased accuracy on the more difficult items in the RtME task. Interestingly, a more recent study by Guastella and colleagues (2010) found that OT administration improved task accuracy for a group of adolescents diagnosed with Autism, but in this case the effects were more robust for those items considered to be easy. Consistent with these findings regarding the effects of OT on RtME performance, Rodrigues and colleagues (2009) found that having a particular variant of the oxytocin receptor polymorphism is related to enhanced accuracy in the task. And finally, Adams et al. (2010) created a variant of the task using photographs of Asian faces and found that both Japanese and American participants were significantly more accurate when judging the mental states of same- versus other-culture photographs. In sum, these studies suggest that performance on the RtME task is related to physiological, personality and contextual differences within non-clinical populations.

Neurobiology supporting the RtME task

In terms of brain regions recruited during the RtME task, healthy populations reliably activate regions thought to be important for mentalizing (mPFC (BA9), temporal poles and temporo-parietal regions), as well as regions of the brain thought to be part of a functional system for understanding facial expressions, including putative mirror neuron regions (inferior frontal gyrus [IFG] [BA 44], middle and superior temporal gyri). In addition, the task recruits brain activity in areas important for the experience and understanding of emotion (amygdala, bilateral insula), as well as in the hippocampus and striatum (Adams et al. 2010; Baron-Cohen et al. 1999).

In further support of the role of these regions for accurately reading emotions based on the eye region, investigators find consistent patterns of hypoactivation related to poor performance on the task. For example, Baron-Cohen found that compared to a control group, an autistic population showed reduced neural responses in the amygdala, insula and IFG (Baron-Cohen et al. 1999). Healthy parents of autistic children, when compared to controls, also show reduced activation in IFG and in the middle temporal gyrus (Baron-Cohen et al. 2006). The pattern of IFG and temporal lobe hypoactivation in schizophrenic populations is very similar to that of autistic populations (Russell et al. 2000).

Even within non-clinical populations, differences in activation are related to differential task performance. For example, Baron-Cohen (2006) found sex differences in brain activity during the task, with men showing more activation in the dorsolateral prefrontal cortex and females showing more activation in bilateral IFG (BA 44). Castelli et al. (2010) found that a population of elderly subjects did not activate the amygdala during the task while a young adult population did, but activated the mirror neuron system more extensively. Because there was no difference in performance between the age groups, the authors suggested that the elderly population was using a compensatory mechanism to make up for decreased amygdala activation during the task. Adams and colleagues (2010) found that activity in the posterior STS was increased when subjects performed a same-culture compared to other-culture RtME and that this difference in activation was correlated with performance biases in the same-culture task. Thus, a pattern emerges in studies of healthy and clinical populations suggesting that accurate performance on the RtME task is related to brain activation in the amygdala, IFG, temporal poles, STS, TPJ, and dmPFC.

Goals of this study

In keeping with the larger goals of this dissertation, the RtME task was used to explore individual variation in aspects of prosocial emotions and behavior as well as to investigate factors that mediate and moderate this variation. The RtME task was included in our full study as a measure of empathic accuracy, and was employed in the fMRI scanner in order to investigate the neurobiology of accurate emotion identification. With regards to its place in the full study, we intend to assess changes in accuracy as well as task-related brain activity that may result from training in and practice of compassion meditation. Before testing our meditation-related hypotheses (in subsequent chapters), we will investigate the task itself in order to verify that it is a meaningful task of empathic accuracy. We also intend to explore individual variation in both task performance and in the neural correlates of task accuracy in order to more fully understand how engagement with a meditative practice may modify these processes. More specifically, we sought to:

1. **Replicate previous findings related to the RtME task, using a slightly modified version of the task.** As will be discussed in more detail in the methods section, we adapted the original (non-scanner) RtME task for use in the full study. In particular, we attempted to maintain the difficulty of the original RtME task, while others who have adapted the original task for use in the fMRI scanner have adapted the task in a different way. Thus, it is crucial that we assess whether task performance results in changes in activity in the same neural regions that have been shown to be active in other RtME studies.

2. **Conduct a preliminary comparison of RtME accuracy and neuroimaging results collected twice from the same subjects.** Because the RtME task was used in the longitudinal design employed for the full study, we have scanned the majority of our subjects twice using this task. To the best of our knowledge, this

is the first time that the task has been utilized twice in the same subjects. Thus, we are in a unique position to do a preliminary evaluation of test-retest reliability. It should be stressed, however, that subjects have gone through a behavioral intervention between scanning sessions, and thus are not the same at Time 2.

3. **Extend previous findings by investigating the relationship between task performance and brain activity during the task with individual variation in self-reported empathy, psychopathy, stress, anxiety and depression.** Despite the emerging findings when the RtME task has been used as a test of empathic accuracy, there remains much that is unknown, and some inconsistencies remain. First, it is unclear how self-reported empathy and perspective taking is related to the neural systems that underlie empathic accuracy. Moreover, while individuals with psychopathy may do equally well on the task, it remains possible that psychopathic personality features are related to a different pattern of brain activity during the task. In addition, there is a lack of convergence concerning the relationship between performance on the RtME task and aspects of well-being such as depression. While this likely reflects the heterogeneity of depressive states, it is worth further exploration of this relationship with neuroimaging assessments.

To these ends, we hypothesized that:

1. The version of the RtME task used here will activate the aforementioned brain regions found in other RtME studies, including dmPFC, IFG, temporal pole, STS, amygdala and TPJ.
2. Self-report measures of empathy will be positively related to RtME scores and related brain activity, and psychopathy scores will be negatively related to brain activity during the task.
3. Self-reported levels of stress, anxiety and depression will be negatively related to RtME scores and related brain activity.

Methods

Participants

Twenty-nine (16 male) participants from the Atlanta area were recruited using a combination of fliers and electronic notifications posted at several local universities, as well as electronic advertisements on Craigslist. Participants were between the age of 25 and 55 (M = 31.0; SD=6.02), were screened and excluded for (self-reported) use of any psychotropic medication (i.e. antidepressants, anxiolytics, psychostimulants, or mood stabilizers) within one year of screening, as well as for regular use of any medications that might influence activity of the autonomic nervous system, HPA axis or inflammatory pathways. Subjects' were also excluded for any serious ongoing medical or psychiatric condition that might influence the results of the study, including post-traumatic stress disorder (PTSD), chronic pain or other pain disorders, depression, anxiety disorders or a history of schizophrenia or bipolar disorder, as well as for substance abuse occurring within one year of study entry. Subjects were screened for MRI safety, handedness (only right handed participants were included in the study), and all participants had normal or corrected-to-normal vision.

During a second visit approximately 10 weeks after the first, subjects were scanned a second time using the same RtME paradigm. Due to subject attrition, only 21 (12 male) subjects were scanned the second time. It is important to note that each subject participated in an 8-week behavioral intervention in the interim time between scans, and thus differences between the two scanning sessions may be attributable to real changes that the subjects underwent as part of the intervention. Nevertheless, where appropriate, time 2 findings will also be reported here and caveats to these findings will be considered in the discussion session (see **table 2-1** for descriptive statistics of both Time 1 and 2 samples).

Stimuli

The stimuli used in the task were modified from the original RtME task (Baron-Cohen et al. 2001), which consists of 36 black and white photographs depicting the eye region of an equal number of male and female Caucasian adults. The adults in the photographs are actors and actresses portraying an emotional state. The photographs span the width of the face from midway up the nose to just above the eyebrows (see **figure 2-2** for an example item). Along with the photograph, participants see 4 mental state choices, one correct answer and 3 foil words. The creators of the task attempted to ensure that the 3 foil words have the same emotional valence as the correct answer, all mental states words are considered complex mental states, as no basic emotions (happy, sad, angry, afraid, disgust) are used.

In order to construct the block design used in the fMRI scanner, the original RtME task was modified in the following ways.

1. The original 36 items were narrowed down to 30, with the 6 easiest items (in the author's judgment) omitted.
2. 30 matching control items were created using the same 30 photographs used in the emotion task, with gender choice replacing the mental state words. The order of the gender choice was randomly alternated so that the subjects had to read the choices for each item (see **figure 2-2** for example items). The 60 items (30 emotion, 30 gender) were grouped into 6 alternating blocks, with 10 items per block. There was a 20 s. rest period between each block.
3. Subjects were given up to 8 seconds to view the eyes and choose their answer. After they chose an answer, a screen indicated to them which answer they chose in order to ensure that they did not get confused with the button box during the task. If they did not make an answer choice during the 8 seconds, the item disappeared, they were told that they did not make a choice and the next item appeared (see **figure 2-3** for schematic of the task).

Of note, while all previous fMRI studies utilizing the RtME task have used a modified version of the RtME that uses only two emotion word choices in the emotion task (in order to more closely match the control task), we preserved the original 4-choice design. This was done in order to maintain the difficultly of the original task, and thereby reduce the risk of a ceiling effect so as to leave room for subjects to increase their accuracy at Time 2 for the Main study. This meant that the Emotion task was more difficult and time-consuming than the gender task, and it remains possible that this influenced the results. This will be discussed further in a later section.

Upon entering the Imaging Center, subjects were seated in a testing room outside of the fMRI scanning room. They were given a health screening form, a consent form and a HIPPA form. They were also asked to complete the following psychometric instruments, in this order:

Interpersonal Reactivity Index (IRI) (Davis 1983): This 28-item instrument uses a likert scale of 0-4 and indexes 4 different emotional responses related to empathy: a perspective-taking scale (“When I’m upset at someone, I usually try to “put myself in his shoes” for a while.”) assesses one’s ability and propensity to adopt another person’s perspective; a fantasy scale which measures the tendency to identify with fictional characters in movies, plays or books (“When I watch a good movie, I can very easily put myself in the place of a leading character”); an empathic concern scale which measures ones’ feelings of concern and compassion for others (“When I see someone being taken advantage of, I feel kind of protective toward them.”) and a personal distress scale which measures personal feelings of anxiety or discomfort when faced with another’s suffering (“In emergency situations, I feel apprehensive and ill-at-ease.”). In particular, we focused on the perspective-taking and empathic concern subscales.

The Psychopathic Personality Inventory (PPI) (Lilienfeld and Andrews 1996): This 56-item instrument asks subjects to rate on a likert scale of 1-4 how true each item is as applied to the subject. It has subscales that measure Machiavellian Egocentricity (“I sometimes try to get others to “bend the rules” for me if I can’t change them any other way.”), Social Potency (“I am a good conversationalist.”), Coldheartedness (“I often become deeply attached to people I like.”), Carefree Nonplanfulness (“I generally prefer to act first and think later”), Fearlessness (“I might enjoy flying across the Atlantic in a hot-air balloon”), Blame Externalization (“People whom I have trusted have often ended up “double-crossing” me.”), Impulsive Nonconformity (“Many people think of my political beliefs as “radical.”), and Stress Immunity (“I can remain calm in situations that would make many other people panic.”). We were particularly interested in three dimensions of the PPI: An Emotional-Interpersonal factor (factor 1) that includes the Carefree Nonplanfulness, Blame Externalization, Machiavellian Egocentricity and Impulsive Nonconformity subscales and which loads onto factor 1 of the Psychopathy Checklist –Revised (PCL-R); a Social Deviance factor (factor 2) which includes the Social Potency, Stress immunity and Fearlessness subscales; and the Coldheartedness subscale which did not load onto either factor and which is thought by the authors to reflect an unreactivity to another’s distress and an inability to imagine. While factors 1 and 2 are often correlated, they predict distinct behavioral and personality features, as factor 2 taps in to the impulsive and antisocial deviance aspect of psychopathy and is more related to self- (suicidality, alcohol abuse) and other-directed (domestic abuse, assaults) impulsive behaviors. In contrast, factor 1 taps in to the affective and interpersonal features of psychopathy and is more related to narcissistic tendencies as well as to more instrumental forms of aggression (Benning et al. 2003).

The Depression Anxiety Stress Scale (DASS) (Lovibond and Lovibond 1995): This 42-item scale asks subjects to rate how much each item applied to them over the past week, on a likert scale of 0-3 (with 0 being "Did not apply to me at all", and 3 being "Applied to me very much, or most of the time"). The scale has three subscales: Depression (sample item: "I couldn't seem to experience any positive feeling at all"), Anxiety (sample item: "I had a feeling of shakiness (e.g., legs going to give way)"), and Stress (sample item: "I found myself getting upset by quite trivial things."). The DASS has proven to have satisfactory psychometric properties, has convergence with Beck Depression Index, and the three subscales have been shown to be reliably discriminated from one another.

All scales were administered again prior to the second scanning session, with the exception of the PPI, which was omitted for the sake of brevity.

Image Acquisition

All MR images were acquired on a Siemens 3T Trio scanner. Functional images were acquired using an EPI sequence with the following parameters: TR=2000 ms, TE=28 ms, matrix=64 x 64, FOV=192 mm, slice thickness=3 mm, gap=0.45 mm, 34 axial slices. We also acquired a 4.5 minute T1-weighted MPRAGE scan (TR=2600 ms, TE=3.02 ms, matrix=256 x 256, FOV=256 mm, slice thickness=1.00 mm, gap=0 mm) for anatomical localization of fMRI activations.

fMRI Image Preprocessing and Analysis

Image preprocessing was conducted using Brain Voyager QX (version 2.0.8) software (Brain Innovation, Maastricht, The Netherlands). The first 6 volumes of each run were discarded in order to allow the tissue magnetization to equilibrate. Preprocessing involved slice scan time correction, 3D motion correction and temporal filtering by linear trend removal and high pass filtering of frequencies below two cycles per run length. Next, images were normalized into Talairach space (Talairach and Tournoux 1988), and spatially smoothed with an 8-mm full width at half maximum (FWHM) Gaussian kernel. A separate general linear model (GLM) was defined for each subject that examined the neural response to the two task conditions: gender and emotion. For each subject, the contrast in parameter estimates (i.e. emotion – gender) was calculated at every voxel in the brain.

A one-sample t test was used to identify voxels in which the average contrast for the whole group (n=29 subjects) differed significantly from 0 (i.e. a random-effect analysis). The resulting map of the t statistic was thresholded at $p < 0.001$, with a spatial extent threshold of 10 contiguous voxels.

Functional regions of interest (ROIs) were defined from the activation map using the following method. For each region, the peak voxel was identified and a 15 mm isotropic cube was centered on that voxel. Given the small anatomical volume of the amygdala, the left amygdala ROI was limited to a 10 mm isotropic cube centered on the activation peak. In addition, two ROIs were defined based on the peak activation found in a previous study that employed the RtME task (Adams citation): right inferior frontal gyrus (rIFG) and the left fusiform gyrus. For these two ROIs, a 15 mm isotropic cube was centered on the peak activation reported in the study. All ROIs were then explored in correlation analyses with scores on self-report personality measures as well as with scores on the task. These ROIs were also used in longitudinal analyses to investigate changes related to meditation training, and these results will be discussed in chapters 4 and 5. In particular, we focused on functional ROIs encompassing the following anatomical regions: supplementary motor area, dmPFC, anterior paracingulate cortex, bilateral IFG and temporal poles, regions along the anterior, mid and posterior STS, caudate, and amygdala.

Finally, in an exploratory whole-brain analysis, we entered personality scores as a covariate in the GLM and tested for correlations between subject contrast values and scores on a voxel-by-voxel basis. Maps of the correlation coefficient were thresholded at $p < .001$, with a 10-voxel spatial-extent threshold.

Results

Behavioral

RtME accuracy was defined as the number of emotion questions answered correctly. For the 30 emotion items, all subjects scored above chance (i.e., more than 7 correct answers). A paired-samples T test confirmed that the emotion task was more difficult than the gender control task, as subjects scored significantly lower ($t(28)=-12.90$; $p<0.0001$) on the emotion task ($M = 18.95$; $SD = 2.92$) compared to the gender task ($M = 27.90$; $SD = 2.23$) (see **table 2-2** for descriptive statistics of the two tasks, and **figure 2-4** for comparison). There was no significant correlation between correct answers on the emotion task and correct answers on the gender task (Time 1: $r(27) = 0.09$, $p=0.63$; Time 2: $r(27) = .045$, $p = 0.85$), indicating that they were tapping into a different skill set.

Independent-samples t-tests revealed a significant gender difference in accuracy for the RtME emotion task ($t(27) = 2.15$, $p=0.04$), with female subjects scoring higher than males (females: M = 19.85; SD 3.56; males: M = 16.88; SD = 3.83). This effect was absent for the RtME gender task (females: M = 28.08; SD = 1.89; males: M = 28.25; SD = 1.69) $t(27) = 0.26$, $p = 0.80$). This effect was not significant at Time 2, however, there was a trend in the same direction ($t(27) =1.46$, $p = 0.16$) and the absence of a significant effect may be attributed to the decrease in sample size. See **table 2-2** for descriptive statistics broken down according to sex and **figure 2-5** for comparison.

The anxiety subscale of the DASS was negatively correlated with accuracy on the RtME emotion task ($r(27) = -0.37$, $p = 0.05$) (see **figure 2-6**). This relationship was non-significant for the RtME gender task ($r(27) = -0.03$, $p = 0.88$). None of the other DASS subscales were correlated with RtME performance, nor were any of the subscales of the IRI or PPI.

Test retest reliability was assessed with a bivariate correlation analysis for Times 1 and 2 data for both the emotion and gender tasks (emotion: $r(19) = 0.48$, $p = 0.03$; gender: $r(19) = 0.51$, $p = 0.02$).

fMRI

The contrast between the Emotion and Gender tasks revealed a main effect in brain regions previously identified as important for inferring the emotions of others based on their facial expression. In particular, the temporal poles, right anterior STS and inferior frontal gyrus (all bilateral), the dmPFC (BA 8 or 9 depending on atlas) and anterior paracingulate cortex (BA 32), and the left amygdala were more active during the emotion task than the gender task. In addition, this contrast identified regions related to the increased demands of the emotion task such as those important for verbal processing (left IFG, left superior temporal sulcus) and action planning (the supplementary motor area; BA6) were more active during the emotion task (see **figure 2-7** for activations, and **table 2-3** for a list of activations).

Several regions that are commonly active during the RtME task were not identified at the statistical threshold employed, including left and right fusiform gyrus, right temporo-parietal junction and right posterior STS. Possible reasons for these negative findings will be discussed in more detail below.

Relationship between personality variables and brain activity

In contrast to previous studies, ROI analysis for the Time 1 scan did not indicate that any regions were more active in females than in males. However, at Time 2 females did have significantly more activity in the supplementary motor region ($t(19)=2.99$, $p = 0.007$), r IFG ($t(19)=3.41$, $p=0.003$), left amygdala ($t(19)=2.44$, $p = 0.02$), anterior paracingulate ($t(19)=2.19$, $p=0.04$), and left fusiform ($t(19)=2.945$, $p=.008$) (see **figure 2-8**). Moreover, the whole brain covariate analysis that searched for correlations outside of ROIs revealed that a portion of the medial OFC was more active in females than in males (see **figure 2-9**). No areas were found to be more active in males at either time point, either using ROI or whole brain analyses.

At time 1, no regions were related to task accuracy. However, at Time 2, correct answers on the emotion task (and not the gender) were positively related to activity in the left posterior STS (r = 0.45, p = 0.04) (see **figure 2- 10**). At neither time were any areas identified in the whole brain analysis.

We also found a significant positive correlation between anxiety scores and activity in the anterior paracingulate (r(27) = 0.61, p<.001), supplementary motor (r(27) = 0.41, p = 0.03) and left fusiform gyrus (r(27) = 0.44, p = 0.02) ROIs (see **figure 2-11**). Interestingly, at Time 2, there was a negative correlation between anxiety scores and left temporal pole activation (r(19) = -0.57, p=0.007) and a trend in the right temporal pole ((r(19) = -0.43, p = 0.05). A whole brain covariate analysis revealed that regions in the anterior insula and dACC that were positively related to anxiety scores (see **figure 2-12**).

For the PPI, scores on the Coldheartedness subscale were negatively correlated with activity in the left temporal pole (r (27) = -0.46, p=0.01), and scores on factor 2 of the PPI were negatively related to anterior right STS activity (r (27) = -0.46, p=0.01) (see **figure 2-13**). PPI data were not collected at Time 2.

Discussion

In this fMRI study we investigated personality and neural correlates of empathic accuracy. The RtME task was used as a task of empathic accuracy, and individual differences in several personality variables were related to performance and concomitant brain activity.

Sex Differences: The finding that females were significantly more accurate in the RtME task is quite striking given that our study had almost half the statistical power as Baron-Cohen and Hammer (1997). However, with regards to the significant sex difference found in this investigation, several points must be made. First, while the RtME is an empathic accuracy task, these results should not be necessarily taken as evidence that females are more accurate than males. A meta-analysis by Ickes and colleagues (2000) found that the degree to which women out-perform men on tasks of empathic ability is directly related to the degree to which situational cues prompt women to think of themselves as the more empathic gender. A similar finding appears when reviewing sex differences in self-reported empathy: In one large review, Eisenberg and Lennon (1983) concluded that the main feature that determined sex differences when self-report measures were used was the obviousness of the particular measure – sex differences appear when it is clear to subjects that empathic reactions are being indexed. This contextual enhancement of gender differences has been demonstrated in other domains (e.g. (Krendl et al. 2008), and Ickes et al. suggest that with regards to empathy, apparent gender differences often reflect a difference in motivation rather than ability. In fact, a study by Klein and Hodges (2001) showed that gender differences in empathic accuracy disappeared when subjects were paid for their performance. Future studies might explore whether males "catch" females on the RtME task if they are compensated based on their performance.

Second, regardless of whether the results herein reflect a sex-difference in motivation *or* accuracy, it is not clear whether this result is due to underlying genetic factors, the effects of a lifetime of socialization, or a combination of the two. The complexity of this question becomes evident when we reflect on the real possibility that there are genetic *and* environmental determinant of sex-differences in motivation *and* in accuracy, and that all of these factors are likely intertwined. It is with this acknowledgement that researchers, ourselves included, should investigate any question of sex-differences in empathy.

In addition, a portion of the medial OFC was significantly more active in females during the Time 1 task. While activity in this area does not appear to be specific to the task, it is well-recognized for its role in positive reward (O'Doherty et al. 2001) and in moral reasoning (Moll et al. 2005). Moreover, Time 2 data replicated the finding from other groups that females have more activity in the right IFG. This finding is also consistent with the findings of Schulte-Ruther et al. (2008), who showed that females activated IFG and superior temporal regions more during an emotional attribution task. It is also consistent with recent morphometric studies, suggesting that females have more regional gray matter in IFG (Yamasue et al. 2008). Moreover, this study identified sex differences in areas thought to be crucial for emotion understanding and theory of mind, specifically the amygdala and anterior paracingulate. It is unclear why these sex differences were not identified at Time 1.

Task Accuracy: In terms of brain regions that specifically support accurate emotion recognition, our finding that Time 2 activity in the posterior STS was related to performance partially replicated the finding by Adams and colleagues (2010). However, the left posterior STS region that Adams found was more posterior to the one identified in this study. It is important to note that in contrast to our task, their task used the original, self-paced task outside of the scanner and then correlated these outside scores to brain activity that occurred during a modified (2-choice) version of the task. We should also stress that, to the best of our knowledge, no other fMRI study that has utilized the

RtME has shown a relationship between accuracy and brain activity in any region. Thus, it is not entirely surprising that this investigation did not find any clear relationship.

Self-reported Empathy: Contrary to our hypothesis, we did not find any regions that were related to aspects of self-reported empathy. This highlights an important critique found in much of the research on empathy; that is, the inherent problems with self-report biases. For example, Davis and Kraus (1997) reported that dispositional measures of empathy were completely unrelated to indexes of accuracy in interpersonal interactions used in their study – people who report that they are highly empathic may not be good judges of other's emotions. In fact, Ickes (1997) has suggested that people have very little insight into how accurate they are in judging other's emotions and mental states. Moreover, Davis and Franzoi (1991) point out the difference between measuring 'capacity' versus 'tendency'. In other words, it remains possible that individuals who are quite capable of accurately reading others' emotions (and thus score high on the RtME task) nevertheless self-report a low tendency to do so, and vice versa.

Self-reported well-being: With respect to the finding that anxiety scores were negatively related to empathic accuracy, it should first be stressed that the anxiety subscale of the DASS reflects how frequently subjects experience panic-related symptoms. In other words, this does not tap into features of social anxiety or phobia. While it is plausible that panic-related symptoms may have been exacerbated by the fMRI scanner, it is important to note that there was no correlation between anxiety and scores on the gender task. Thus, the effect of anxiety seems to specifically hamper empathic accuracy. This finding is in accord with other studies which have shown a negative relationship between a performance-based measure of emotional intelligence and anxiety (MacCann and Roberts 2008). In addition, it is important to note that the underlying mechanisms and causative relationship are not clear from our analysis. While it remains possible that panic-related anxiety symptoms hamper one's ability to read others emotions, it could also be the case that people who are poor at reading the emotions of others have poorer quality relationships and less social support and therefore, more anxiety. Consistent with the idea that poor empathic accuracy leads to poor relationships, Losh and Pivens (2007) found that only a subgroup of (healthy) parents of autistic children were impaired in RtME, and these were the parents who were behaviorally coded as "aloof" and of low "friendship quality."

While anxious subjects performed worse on the task, they had more brain activity in several regions, including the anterior paracingulate cortex and left fusiform. This is somewhat counterintuitive, except that the activity in anterior paracingulate and left fusiform appear to be unrelated to task performance. In other words, anxious subjects may be attending to the eyes and putting more effort into mentalizing, and yet, still be bad at it.

Psychopathy: Consistent with previous findings, we found no significant relationship between scores on the RtME task and aspects of psychopathy. However, we did uncover significant negative relationships between brain activity during the task and levels of psychopathy. Specifically, subjects who scored higher on the Coldheartedness subscale had less neural activity in the left temporal pole, and those who scored higher on the

Social Deviance factor (2) of the PPI had less activity in anterior right STG. This finding, that a personality variable does not differentiate people based on behavior but relates to a differing profile of brain activity, has been shown elsewhere using the RtME task. Castelli and colleagues' aging study (2010) as well as Baron Cohen's study of parents of autistic children (2006) showed that while there was no performance difference, there were different patterns of neural activity between the population of interest and the control group. Of interest here, our results suggest that psychopathic features may not impair empathic accuracy but may be related to alternative neural mechanisms by which people accurately infer others' emotions. Moreover, it may be the case that these individuals, while just as accurate, have a different experience of others' facial expressions.

Finally, we would like to address the fact that several of the regions typically found active during the RtME task were not significantly active during the version of the task used here, specifically, the fusiform gyrus, right TPJ and right posterior STS. First, as noted previously, the emotion task used here was slightly different than that used in all other fMRI RtME tasks in that it involved choosing the correct answer from 4 rather than 2 choices. This made it a more difficult task and necessitated far more linguistic processing for each item. Thus, it may have been the case that subjects had less time to simulate the facial expression and reason about the mental state of the person in the photograph. This was not our intention, but may have been a consequence of our goal of preserving task difficulty. A related problem may have been that the control task used here was far easier than the task of interest, and subjects may have spent relatively more time looking at the faces than at the answer choices. In the future, better results might be gained by employing an equally difficult control task. One possibility would be to use a control task in which the subject is asked to judge the age of the person in the photographs. The subject would have four age words to choose from (spelled out to match semantic processing demands of emotion words) and these word choices would be different for each item so that the subject always has to read all of the answer choices. In this way, the difficulty of the original non-scanner RtME task would be maintained while better controlling for the non-specific effects of the task of interest, such as visual and linguistic processing. Alternatively, future studies could employ the simplified, 2-choice version of the emotion task in the scanner and subsequently have the subjects complete the more difficult 4-choice task outside of the scanner as a metric of accuracy.

In summary, the study described here replicated previous findings indicating that there are sex differences both in empathic accuracy as measured by the RtME task, as well as in brain activity related to the RtME task. Our findings also suggest that individuals suffering from panic-related anxiety are less accurate in reading others' emotions, even while task-relevant brain activity is increased during the task. Finally, our results indicate that, while psychopathic personality traits may not impair individuals in reading others' emotions, these traits are associated with a decrease in task-related brain activation as well as increased activations in areas related to reward processing.

With relation to the full study, these results indicate that the version of RtME task used here is, for the most part, activating brain regions hypothesized to be important for empathic accuracy. Test retest reliability was relatively good for a behavioral measure, particularly considering the relatively large amount of time that passed between testing sessions. Moreover, we feel confident that there is a sizeable amount of individual variation within this non-clinical population, and that compassion meditation may work within this existing variation to enhance empathic accuracy in practitioners.

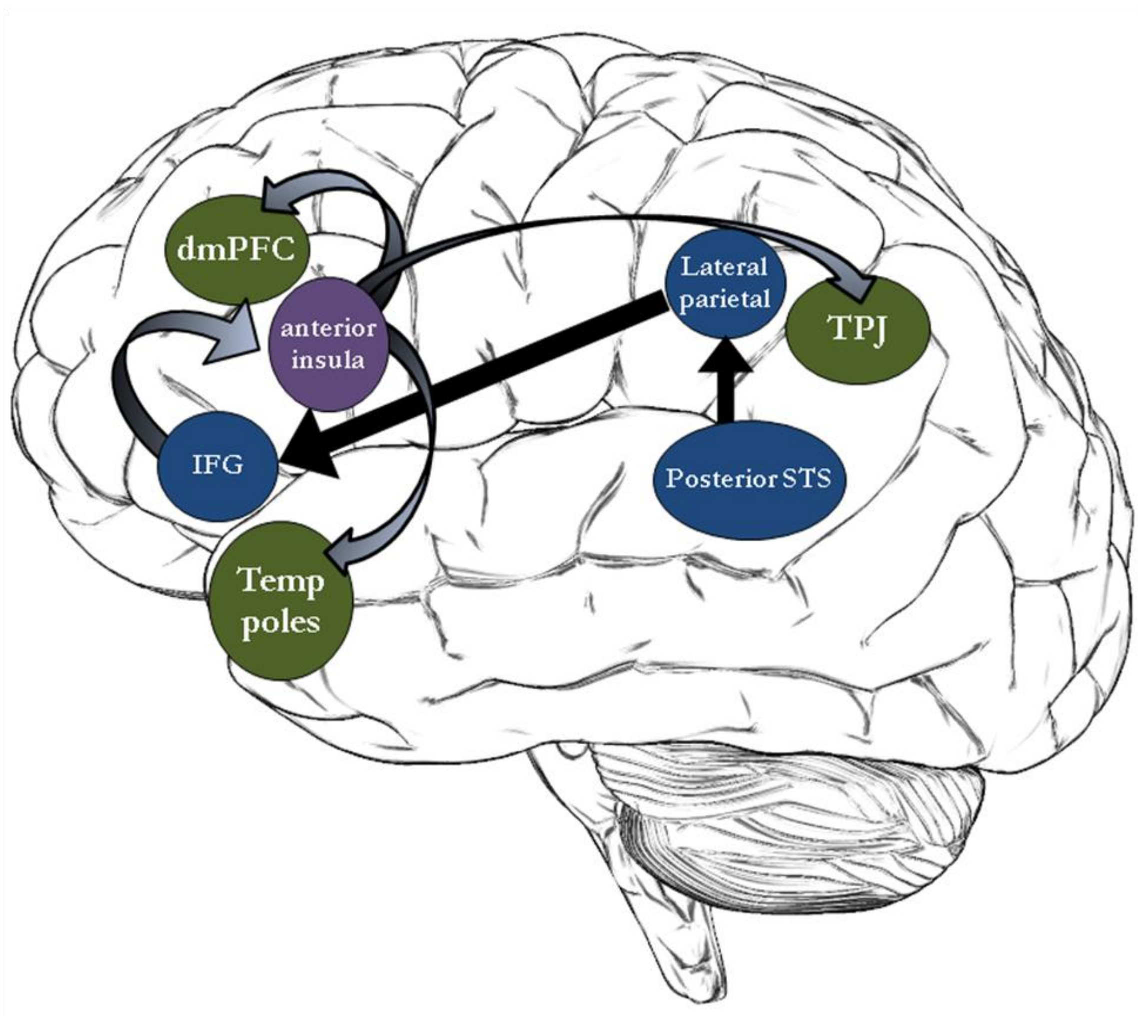

Figure 2-1: Schematic of neural processes involved in accurately inferring another's emotions based on their facial expression. Arrows denote functional directionality but not necessary direct anatomical connection.

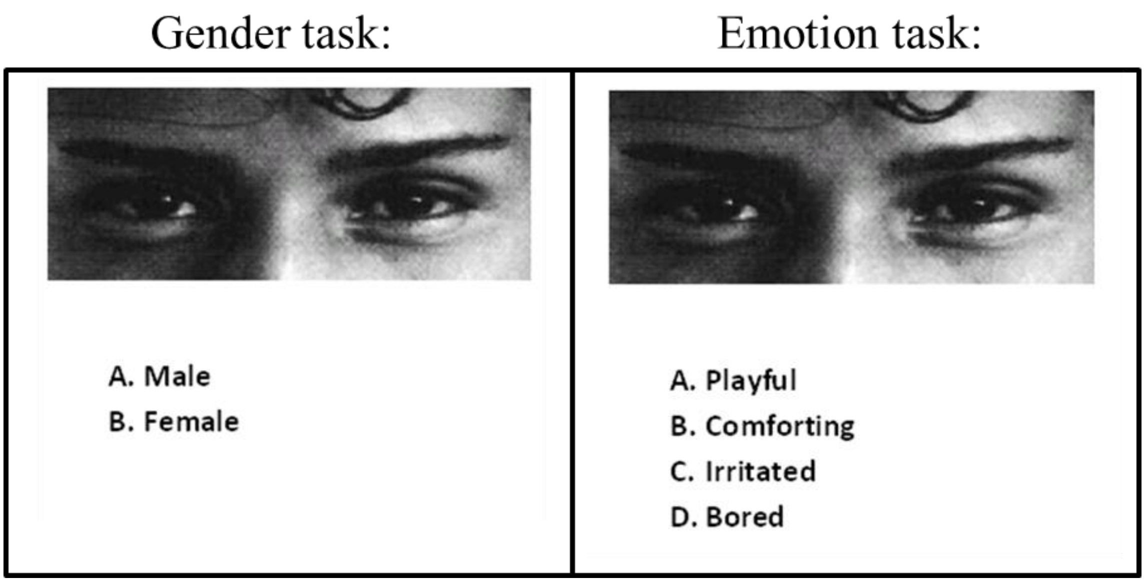

Figure 2-2: Example items from the Gender and Emotion tasks.

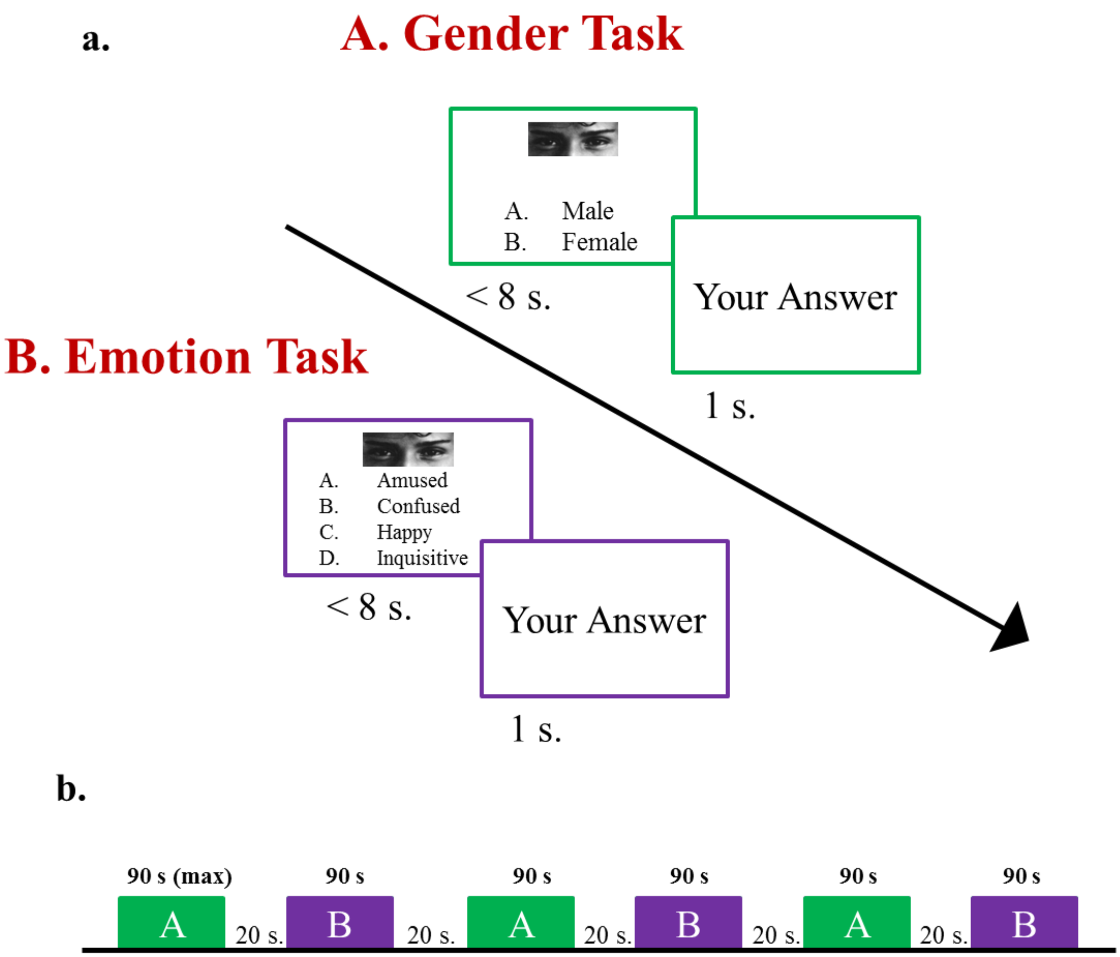

Figure 2-3: (a.) Schematic representing item timing for the gender and emotion tasks; (b.) Schematic of alternating block design (A is the gender task and B is the emotion task).

Time 1	Emotion correct	Gender correct
N	29	29
Mean	18.21	28.17
Median	19.00	29.00
Std. Deviation	3.94	1.75
Variance	15.53	3.08
Minimum	9	24
Maximum	25	30

Time 2	Emotion correct	Gender correct
N	21	21
Mean	18.95	27.90
Median	19.00	28.00
Std. Deviation	2.92	2.23
Variance	8.55	4.99
Minimum	14	20
Maximum	24	30

Table 2-1: Descriptive statistics of performance on the Emotion and Gender tasks at Time 1 and 2.

Time 1		Mean	Std. Deviation
Emotion correct	Males (n=16)	16.88	3.83
	Females (n=13)	19.85	3.56
Gender correct	Males (n=16)	28.25	1.69
	Females (n=13)	28.08	1.89

Time 2		Mean	Std. Deviation
Emotion correct	Males (n=12)	18.17	3.10
	Females (n=9)	20.00	2.45
Gender correct	Males (n=12)	28.33	1.50
	Females (n=9)	27.33	2.96

Table 2-2: Descriptive statistics of Emotion and Gender tasks broken down according to sex.

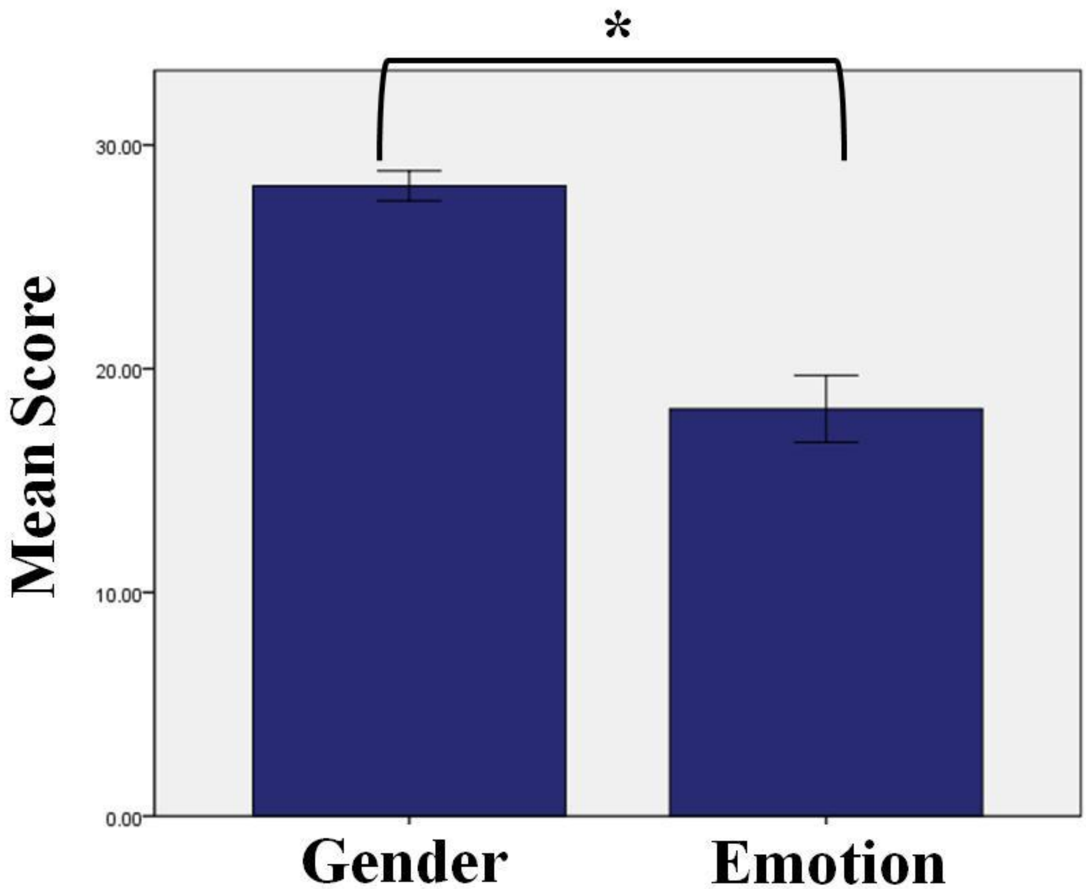

Figure 2-4: Performance on the Gender and Emotion tasks ($t(28) = -12.90$; $p < 0.0001$).

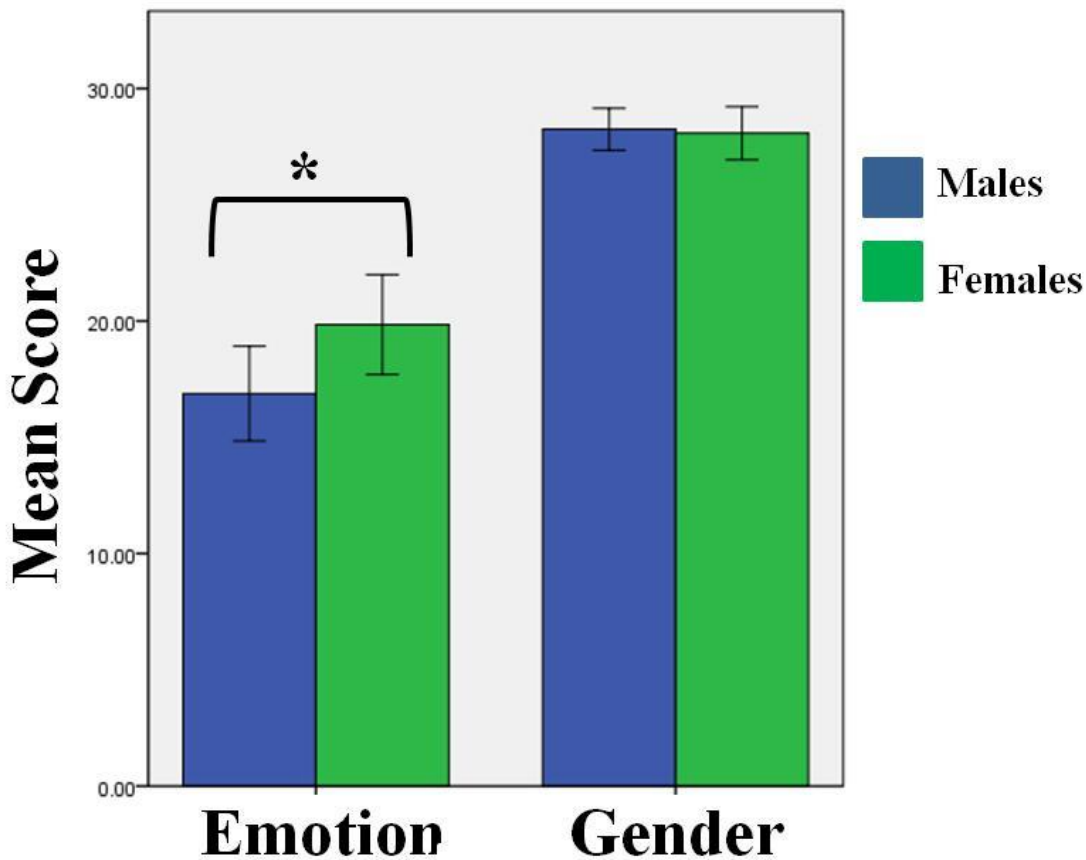

Figure 2-5: Performance on the Emotion and Gender tasks according to sex at Time 1 (Emotion: t(27) = 2.15; p =0.04; Gender: t(27) = 0.26; p = 0.80)

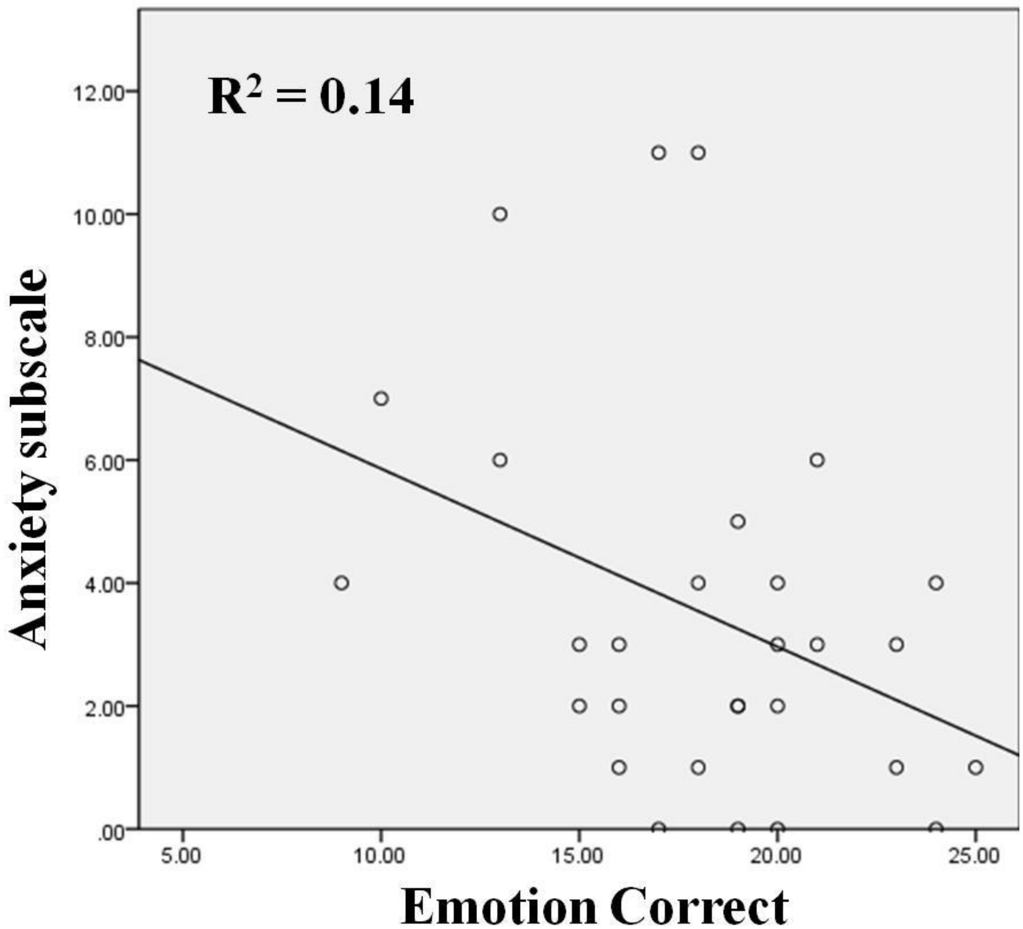

Figure 2-6: Correlation between scores on the anxiety subscale of the DASS and correct answers on the Emotion task at Time 1 ($r(27) = -0.37$; $p = 0.05$).

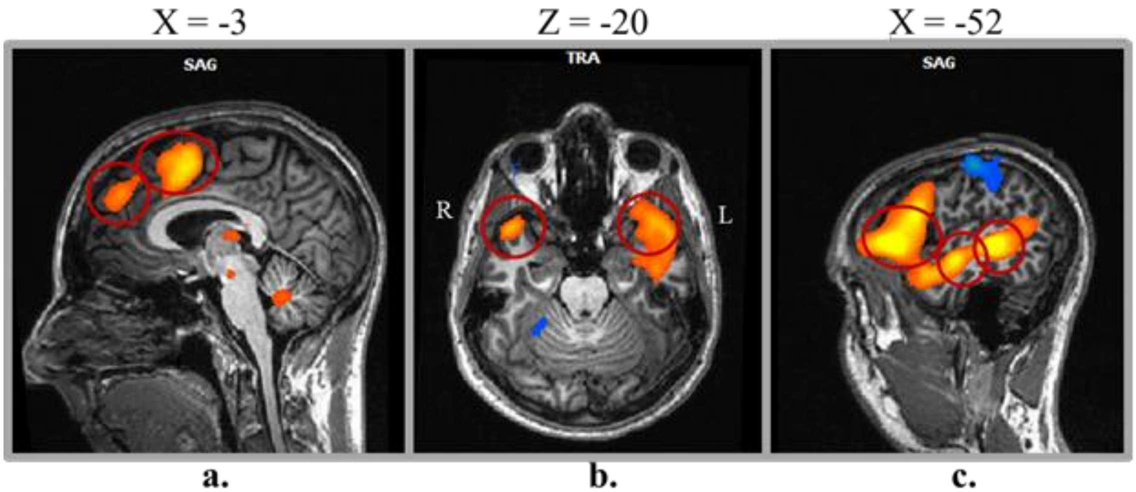

Figure 2-7: Main effect for the contrast of interest [Emotion – Gender] at threshold t(28) = 3.67, $p < 0.001$. Panel **(a.)** shows dmPFC and supplementary motor activations in the sagittal plane. Panel **(b.)** shows the right and left temporal pole activations in the axial plane. Panel **(c.)** shows the left IFG, mid STS and posterior STS activations in the sagittal plane.

Brain Region	Brodmann's Area	X	Y	Z	Voxels	Peak t
Supplementary Motor	6	-6	14	46	14625	8.51
dmPFC	8	-9	50	37	↓	7.09
dACC	32	12	14	34	315	4.97
L Inferior Frontal Gyrus		-45	29	4	72831	14.09
L Post Superior Temporal Gyrus	22	-51	-31	4	↓	11.91
L Mid Superior Temporal Gyrus		-51	-10	-5	↓	8.26
L Temporal Pole		-48	14	-17	↓	7.58
L Amygdala		-30	-4	-17	↓	5.32
R Temporal Pole	20	42	17	-20	2184	7.04
R Caudate		15	14	13	496	5.01
R Caudate		21	-37	19	308	4.79
R Inferior Frontal Gyrus*		56	28	9	3375	3.73
R Anterior Superior Temporal Gyrus	21	51	-7	-11	168	4.16
L Caudate		-12	-28	22	2378	6.38
L Fusiform*		-41	-49	-7	3375	5.08
Cerebellum		15	-67	-29	6657	7.52
Cerebellum		-3	-49	-23	991	4.46
Brainstem		-6	-16	-11	173	4.02
Thalamus		-3	-19	13	312	4.62
Occipital Lobe	18	-24	-85	-2	719	4.31

Table 2-3: Brain regions that showed a significant main effect for the contrast of interest at Time 1 [Emotion – Gender] at threshold $t(28)=3.67$, $p< 0.001$. For regions that were subdivided into smaller ROIs using the local maxima, an "↓" is entered for number of voxels, which means that the size of the entire activation is listed above.

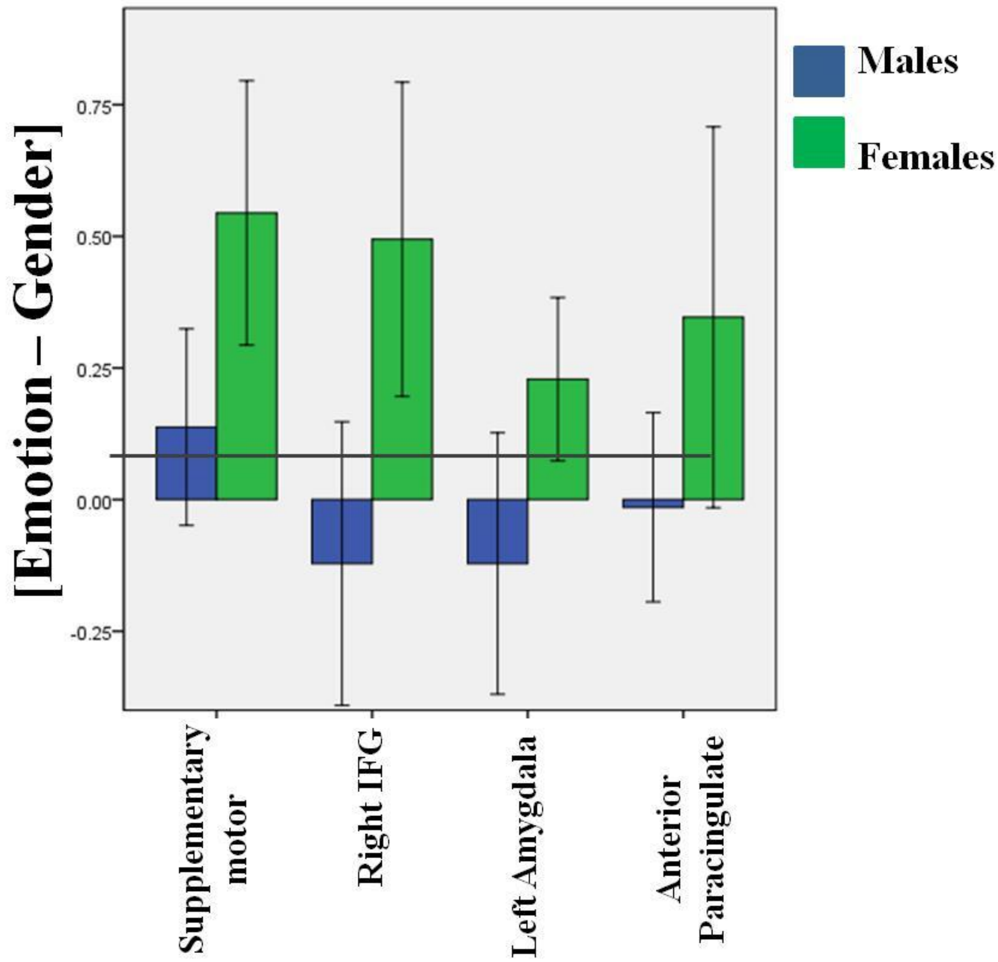

Figure 2-8: Time 2 comparison of male and female responses to the contrast of interest [Emotion – Gender] in the supplementary motor cortex (t(19) =3.00, p = 0.007), right IFG (t(19) = 3.41, p = 0.003), left amygdala (t(19) = 2.44, p = 0.02) and anterior paracingulate (t(19) = 2.19, p = .04) functionally defined regions of interest.

X = -12

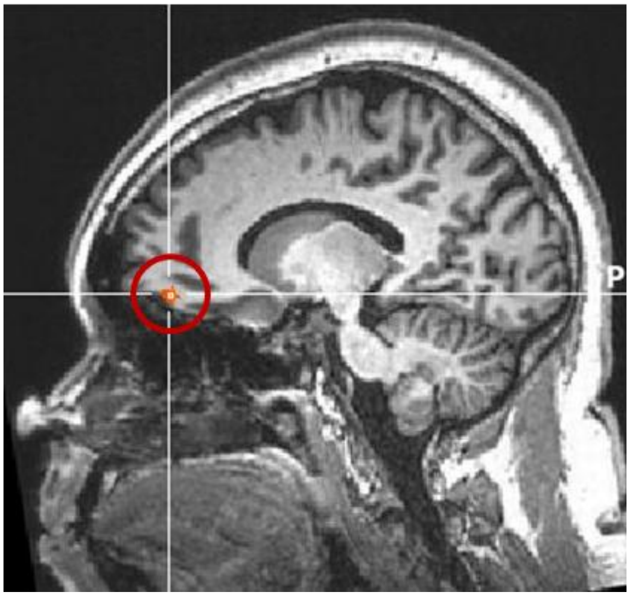

Figure 2-9: Area in the OFC that was significantly more active in females than in males. Found in whole brain analysis with $p < 0.001$.

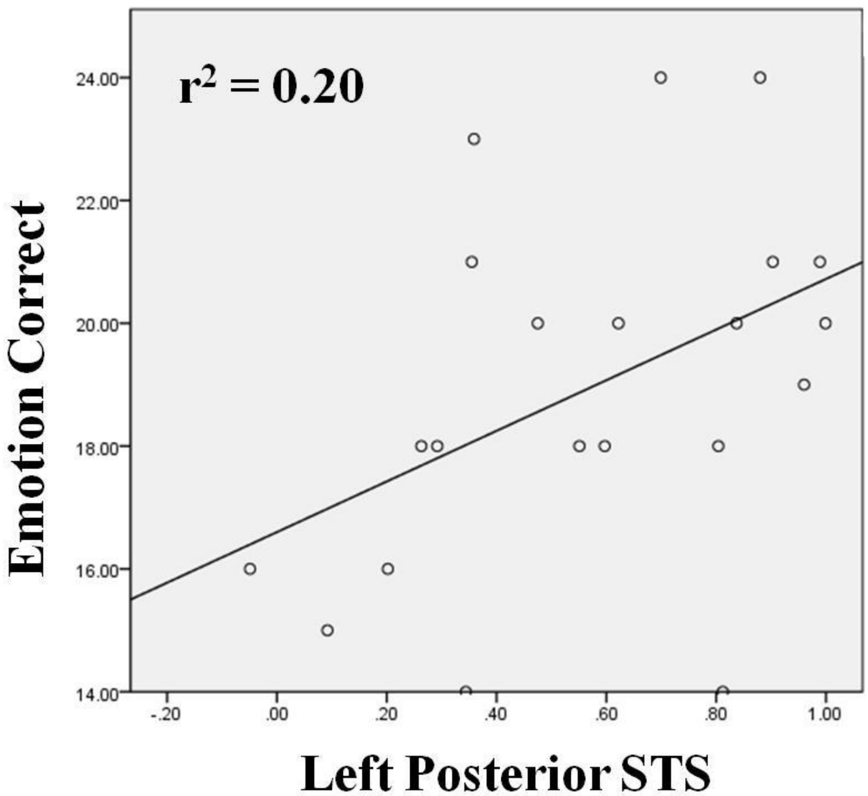

Figure 2-10: Bivariate correlation between Time 2 correct emotion answers and activity in the left posterior STS functionally defined ROI ($r(19) = 0.45$; $p = 0.04$).

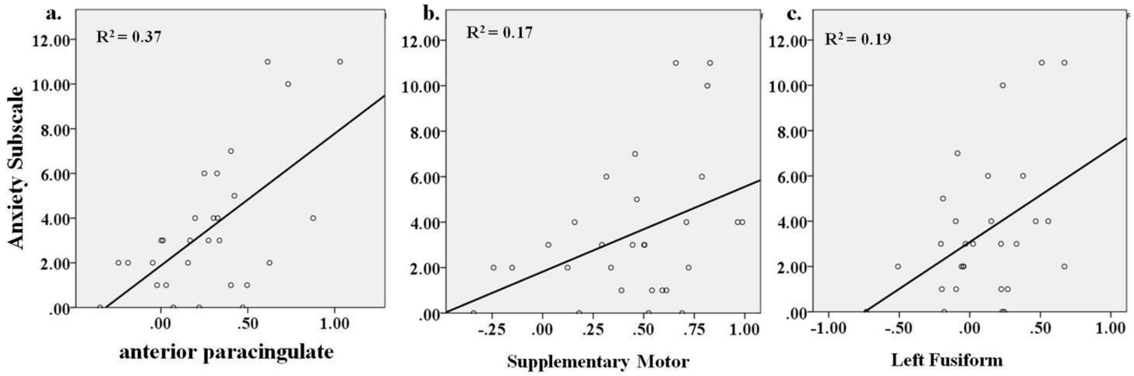

Figure 2-11: Bivariate correlation analyses with brain activity for the Time 1 contrast [Emotion – Gender] and the anxiety subscale of the DASS in **a.)** anterior paracingulate: ($r(27) = 0.61$; $p < 0.001$); **b.)** supplementary motor: ($r(27) = 0.41$; $p = 0.03$) and **c.)** left fusiform: ($r(27) = 0.44$; $p = 0.02$).

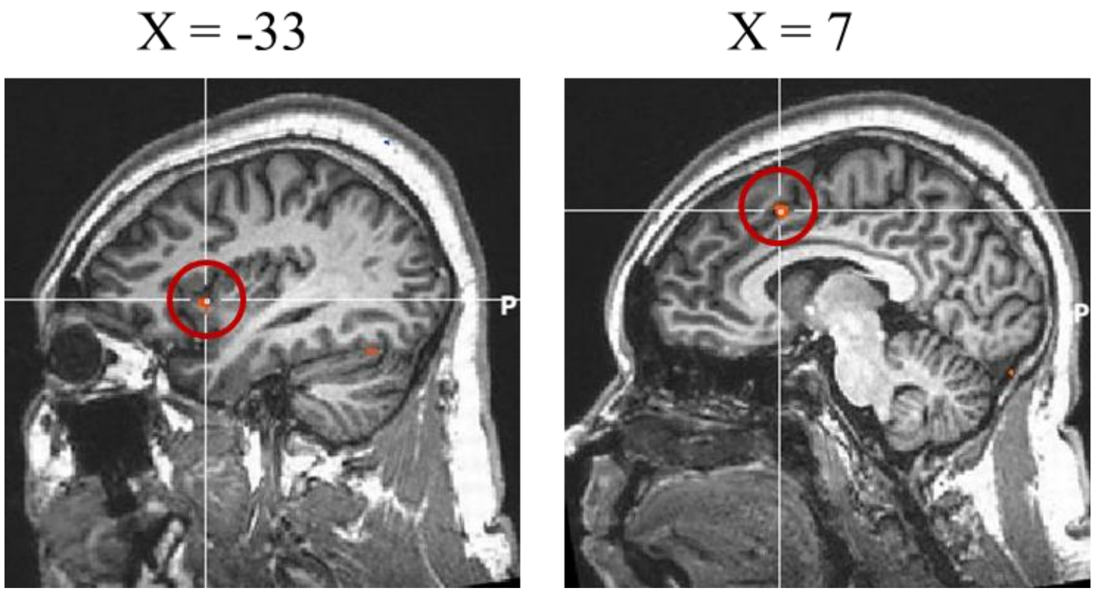

Figure 2-12: Significant correlation between scores on the anxiety subscale of the DASS and activity in anterior insula (left) and dACC (right); revealed with whole brain analysis with threshold $p < 0.001$.

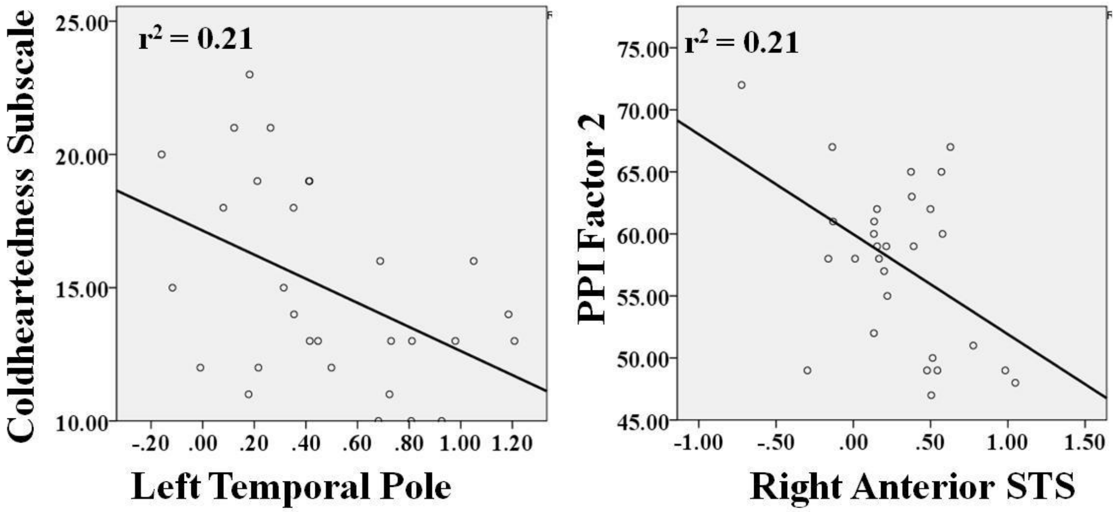

Figure 2-13: Bivariate correlation analysis between psychopathy subscales and brain activity at Time 1 for the contrast [Emotion – Gender].

Chapter 3

Empathy for Pain

Introduction

Empathy is defined as the ability to understand what another individual feels by experiencing the affective state of the observed individual (de Vignemont and Singer 2006). Several researchers have suggested that empathy functions as a prosocial motive, and a multitude of studies have shown that levels of empathy predict helping behavior (for reviews Batson 1998; Hoffman 2001). Moreover, several studies have shown that empathy has an inverse relationship with aggression (Feshbach and Feshbach 1969; Hoffman 2001), and that empathy deficits are characteristic of disorders typified by aggressive behavior.

In addition to the benefits to others that result from empathy, there is an emerging literature regarding the increases in well-being that occur for the empathic person. For example, Barraza and Zak (2009) found that the empathic feelings elicited by an emotion-inducing video were related to a spike in oxytocin, a neurohormone known to have stress-protective benefits (Heinrichs et al. 2003). This oxytocin increase, in turn, predicted compassionate behavior toward others. What is more, compassionate attitudes and behaviors account for much of the observed association between religiosity and improved emotional health (Steffen and Masters 2005). In fact, simply watching another person engage in compassionate behavior leads to beneficial boosts in the observer's immune system (McClelland and Kirshnit 1988). Taken together, these data create a picture in which empathic reactions lead to prosocial behaviors toward others and enhance the well-being of the empathizer, the target of the empathy and witnesses to the process.

Background: Neurobiological Processes supporting empathy for pain

Several different paradigms have been used to investigate the neurobiology of the empathic response. Depending on the task used, fMRI results have identified brain activity related to some or all of three different parts of the empathic response: (1) Perceptual processes related to observing another individual, (2) The affective component of the empathic response, and (3) The cognitive component of the empathic response. These will be discussed in turn.

Perceptual Processes: When witnessing someone else's suffering, the initiation of an empathic response often relies on the perception of the suffering. In particular, this involves a putative mirror neuron circuit, consisting of pars opercularis in the inferior frontal gyrus (IFG) and the inferior lateral parietal cortex (Lamm et al. 2011). Some propose this to be a crucial network for understanding others' actions, behaviors and facial expressions (Iacoboni and Dapretto 2006). If this is the case, this mirroring process during Empathy for Pain (EFP) may be related to understanding the content of a situation, which may then initiate processes related to affective empathy.

Affective Empathy: The most widely utilized paradigm by social cognitive neuroscientists to study the neural correlates of empathy has been one in which subjects are exposed to empathy-for-pain (EFP) stimuli. These studies have shown that when subjects either watch another person experience pain or are given a cue indicating that someone is in pain, a network of brain regions are commonly activated including the anterior mid cingulate cortex (aMCC) and bilateral anterior insula stretching into the ventral frontal operculum. Importantly, these regions are also active during the direct experience of pain and are thought to underlie the affective dimension of the direct experience of pain (Botvinick et al. 2005; Jackson et al. 2005; Lamm et al. 2011; Morrison et al. 2004; Simon et al. 2006; Singer et al. 2004).

In fact, with a few exceptions, the results in these studies are remarkably consistent despite slight variations in the tasks used, causing some to label these areas as a "core neural network for pain empathy" (Lamm et al. 2011 p. 2497). Speculations have been advanced regarding the function of this network. One of the primary viewpoints is that AI and aMCC comprise a network that represents the subjective sense of the physical state of the body, and that humans incorporate this awareness to form the subjective experience of emotions (Craig 2002; Craig 2009). Within the network, it has been suggested that the AI specifically encodes the representation of the affective state, while the ACC is involved in the motivational (Singer and Lamm 2009) or attentional aspects (Paulus and Stein 2006). In the case of empathy then, activity in the AI may be a simulated mapping of the observed individual's body state onto one's own. Consistent with this view, efforts by Gu et al. (2010) to dissociate AI and ACC activity during empathy for pain suggest that AI is more specific to the empathic reaction.

Cognitive Empathy: A full empathic response necessitates a cognitive perspective-taking component. In other words, empathy has some element of *understanding*, such that the empathizer knows that the affective response that they are having is related to another's emotional state. If this is not present, the affective response is more akin to emotional contagion and personal distress. The ability to take the perspective of another likely rests on neural processes related to basic mentalization skills that allow one to reflect on the emotions or thoughts of another. For example, one group has found that effortful third-person perspective taking, as happens when a study participant is asked to take the perspective of another person, activates ventromedial PFC, left superior temporal sulcus and temporal pole (Ruby and Decety 2004). Another study found that top-down appraisal during the observation of painful stimulation is related to activity in the perigenual ACC, ventromedial OFC and middle frontal gyrus (Lamm et al. 2007). It is also likely that the cognitive aspect of the empathic response is related to activity in areas important for ToM such as dmPFC or TPJ (Saxe 2006). In addition to mentalization, it is likely that the ability to maintain a self/other distinction may be crucial for a full empathic response. For, if this awareness is missing, the observer will experience a more personal form of distress rather than an empathic response (Decety and Lamm 2006).

The ways in which perceptual, affective and cognitive processes interact to support a full experience of empathy are just beginning to be understood. And while simulationist accounts of affective empathy are often pitted against higher-level accounts of cognitive perspective-taking, many have recently posited that higher-level mentalizing may depend upon lower-level simulation processes (Keysers and Gazzola 2007; Uddin et al. 2007). Recent studies support this view, as Jabbi and Keysers (2008) found that BA 45 (part of the putative human mirror neuron system) and the anterior insula/fronto-orbital (IFO) region were significantly more functionally connected when subjects viewed facial expressions of disgust compared to neutral facial expressions. Results from a granger causality analyses suggested that activity in BA 45 preceded and caused activity in IFO, providing support for the notion that perceptual mirroring properties may initiate or drive the affective component of empathy. A more recent study used functional connectivity to show that mentalizing about oneself and others increased the functional connectivity between areas important for mentalizing (vMPFC, PCC, and RTPJ) and areas such as AI and caudal ACC, thought to be important for affective empathy (Lombardo et al. 2010).

Novel aspects of this study

Empathy for dynamic pain stimuli: Despite the recent abundance of studies investigating empathy for pain, there is much that remains to be learned. For example, most of the EFP tasks that have been used employ still photographs, either of limbs in painful positions or faces of people who are in pain. Very few studies have used dynamic film clips of others experiencing pain to elicit empathy. The two studies in which subjects viewed video clips of dynamic facial expressions of pain elicited amygdala activity in addition to ACC and AI activity (Botvinick et al. 2005; Simon et al. 2006). Still photographs of facial expressions of pain did not elicit amygdala activity (Gu and Han 2007a), and neither did any other tasks that did not show faces. While Botvinick and colleagues suggest that the amygdala activity found in their study could reflect fear conditioning, Simon et al. point out that a situation in which an individual views a dynamic facial expression of pain, but cannot see the source of the pain reflects an ambiguous threat and may initiate amygdala activity as a result. Our study may be able to disentangle these two explanations, since we will have dynamic stimuli in which subjects see and experientially understand the source of the threat.

Empathic anticipation of pain: A second feature that has been relatively unexplored by researchers investigating empathy for pain is empathy for the anticipation of pain. Given the real possibility that the anticipation is more aversive than the stimulations themselves, it is important to explore this portion of the empathic response. To the best of our knowledge, only one other study has included an anticipation epic in their study of empathy for pain (Morrison et al. 2007), but no study to date has explicitly modeled brain activity in observers while they watch others anticipate pain. However, two previous findings allow us to make a priori hypotheses regarding brain activation during anticipation of others' pain. First, investigations of anticipation of the experience of pain show that anticipation is related to activity in the ACC and insula, but more anterior to activations seen with the experience of pain (Ploghaus et al. 1999; Porro et al. 2002). Second, the anterior insula activates during the anticipation of aversive emotional stimuli (Simmons et al. 2004). Thus, we expect that empathic anticipation will activate the ACC and anterior insula.

Relationship between Empathy and Compassion: As Singer and Lamm (2009) point out, there is very little understanding of the relationship between empathy and compassion. If the model proposed by others and presented in our introductory chapter is correct, we should expect that there is some neurobiological process by which empathy is translated into compassion. Yet, the mechanistic underpinnings of this transition are murky and there are very few, if any, studies that investigate this process. One study has investigated this relationship and found that individual differences in activity in the left anterior insula were related to costly helping at a later time (Hein et al. 2010). Similarly, a study by Masten and colleagues (2010) found that activations in the medial PFC and anterior insula while watching others being ostracized were related to compassionate behavior at a later time. However, based on the above model, compassionate behavior necessitates adequate emotion regulation to allow an individual to empathize with the distress of another without becoming mired in personal distress (Batson 1998; Eisenberg 2000). If this is the case, we might expect that activation of neural regions related to emotion regulation, such as the dorso- and ventrolateral PFC and orbitofrontal cortex, (Ochsner and Gross 2005) would predict compassionate behavior. We will test this hypothesis.

Individual variation in EFP: While several EFP studies have explored the links between self-reported trait empathy and the neurobiology of the empathic response, to the best of our knowledge no one has investigated the relationship between EFP and psychopathic personality traits in non-clinical population of adults. This is curious given that psychopathy is characterized in large part by deficits in empathy (Blair 2005) and both adults and children with psychopathic traits are less responsive to distress cues of others (Blair et al. 1997; Blair 1999). In addition, children diagnosed with conduct disorder, a precursor to antisocial personality disorder in adulthood, have decreased coupling of the amygdala and PFC when watching others deliberately inflict pain on another (Decety et al. 2009). For this reason we will administer the Psychopathic Personality Inventory (PPI) to investigate the relationship between EFP and psychopathic personality traits.

In addition, it is reasonable to suspect that an individual's well-being may be related to their EFP response, particularly given the link between dispositional empathy and frequency of negative emotionality (reviewed in Eisenberg 2000). Conversely, the more cognitive aspects of the empathic response are inversely related to negative emotionality (Okun et al. 2000) and personal distress (Davis and Franzoi 1991). However, we are aware of no EFP studies that have investigated this relationship. For this reason, we will administer the Depression Anxiety and Stress Scale (DASS) and will explore the relationship between clinical symptomatology and empathy.

Goals of this study

This study is an attempt to explore the aforementioned unresolved issues in our understanding of empathy for pain. We employed dynamic video clips showing people waiting for and receiving painful and non-painful stimulations to their wrist. The people in the clips were actually receiving the stimulations and were instructed to act as came naturally. We did not omit video clips based on pain expressions, and thus the stimuli set were heterogeneous in terms of the extent to which people responded to the stimulations that they received.

In keeping with the larger goals of this dissertation, we utilized an EFP task in order to explore individual variation in aspects of prosocial emotions and behavior as well as to investigate factors that mediate and moderate this variation. With regards to its place in the full study, we intend to assess changes in EFP that may result from training in and practice of compassion meditation. Before testing our meditation-related hypotheses (in subsequent chapters), we will investigate the task itself in order to verify that it is a meaningful task of empathy for pain and to investigate the relationship between empathy and compassion. We also intend to explore individual variation in brain activity during the EFP task in order to more fully understand how engagement with a meditative practice may modify the neural processes involved in empathy. More specifically, we sought to:

4. **Verify that our empathy for pain task activates neural regions previously found to be important for empathy for pain**.

5. **Investigate empathy for the anticipation of pain.**

6. **Investigate the relationship between empathy for pain and compassionate behavior.**

7. **Extend previous findings by investigating the relationship between the neural correlates of empathy for pain and individual variation in self-reported well-being, clinical symptomology and psychopathy.**

To this end, we hypothesize:

1. That our EFP task will activate neural regions involved in the affective simulation of pain (the anterior insula and mid cingulate), the mirror neuron system (posterior STS, lateral parietal and inferior frontal gyrus), and regions involved in the cognitive aspect of the empathic response (dmPFC).

2. The empathic anticipation epic will engage areas related to pain anticipation, including the anterior insula.

3. Individual's compassionate behavior after the EFP task will be related to their EFP neural response as well as to activity in regions important for emotion regulation.

4. Individual differences in psychopathy scores will be inversely related to state empathy during the EFP task, to the EFP neural response, and to compassionate behavior.

5. Individual differences in clinical symptomatology (stress, anxiety and depression) will be positively related to activity in brain regions related to distress (e.g. amygdala), and inversely related to activity in regions related to cognitive empathy and emotion regulation (e.g. dmPFC and ventrolateral PFC).

Methods

Other-Pain Stimuli Construction

The empathy for pain video stimuli were created using the following protocol. Approximately 25 subjects were recruited from the Emory campus using fliers. Attempts were made to get a diverse sample in terms of age and ethnicity. Volunteers met researchers in an empty testing room and were seated in a chair and positioned such that they could both view a laptop computer and face directly toward the video camera. We explained that the video clips would be used as stimuli in an fMRI study of empathy, and told the subjects that while we did not want them to give artificial reactions to the stimulations, they did not have to work hard to be stoic and they were welcome to make any facial expressions that came naturally.

Volunteers were outfitted with 2 electrode pads on the inside of their right wrist and hooked to the GRASS SD-9 stimulator, which was our method of administering stimulations. First, participants' pain tolerance were assessed by administering a series of stimulations and asking the subject to rate the stimulations on a 10-point intensity rating scale (0='don't feel anything', 1='can feel something but not painful', 8='maximum tolerable pain', and 10='worst imaginable pain'). The 1 setting was used for the 'no pain' stimuli and the 8 setting was used for the 'pain' stimuli. Upon finding the settings for the non-painful and painful stimulations for each participant, we administered 3 of each in pseudorandom order. Prior to each stimulation, the laptop screen next to the subjects showed a colored screen for 6 seconds indicating to them which level they were about to receive (a red screen indicated that they would receive a painful stimulation, a blue screen indicated that they would receive a non-painful stimulation). Next, they received the stimulations for approximately 3 seconds each. Volunteers were compensated $30.00.

The video clips were assembled into one video stimuli set. Each participant appeared twice within the video, once receiving a 'no-pain' stimulation and once receiving a 'pain' stimulation. The clips appeared in a pseudorandom order and were assembled into two blocks, separated by a one minute rest period.

Full Study Participants

Twenty-nine (16 male) participants from the Atlanta area were recruited using a combination of fliers and electronic notifications posted at several local universities, as well as electronic advertisements on Craigslist. Participants were between the age of 25 and 55, were screened and excluded for (self-reported) use of any psychotropic medication (i.e. antidepressants, anxiolytics, psychostimulants, or mood stabilizers) within one year of screening, as well as for regular use of any medications that might influence activity of the autonomic nervous system, HPA axis or inflammatory pathways. Subjects were also excluded for any serious ongoing medical or psychiatric condition that might influence the results of the study, including post-traumatic stress disorder (PTSD), chronic pain or other pain disorders, depression, anxiety disorders or a history of schizophrenia or bipolar disorder, as well as for substance abuse occurring within one year of study entry. Subjects were screened for MRI safety and handedness (only right handed participants were included in the study), and all participants had normal or corrected-to-normal vision. During a second visit approximately 10 weeks after the first, subjects were scanned a second time using the same EFP paradigm. Due to subject attrition, only 21 (12 male) subjects were scanned the second time.

Data Collection

Upon entering the Imaging Center, subjects were seated in a testing room outside of the fMRI scanning room. They completed a health screening form, a consent form and a HIPPA form. They also completed the following psychometric instruments, in this order:

Interpersonal Reactivity Index (IRI) (Davis 1983): explained in previous chapter

The Psychopathic Personality Inventory (PPI) (Lilienfeld and Andrews 1996): explained in previous chapter

The Depression Anxiety Stress Scale (DASS) (Lovibond and Lovibond 1995): explained in previous chapter

After completing these questionnaires, subjects were given a detailed explanation of what they would be asked to do in the fMRI scanner. Next, their pain tolerance was titrated, and pain and no-pain levels were documented. Subjects were then placed in the scanner.

Experimental Paradigm

The EFP task used here followed other fMRI paradigms that have successfully identified an empathy-for-pain response (Botvinick et al. 2005; de Vignemont and Singer 2006; Jackson et al. 2005; Singer et al. 2004) (**Figure 3-1**). First, subjects completed a short 'self pain' paradigm, in which they received moderately painful and nonpainful stimulations to the inside of their wrist. We included the 'self pain' portion for two reasons. First, we wanted to have the ability to use neural activations to self pain as functional localizers for analysis in the other pain paradigm. Second, the self-pain paradigm also ensured that subjects experienced the painful stimuli that they observed others experience, and thus, would be more apt to empathize (Preston et al. 2007). Pain stimuli were delivered by the same GRASS SD-9 stimulator.

Prior to both the Time 1 and Time 2 scans, we indexed the subjective pain tolerance of each subject by asking them to judge the painfulness of stimuli on a 10-point intensity rating scale (0='don't feel anything', 1='can feel something but not painful', 8='maximum tolerable pain', and 10='worst imaginable pain'). The 1 setting was used for the ‘no pain’ stimuli and the 8 setting was used for the ‘pain’ stimuli. After explaining the subjective scale to each subject, we explained that, “level 8 is that point where you think, that hurts and I don’t want you to go any higher.” They were then informed that they would receive each stimulation for approximately 3 seconds, and that they would receive approximately 10 of each type of stimulation. They were told that the level of stimulation was randomly determined.

In the ‘self-pain’ paradigm, while lying in the scanner, the subject saw either a green or a yellow colored screen (the anticipation cue) for 6 seconds, which indicated to them whether they were about to receive a painful or a non-painful stimulus. The stimulus was then delivered for 3 seconds, and was followed by a fixation period of 12-16 (14 +/- 2 seconds jittered) seconds. Pain and no-pain stimuli were each presented 10 times. We also included 6 null trials (3 painful, 3 non-painful), in which subjects saw the anticipation cue but did not receive a stimulation.

Following the “self-pain” paradigm, subjects completed the “other-pain” paradigm, in which they saw video clips of other people anticipating and receiving the same stimuli that they received. Both the subject and the person in the video saw the anticipation cue (red = painful, blue = nonpainful), signifying whether the pending stimulus would be painful or not. The video clips then showed the person receiving the stimulus for 3 s, followed by a 12-16 s (jittered) fixation period. The “other pain” paradigm consisted of 2 blocks of stimuli, each consisting of 10 pain and 10 no-pain events distributed randomly (thus, each subject viewed 20 pain and 20 no-pain conditions). There was a one minute break between blocks, during which the subject saw a fixation cross. Again, 12 null trials (6 pain, 6 non-pain) were included in which the subject saw a video clip of a person viewing the anticipation cue, but they did not see the person receive the stimulation. Each video clip was of a different person, so that subjects saw 1 pain and 1 no-pain stimulus for each person.

Upon completion of the Self and Other paradigms, subjects were asked to rate on a scale from 1-5 (with 1 being least and 5 most) how aversive they found it to: 1. Receive the nonpainful stimulations, 2. Receive the painful stimulations, 3. Watch others receive the nonpainful stimulations, and 4. Watch others receive the painful stimulations. Self Pain and Other Pain (state empathy) ratings were generated for each subject by subtracting the NoPain rating from the Pain rating for both self and other.

After the Time 2 (post-intervention) scanning session, subjects were removed from the scanner and brought to a private testing room. They were compensated and then told to wait while the experimenter went to another room to print off a receipt for them. They were asked, in the meantime, to read a flier regarding an unfortunate event that occurred to one of the study participants. Subjects were given 60 seconds (alone) to read the flier, which had a still photograph taken of one of the video stimuli participants. Under the photograph was the following text:

> "This woman volunteered for our study – you may remember her from the video clips that you saw earlier in the scanner. Unfortunately, she was in a moderately severe car accident just down the street from our building and injured her neck. Because she was in the accident after participating in our study, we feel pretty bad about the situation and we are all trying to pool money to help her with her day to day expenses, as she has been unable to work. Obviously you are in no way

obligated to her, but if you would like to donate confidentially, you can place any amount of money in this donation box."

Next to the flier was an opaque donation box. After 60 seconds, the experimenter came back into the room and debriefed the participant. Participants were told they could take any donations out of the box and they were asked to show the experimenter how much money they had donated. Finally, they were queried as to whether they found the story suspicious in any way.

Image Acquisition: All MR images were acquired on a Siemens 3T Trio scanner. Functional images were acquired using an EPI sequence with the following parameters: TR=2000 ms, TE=28 ms, matrix=64 x 64, FOV=192 mm, slice thickness=3 mm, gap=0.45 mm, 34 axial slices. We also acquired a 4.5 minute T1-weighted MPRAGE scan (TR=2600 ms, TE=3.02 ms, matrix=256 x 256, FOV=256 mm, slice thickness=1.00 mm, gap=0 mm) for anatomical localization of fMRI activations.

fMRI Image Preprocessing and Analysis: Image preprocessing was conducted using Brain Voyager QX (version 2.0.8) software (Brain Innovation, Maastricht, The Netherlands). The first 6 volumes of each run were discarded in order to allow the tissue magnetization to equilibrate. Preprocessing involved slice scan time correction, 3D motion correction and temporal filtering by linear trend removal and high pass filtering of frequencies below two cycles per run length. Next, images were normalized into Talairach space (Talairach and Tournoux 1988), and spatially smoothed with an 8-mm (for self pain) and 5-mm (for other pain) full width at half maximum (FWHM) Gaussian kernel. A smaller smoothing kernel was used for the other pain run in order to preserve spatial resolution that would allow us to dissociate activations in the inferior frontal gyrus from anterior insula.

A separate general linear model (GLM) was defined for each subject that examined the neural response during the entirety of run. We defined four regressors for both the “self” and “other” runs: Pain Anticipation, NoPain Anticipation, Pain, NoPain. The following contrasts were specified and, for the sake of clarity, will be referred to as follows:

1. Self Pain: [Self Pain – Self NoPain]
2. Other Pain: [Other pain – Other NoPain]
3. Other Anticipation: [Other Pain Antic – Other NoPain Antic]

Within each of these contrasts, a one-sample t test was used to identify voxels in which the average contrast for the whole group (n=29 subjects) differed significantly from 0 (i.e. a random-effect analysis). The resulting map of the t statistic was thresholded at $p < .001$, with a spatial extent threshold of 10 contiguous voxels.

Functional regions of interest (ROIs) were defined from each of the four activation maps (Self Pain, Self Anticipation, Other pain, Other Anticipation) using the following method. For Self Pain and Other Anticipation, the activation map was thresholded at $p < .001$. Because the activations during Other Pain were more robust, the activation map was thresholded at $p < .0001$ in order to better delineate the structure where the activation was taking place. For each activation of interest, the peak voxel was identified and a 15 mm isotropic cube was centered on that voxel. Given the small anatomical volume of the amygdala, the functional ROIs comprised a 10 mm isotropic cube centered on the voxel of peak activation. Functional activations that spanned multiple anatomical regions were separated by finding the local maxima of each activation. All ROIs were then explored in correlation analyses with self-report personality measures as well as with state empathy ratings during the task. These ROIs were also used in longitudinal analyses to investigate changes related to meditation training, and these results will be discussed in a later chapter.

Finally, in an exploratory whole-brain analysis, we entered personality scores as a covariate in the GLM using each of the four contrasts, and tested for correlations between subject contrast values and scores on a voxel-by-voxel basis. Maps of the correlation coefficient were thresholded at $p < .001$, with a 10-voxel spatial-extent threshold.

Results

Behavioral: One subject's Other Pain and NoPain ratings were excluded due to suspicion that he was confused about how to use the button-box (he rated the nonpainful as more aversive than the painful). A paired samples t-test revealed that subjects rated both the Self Pain (n=29) and Other Pain (n=28) as more aversive than the Self NoPain ($t(28) = 8.65$; $p < .001$) and Other NoPain ($t(27) = 5.35$; $p < .001$). Subjects found the Self Pain more aversive than the Other Pain (paired $t(27)=2.83$; $p < 0.01$) (see **figure 3-2**).

Next, personality variables and pain ratings were entered into a bivariate correlation analysis. There was a significant negative correlation between state empathy ratings and the coldheartedness subscale of the PPI ($r(27) = -0.57$; $p = .001$) (see **figure**

3-3). There were no other significant correlations, although there was a trend suggesting that empathic concern scores were related to other pain ratings (r (26) = .35; p = .07).

In terms of compassionate behavior, 17 of the 21 subjects made some monetary donation (M = 4.76, SD = 4.3) (see **figure 3-4** for histogram). One subject chose not to reveal how much money he had donated. As it was clear that he had donated something, a mean-replace was performed for his donation amount. There was one subject in the control group who donated a sum of money that was greater than 3 standard deviations above the mean ($20.00). There was a positive relationship between donation and self-reported stress (r(19) = 0.44, p = 0.05) and anxiety (r(19) = 0.52, p = 0.02). However, this relationship was non-significant if the outlier was removed. There was no relationship between any of the subscales of the IRI and donation amount.

fMRI

Self Pain: The contrast Self [Pain – NoPain] revealed expected neural activations in areas related to the perception of pain, including S1 and posterior insula. Also active were areas related to the affective and evaluative dimensions of pain, including anterior insula, dACC, mid cingulate and amygdala (see **figure 3-5** and **table 3-2** for activations)

An independent samples t test indicated that women had more activity in the right amygdala (t(27)=2.67; p = .01) (see **figure 3-6)** and there was a strong trend indicating that they had more activity in the right (t(27) = 1.76; p = .09) and left (t(27) =2.00; p = .06) anterior insula during the self pain task. Moreover, scores on the personal distress subscale of the IRI were positively related to almost all activations related to pain, including the right amygdala (r(27) = 0.48; p = 0.01), mid cingulate (r(27) = 0.63; p <

.001), dorsal ACC (r(27) = 0.47; p = .01), right anterior insula (r(27) = 0.45; p = 0.01), left anterior insula (r(27) = 0.50; p = 0.01), posterior insula/S2 (r(27) = 0.49; p = 0.01) and left S1 (r(27) =0.51; p = 0.01)(see **figure 3-7**). Finally, there was a strong trend suggesting that scores on the depression subscale were negatively related to activity in the anterior insula (r(27) = -0.36; p = 0.05).

Other Pain: The contrast Other [Pain – NoPain] revealed activations related to empathy for pain, such as in the anterior insula, mid cingulate, inferior frontal gyrus and amygdala. See **figure 3-8** and **table 3-3** for a list of activations.

Bivariate correlation analyses (n=28) revealed that state empathy ratings were positively related to activity in the left amygdala (r(26) = 0.41, p = 0.03) (see **figure 3-9**). There was a trend suggesting that factor 2 of the PPI was inversely related to activity in the left anterior insula (r(27) = -0.36, p = 0.06) and left IFG (r(27) = -0.35, p = 0.07). There was also a significant negative relationship between scores on the depression subscale of the DASS and activity in the right amygdala (r(27) = -0.42, p = 0.03) (see **figure 3-10**). There was also a strong trend suggesting that females engage the left amygdala more than males (t(27) = 1.94, p = 0.06). There were no other significant relationships between personality variables and brain activity for this contrast.

Other Anticipation: The contrast Other [Pain Anticipation – NoPain Anticipation] revealed activations in areas related to pain anticipation, including the anterior insula bilaterally. See **figure 3-11** and **table 3-4** for list of activations.

Bivariate correlation analyses (n=28) revealed that state empathy ratings were positively correlated with neural activity in the right (r(26) = 0.45; p=0.02) and left (r(26)

= 0.59; p = .001) anterior insula (see **figure 3-12**). The coldheartedness subscale of the PPI was negatively related to activity in the right anterior insula (r(27) = -0.45; p = .02) and there is a trend in the same direction for the left anterior insula (r(27) = -0.36; p = 0.05) (see **figure 3-13**). The whole brain ANCOVA did not reveal any areas in which activity was correlated with personality variables at a threshold of $p < 0.001$.

Discussion

The goal of this study was to validate an EFP paradigm using dynamic video stimuli so that it could be utilized in a longitudinal investigation of meditation. Moreover, we attempted to add to what is known about the neurobiology of empathy by exploring the period of time in which participants watch others anticipate a painful stimulation, and by investigating the relationship between empathy for pain and future compassionate action. Finally, we probed for relationships between empathy and individual variation in well-being and psychopathy. Each of these aspects of the study will be discussed in turn.

EFP Paradigm Validation: With regards to the first aim, to validate an EFP task, it is clear from our results that the video stimuli elicit robust neural activations commonly found in other EFP paradigms. While watching others receive painful compared to non-painful stimulations, participants engage the putative mirror neuron system (lateral parietal, STS and IFG), regions related to the affective and evaluative dimension of pain (anterior insula, aMCC and amygdala), as well as regions related to mentalizing (dmPFC).

Of interest, we did see robust activation in the amygdala, suggesting that amygdala activation during EFP is related to fear conditioning rather than to ambiguous threat. This interpretation is consistent with the fact that the portion of the amygdala that is active is likely the central and centromedial nucleus of the amygdala, which has dense connections to the hypothalamus and midbrain and is thought to be important in mediating the physiological response to fear and anxiety (Davis 1992; Kalin et al. 2004). In fact, this was the only region of activation that was related to state empathy during the EFP task.

Empathic Anticipation: Neural activity in the anterior insula during empathic anticipation was more strongly correlated with self report measures of state empathy and psychopathy than neural activity during EFP. While several EFP studies have reported a relationship between brain activity and state and trait empathy, there is very little consistency across studies. For example, some studies find that either state *or* trait measures (but not both) are related to activity (e.g. Jackson et al. 2005). What is more, some studies show that measures are related to activity in the anterior insula, while a handful find relationships only with activity in dACC. The results presented here are consistent with those of Gu and colleagues (2010) who found that activity in the anterior insula was more related to empathy for pain than aMCC was.

It is unlikely that the finding that empathic anticipation is related to state and trait measures is spurious or that it reflects some anomalous aspect of one of the ratings systems, as the activity in the empathic anticipation epic is correlated with two different aspects of self-reported empathy (psychopathy and state empathy). However, we do not believe that it is the case that the empathic anticipation period was more salient to subjects, as the activity in our regions of interest was actually more robust during EFP than during empathic anticipation. Moreover, we do not suspect that there was a ceiling effect. If there was a ceiling effect, we would expect to see less variation across subjects in activation during EFP than from empathic anticipation. However, taking the anterior insula as an example, there is more variance in activity in the right and left anterior insula during empathy for pain (SD = 0.77 and 0.64) than there was during empathic anticipation (SD = 0.12 and 0.15). We suspect that this is a fruitful avenue for follow-up investigations that are specifically designed to explore empathic anticipation.

Compassion: Based on ROI and whole brain analyses, no brain regions were identified in which activation during EFP or empathic anticipation predicted donation at a later time. This is likely due to the nature of our donation induction, which only provided one measure of costly helping. In contrast, the study in which there was an observed relationship between anterior insula activity and altruistic behavior employed a methodology in which the subjects were faced with multiple instances in which they could behave altruistically (Hein et al. 2010). A study design such as this provides far more power, and should be used in the future. In fact, others have set out to study the neurobiology of compassion without confirming their hypotheses (Zahn et al. 2009), and such a complex emotion is difficult to experimentally invoke and model.

Individual variation in well-being and psychopathy: The results presented here do not confirm our hypothesis that well-being will be inversely related to the distressing aspects of EFP, as the extent to which participants endorsed depressive symptoms was negatively related to amygdala activity. This finding is in contrast with other studies that link amygdala *hyper*activity with depressive states (e.g. Sheline et al. 2001; Yang et al. 2010). It is important to note that our participants were all healthy, depression-free adults, and thus our finding may be related to subtle mood differences within a healthy population. In fact, a recent study by Han and colleagues (2009) found that the affective empathic neural responses in the aMCC were attenuated when the EFP stimuli was viewed in the context of positive and negative emotional facial expressions. The authors interpreted this result as a decrease in the affective response to others in pain during emotional contexts, and it may be that our results are reflecting a similar type of effect for individuals who are feeling more depressive mood states. It may be the case that individuals experiencing more depressive mood states are more introspective and less attentive to the video clips.

With regards to individual differences in psychopathic personality features, there was confirmation for the hypothesis that those who endorsed more features of psychopathy would have reduced state empathy during the task as well as reduced neural activity. In addition, the fact that scores on the Coldheartedess subscale were negatively related to activity in the right anterior insula during empathic anticipation are consistent with studies showing that children with conduct disorder have reduced gray matter in the anterior insula (Sterzer et al. 2007). Again, it is important to note that the population studied here was non-clinical, and thus it is interesting that we find these results even within a group of individuals who have not been diagnosed with psychopathy.

In conclusion, the EFP paradigm used in this study proved to be a robust elicitor of neural activity previously shown to be related to empathy for pain. In fact, the dynamic video stimuli used here identified amygdala activity that is often not seen in EFP paradigms that use still photographs of others in pain. Further, we found that neural activity during empathic anticipation may be a better indicator of subjective empathic feelings, since it was more closely related to both state and trait aspects of empathy. With regard to the relationship between individual differences in well-being, we found that depressive mood states, even within a healthy population, impacted aspects of the EFP response. Similarly, our study shows that even within a non-clinical population, psychopathic personality features are related to the neurobiology of the empathic response.

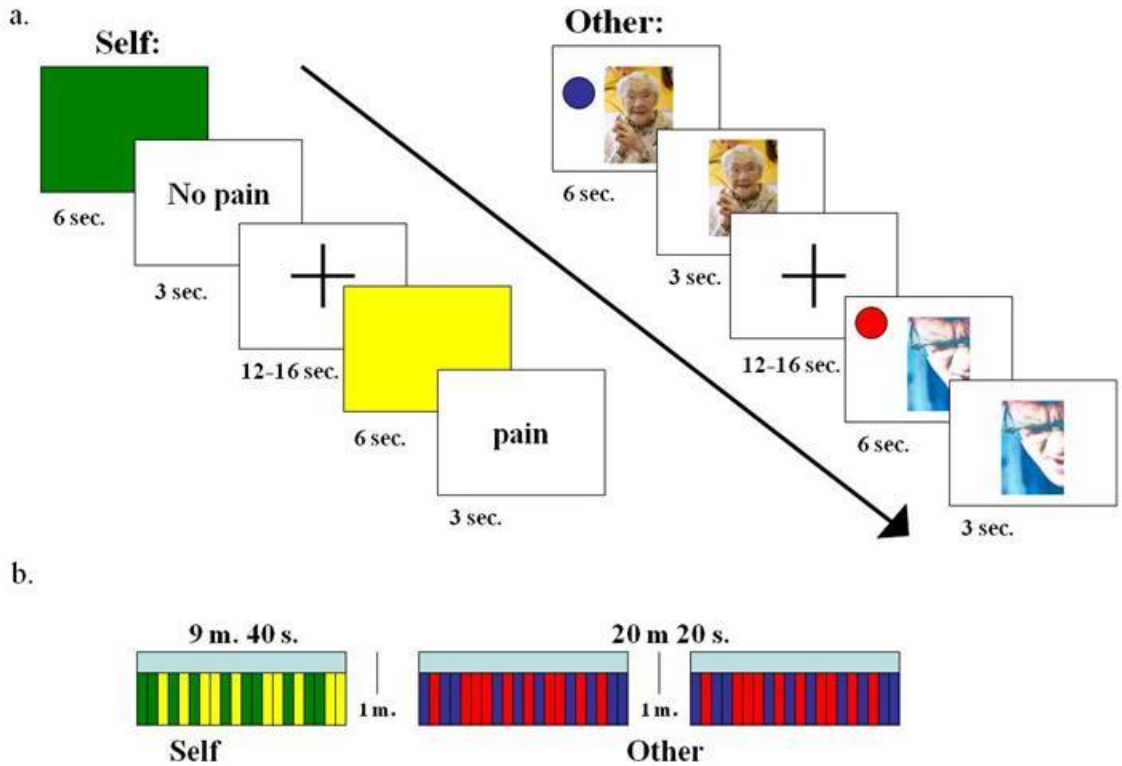

Figure 3-1: Schematic of the Empathy for Pain (EFP) (Self Pain and Other pain) paradigm. (a.) Example of individual trials for Self Pain and Other Pain; (b.) Event related design of Self Pain and Other Pain.

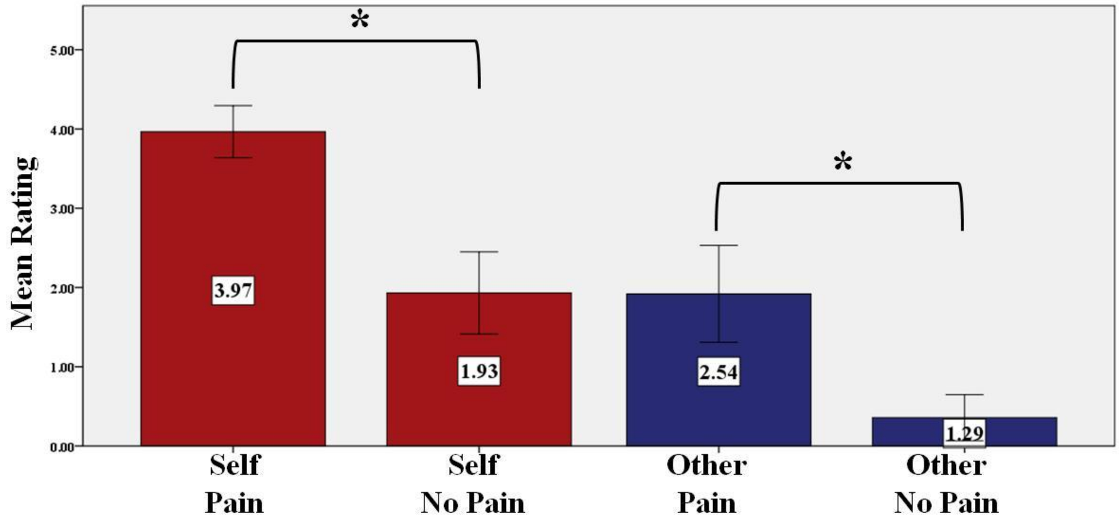

Figure 3-2: Mean aversiveness ratings for Self and Other Pain and No-Pain.

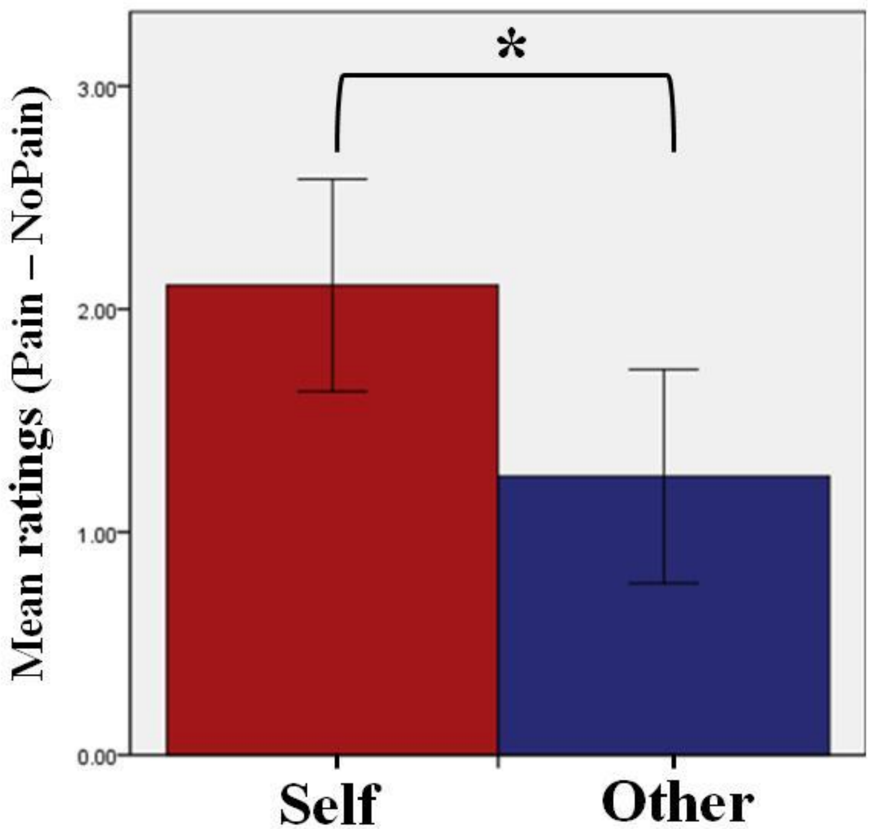

Figure 3-3: Mean aversiveness ratings (Pain – NoPain) for self (red) and other (blue) ($t(27) = 2.83$, $p < 0.01$).

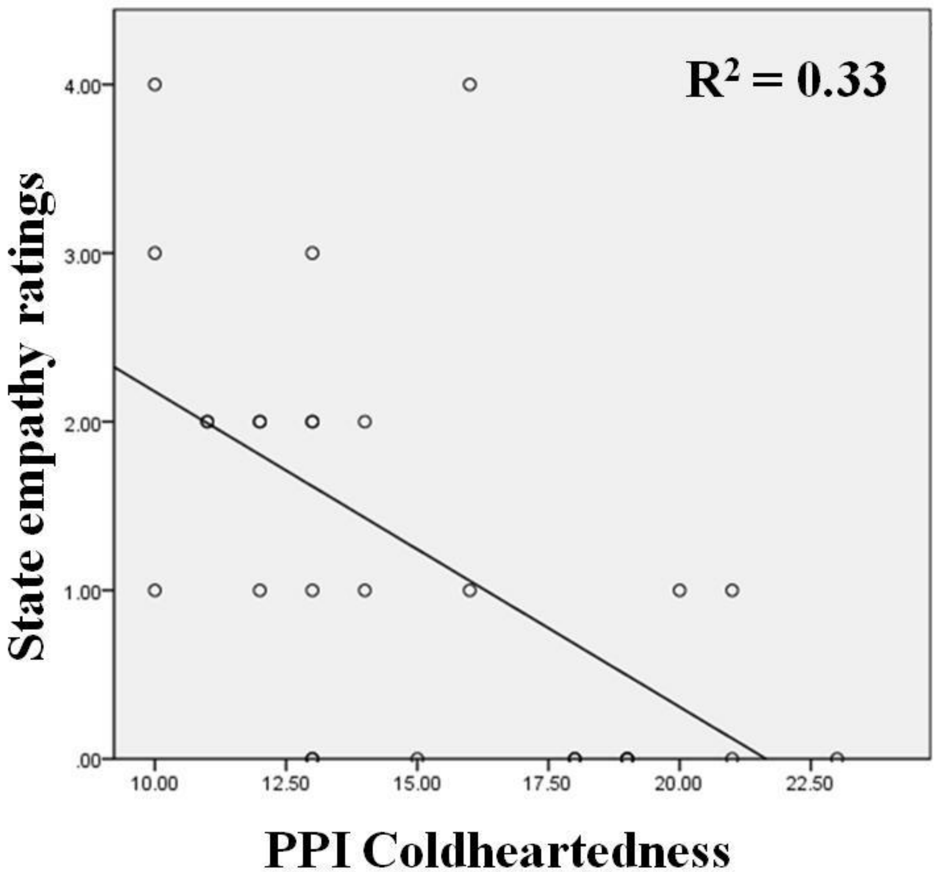

Figure 3-4: Bivariate correlation between state empathy ratings (Pain – NoPain) and the Coldheartedness subscale of the PPI (r(26) = -.574, p = .001).

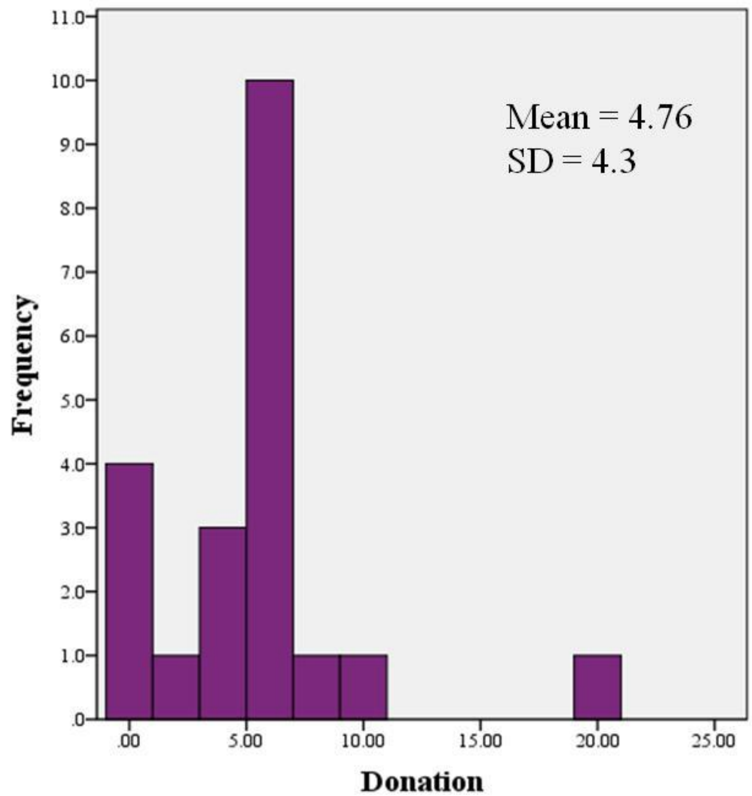

Figure 3-5: Histogram of donations during compassion induction.

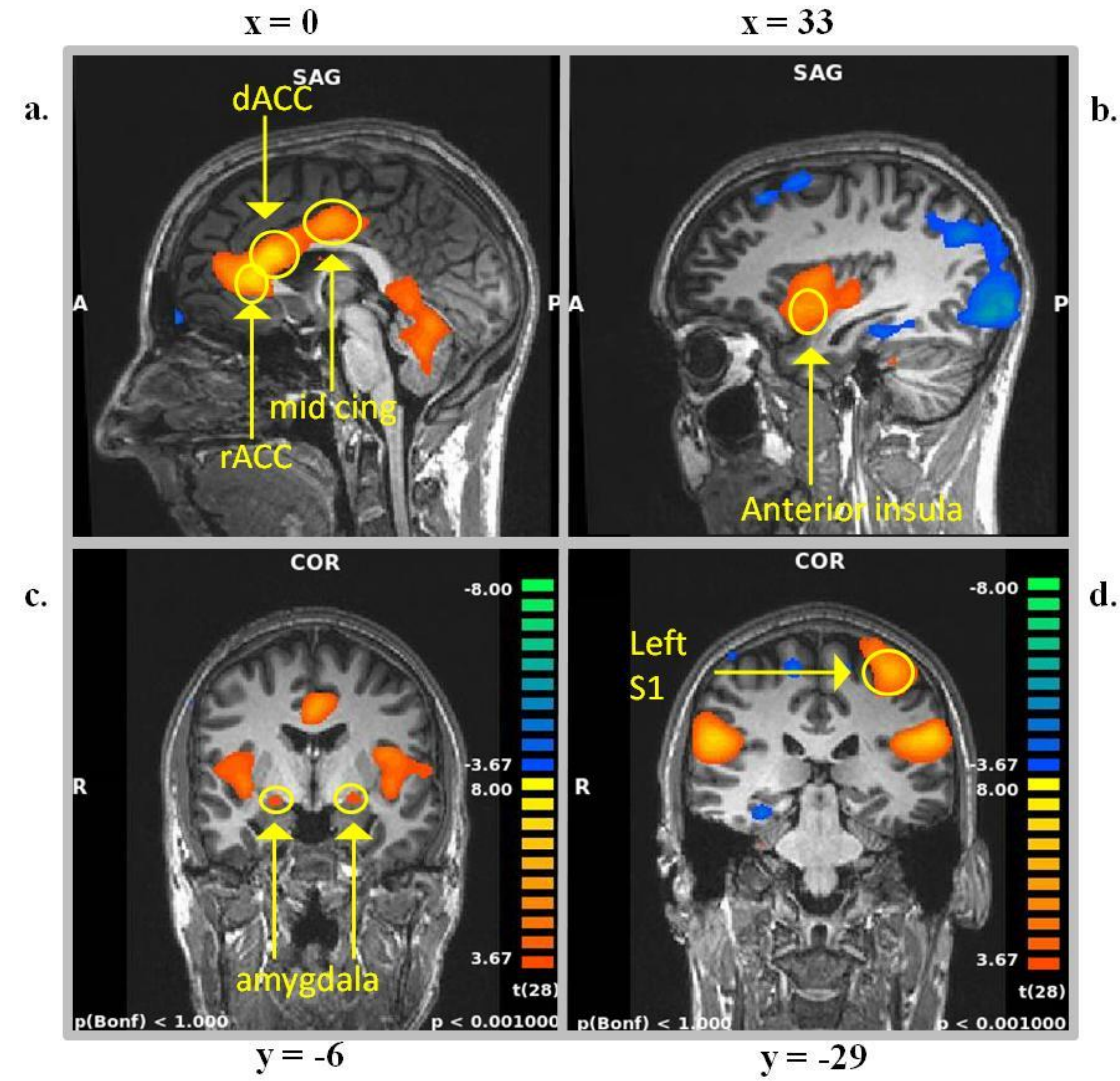

Figure 3-6: Main effect of Self Pain [Pain – NoPain] at threshold t(28) = 3.67, $p < 0.001$. Panel **(a.)** shows rostral ACC (rACC), dACC and mid cingulate in the sagital plane. Panel **(b.)** shows the right anterior insula in sagital plane. Panel **(c.)** shows the right and left amygdala in coronal plane. Panel **(d.)** shows the left primary somatosensory cortex in coronal plane.

Brain Region	Brodmann's Area	X	Y	Z	Voxels	Peak t
R amygdala		21	-7	-8	184	4.15
L amygdala		-18	-10	-5	383	4.22
dACC	24	3	23	25	20236	7.99
Mid Cingulate	24	0	-7	40	↓	5.97
Rostral ACC	24	0	32	13	↓	7.72
R Inferior Parietal	40	54	-28	25	23708	7.27
R Ant Insula	14	36	8	-2	↓	6.34
L Post Insula	13	-48	-19	19	26277	7.81
L Ant Insula	14	-39	5	1	↓	7.16
L S1	3	-36	-28	58	16372	6.64
Cerebellum		18	-43	-17	8932	6.49
Cerebellum		-30	-43	-23	645	4.93

Table 3-1: Main effect of the Self Pain task [Pain – NoPain]. For regions that were subdivided into smaller ROIs using the local maxima, an "↓" is entered for number of voxels, which means that the size of the entire activation is listed above.

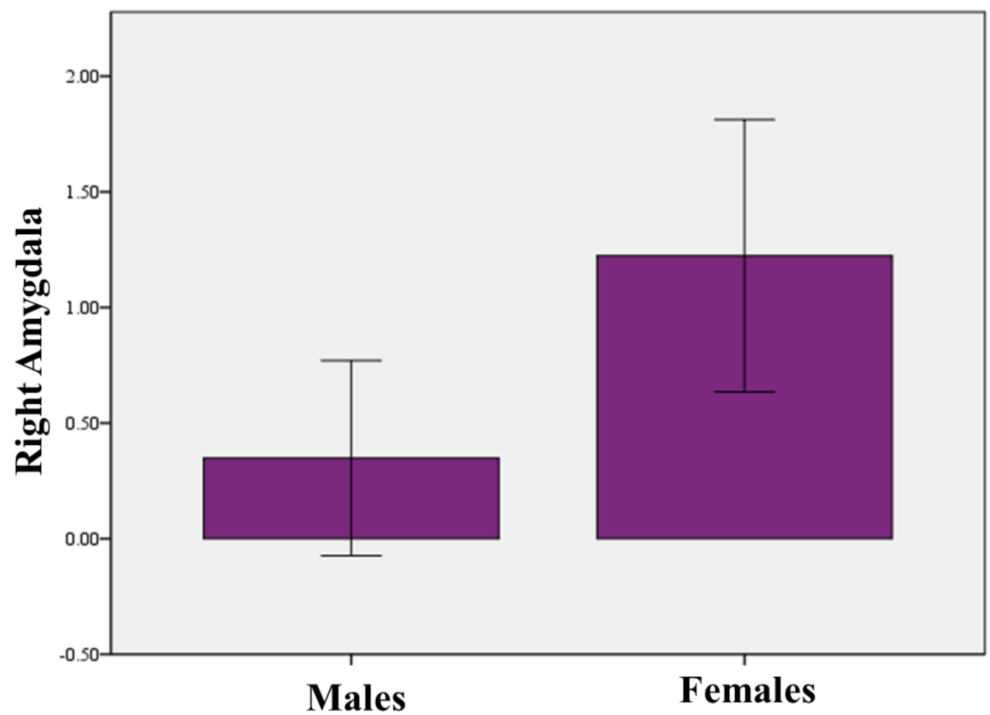

Figure 3-7: Plot of the mean beta contrast value in the Self Pain task [Pain – NoPain] in the right amygdala in males and females (t (27) = 2.67, p = 0.01).

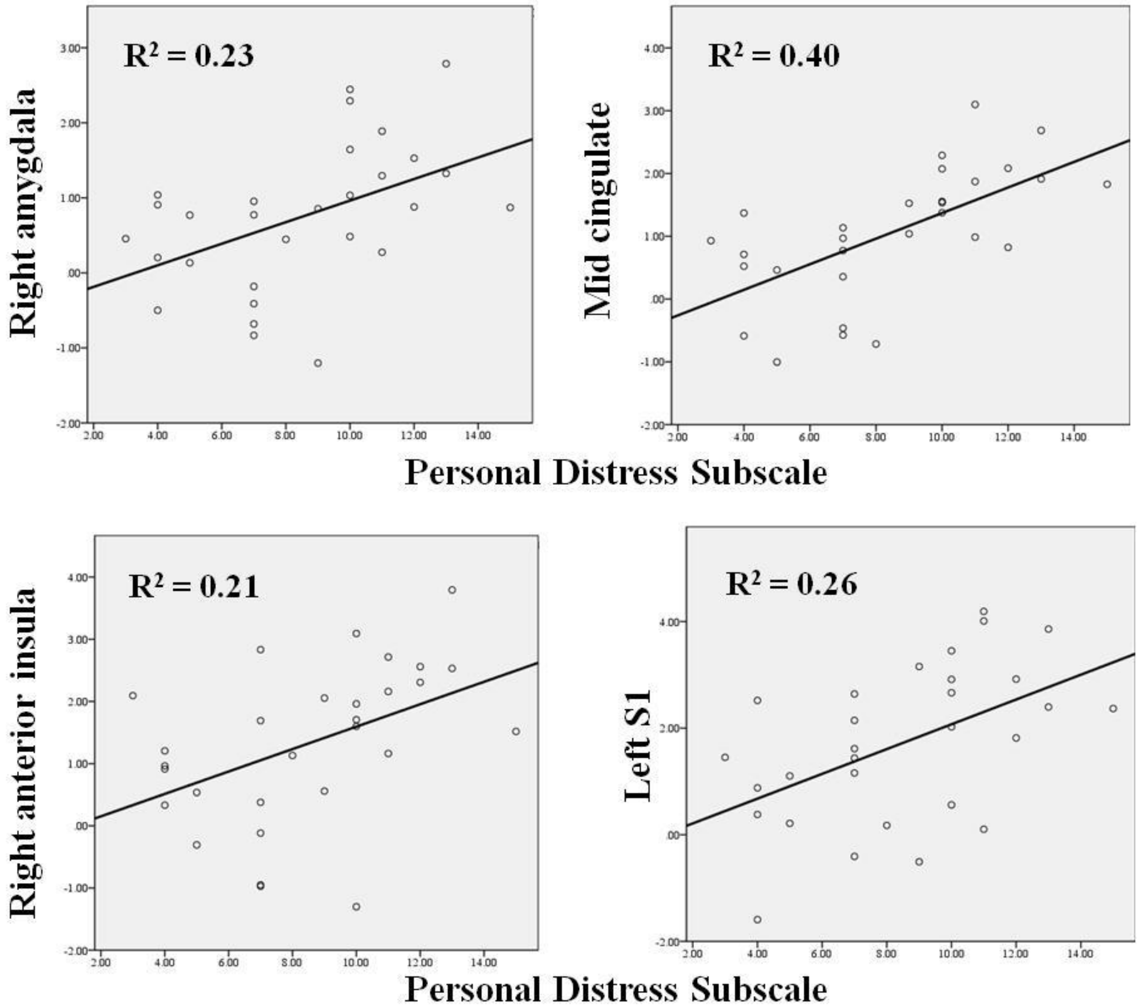

Figure 3-8: Plots of bivariate correlations for personal distress subscale of the IRI with beta contrast values in the Self Pain task [Pain – NoPain] in the right amygdala ($r(27) = 0.48$, $p = 0.01$), mid cingulate ($r(27) = 0.63$, $p < 0.001$), right anterior insula ($r(27) = 0.45$, $p = 0.01$), and left somatosensory cortex ($r(27) = 0.51$, $p = 0.01$).

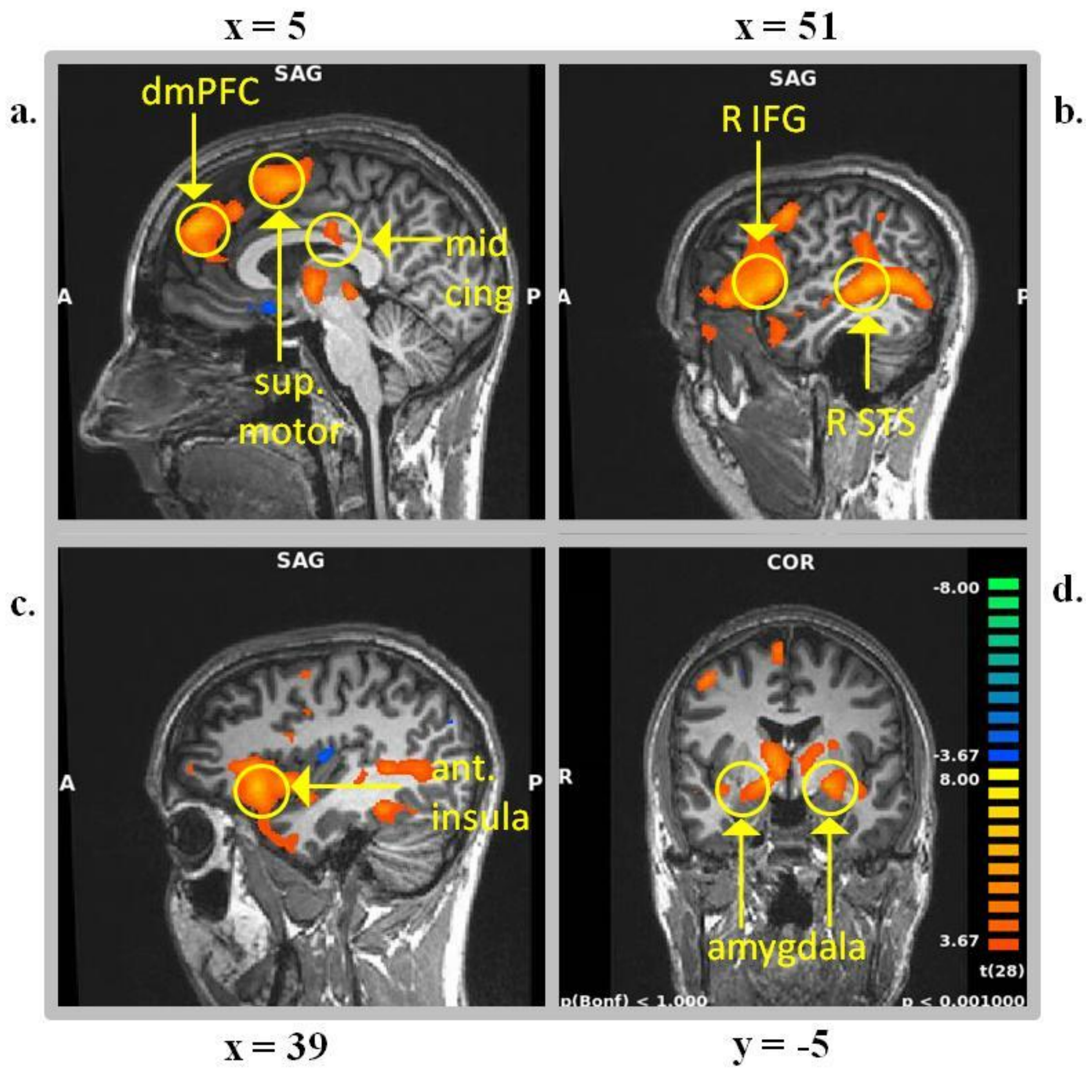

Figure 3-9: Main effect of Other Pain [Pain – NoPain] at threshold $t(28) = 3.67$, $p < 0.001$. Panel **(a.)** shows dmPFC, supplementary motor and mid cingulate activations in the sagital plane. Panel **(b.)** shows the right inferior frontal gyrus and STS activations in sagital plane. Panel **(c.)** shows the right anterior insula activation in sagital plane. Panel **(d.)** shows the left and right amygdala activations in coronal plane.

Brain Region	Brodmann's Area	X	Y	Z	Voxels	Peak t
dmPFC	9	6	50	37	15191	7.19
Supplemantary Motor	6	6	8	58	↓	6.72
Cingulate Gyrus	24	3	-16	34	2040	5.04
R Inferior Frontal	44	54	14	7	59101	7.28
R Anterior Insula	13	39	23	-2	↓	7.31
R Superior Temporal Gyrus	22	45	-31	1	16538	7.84
R Lateral Inferior Parietal/TPJ	22	52	-37	22	↓	5.16
L Amygdala		-21	-7	-2		7.11
R Amygdala		14	-4	-2		6.80
R Thalamus		6	-4	4		6.03
L Anterior Insula	13	-36	23	10		7.26
L Lateral Inferior Parietal TPJ	40	-54	-37	25	12641	8.03
L Middle Temporal Gyrus	41	-54	-46	7	↓	7.30
L Inferior Frontal	44	-48	14	13		6.51
R Fusiform Gyrus	20	39	-40	-14	574	5.31
L Superior Temporal Gyrus	22	-48	-22	-2	323	4.54
Cerebellum		27	-76	-29	1397	5.76
Cerebellum		-3	-43	-32	324	4.97
Cerebellum		-12	-67	-26	6850	6.11

Table 3-2: Main effect of Other Pain [Pain – NoPain].

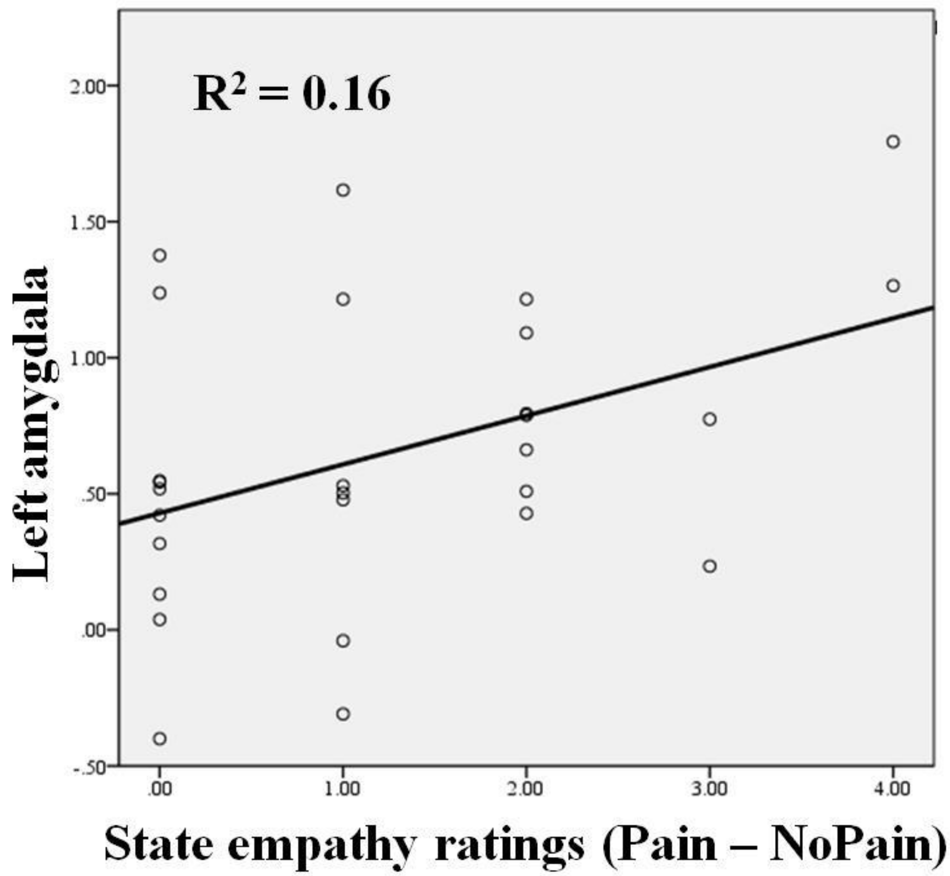

Figure 3-10: Plot of bivariate correlation between state empathy ratings (Pain – NoPain) and beta contrast values for the other pain task [Pain – NoPain] in the left amygdala ($r(26) = 0.41$, $p = 0.03$).

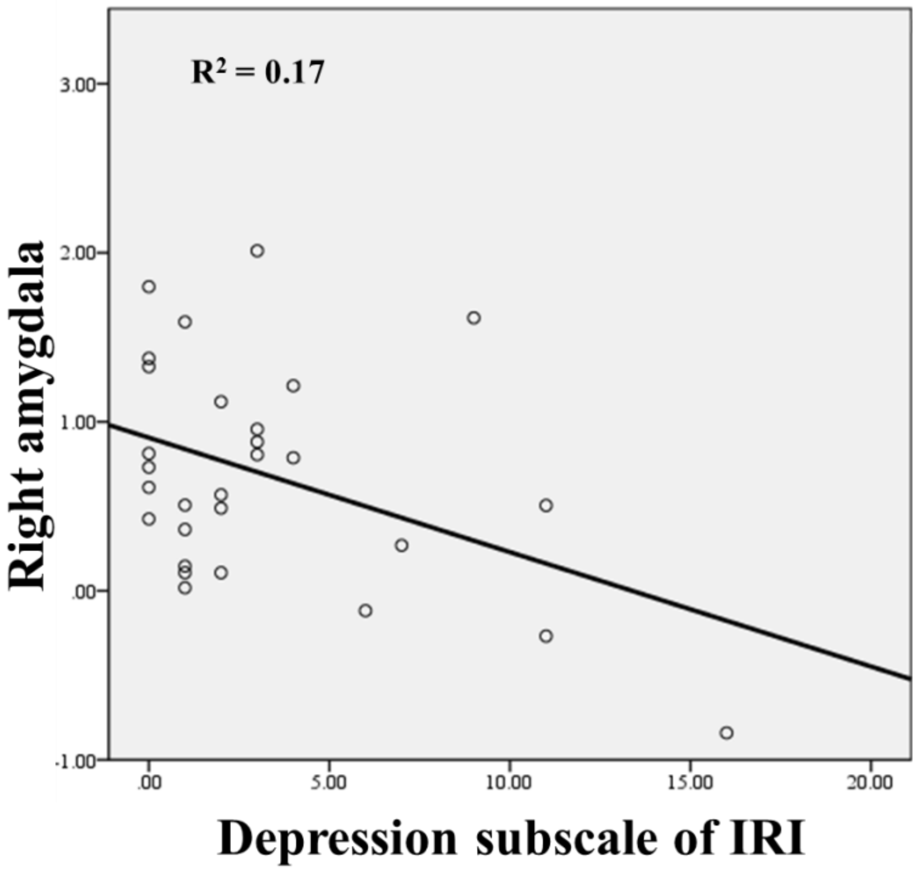

Figure 3-11: Plot of bivariate correlation between depression scores and beta contrast values for the Other pain task [Pain – NoPain] in the right amygdala (r(27) = 0.42, p = 0.03).

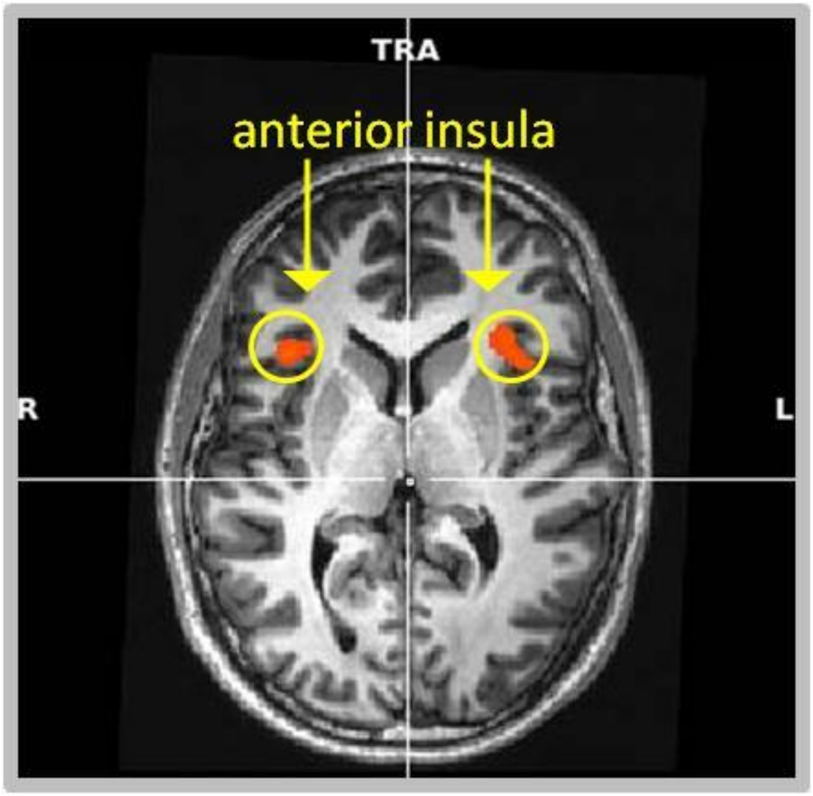

Figure 3-12: Main effect during Other Pain for the contrast [PainAntic – NoPain Antic] at threshold $t(28) = 3.67$, $p < 0.001$, in axial plane ($z = 7$).

Brain Region	Brodmann's Area	X	Y	Z	Voxels	Peak t
R Anterior Insula	13	39	17	4	465	4.58
L Anterior Insula	13	-33	20	4	790	4.86
Midbrain/Thalamus		-3	-22	-2	593	5.16

Table 3-3: Main effect during Other Pain for the contrast [PainAntic – NoPain Antic].

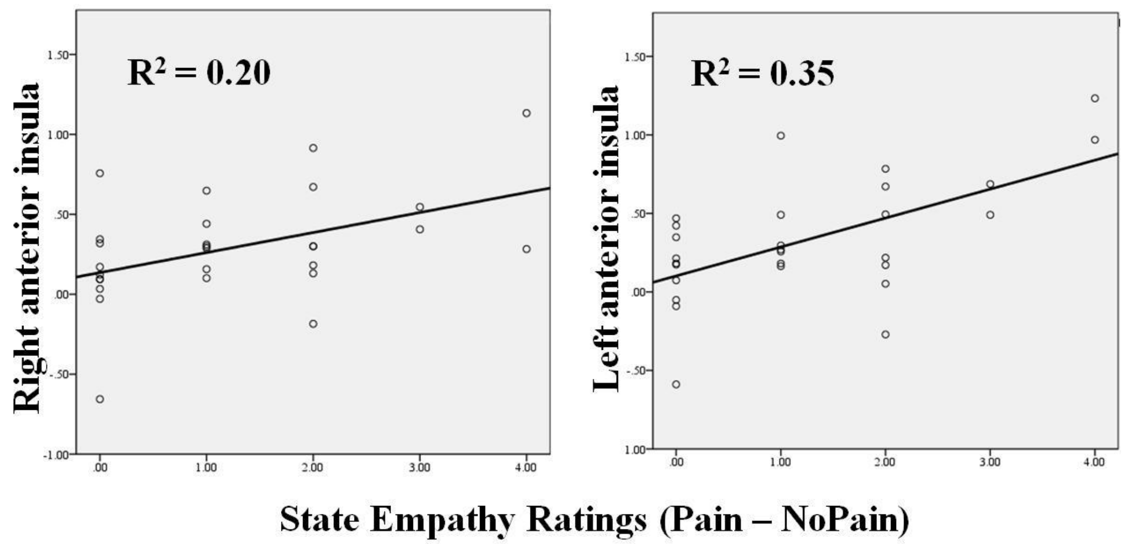

Figure 3-13: Plot of bivariate correlation between state empathy ratings (Pain – NoPain) and beta contrast values for the other pain task [PainAntic – NoPainAntic] in the right (r(26) = 0.45, p = 0.02) and left (r(26) = 0.59, p = 0.001) anterior insula.

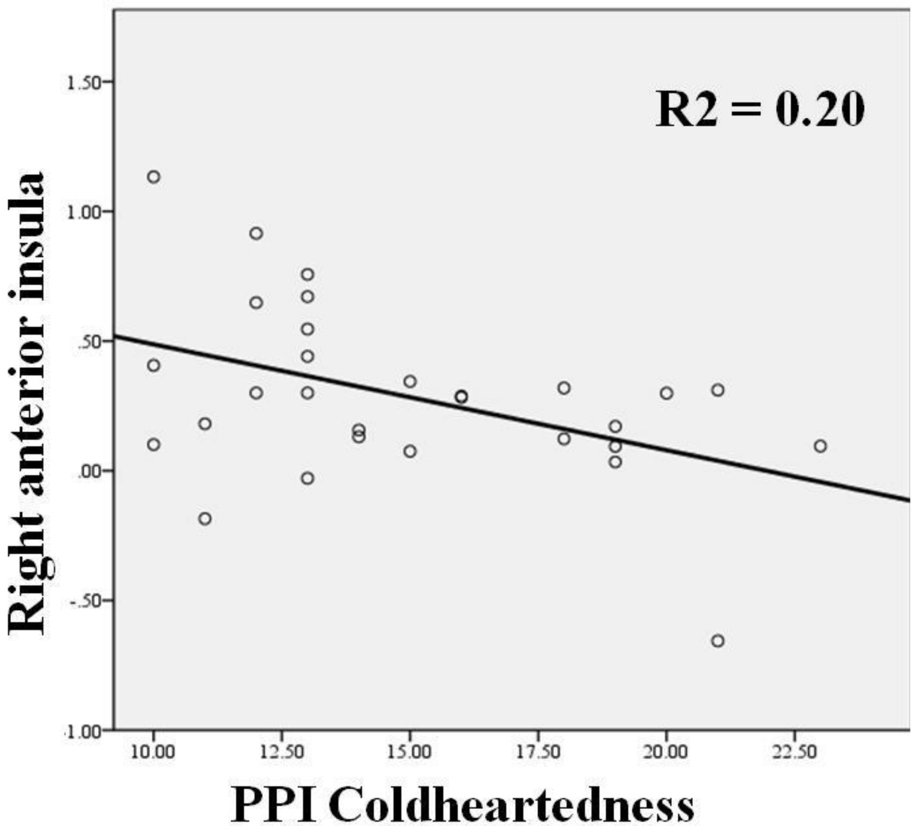

Figure 3-14: Plot of bivariate correlation analysis of beta contrast values during the other pain task [Pain Antic – NoPain Antic] in the right anterior insula with scores on the Coldheartedness subscale of the PPI (r(27) = -0.45, p = 0.02).

Chapter 4

Longitudinal investigation of compassion meditation

Introduction

During the last half century, meditation has come to the West in waves and carved out a distinctive and distinguished place in secular, religious, and clinical contexts. In fact, it is difficult to watch CNN or to read the New York Times without finding some reference to the physical, mental and social health benefits of various meditative practices. Yet, while meditation is increasingly incorporated into clinical treatments for a variety of mental and physical ailments and is offered to the public in multiple domains with claims of increasing overall well-being, there are sizeable gaps in our understanding of how meditation affects well-being and of the neurobiological mechanisms by which it is translated into these outcomes in practitioners. First, very little is known about how meditation affects social cognition and the neural processes that support it. This gap in our understanding appears cavernous when we reflect that, according to Buddhist philosophy, one of the fundamental goals of meditative practice is to cultivate compassion and empathy towards others (HHDL 1995; Wallace 2001). And so, while Buddhist meditative techniques have been employed for hundreds of years to enhance prosocial traits, the assumption that meditation enhances empathy has not been rigorously evaluated. Second, much of the current research on meditation is fraught with flawed experimental designs and incomplete assessments of practitioners, such that many have called into question *any* conclusions regarding the effects of meditation practices in healthcare (Ospina et al. 2007). As such, we have little understanding of which aspects of meditation affect health outcomes, or of the physiological mechanisms that mediate these outcomes. To address these issues, the current study has been designed to evaluate whether a Tibetan Buddhist meditation that is thought to cultivate empathy and compassion will, in fact, enhance empathy and the neural correlates of empathy when compared to an active control condition consisting of a health discussion control group.

What's missing from meditation research?

Analytical styles: In one of his dialogues with contemplative researchers and practitioners, His Holiness the XIVth Dalai Lama pointed out that Buddhist meditative practices are traditionally divided into two categories: analytical, in which the practitioner engages in the examination or cognitive inquiry of some object or subject matter, and non-analytical . He noted that scientific investigation has largely been limited to non-analytical practices, particularly mindfulness practices. In fact, of late, meditation has become almost synonymous with mindfulness practices, and by far the most widely applied meditative program is Mindfulness-Based Stress Reduction (MBSR) (there are over 240 clinics worldwide with MBSR programs). Through his program, Jon Kabat-Zinn has popularized the idea of mindfulness as "paying attention in a particular way: on purpose, in the present moment, and non-judgmentally" (Kabat-Zinn 1994 p.4). While Kabat-Zinn does speak of ethics in his books, (for example, Kabat-Zinn 2005, p. 102), the oft-cited definition and instructions that are used in these contexts emphasizes acceptance of all thoughts and a goal-less attitude. For example, instructions often run something like this: "In meditation, thoughts and emotions that inevitably arise are simply accepted and observed; there are no attempts to change or escape from anything, nor are there attempts to hold on to or prolong anything." (Bishop 2002 p. 74) Similarly, "phenomena that enter the individual's awareness during mindfulness practice, such as perceptions, cognitions, emotions, or sensations, are observed carefully but are not evaluated as good or bad, true or false, healthy or sick, or important or trivial" (Baer 2003 p. 125). In this way, mindfulness practices are decidedly non-analytical, as the goal of the practice is to change one's relationship to their thoughts, rather than to modify the content of their thoughts (Kabat-Zinn 1990). And while studies of mindfulness approaches largely support its use in the alleviation of suffering from a host of clinical conditions (Chiesa and Serretti 2010), this emphasis on non-analytical practices has left a significant gap in our understanding of a wide range of diverse contemplative practices (Ozawa-de Silva and Dodson-Lavelle 2011).

Non-clinical assessments: Religious scholars have pointed to the "psychologization" that characterizes modern Buddhism all over the world (McMahan 2008 p. 52). In particular, this process has afforded a unique place for Buddhist theory and practice in the modern west, and has led to its incorporation into the scientific and medical community. For example, clinical researchers are increasingly applying mindfulness meditative techniques as treatments to reduce depression (Teasdale et al. 1995; Teasdale et al. 2000) and anxiety (Kabat-Zinn et al. 1992) , increase immune functioning (Davidson et al. 2003) , and benefit those with chronic pain (Kabat-Zinn 1982), cancer (Speca et al. 2000), and eating disorders (Kristeller 2004). While results of these treatments suggest that meditation holds promise for alleviating suffering related to clinical disorders, the medicalization of these processes have brought the investigative focus on distinctly “extra-Buddhist goals” (McMahan 2008 p. 57), such as the alleviation of symptoms of various psychological and physical clinical conditions. Very little research has been directed toward understanding how meditative practices influence those positive personality traits, such as empathy and compassion, which some have suggested are most emphasized, particularly within Tibetan Buddhism (Wallace 2001; Wallace and Shapiro 2006).

In fact, the focus on illness and disease has largely characterized western biomedicine in research and in practice, and recent reactions to this have spurred movements within psychology (the positive psychology approach, coined and emphasized by Seligman and Csikszentmihalyi (2000)) and anthropology (the study of the “social production of health” Levin and Browner (2005)). Yet, this more holistic approach is largely missing from meditation research. This gap in our understanding is particularly unfortunate for two reasons. First, the scientific community has largely missed the opportunity to investigate meditative traditions on their own terms. Second, placing meditation back in a scientific and clinical context, if a meditative technique is found to enhance empathy and compassion, it might represent a powerful practice for the cultivation of well-being across various age groups and in various populations, including those characterized by a lack of empathy such as individuals with autism (Baron-Cohen and Wheelwright 2004; Yirmiya and Sigman 1992) and psychopathy (Blair 2005).

Despite the lack of studies regarding the effects of meditation on prosociality, there is good reason to suspect that meditative practices may have beneficial effects beyond stress reduction. For example, Hutcherson and colleagues (2008) found that study participants randomized to a 7 minute Loving Kindness Meditation, compared to those randomized to a control condition, became more positive toward others in an implicit social task. In another study, Lutz and colleagues (2008) asked adepts and controls to perform compassion meditation, in which the meditator generates an "unconditional feeling of loving-kindness and compassion." Subjects were asked to meditate in blocks, interspersed with blocks of rest. During both meditation and rest, subjects heard emotional vocal stimuli. After the sessions were complete, subjects were asked to rate each meditation session according to how successful they thought they were in cultivating the meditation state. They found that the meditation state was related to activation in the anterior insula and areas known to be important for theory of mind – temporal lobes, posterior STS, temporo-parietal junction, medial prefrontal cortex and precuneus. The expert meditators had more neural activation in areas related to empathy, including the insula and secondary somatosensory cortex, in response to emotional vocalizations during meditation. Furthermore, the insula activation was related to self-reported intensity of meditation session.

Off the cushion and into real life: A third area in which meditation research is lacking, particularly in the basic science (i.e. non-clinical) studies of meditation, is that much of it points its magnifying glass to the physiological changes that occur during the meditation itself. However, many contemplative scholars note that "the states developed in meditation are usually thought to create a post-meditative effect" (Lutz et al. 2007 p. 505), and that the point of meditation is to cultivate changes that continue "off the cushion" and permeate one's life (HHDL 2001). If this is the case, then we should be exploring the potential of meditation to act as a scaffold for off the cushion changes. This approach is particularly lacking within the neuroscientific study of meditation. For, while several researchers have employed neuroimaging methodologies to study the neural correlates of meditation itself (for a review, see Lutz et al. 2007), very few have explored the ways in which meditative practice might affect the neural correlates of everyday mental processes outside of the context of meditation. If practitioners are taught to cultivate cognitive skills or attributes in such a way that they can be practiced during all facets of the practitioner's life, it is important to systematically explore the ways in which a meditative practice affects every day processes and the neural correlates of these processes.

Appropriate study designs: While the sheer number of scientific articles purporting to show beneficial effects of meditation suggest its value as a tool for cultivating well-being, in general, reviews have been critical of the study designs employed as well as the conclusions drawn from these studies. For example, many of the early studies used inappropriate statistics and invalidated psychometric and clinical measures (Bishop 2002). Even more problematic, many of the initial clinical studies included patients who were simultaneously treated either pharmaceutically or with other therapies. Moreover, Bishop notes that outcomes often cannot be definitively attributed to the meditation, per se, as most studies have used an inadequate control group or no control group at all. In fact, Kabat-Zinn has stated that because MBSR was designed for maximal clinical utility, the course emphasizes aspects of personal development beyond mindfulness, and "the positive placebo effect was maximized."(Kabat-Zinn 1982 p. 35) These methodological issues are emblematic of meditation studies as a whole. In fact, an exhaustive review by Ospina and colleagues (2007) summed up the state of meditation research by asserting that "most clinical trials on meditation practices are generally characterized by poor methodological quality with significant threats to validity in every major quality domain assessed" (p. 1199).

In addition to these problems associated with clinical research on meditation, much of the more theoretical research on contemplative techniques is dogged by study designs that muddle our understanding of specific practices, as it often relies on meditation "adepts" with thousands of hours of training in varied techniques. For example, the aforementioned study investigating compassion meditation focused on Tibetan monastics with between 10,000 and 40,000 hours of meditation practice. While this quite selective group of individuals presents a fantastic opportunity for investigation, this type of study design makes conclusions about the specific effects of meditation problematic. First, it is quite clear that Tibetan monastics with such a high degree of training were likely not your run-of-the mill people to begin with. Rather, this is a self-selected population who, we can only imagine (until there is more research to draw from), enter the monastic world with extraordinary levels of conscientiousness, self-discipline, and intelligence and who carry with them a distinct set of spiritual and cultural beliefs. Moreover, most of these monks have a long history of engagement with multiple contemplative practices (Wallace 2006). Thus, if and when an outcome is found, it is not possible to causally link this outcome with a single meditative technique, or to generalize this outcome to a wider population.

With these methodological issues in mind, we believe that the most definitive empirical investigation of meditation necessitates a longitudinal design in which novices are randomized to either meditate or to participate in a control group designed to control for non-specific aspects of meditation.

Goals of study

The overall goal of this study fits into the larger goals of the dissertation. The longitudinal, randomized investigation of compassion meditation described in this chapter was designed to address the aforementioned gaps in the literature. On the one hand, we feel that research on meditative techniques should include a more macroscopic approach that shifts the point of inquiry toward the everyday behaviors and cognition of people that meditate. On the other hand, we felt it was necessary to include systematic testing of an isolated meditative practice in order to definitively investigate outcomes that may be related to practice. With such a rigorous analysis, we can begin to identify the neural mechanisms by which a Buddhist meditative practice may lead to positive health and social outcomes.

In addition to our approach to the meditation itself, we also wanted to include assessments that would allow us to test mechanistic models of empathy and to ask whether meditation modulated each component. To this end, we included assessments that would allow us to probe for changes in the neurobiology of (1) the perceptual aspects of empathy (e.g. the mirror neuron system), (2) the affective components of empathy (e.g. the anterior insula), and (3) the cognitive components of empathy (e.g. dmPFC). In this way, we can assess whether compassion meditation differentially affects aspects of the empathic response. In addition, we felt it was crucial to include assessments of empathic accuracy as well as compassionate behavior so that we could more fully explore how meditation might enhance real-world behavior. Finally, we included measures of well-being and spiritual meaning, as well as an instrument designed to probe participants' goals and attitudes about meditation in order to get a more nuanced picture of how the meditative technique "works" in people. In other words, is meditation more or less efficacious, depending on underlying personality variables, attitudes and beliefs? A subsequent chapter will discuss this exploration.

Hypotheses:

1. Subjects randomized to the meditation group, when compared to the control group, will report increased state and trait empathy.

2. Subjects randomized to the meditation group, when compared to the control group, will show more compassionate behavior during the donation induction.

3. Subjects randomized to the meditation group, when compared to the control group, will show increased brain activity in brain regions related to the Empathy for Pain (EFP) task, including the anterior insula, dmPFC and mid cingulate.
    a. Increased brain activity in meditation group will be related to increase is self-reported empathy and to compassionate behavior.

4. Subjects randomized to the meditation group, when compared to the control group, will show increased empathic accuracy during the Reading the Mind in the Eyes (RtME) task.

5. Subjects randomized to the meditation group, when compared to the control group, will show increased brain activity in regions related the RtME task, including dmPFC and the inferior frontal gyrus.
    a. Increased brain activity during the task in the meditation group will be related to increased empathic accuracy scores.

Methods

The Meditation: While Buddhist practices aimed at cultivating compassion are among the oldest and most widespread practices, they vary in terms of their emphasis on the cultivation of the affective dimension of compassion or involvement of discursive strategies aimed at cognitive restructuring (Lutz et al. 2007). The compassion meditation protocol utilized in this study was designed by Geshe Lobsang Tenzin Negi in response to the Dalai Lama's call for more research on analytical styles of compassion meditation. It is heavily based on the 11th century Tibetan Buddhist *lojong* tradition, and was given the title cognitive-based compassion training (CBCT) in order to diminish the baggage that comes when the word *meditation* is included. In its operationalization, there were two important modifications made. First, the program was presented in a secular manner; thus, all discussions of soteriological or existential themes (e.g. the attainment of Buddhahood, Karma) were omitted. Second, participants were taught one week each of concentrative (i.e. shamatha) and open-presence (i.e. vipassana) practices at the beginning of the course. While these techniques are generally considered quite advanced according to the Tibetan tradition, they are often practiced alongside compassion practices and are thought to be necessary for establishing the focus and awareness necessary to engage in analytical practices (HHDL 2001; Wallace 2006). As such, the course content proceeding according to the following schedule:

Week 1: Developing Attention and Stability of Mind: The foundation for the practice is the cultivation of a basic degree of refined attention and mental stability.

Week 2: Cultivating Insight into the Nature of Mental Experience: The stabilized mind is then employed to gain insight into the nature of the inner world of thoughts, feelings, emotions and reactions.

Week 3: Cultivating Self-Compassion: The student participant observes the innate aspirations for happiness and wellbeing as well as those for freedom from unhappiness and dissatisfactions, i.e., which mental states contribute to fulfillment and which ones prevent it. The participant then makes a determination to emerge from the toxic mental and emotional states that promote unhappiness.

Week 4: Developing Equanimity: Normally one tends to hold fast to categories of friends, enemies, and strangers and to react unevenly to people, based on those categories, with over-attachment, indifference and dislike. By examining these categories closely, the participant comes to understand their superficiality and learns to relate to people from a deeper perspective: everyone is alike in wanting to be happy and to avoid unhappiness.

Week 5: Developing Appreciation and Gratitude for Others: Although people view themselves as independent, self-sufficient actors, the truth is that no one can thrive or even survive without the support of countless others. When the participant realizes interdependence with others and the many benefits which others offer every day, the participant develops appreciation and gratitude for them.

Week 6: Developing Affection and Empathy: Deeper contemplation and insight into the ways in which myriad benefits are derived from countless others, along with awareness that this kindness should by rights be repaid, enables the participant to relate to others with a deeper sense of connectedness and affection. By relating to others with a profound sense of affection and endearment, the participant is able to empathize deeply with them. The participant cannot then bear to see others suffer any misfortune and rejoices in their happiness.

Week 7: Realizing Wishing and Aspirational Compassion: Enhanced empathy for others, coupled with intimate awareness of their suffering and its causes, naturally gives rise to compassion: the wish for others to be free from suffering and its conditions.

Week 8: Realizing Active Compassion for Others: In the final step, the participant is guided through a meditation designed to move from simply wishing others to be free of unhappiness to actively committing to assistance in their pursuit of happiness and freedom from suffering (Negi 2009).

The compassion meditation courses were taught by two experienced meditators who had undergone extensive training with Geshe Lobsang. Study participants attended two 1-hour classes per week for 8 weeks (Note: subjects in the second cohort attended one, 2-hour class per week in an attempt to increase class attendance). Class sessions combined a didactic teaching and discussion section with approximately 20 minutes of meditation per hour class time. Participants were provided with a meditation compact disc to guide "at-home" practice sessions that reflected in-class material, and were asked to keep track of practice time each day. Practice time was assessed as the sum of the number of classes attended multiplied by 20 minutes plus the recorded, at-home practice time.

Health Control: Participants randomized to the control condition attended a bi-weekly, one-hour discussion group (again, for cohort 2 this was changed to one, 2-hour class per week). Classes were designed and taught by graduate students from the Emory Rollins School of Public Health, and topics included history of medicine, nutrition, sleep, nature, interpreting health information, mental health, health through the lifespan, exercise, stress, infectious disease, sexual health and complementary and alternative medicine. The health discussion group was designed to control for the non-specific effects of the meditation class, including education and social engagement with a collective group. We did not ask subjects to do any "at home" work.

Participants

Twenty-nine (16 male) participants from the Atlanta area were recruited using a combination of fliers and electronic notifications posted at several local universities, as well as electronic advertisements on Craigslist. Participants were between the age of 25 and 55 (M = 31.0; SD =6.02), were screened and excluded for (self-reported) use of any psychotropic medication (i.e. antidepressants, anxiolytics, psychostimulants, or mood stabilizers) within one year of screening, as well as for regular use of any medications that might influence activity of the autonomic nervous system, HPA axis or inflammatory pathways. Subjects' were also excluded for any serious ongoing medical or psychiatric condition that might influence the results of the study, including post-traumatic stress disorder (PTSD), chronic pain or other pain disorders, depression, anxiety disorders or a history of schizophrenia or bipolar disorder, as well as for substance abuse occurring within one year of study entry. Subjects were screened for MRI safety, handedness (only right handed participants were included in the study), and all participants had normal or corrected-to-normal vision.

During a second visit approximately 10 weeks after the first, subjects were scanned a second time using the same scanning paradigm. Due to subject attrition, only 21 (12 male) subjects were scanned the second time (*M* age = 31.9; *SD* = 6.70). See **figure 4-1** for a schematic of the entire study design and table 1 for subject demographics. Unexpectedly, there was a significant difference between the mean age of the meditation and control group (t(19) = 2.40, p = 0.03) with the control group being older (M age = 35.9; SD = 8.06) than the meditation group (M age = 29.4; SD = 4.43). It should be noted that one subject refused to do the Self Pain task at the Time 2 scanning session because she said she found it too aversive the first time, so we only acquired complete data for 20 subjects for the Self Pain task.

Scanning paradigm

Upon entering the Imaging Center, subjects were seated in a testing room outside of the fMRI scanning room. They were given a health screening form, a consent form and a HIPPA form. They were also asked to complete the following psychometric instruments, in this order:

Interpersonal Reactivity Index (IRI) (Davis 1983) (described more fully in chapter 2)

The Psychopathic Personality Inventory (PPI) (Lilienfeld and Andrews 1996) (described more fully in chapter 2)

The Depression Anxiety Stress Scale (DASS) (Lovibond and Lovibond 1995)

(described more fully in chapter 2)

The Spiritual Meaning Scale (SMS) (Mascaro and Rosen 2006; Mascaro et al. 2004)

The SMS is a 15-item self-report instrument that asks people to rate on a scale from 1-5 (*I totally disagree* to *I totally agree*) how much they endorse each item, and has good psychometric properties. The authors designed the instrument to measure "the extent to which an individual believes that life or some force of which life is a function has a purpose, will, or way in which individuals participate" (p. 847). Items were selected that were not related to socially desirable responding or with overly concrete thinking related to "an unthinking acceptance of ideas due to socialization." The SMS generally has an inverse relationship with levels of depression, anxiety and antisocial features.

All scales were administered again prior to the second scanning session, with the exception of the PPI and the KIMS, which were omitted for the sake of brevity.

After giving consent and completing the self-report questionnaires, subjects' pain levels were titrated (described in previous chapter). Next, subjects were placed in the fMRI scanner where they completed three tasks in the same order: a Self Pain task, an Other Pain task, and the Reading the mind in the eyes (RtME) task. Each of these individual tasks has been described in more detail in previous chapters. The timeline for the entire scan is shown in **figure 4-2**. The Time 2 sessions were exactly the same, except that the donation induction was performed at the end of the Time 2 session (described in more detail elsewhere).

Image Acquisition

All MR images were acquired on a Siemens 3T Trio scanner. Functional images were acquired using an EPI sequence with the following parameters: TR=2000 ms, TE=28 ms, matrix=64 x 64, FOV=192 mm, slice thickness=3 mm, gap=0.45 mm, 34 axial slices. We also acquired a 4.5 minute T1-weighted MPRAGE scan (TR=2600 ms, TE=3.02 ms, matrix=256 x 256, FOV=256 mm, slice thickness=1.00 mm, gap=0 mm) for anatomical localization of fMRI activations.

fMRI Image Preprocessing and Analysis

All image preprocessing has been described in more detail in the previous two chapters. In order to statistically evaluate the study hypotheses, single subject contrasts were pooled to create average maps separately for the two groups (meditators and controls) at each time point (Time 1 and Time 2). Functional regions of interest (ROIs) were defined at time 1 for relevant contrasts for each of the three tasks (Self Pain, Other Pain, RtME). The definition of these ROIs was described in the previous two chapters. Contrast values were generated for each contrast of interest, averaged across all voxels within each of the ROIs, at both Time 1 and Time 2.

The first experimental question was whether the groups (meditation and control) differed from each other at Time 1 due to chance. To determine this, independent t-tests were used to compare contrast values in each ROI across the two groups. This was done for each of the three Time 1 tasks (Self Pain, Other Pain, RtME).

The next question was whether brain activity changed from Time 1 to Time 2, irrespective of group. Paired-samples t-tests were conducted using the contrast values in each ROI for each of the three tasks at Times 1 and 2.

In order to test the hypotheses that subjects randomized to the meditation group showed an altered change in neural activity from Time 1 to Time 2 compared to the control group, the contrast values from each ROI at Times 1 and 2 were entered into a repeated measures ANOVA and tested for an interaction effect (group by time). However, if the groups differed at Time 1 (due to chance), we tested for group effects by running a univariate ANOVA, which asks if the contrast values at Time 2 varied by group, while controlling for Time 1 contrast values (entered as a covariate). In addition, for the 21 subjects who completed both scans, an exploratory whole-brain analysis was conducted, in which Time 1 and 2 data were entered into a whole-brain repeated measures ANOVA. Resulting maps were thresholded at $p < .001$, with a 10-voxel spatial-extent threshold.

Finally, for brain regions that changed as a function of meditation, we ran linear regression analyses to investigate whether changes in brain activity were related to changes in self-reported empathy or empathic accuracy. In other words, , controlling for Time 1 brain activity and Time 1 empathy (self-report or accuracy) levels, does the residual change in brain activity account for a significant amount of the variance in time 2 empathy (self-report or accuracy). **Figure 4-3** shows the relationships we will investigate.

Results

Behavioral

Self-report: Independent samples t-test indicated that there was no difference between the two groups at Time 1 for any of the self-report measures (see **table 4-2**). A mixed design ANOVA revealed a significant interaction (group by time) effect for stress (F(19)

= 5.49, p = 0.03) and a strong trend for depression (F(19) = 4.28, p = 0.05) (see **figure 4-4** for plot). For both of these measures, the meditation group endorsed a greater increase in symptoms compared to the control group. There were no other self-report measures (state or trait) that showed an interaction effect.

Donation: With regards to the compassion induction, 17 of the 21 subjects made some monetary donation (M = 4.76, SD = 4.3) (see **figure 4-5** for histogram). One subject chose not to reveal how much money he had donated. As it was clear that he had donated something, we did a mean-replace for his donation amount. Independent samples t-tests indicated that there was no group difference in terms of compassionate behavior during the donation induction. There was one subject in the control group who donated a sum of money that was greater than 3 standard deviations above the mean ($20.00), but even when he was removed the groups were not significantly different (with outlier: M control group = $5.00; M Meditation group = $4.62; outlier removed: M control group = $2.86; M Meditation group= $4.62).

Empathic accuracy: Independent samples t-tests indicated that the groups were not significantly different at Time 1 in terms of RtME scores (t (19) = -0.10, p = 0.92). Paired samples t-tests revealed that subjects (not split by group) did not get significantly more accurate from Time 1 to Time 2 (t (19) = -0.65, p = 0.52). However, there was a trend for a significant interaction (group by time) effect (F (19) = 3.28, p = .09) with meditators getting more accurate in the task (see **figures 4-5** and **4-6** for plots of this effect). There was no trend for an interaction effect for accuracy in the gender task. Moreover, the trend for the emotion task was not driven by outliers (see **figure 4-7** for scatter plot of changes in accuracy for each subject, separated by group). Chi square tests revealed that the meditation group differed significantly from what we would expect based on chance in terms of the number who became more accurate after the training, $c^2(1, N=21) =4.86$, $p = 0.03$. In addition, an odds ratio analysis revealed that participants randomized to the meditation group had 11.2 greater odds of increasing their empathic accuracy. Finally, given that the meditation group also increased self-reported stress symptoms (based on the stress subscale of the DASS) compared to the control group, we performed linear regression to test whether changes in stress levels accounted for a significant amount of the variance in changes in accuracy, and they did not, $r^2 = 0.03$, $F(1,17) = 0.39$, $p = 0.55$.

fMRI

Self Pain: Independent samples t-tests indicated that the groups were not significantly different at Time 1 in any of the ROIs (see **table 4-3** for statistics). Paired samples t-tests revealed that there was no significant attenuation of brain activity from Time 1 to Time 2 in any ROI tested (see **table 4-4** for statistics). There was not a significant interaction (group by time) effect in any of the ROIs tested, however, there was a trend in the right ($F(18) = 3.78$, $p = .07$) amygdala which suggested that neural activity in these areas increased for the control group but decreased for the meditation group (see **figure 4-8**).

OtherPain: Independent samples t-tests indicated that the groups were not significantly different at Time 1 (see **table 4-5** for statistics). Paired samples t-tests revealed that there was significant attenuation of brain activity in every ROI tested, including in the inferior frontal gyrus (bilaterally), right anterior insula, dmPFC, and in bilateral amygdala (see **table 4-6** for statistics). In addition, there were no ROIs in which there was a significant interaction (group by time) effect for the contrasts [Pain – NoPain] or [Pain Anticipation

– NoPain Anticipation]. While none of these analyses was close to significant, a qualitative analysis showed that there was more attenuation in almost every ROI for the meditation group compared to the control group. The whole brain analysis using the contrast [Pain – NoPain] revealed areas in the inferior temporal gyrus and superior temporal sulcus that were more attenuated in the meditation group than in the control group (see **figure 4-9**). There was no area that was enhanced (or less attenuated) in the meditation group at a threshold of $p < 0.001$, nor were there any areas that were significantly different between groups for the contrast [Pain Anticipation – NoPain Anticipation].

RtME: Independent samples t-tests indicated that the groups differed significantly at Time 1 in terms of the magnitude of activation in the left mid STS ($t(19) = 2.24$, $p = 0.04$) and in the right temporal pole ($t(19) = 2.82$, $p = 0.01$) (see **table 4-7** for complete statistics). There was also a trend in the dmPFC and in the right anterior STS. For all four of these ROIs, subjects who would be randomized to the control group had a higher mean activation than those subjects randomized to meditation. Paired samples t-tests revealed that there was significant attenuation of brain activity in the left mid STS and right anterior STS ROIs (see **table 4-8** for complete statistics). A mixed design ANOVA revealed a significant interaction (group by time) effect for brain activity in the left IFG ($F(19) = 7.05$, $p = 0.02$), right caudate ($F(19) = 4.60$, $p = 0.05$), and right IFG ($F(19) = 8.18$, $p = 0.01$), and trends in the left posterior STS ($F(19) = 4.20$, $p = 0.06$) and left fusiform ($F(19) = 3.69$, $p = 0.07$) (see **figure 4-10** for plots). Looking at the change in each individual subject as a function of group reveals that these interaction effects were not driven by outliers, but rather by a fairly consistent pattern in which we see attenuation in activity in the control group and enhanced activity in the meditation group (see **figure 4-11** for an example). While there was also a significant interaction effect for the dmPFC and right temporal pole ROIs, we performed a stricter univariate analysis controlling for Time 1 beta contrast values due to the fact that there was a significant group difference at Time 1. This revealed that there was not a significant group difference in either ROI, although there was a trend in both for the meditation group to have increased activity (dmPFC: $F(19) = 2.271$, $p = .149$; right temporal pole: $F(19) = 2.496$, $p = .132$).

We next assessed whether changes in brain activity were related to changes in accuracy using a series of hierarchical regression analyses. We tested for this in all of our ROIs that showed a significant group by time interaction effect. After controlling for Time 1 RtME scores and brain activity, the residual change in activity in the left IFG accounted for a significant amount of the variance in Time 2 empathic accuracy, $R^2 = 0.23$, F-change(1, 17) = 7.60, $p = 0.01$ and there was a strong trend suggesting that changes in right IFG accounted for a significant amount of the variance, $R^2 = 0.14$, F-change(1, 17) = 3.62, $p = 0.07$. Other areas, where changes in brain activity are related to changes in accuracy include the dmPFC ($R^2 = 0.24$, F-change(1,17) = 8.25, $p = 0.01$), left posterior STS ($R^2 = 0.29$, F-change(1, 17) = 10.70, $p = 0.01$) , and right temporal pole ($R^2 = .15$, F-change(1, 17) = 4.57, $p = 0.05$).

Discussion

The randomized, longitudinal study described here investigated the effects of compassion meditation on various aspects of empathic emotions, behaviors, and neural activity and indicated that training in compassion meditation enhances some aspects of the empathic system while leaving other aspects unchanged. In terms of self-reported changes in empathy (state and trait) and well-being, the only significant finding was that those randomized to compassion meditation endorsed more symptoms of stress and depression. Those randomized to meditation did not report increases in state or trait empathy or spiritual meaning and did not exhibit more compassionate behavior when compared to the control group. Subjects randomized to meditation did have an increase in accuracy on an empathic accuracy task. Moreover, they did not show the attenuation from Time 1 to Time 2 of brain activity during the RtME task that the control group showed, and this difference in brain activity accounted for a significant amount of the variance in the enhanced accuracy (see **figure 4-12** for schematic of findings). Each of these findings will be discussed in more detail below.

Behavioral findings: In contrast to what was hypothesized, we did not find that meditation led to enhanced levels of self-reported state or trait empathy in response to viewing others in pain. Given that we do see changes in empathic accuracy, this lack of a finding regarding trait empathy suggests that subjects may be unaware of changes that have occurred and thus are not able to report them. As discussed elsewhere in the dissertation, previous studies have suggested that people are not very good at accurately assessing and reporting their levels of empathy (Ickes 1997).

However, there were increases in the extent to which meditation subjects, compared to control participants, endorse symptoms of stress. Perhaps these aspects of well-being are more salient than empathy, and thus more subject to self-report. This was a surprising finding, however, given the results of a previous study that investigated the effects of a very similar compassion protocol on undergraduate students, which showed that compassion meditation training buffered students against the deleterious effects of psychosocial stress (Pace et al. 2009). It is important to note that the symptoms of “stress” referred to in this psychometric instrument are akin to a generalized type of worry or anxiety, not to physiological or behavioral responses to an acute insult. Moreover, the assessments used in this previous study by Pace and colleagues were different than the self-report measures used in our current study, and thus may have tapped into a different construct. It is also possible that differences in study populations in the two studies may have lead to differential outcomes of meditation practice. In comparison to the undergraduates in the previous study, the population of participants in our study was older. Perhaps the meditation practice caused them to more fully take on the suffering of others that they interact with, which may have led to dips in well-being. In fact, George Dreyfus has written of beginning bodhisattvas who “are often described as being overwhelmed by compassion. They can be deeply moved by compassion and sometimes cry…” However, he notes that as they progress, the compassion seems to change in important ways: “It is less clearly emotional in the usual sense of the word. Such a compassion is described as being equanimous. It is very strong, even stronger than that of beginning bodhisattvas, but it is more balanced and does not lead to the kind of emotional outburst mentioned previously.” (in Davidson and Harrington 2001 p. 43) Similarly, the Dalai Lama notes that in the early stages, compassion practices are often accompanied by visceral feeling and emotional reaction, but “the final phase of developing compassion is meant to go beyond that state to one that is both more stable and also more engaged with aiding others” (Lutz et al. 2007 p. 516). Perhaps adults are more like beginning bodhisattvas, and our study is capturing only the beginnings of the cultivation of compassion. With respect to this idea, it is important to note that increases in stress do *not* account for changes in empathic accuracy, suggesting that increases in stress are not crucial to the cultivation of empathy and compassion.

There was no support for the hypothesis that meditation training was related to increased compassionate behavior during the donation induction. This may have been due to limitations in the task design, which only allowed a single assessment of compassionate behavior. Related to this, it may be that our sample size was too small to find a behavioral difference given a one-shot assessment (i.e. there was too little signal and too much noise). While the single assessment of compassionate behavior, in hindsight, was not ideal for drawing statistical inferences, we do feel strongly that this was a meaningful instrument. For one thing, the majority of participants donated some amount of money, suggesting that the story was believable and that it resonated with them, at least to some extent. Secondly, a qualitative look at the statements that participants made when the deception was revealed to them shows that participants made statements that are very consistent with the compassion training. For example, one participant who was in the meditation group said, “Oh, my heart had went out to her. I thought, well, coulda been me…” , Moreover, we feel that this compassion induction modeled important aspects of real situations that humans are faced with when they encounter another who is suffering. For example, when asked if they were suspicious of the story, some participants said that they were. What is interesting is that, of those that said they were suspicious, some still chose to donate “just in case” it was real. We believe that this nicely models the noisy situations that human beings are faced with regarding who honestly needs help, as well as the evaluative processes that go into our decisions about who deserves help, when and why.

Moreover, meditation training was associated with increases in empathic accuracy. While there was not a significant change within the meditation group alone, there was a trend suggesting that they got more accurate. Given that this was an extremely small sample size in which to see a significant behavioral change, we find these results compelling. Moreover, more participants randomized to meditation increased their accuracy than would have been expected by chance, and we see a strong trend for an interaction between group and time. While two other studies have found that an experimental manipulation in which participants are administered oxytocin enhances accuracy on the RtME task, to the best of our knowledge this is the first to show that a behavioral intervention can increase empathic accuracy.

fMRI findings: In terms of how meditation changed brain activity during empathic tasks, the majority of significant findings were within the RtME task. In particular, when compared to the control group meditation significantly enhanced activity in the inferior frontal gyrus bilaterally and in the right caudate during the RtME task. There were trends in the posterior STS and in the left fusiform. It was unfortunate that the groups differed at Time 1 in activity in the dmPFC and right temporal pole, as this random factor may have rendered us unable to find effects in these areas.

In addition, the changes in activity in left and right IFG, but not in the caudate, accounted for variance in change in accuracy. That is, those who showed a larger increase in accuracy also showed a larger increase in left IFG activation. While mirror neuron activity has often been associated with the right hemisphere, and the left IFG activity that we see in our study may be primarily related to enhanced language processing, MNS-like activation patterns are found bilaterally (e.g. Aziz-Zadeh et al. 2006), and a recent meta-analysis led authors to argue that the MNS is bilateral (Caspers et al. 2010). We feel it is plausible, therefore, to think that the enhanced activity in bilateral IFG is related to enhanced activity in the mirror neuron system. Other studies have shown that experience modulates the MNS. For example, musicians and dancers have more activity in their MNS, compared to controls, when they watch others perform their respective artistic endeavor (Cross et al. 2006; Haslinger et al. 2005). Moreover, monkeys who have the opportunity to both observe humans using tools and manipulate the tools themselves, develop neurons with mirroring properties (Ferrari et al. 2005). However, to the best of our knowledge this is the first study to show enhancement of MNS activity related to the observation of facial expressions. Taken together, our findings suggest that meditation enhances neural activity in putative mirror neuron regions, and that this enhanced activity leads meditators to more accurately infer the emotions of others.

Given the aforementioned finding regarding the putative MNS, we find it quite interesting that we do not see an enhancement of neural activity in similar regions that are active during the EFP task. In fact, the only changes that we saw as a function of group assignment was that participants randomized to the control group had less attenuation in regions in the temporal lobe. Thus, it is curious that meditators only increase mirror neuron activity during the RtME task and not during the EFP task. This differential profile of results may stem from the fact that the EFP task is an implicit empathy task, as we do not explicitly ask subjects to reflect on what others are feeling or thinking. In contrast, the RtME task is more explicit and it may be the case that participants in the meditation group were primed to pay more attention to the task. In fact, the MNS is subject to modulation by attention demands (Muthukumaraswamy and Singh 2008). Similarly, it may be the case that the EFP task is not an optimal assessment for a pre/post design, since the very pronounced observed habituation effects suggest that participants may not have attended as carefully during the Time 2 task. A third possibility is that there were ceiling effects for the Time 1 EFP task, and thus there was no room for increase in brain activity related to empathy for pain. Alternatively, it may be that the compassion meditation training used in this study does not affect the neural circuitry related to empathy for pain. It remains to be seen whether a practice that more focally entrains the affective dimension of empathy would have differential results.

If compassion meditation does, in fact, make practitioners more primed to attend to others, this may be a mediating factor by which compassion meditation confers its benefits. It may, quite simply put, just remind people to pay attention to others. This idea is in line with what the Dalai Lama has asserted: “We should ensure that whatever we do, we maintain some effect or influence from our meditation so that it directs our actions as we live our everyday lives. By our doing so, everything we do outside our formal sessions becomes part of our training in compassion.” (HHDL 2001 p. 104)

Overall, these findings suggest a potential mechanism by which meditation may confer prosocial outcomes. For example, it is noteworthy that the complete profile of results mirror previous findings regarding how oxytocin mediates empathy. One recent study showed that oxytocin administration decreases neural activity in the amygdala during self pain, but has no effect on neural activity during an EFP paradigm (Singer et al. 2008). Three different studies showed that the oxytocin system in important for empathic accuracy during the RtME task (Domes et al. 2007; Guastella et al. 2010; Rodrigues et al. 2009). Our pattern of results is consistent with these discrepant findings, making it plausible that compassion meditation augmented the oxytocin system in our subjects, leading to the observed profile of results. We will do a preliminary investigation of this relationship using plasma oxytocin samples acquired before and after meditation training.

As with all studies, the one described here includes confounds that place limits on the conclusions that can be made. First, in attempting to design a meditation program that would be attractive to a Western population, all specific theological references such as *Karma* and *Dharma* have been removed. So while this design allowed us to see the specific effects of a meditation practice, we may have lost some of the power that is inherent when a philosophical model is intertwined with meditation practice. Moreover, we cannot investigate the effects that such a philosophical model may have on levels of prosociality. This speaks to a larger issue within this study, which is that, while we have attempted to investigate a traditional Tibetan practice, we have removed this practice from its original cultural and historical context. Thus, we cannot investigate how such a compassion meditation practice may affect Tibetan Buddhist practitioners; rather, we have explored how an adaptation of this traditional practice affects an American population. In addition, we recognize that the argument could be made that all of the effects generated by the compassion meditation were simply due to the two weeks of non-analytical, attentional practices at the beginning of the course. In the future, it will be quite important to include a mindfulness group to this study design in order to assess the effects of attention training on the empathy and compassion measures employed in this study. Despite these limitations, we feel that our results provide some illumination into this practice of compassion meditation, and our distinct profile of results point to the mechanisms by which this practice may confer benefits to practitioners and beyond.

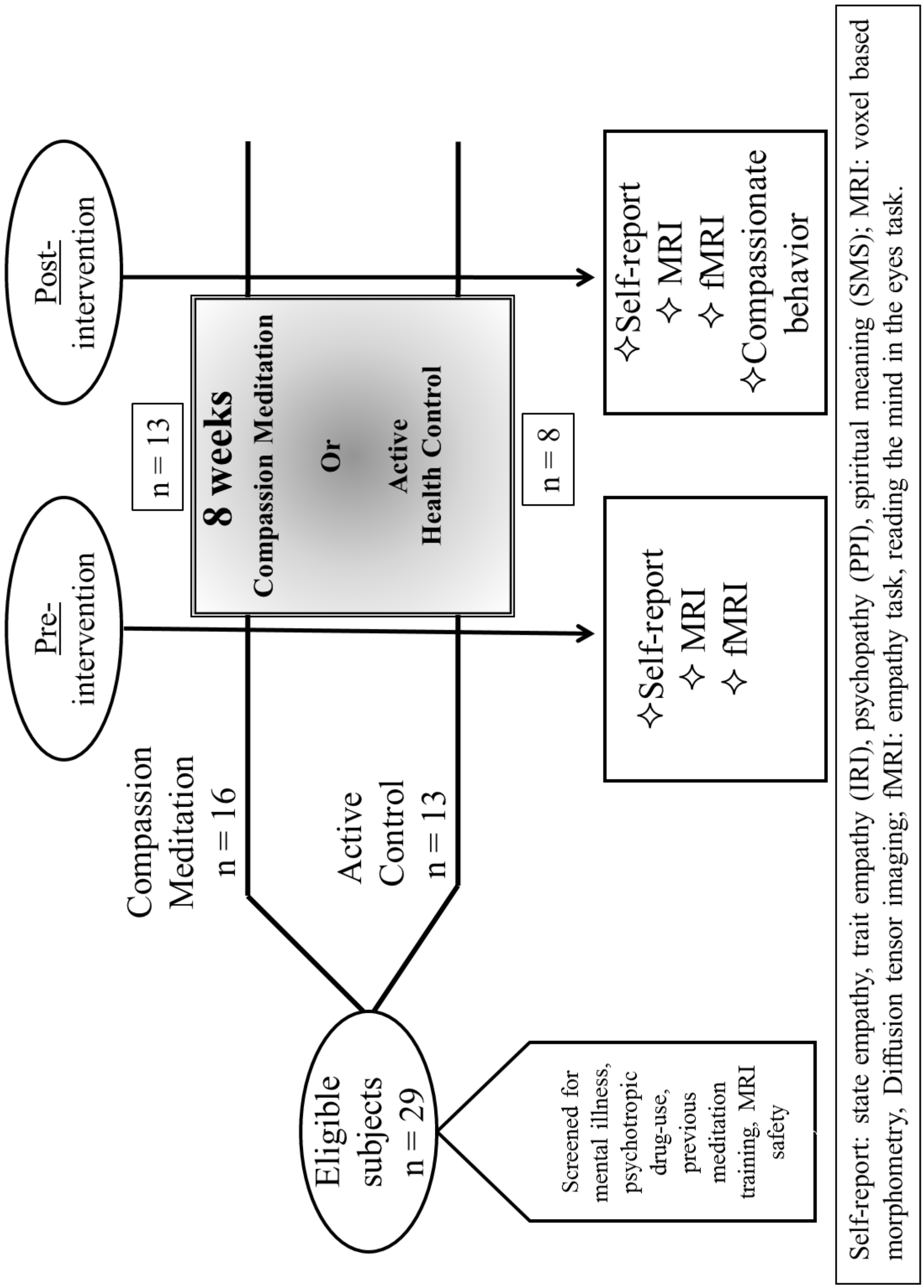

Figure 4-1: Schematic of the randomized, controlled longitudinal study design.

	Age (M; SD)	Gender
Total (n = 21)	31.9; 6.70	12 males, 9 females
Meditation (n = 13)	29.4; 4.43	6 males, 7 females
Control (n = 8)	35.9; 8.06	6 males, 2 females

Table 4-1: Demographics of participants who completed all assessments

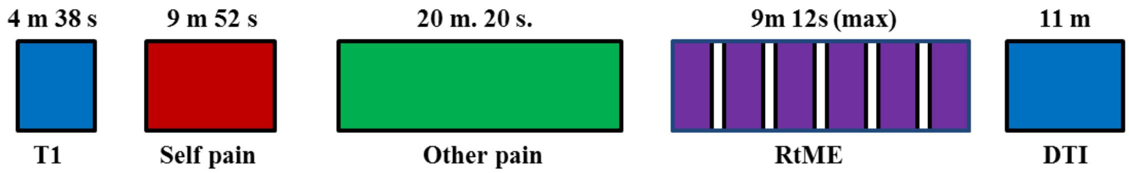

Figure 4-2: Schematic of entire scan.

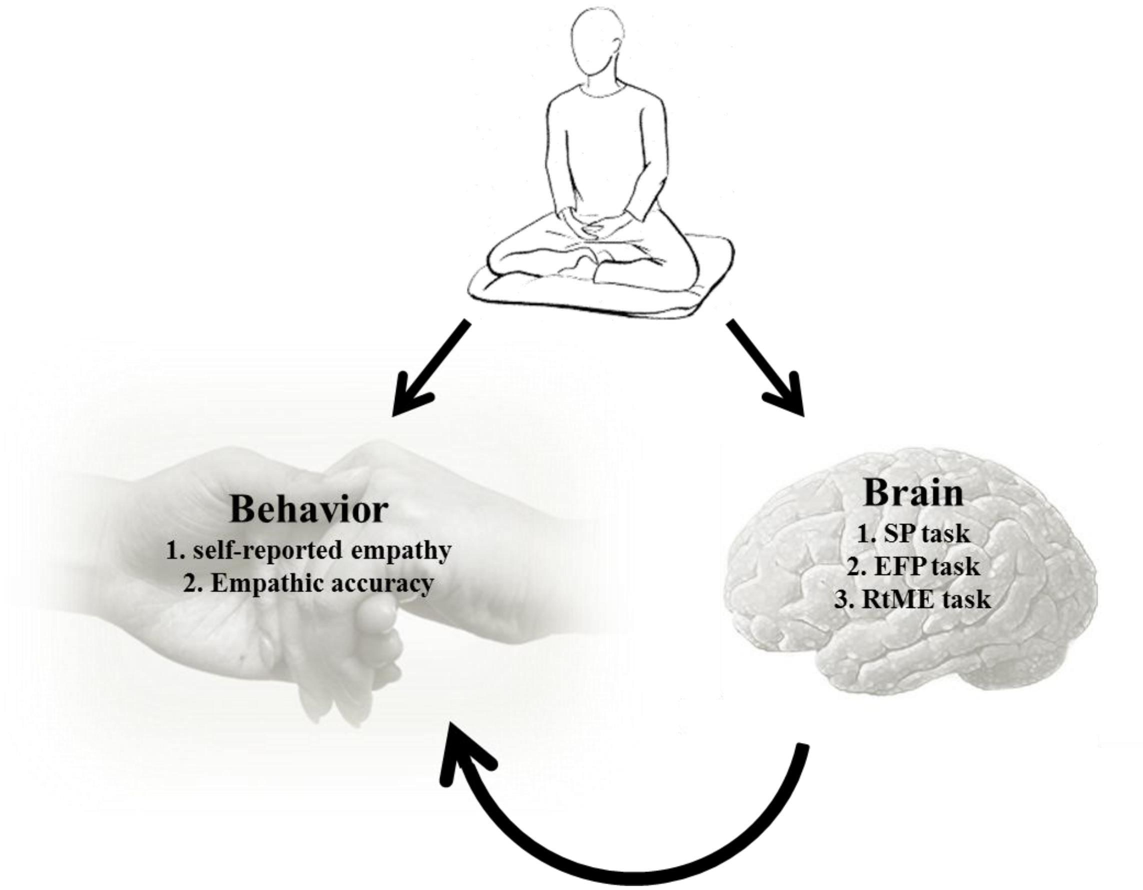

Figure 4-3: Schematic of the causal relationships we will test in this study. SP: Self Pain; EFP: Empathy for Pain; RtME: Reading the Mind in the Eyes.

	group	N	Mean	Std. Deviation	Std. Error Mean	t	Sig. (2-tailed)
Fantasy	Controls (C)	8	16.5	5.68205	2.00891	-1.246	0.228
	Meditators (M)	13	19.5385	5.26965	1.46154		
Perspective Taking	C	8	19.125	3.52288	1.24553	-1.91	0.071
	M	13	21.6154	2.46774	0.68443		
Empathic Concern	C	8	18.5	4.30946	1.52362	-1.838	0.082
	M	13	21.5385	3.25616	0.9031		
Personal Distress	C	8	7.75	3.01188	1.06486	0.265	0.794
	M	13	7.3846	3.09673	0.85888		
PPI total	C	8	122.875	12.14716	4.29467	-0.027	0.979
	M	13	123	9.35414	2.59437		
SMS	C	7	64.1429	8.23465	3.11241	0.237	0.815
	M	13	63.0769	10.19364	2.82721		
Stress	C	8	6.125	4.54933	1.60843	0.625	0.539
	M	13	4.9231	4.11221	1.14052		
Anxiety	C	8	2.75	3.32738	1.1764	-0.673	0.509
	M	13	3.6923	2.98286	0.8273		
Depression	C	8	3.375	3.70087	1.30845	0.227	0.823
	M	13	3	3.65148	1.01274		
PPI Coldheart	C	8	14.625	3.06769	1.08459	-0.407	0.689
	M	13	15.3077	4.0699	1.12879		
State Empathy Ratings	C	8	1	0.92582	0.32733	-0.407	0.689
	M	13	1.2308	1.42325	0.39474		
RtME correct	C	8	18.375	3.42	1.20915	-0.1	0.921
	M	13	18.5385	3.75534	1.04154		

Table 4-2: Time 1 scores for all self-report and behavioral measures.

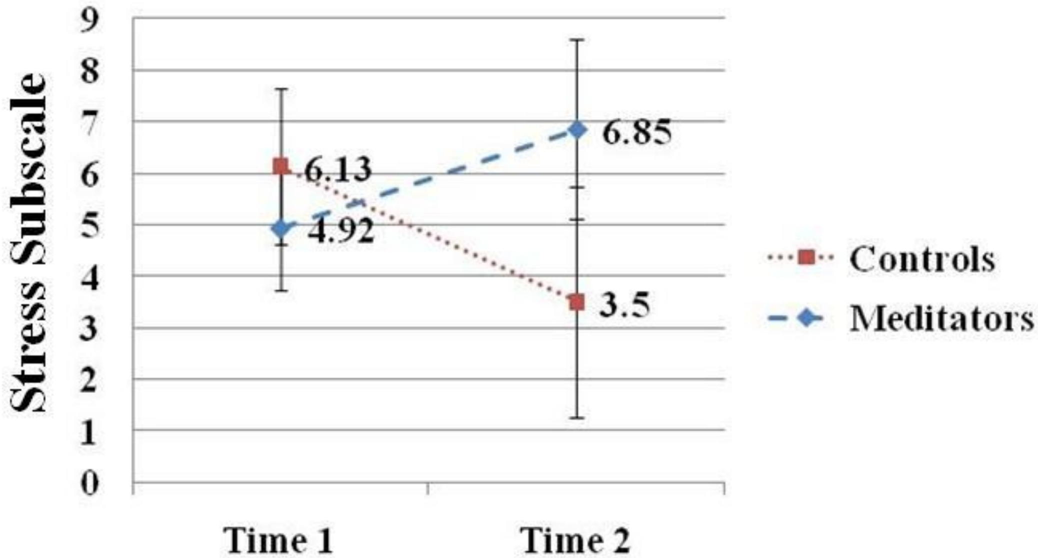

Figure 4-4: Plot of repeated measures ANOVA for the stress subscale of the DASS. There was a significant interaction (group by time) effect (F (19) = 5.49, p = 0.03). (standard error bars)

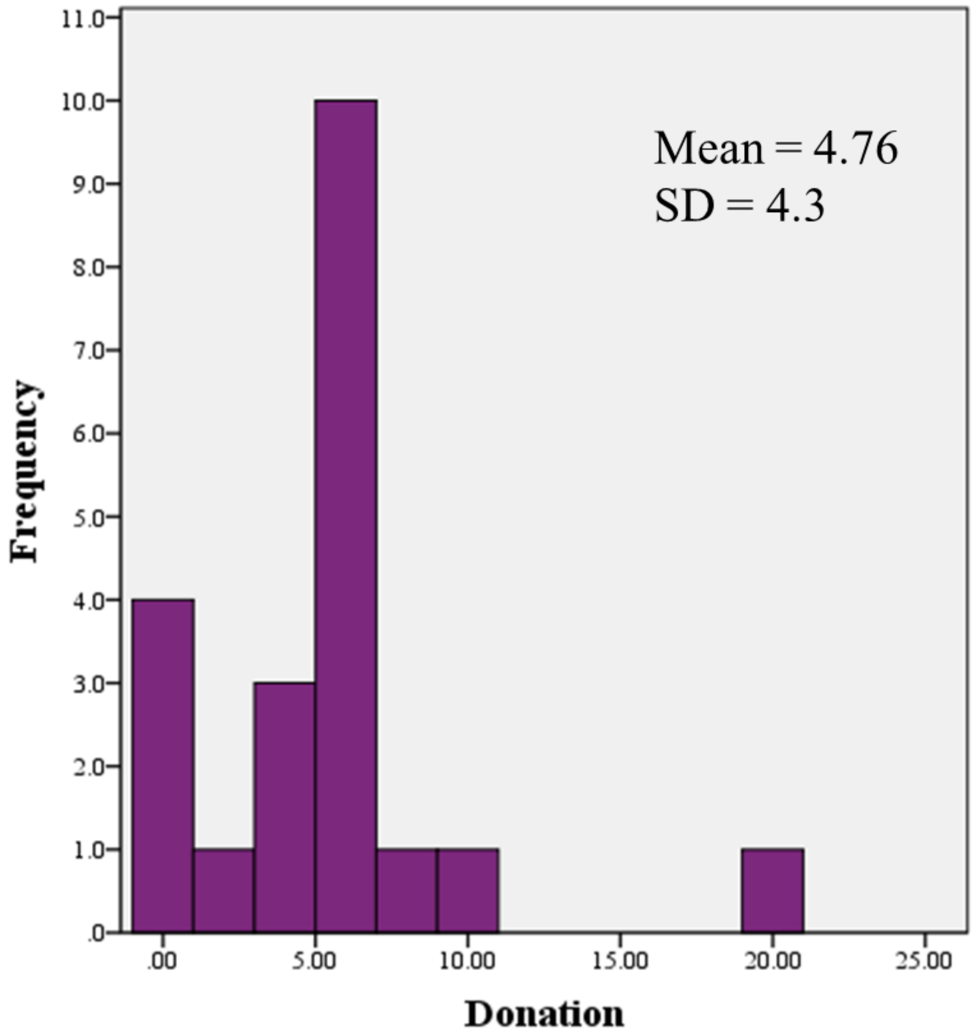

Figure 4-5: Histogram of donations made during compassion induction.

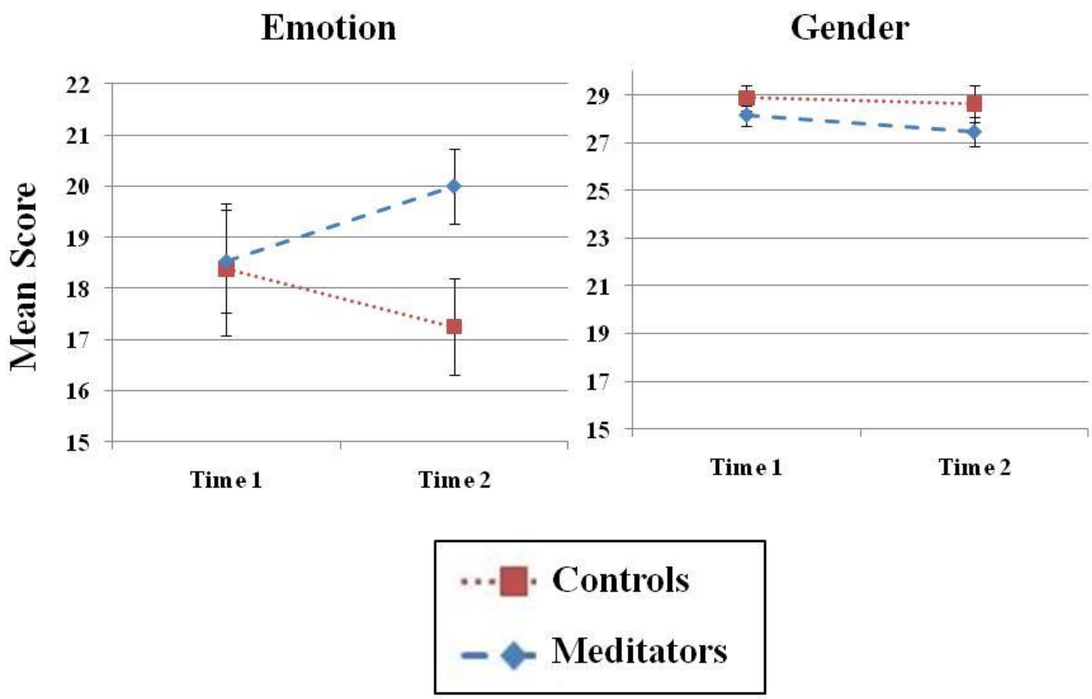

Figure 4-6: Plot of the repeated measures ANOVA for the Emotion and Gender tasks. There was a strong trend for an interaction (group by time) effect for the emotion task (F (19) = 3.28, p = .09).

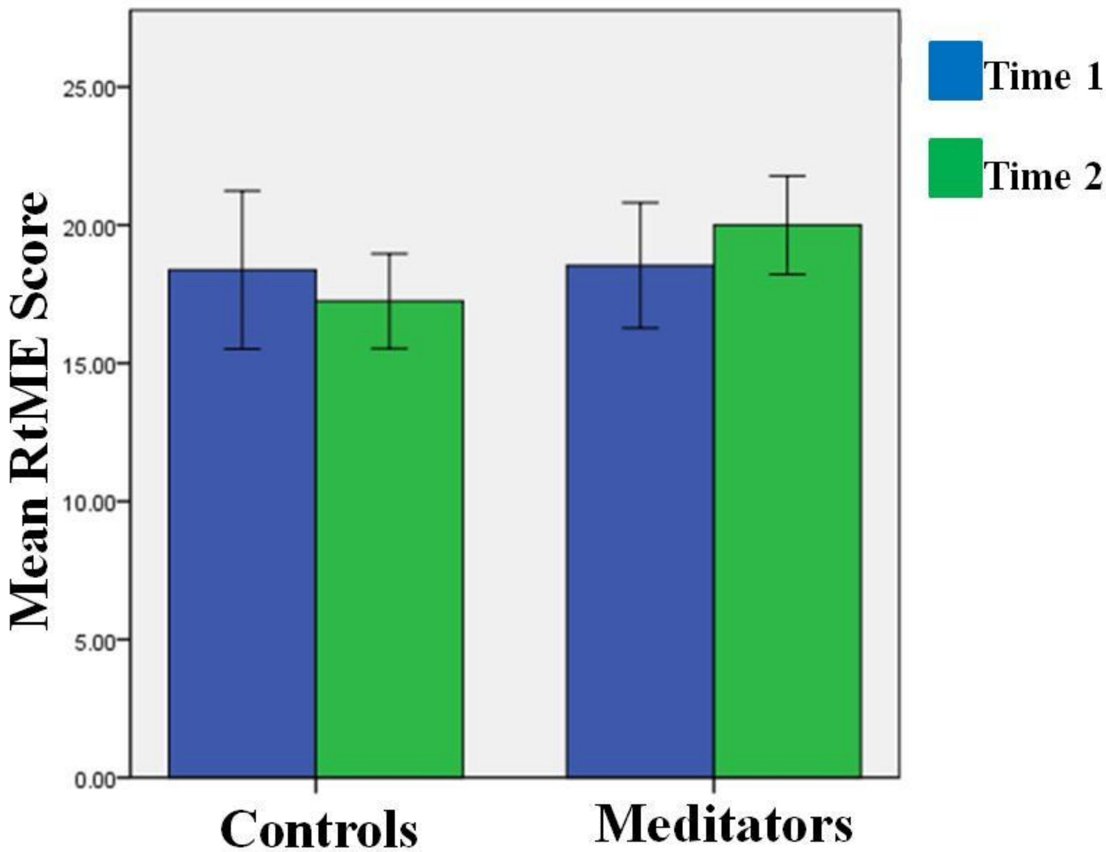

Figure 4-7: Plot of Mean RtME scores at Time 1 and 2 according to group.

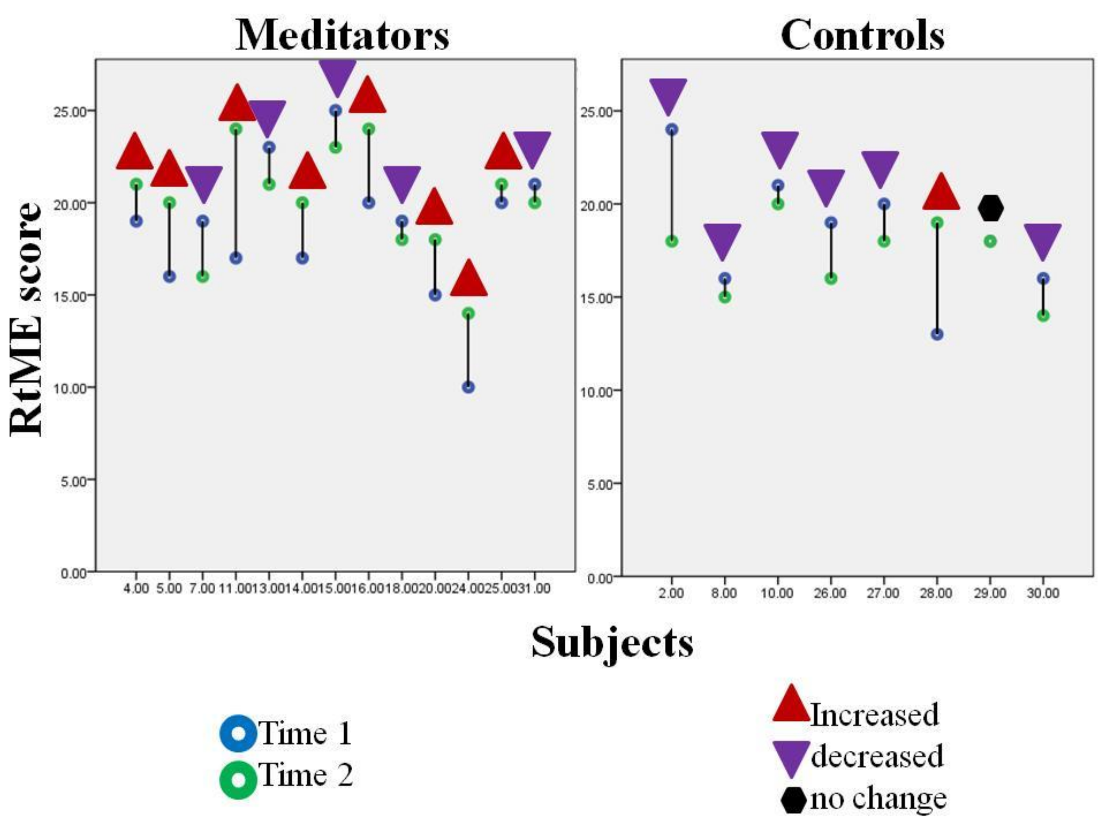

Figure 4-8: Scatter plot of Time 1 (blue circles) and 2 (green circles) scores for each subject, broken up according to group. Red triangles represent subjects whose scores increased from Time 1 to Time 2, and purple triangles represent subjects whose scores decreased from Time 1 to Time 2.

Region of interest	group	N	Mean	Std. Deviation	t	df	Sig. (2-tailed)
Right amygdala	Controls	8	0.588	1.118	-0.298	19	0.769
	Meditators	13	0.741	1.154			
Left amygdala	Controls	8	0.743	1.294	-0.267	19	0.792
	Meditators	13	0.910	1.448			
Mid cingulate	Controls	8	1.278	1.168	1.132	19	0.272
	Meditators	13	0.696	1.131			
Rostral ACC	Controls	8	1.342	1.137	1.643	19	0.117
	Meditators	13	0.719	0.611			
Dorsal ACC	Controls	8	1.332	1.225	1.081	19	0.293
	Meditators	13	0.883	0.691			
Right anterior insula	Controls	8	1.451	1.442	0.715	19	0.484
	Meditators	13	1.032	1.215			
Left anterior insula	Controls	8	1.116	1.488	0.384	19	0.706
	Meditators	13	0.902	1.074			
Left posterior insula/ SII	Controls	8	1.657	1.803	0.779	19	0.446
	Meditators	13	1.148	1.209			
Left primary somatosensory cortex	Controls	8	1.931	1.149	1.078	19	0.294
	Meditators	13	1.239	1.567			

Table 4-3: Independent samples t-tests performed on all Self Pain [Pain – NoPain] ROIs. There were no regions that differed significantly by group at Time 1.

Paired Samples Test			
Region of Interest	**t**	**df**	**Sig. (2-tailed)**
Right amygdala	1.04	19	0.311
Left amygdala	1.006	19	0.327
Mid cingulate	0.16	19	0.875
Rostral ACC	0.546	19	0.591
Dorsal ACC	0.526	19	0.605
Right anterior insula	0.286	19	0.778
Left anterior insula	-0.311	19	0.759
Left posterior insula/ SII	-0.199	19	0.845
Primary Somatosensory cortex	-0.096	19	0.925

Table 4-4: Paired samples t-tests performed on all Self Pain [Pain – NoPain] ROIs. There were no regions in which activations changed from Time 1 to Time 2.

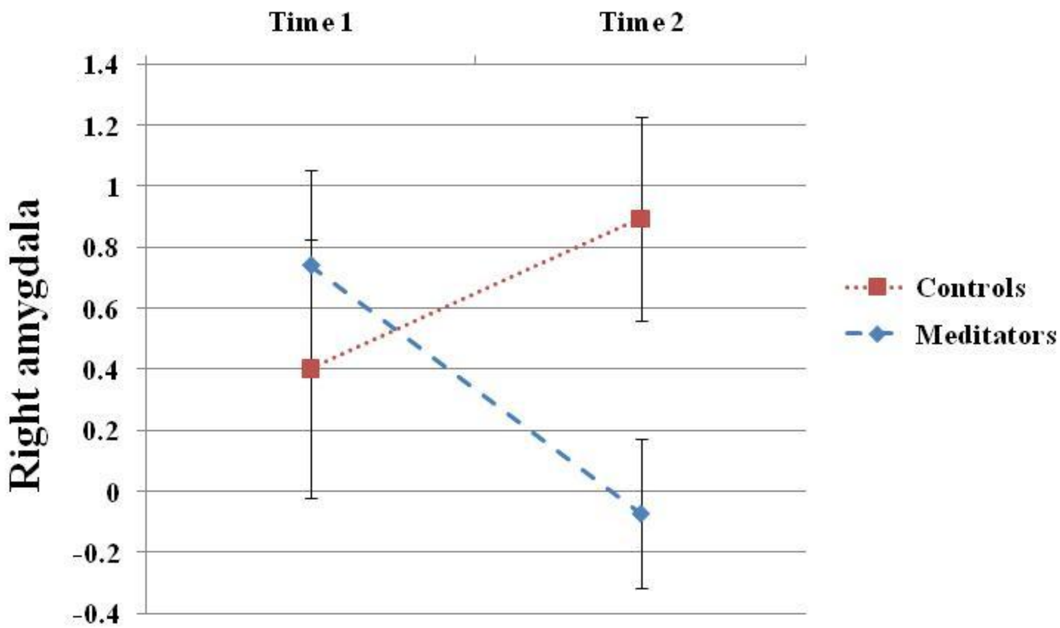

Figure 4-9: Plots of repeated measures ANOVA in right amygdala during Self Pain [Pain – NoPain]. Strong trend suggests that amygdala activity decreases in meditators and increases in controls, ($F(19) = 3.78$; $p = 0.07$).

Regions of interest	group	N	Mean	Std. Deviation	t	df	Sig. (2-tailed)
Right inferior frontal	Controls	8	0.885	0.399	-0.215	19	0.832
	Meditators	13	0.971	1.071			
Left inferior frontal	Controls	8	0.820	0.625	0.017	19	0.986
	Meditators	13	0.814	0.825			
Right amygdala	Controls	8	0.636	0.632	-0.723	19	0.478
	Meditators	13	0.859	0.717			
Left amygdala	Controls	8	0.502	0.432	-1.274	19	0.218
	Meditators	13	0.841	0.667			
Right anterior insula	Controls	8	1.207	0.495	0.561	19	0.581
	Meditators	13	0.986	1.037			
Left anterior insula	Controls	8	0.840	0.532	-0.071	19	0.944
	Meditators	13	0.867	0.969			
dmPFC	Controls	8	0.942	0.536	0.233	19	0.818
	Meditators	13	0.857	0.934			

Table 4-5: Paired samples t-tests performed on Other Pain [Pain – NoPain] ROIs. There were no regions that differed significantly by group at Time 1.

Paired Samples Test

Region of Interest	t	df	Sig. (2-tailed)
Right Inferior Frontal Gyrus	2.72	20	0.013
Right Anterior Insula	2.821	20	0.011
dmPFC	3.23	20	0.004
Left Inferior Frontal Gyrus	2.349	20	0.029
Left Amygdala	3.928	20	0.001
Right Amygdala	2.442	20	0.024

Table 4-6: Paired samples t-tests performed on Other Pain [Pain – NoPain] ROIs. All regions showed significant attenuation from Time 1 to Time 2.

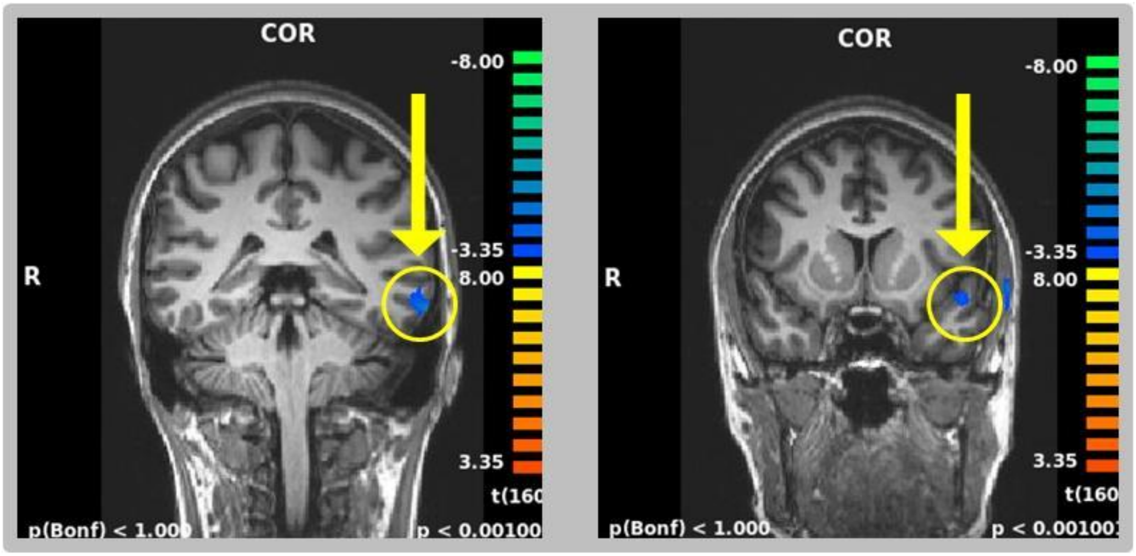

Figure 4-10: Whole brain ANOVA that probes areas that increase significantly in meditators, from Time 1 to Time 2, compared to the control group during Other Pain [Pain – NoPain], thresholded at p < 0.001. Areas shown here increased more in the control group (or attenuated less) than in the meditation group. On left, peak voxel t = -5.06; tal. coordinate: -64, -34, -14. On the right, peak voxel t=-4.05, tal. coordinate = -45, 8, -11.

Region of interest	group	N	Mean	Std. Deviation	t	df	Sig. (2-tailed)
Supplementary motor cortex	Controls	8	0.397	0.358	-0.237	19	0.815
	Meditators	13	0.430	0.283			
dmPFC	Controls	8	0.557	0.277	1.884	19	0.075
	Meditators	13	0.267	0.376			
Left inferior frontal gyrus	Controls	8	0.962	0.285	0.666	19	0.513
	Meditators	13	0.860	0.372			
Left posterior STS	Controls	8	0.790	0.346	0.77	19	0.451
	Meditators	13	0.675	0.325			
Left mid STS	Controls	8	0.757	0.402	2.24	19	0.037*
	Meditators	13	0.375	0.366			
Right temporal pole	Controls	8	0.644	0.315	2.815	19	0.011*
	Meditators	13	0.279	0.273			
Left temporal pole	Controls	8	0.574	0.380	0.863	19	0.399
	Meditators	13	0.434	0.350			
Right caudate	Controls	8	0.209	0.268	-0.146	19	0.885
	Meditators	13	0.223	0.172			
Right inferior frontal gyrus	Controls	8	0.471	0.372	1.235	19	0.232
	Meditators	13	0.199	0.549			
Left amygdala	Controls	8	0.190	0.353	-0.338	19	0.739
	Meditators	13	0.247	0.381			
Right anterior STS	Controls	8	0.479	0.350	1.859	19	0.079
	Meditators	13	0.187	0.349			
Dorsal ACC	Controls	8	0.249	0.315	-0.292	19	0.773
	Meditators	13	0.291	0.314			
Left fusiform	Controls	8	0.077	0.347	-0.126	19	0.901
	Meditators	13	0.095	0.287			

Table 4-7: Paired samples t-tests performed on RtME [Emotion - Gender] ROIs. Beta contrast values in the left middle STS and right temporal pole differed significantly by group at Time 1.

Region of interest	t	df	Sig. (2-tailed)
Supplementary Motor	1.367	20	0.187
dmPFC	0.259	20	0.798
Left inferior frontal gyrus	1.252	20	0.225
Leftposterior STS	1.687	20	0.107
Left mid STS	3.573	20	0.002*
Right temporal pole	0.705	20	0.489
Left temporal pole	1.450	20	0.163
Right caudate	0.792	20	0.438
Right inferior frontal gyrus	1.386	20	0.181
Left amygdala	1.731	20	0.099
Right anterior STS	2.663	20	0.015*
dACC	1.721	20	0.101
Left fusiform	0.370	20	0.716

Table 4-8: Paired samples t-tests performed on RtME [Emotion - Gender] ROIs. Beta contrast values in the left middle STS and right anterior STS showed significant attenuation from Time 1 to Time 2.

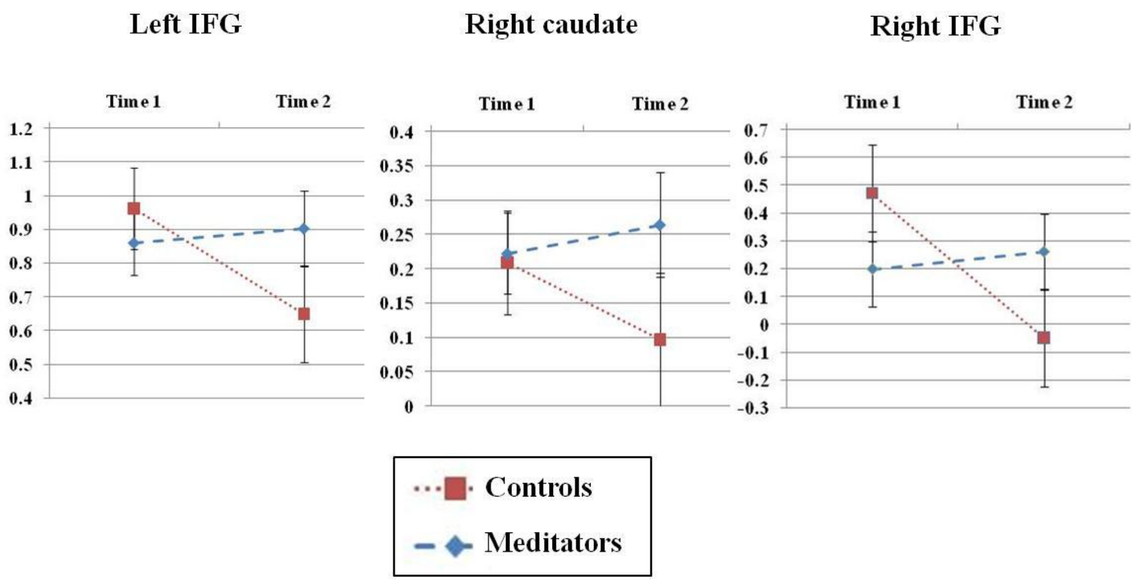

Figure 4-11: Plots of repeated measures ANOVA in bilateral IFG and in the right caudate for the RtME [Emotion – Gender] task. All regions show a significant interaction (group by time) effect: Left IFG: $F(19) = 7.05$; $p = 0.02$; Right Caudate: $F(19) = 4.60$; $p = 0.05$; Right IFG: $F(19) = 8.18$; $p = 0.01$.

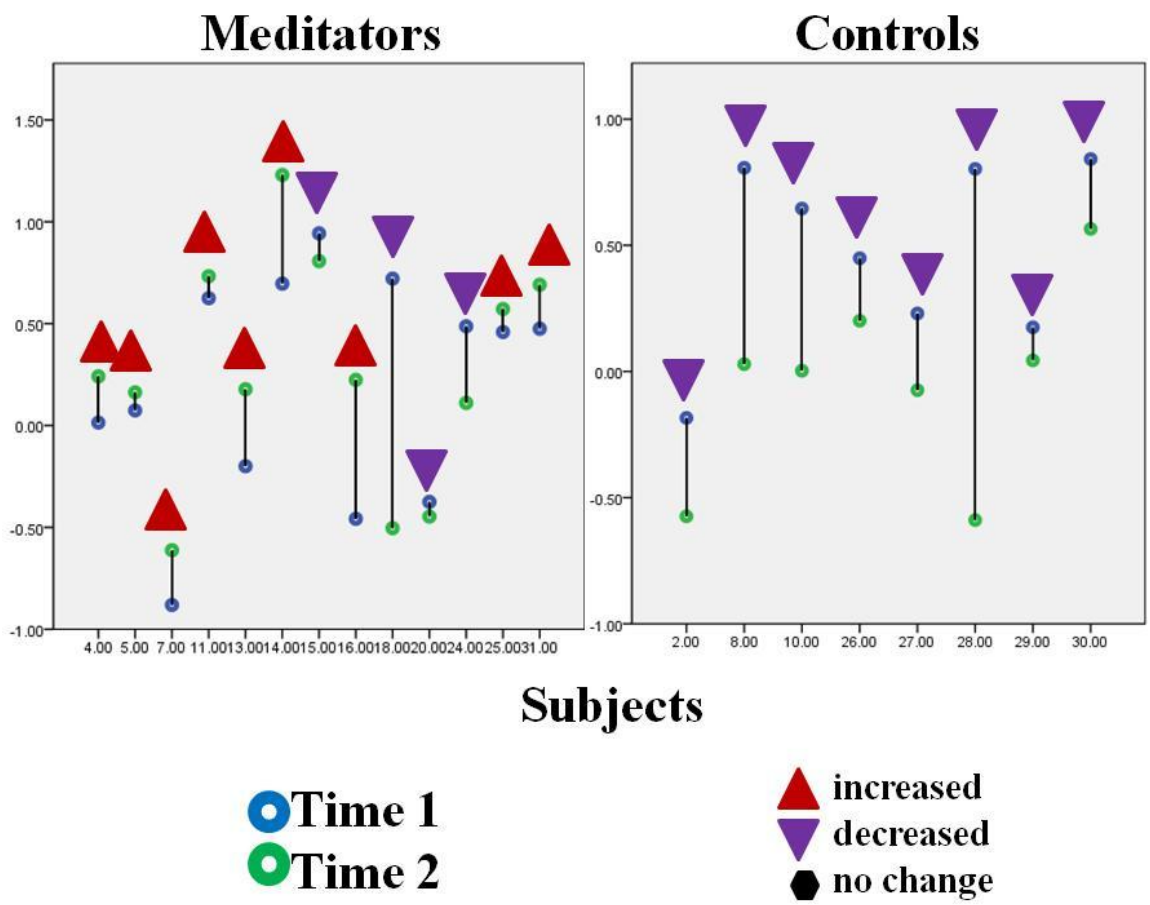

Figure 4-12: Scatter plot of Time 1 (blue circles) and 2 (green circles) RtME beta contrast values [Emotion – Gender] for each subject in the right IFG, broken up according to group. Red triangles represent subjects whose neural activity increased from Time 1 to Time 2, and purple triangles represent subjects whose neural activity decreased from Time 1 to Time 2.

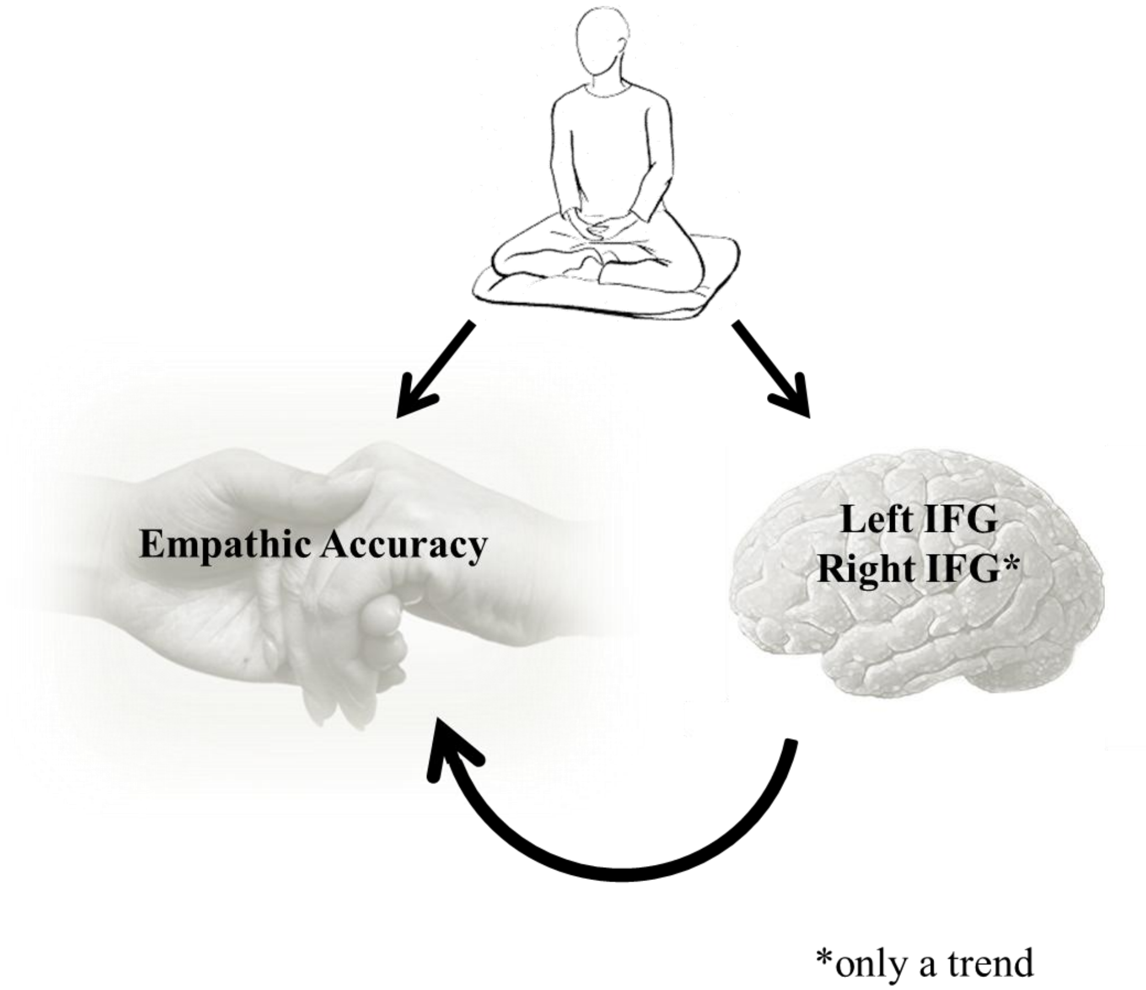

Figure 4-13: Schematic of the significant causal relationships identified in this study.

Chapter 5

Meditation on the ground

Introduction

Along with a dramatic increase in the ways in which meditative practices are currently offered as clinical treatments, aids to personal well-being and as spiritual tools, the investment from the scientific community in meditation research has risen dramatically in the last two decades. A PubMed literature search of the word "meditation" shows that the number of publications has doubled every five years since 1991 (see **figure 5-1**). However, this popularization has not come without criticism regarding the ways in which meditation is incorporated into secular contexts, as well as of the ways in which meditation has been studied. Lutz and colleagues (2007) note that traditional authors emphasize the importance of focusing on other situational factors along with meditation, factors such as the study of Buddhist contemplative philosophy as well as the observance of an appropriate "moral code" (p. 509). The authors point out that these aspects are often ignored when meditation is translated into a scholarly setting. Others have called for an increased focus on the intentions of practitioners when investigating contemplative practices (Shapiro 1992). In fact, to a large extent research on meditation has been conducted under the assumption that all practitioners meditate for a common reason and with common goals, and that meditation acts the same way in all practitioners.

Goals and Intentions: To the best of our knowledge, only one study has explicitly investigated the ways in which a meditator's goals influence their practice as well as the outcomes of their practice. Shapiro (1992) examined Vipassana practitioners with varying degrees of experience and investigated the ways in which their goals affected the outcome of their practice, as well as the ways in which their stated goals changed with practice. He found that people generally attained effects related to the goals they had stated in the outset. For example, if a practitioner reported wanting to decrease their feelings of stress, after their meditation retreat they were more likely to say that the main effect of the retreat was to cause them to feel less stress. He also found that, with experience, meditators' goals shifted from those related to self-regulation (i.e. decreasing stress and anxiety) to those more related to existential changes and increases in prosociality.

With respect to our particular compassion meditation protocol, it is important to study participants' attitudes and goals regarding meditation. McMahan (2008) notes that Western ideas regarding Buddhism, with a particular focus on meditation and an "ethic of compassion" are "a unique confluence of cultures, individuals, and institutions in a time of rapid and unprecedented transformation of societies" (p. 5). As such, we feel strongly that any investigation of meditation should both explicitly describe study participants' varying goals and attitudes, and also explore how these factors may influence the outcomes of their study.

Personality: In addition to the goals and attitudes that a practitioner brings to meditation, it is very likely that study participants' underlying personality features play a large part in determining the outcome of a particular meditative practice. Contemplative scholars such as the Venerable Analayo (2003) have suggested that different types of meditation may better suit individuals of a certain orientation. Alan Wallace (2007) has pointed out that while there are hundreds of meditative techniques taught by Buddhist adepts, it remains unclear whether some are more effective for certain types of people than for others. Beyond the relationship between an individual's cognitive features and meditation outcomes, it remains likely that a meditator's well-being will help determine and characterize their experience with meditation training and practice. This idea is crucial given the increased use of meditative practices in clinical contexts, as underscored by the few who have explored the relationship between well-being and meditation outcomes. For example, Delmonte (1984) found that more extreme symptomatology was related to low meditation practice times within a clinical population, and Carson and colleagues (2004) found that participants who dropped out of a mindfulness-based relationship enhancement intervention were more likely to have been in individual therapy. These data suggest that some minimal degree of mental stability and well-being is necessary to engage with meditation practice.

Over and above baseline well-being, it may be the case that individual differences in spiritual orientation affect the extent to which individuals engage in meditation practice by rendering an individual more open to the practice. Moreover, spiritual orientation may moderate the effects of meditation, rendering a practice more or less effective. This is a particularly interesting, yet neglected, investigation given the characterization of the modern Buddhist movement in the west. Largely appealing to the white, highly educated and upper-middle class, the emphasis within western Buddhism has primarily been on meditation rather than on spiritual or soteriological belief system

(Coleman 2002; McMahan 2008). In fact, the Dalai Lama has emphasized the point that meditation may have universal value (Revel et al. 2000). It remains to be seen how an individual's spiritual orientation relates to their practice of compassion meditation.

Goals of the study: The overall goal of this study is in accord with the larger dissertation goal of exploring variation in prosocial emotions and behaviors as well as the behaviors that impact them. For, if we want to understand how compassion meditation enhances compassion and empathy in practitioners, it is crucial to explore the meditation context to the fullest possible extent. Moreover, it is important to understand how personality variable interact with compassion meditation so that we may understand whether all individuals equally benefit from the practice.

With these goals in mind, we will test the following hypotheses:

1. Participants' meditation goals will be related to practice time.
2. Meditation goals will be related to baseline levels of well-being (stress, anxiety and depression) and spiritual meaning.
3. Baseline levels of well-being (stress, anxiety and depression) and spiritual meaning will be related to practice time and to study completion
4. Baseline levels of well-being (stress, anxiety and depression), spiritual meaning, and meditation goals will account for variance in meditation outcomes (empathic accuracy, brain activity during the empathic accuracy task). (see **figure 5-2** for a diagram of the effects we will test).
5. Baseline brain activity during empathy for pain tasks will predict practice time.

Methods

Motivations and goals: The full study design is described in the previous chapter of this dissertation. In addition to the psychometric measures described previously, we also administered a self-report instrument designed to assess study participants' (1) motivation for entering the study, and (2) meditation-related goals. Their instructions were to: "Please answer the following questions as accurately as you can. Please know that there are NO wrong answers, your answers will be anonymous and will not be reviewed until the end of the study."

First, they were asked to "Please list your motivation for enrolling in this study." Next, they were told, "In the space below, please talk about what specifically you hope to gain from the course you are about to take. Feel free to list more than one thing. Please rate on a scale from 1-6 how intense your wish is to achieve each goal (with 1 being "a little bit interested in achieving this effect" and 6 being "extremely passionate about this goal")"

In order to code these data, the following method was used. For the first question ("Please list your motivation for enrolling in this study."), participants were given 1 point if they mentioned meditation or a meditation-related goal. If the participant mentioned a non-meditation related goal (e.g. "to make money"), we entered 0 points. If the participant mentioned both, we entered 0.5. Coding of the second part of the questionnaire ("please talk about what specifically you hope to gain from the course…") was done primarily based on the categories of Shapiro (Shapiro 1992): 1. Self-regulation (e.g. "learn to control my stress better), 2. Self-exploration (e.g. "want to learn more about myself"), and 3. Self-liberation/compassionate service (e.g. "want to place myself in God's presence", "want to deepen my compassion for others"). In addition, we added a category that we called non-meditation related goals (e.g. "make money", "benefit science"). For each of these four possibilities, we entered the rating that they gave (on a scale of 1-6) regarding how intensely they wanted to achieve the goal. If a subject mentioned several goals that fell under the same category (e.g. mentioned several different goals related to self-regulation), we entered it one time and used the highest rated entry. If a subject mentioned goals that fell into different categories (e.g. a self-regulation goal and a non-meditation related goal), we entered both. In summary, there were five columns on which a subject was scored:

1. Motivation for enrolling in the study: 0, 0.5 or 1
2. Self-Regulation Goal: 0 (did not mention) or 1-6 (the rating that they gave)
3. Self-Exploration Goal: 0 (did not mention) or 1-6 (the rating that they gave)
4. Self-Liberation Goal: 0 (did not mention) or 1-6 (the rating that they gave)
5. Non-meditation Goal: 0 (did not mention) or 1-6 (the rating that they gave)

One subject did not fill out the questionnaire as she was late to the scanning session. Thus, we have complete data on 28 participants. With these data, we ran bivariate correlation analyses in order to test the hypothesis that meditation goals predict practice time (**hypothesis 1**). We also asked whether self-reported well-being (stress, anxiety and depression) and spiritual meaning scores were related to meditation goals (**hypothesis 2**). Finally, we used the goal scores in linear regression analyses to investigate whether subjects' goals accounted for a significant amount of the variance in meditation outcomes (as measured by changes in empathic accuracy and brain activity during the empathic accuracy task).

Relationship between baseline well-being and meditation practice: In order to test the hypothesis that baseline levels of well-being and spiritual meaning would predict practice time, we used bivariate correlation analyses. Independent t-tests were run to test the hypothesis that baseline levels of well-being would predict study completion **(hypothesis 3)**.

Factors that moderated meditation success: In order to identify factors that made meditating more or less beneficial (**hypothesis 4**), we tested for personality variables that interacted with group to predict variance in outcomes. To do this, we conducted linear regression analyses in which the Time 2 outcome measure (e.g. empathic accuracy, brain activity related to empathy accuracy) was our dependent variable. We then asked, controlling for the Time 1 levels of the dependent variable, does the interaction of the personality variable with group predict variance in the dependent variable above and beyond that predicted by the personality variable and group independently. So that we did not run into a multiple comparisons problem, analyses were limited to outcome measures that were previously found to be most relevant to mediation, including empathic accuracy scores and neural activity in the right and left IFG.

Predicting practice time using baseline brain activity: To explore whether baseline brain activity during the empathy for pain (EFP) and reading the mind in the eyes (RtME) tasks predicts practice time (**hypothesis 5**), we limited our sample to those randomized to the meditation group (n = 16) and we performed two different investigations. First, we explored whether the subjects who dropped out of the study (n=3) differed in significant ways from the subjects who completed the study (n=13). To do this, we performed independent samples t-tests of the beta values in each ROI for two different tasks: (1) EFP task (contrasts: [Self Pain – Self NoPain], [Other Pain – Other NoPain] and [Other Pain Anticipation – Other NoPain Anticipation]) and (2) RtME [Emotion – Gender]. A whole-brain exploratory analysis was also conducted for each of these contrasts, with a threshold set at $p < 0.001$ with a 10-voxel spatial-extent threshold. Second we entered practice time in bivariate correlation analyses for the beta values in each ROI generated using the above contrasts. Again a whole-brain exploratory covariate analysis was performed by entering practice time as a covariate in each of the contrasts listed above, with a threshold set at $p < 0.001$.

Results

Motivations and goals: With respect to participants' motivations for entering the study, the majority (n=16) only mentioned non-meditation related goals (e.g. "move science forward", "to pay for some spa treatments"). Only 3 participants solely mentioned meditation as their motivation for enrolling, and 9 participants referenced both non-meditation and meditation-related goals.

In terms of goals, no participants mentioned a self-liberation goal. In other words, not a single participant said that they wanted to learn to meditate because they wanted to be more empathic toward others or for any reason related to soteriological or spiritual gains. Fifteen participants referenced self-regulation goals (e.g. "have more patience for life stressors"), 4 mentioned goals related to self-exploration (e.g. "learn about behavior”), and 13 participants referenced non-meditation goals (e.g. “get an MRI”, “promote and support health research”). See **figure 5-3** for a plot of the mean ratings for each category.

In order to address the hypothesis that meditation goals will predict practice time (hypothesis 1), we ran bivariate correlation analyses and found that practice time had a positive correlation with self-regulatory goals ($r(14)= 0.53$, $p = 0.04$), but a negative correlation with non-meditation goals ($r(14)=-0.66$, $p = 0.005$) (see **figure 5-4** for plots). In other words, subjects who wanted to meditate in order to manage stress or increase their well-being were far more likely to report practicing, whereas subjects who said that their goals were to get monetary compensation or to further science were less likely to report practicing.

With respect to the hypothesis that baseline levels of well-being and spiritual meaning were related to meditation goals, bivariate correlation analyses revealed that SMS scores were inversely related to self exploration goals ($r (26) = -0.39$, $p = 0.05$). In other words, the higher people were on spiritual meaning, the less they reported wanting to learn about themselves. There was a significant positive relationship between the number of symptoms of depression that participants endorsed and self-exploration goals ($r(28) = 0.51$, $p = 0.006$) (see **figure 5-5**). However, it should be noted that very few participants endorsed self-exploration goals, which may account for both of these findings.

Predicting meditation success: Of the 29 participants who completed the Time 1 assessments, 8 participants drop out of the study. **Table 1** shows descriptive statistics of the 8 drop-outs compared to the 21 participants who completed the study. Of the drop-outs, half were males, and 5 of the 8 were participants randomized to the control group. With regards to self-reported personality variables, the subgroup of those randomized to meditation that dropped out of the study had a significantly higher score on the personal distress subscale of the IRI (drop outs n = 3; complete n = 13). It appears that this effect is primarily driven by those randomized to compassion meditation - those randomized to compassion meditation who dropped out had significantly higher scores on this subscale (t(14) = 2.29, p = 0.04), while those randomized to the control condition did not have significantly higher personal distress scores. See **figure 5-6** for plot of these effects within those randomized to meditation.

In terms of the hypothesis that baseline personality variables would predict practice time, we did not find any significant correlations between practice time and self-reported well-being, spiritual meaning, or empathy levels. However, we did find that baseline levels of spiritual meaning (r(25) = -0.43, p = 0.03) and personal distress (r(27) = -0.48, p = 0.008) were negatively related to class attendance.

Next, used linear regression analyses were used to identify baseline personality variables or goals that predicted changes in empathic accuracy. There was a trend suggesting that self-regulation goals account for a significant amount of the variance in Time 2 empathic accuracy scores, controlling for Time 1 scores and group (b = 0.34, R^2 change =0 .10, F (17) = 3.53, p = .08). In other words, no matter the intervention, participants who reported goals related to self-regulation, such as wanting to better learn to cope with stress, had more of an increase in empathic accuracy scores. Given this, we did a correlation analysis to investigate whether meditation goals were related to Time 1 levels of empathic accuracy, and found that the extent to which participants endorsed non-meditation related goals was correlated with lower scores on the empathic accuracy task ($r(28) = -0.41$, $p = 0.03$). No other baseline personality variable predicted changes in empathic accuracy.

In terms of personality variables and goals that moderated the relationship between group and meditation outcome, we found that both spiritual meaning scores (b = -0.30, R^2 change = 0.16, F-change (1,16) = 5.42, p = 0.04)) and anxiety scores (b = -0.70, R^2 change = 0.13, F-change (1,16) = 4.72, p = .05) at Time 1 moderated the effect of being randomized to the meditation group on empathic accuracy scores. In other words, participants who reported high baseline levels of spiritual meaning and anxiety had *less* of an increase in empathic scores due to meditation. Baseline levels of empathy, psychopathy, stress and depression did not moderate the effects of meditation, and neither did the sex of the participant. We also found that Time 1 anxiety levels showed a 2-way interaction effect in predicting variance in Time 2 neural activity in the right IFG during the RtME task (b = 0.13, R^2 change = 0.15, F-change (1,16) = 5.34, p = 0.03). However, the moderation effect was in the opposite direction, in that high levels of baseline anxiety were related to more brain activity during the empathic accuracy task. Linear regression testing for an interaction effect of goal by group was non-significant (b = -0.27, R^2 change =.00, F-change (1,16) = -.12, p = 0.74).

With respect to our investigation of the relationship between baseline brain activity and meditation success, the drop-out group had significantly less activity in the right thalamus for the Other Pain condition [Pain – NoPain] ($t(14) = 2.79$; $p = 0.02$) (see **figure 5-7** for a plot). There were no significant differences in any other ROI for any of the other contrasts, nor did our whole-brain analyses reveal significant differences between the drop-out and complete groups for any other contrast. Bivariate correlation analyses revealed that practice time was inversely correlated with neural activity in the left amygdala during the Self Pain task [Pain – NoPain] ($r(16) = -.505$; $p < 0.05$) (see **figure 5-8** for a plot). Moreover, there was a positive correlation between practice time and activity during the Other Pain task in several regions, including the right anterior insula ($r(16) = 0.58$; $p = 0.02$), supplementary motor cortex ($r(16) = 0.51$; $p = 0.04$), right STS ($r(16) = 0.55$, $p = 0.03$), right thalamus ($r(16) = 0.73$; $p < 0.01$), and left STS ($r(16) = 0.55$; $p = 0.03$), and a trend in the right lateral parietal ($r(16) = 0.47$; $p = 0.07$) and left anterior insula ($r(16) = 0.47$; $p = 0.07$) (see **figure 5-9** for plots). There was also a positive correlation between practice time and brain activity in the right anterior insula during Other Pain Anticipation [Pain Antic – NoPain Antic] ($r(16) = 0.54$, $p = 0.03$) (see **figure 5-10** for a plot). The whole brain exploratory analyses revealed an inverse relationship between practice time and brain activity during Other Pain Anticipation [Pain Antic – NoPain Antic] in two regions of the ACC (BA 32 and 24), dmPFC (BA 8), visual cortex and middle temporal gyrus (see **figure 5-11** for a plot).

Discussion

Motivations and goals: In terms of study participants’ goals in learning to meditate, stress-related goals were by far the most prevalent. This is consistent with the results of Shapiro (1992), who found that the intentions of most beginning meditators (in his study, Vipassana meditators) are to increase self-regulation (Shapiro 1992). He found that, with practice, these intentions shift along a continuum to self-exploration and then to self-liberation related goals. It would be quite interesting to see whether the same pattern holds true for practitioners of compassion meditation. It was remarkable that, despite the fact that no participant endorsed goals related to increasing empathy, compassion or connections to others, participants in the meditation group did have increases in aspects of empathy, namely increased empathic accuracy and increases in the neural activity related to it. While this is somewhat in contrast to the results of Shapiro, who found that meditation goals were significantly predictive of outcomes, he does note that self-regulatory goals can bridge the way to more lofty outcomes, and tells an anecdote regarding a meditator who began with the goal of stress management and came out of the Vipassana retreat with a strong wish to make the world a better place. It is also important to note that our outcome measure was more objective in nature than that used by Shapiro, who had subjects report on the outcomes related to their meditation practice. This difference in methods could lead to very different results, and it remains possible that participants in our study would not report having attained increases in empathy. In fact, their self-reported trait empathy levels did not increase. In hindsight, it would have been informative to explicitly probe participants regarding what they thought they had gained from the meditation course.

While these results regarding the relationship between self-exploration goals and spiritual meaning and depression should be taken with caution due to so little variance in the sample, we can speculate on other possible explanations. Regarding the fact that spiritual meaning was inversely related to self-exploration goals, our finding is somewhat consistent with that of Shapiro, who reported that 80% of participants attending a Theravada Buddhist Vipassana retreat who reported belonging to a monotheistic religion also reported self-regulation goals as opposed to self-exploration or self-liberation goals.

He interpreted this finding by suggesting that, for those belonging to a monotheistic religion, self-exploration and self-liberation goals are more in conflict with one's religious beliefs. It may be that we are seeing a similar effect; that is, if one endorses monotheistic religious beliefs they may be less apt to say that they want to meditate in order to learn fundamental truths about themselves. It is less clear why depression levels would be positively related to self-exploration goals, but it is worth remembering that these individuals have not been diagnosed with depression, and it remains possible that individuals who are experiencing more symptoms of depression are interested to learn more about themselves. Related, it may be that introspective tendencies lead to symptoms of depression (Nolenhoeksema and Morrow 1993; Roberts et al. 1998; Schieman and Van Gundy 2001).

Finally, it is quite striking that individuals who endorsed non-meditation related goals (e.g. to get an MRI, to advance science) tended to score lower on the empathic accuracy task. There are two possible explanations for this finding. It may be that subjects who were not interested in meditation did not try as hard on the empathic accuracy task. Another interpretation is that individuals who were not interested in meditation are simply less empathic.

Predicting meditation success: With respect to the hypothesis that baseline levels of well-being would predict whether individuals completed the meditation study, scores on the personal distress subscale of the IRI were higher in those participants who dropped out of the study. Importantly, it was participants randomized to the meditation condition who drove this effect. The personal distress subscale was designed to assess the extent to which an individual experiences anxiety or discomfort when observing another's suffering. One plausible interpretation of this finding is that subjects who were more prone to feelings of personal distress had trouble engaging with the meditation protocol, a large part of which involves contemplation of others' suffering.

In addition, spiritual meaning and aspects of well-being (anxiety) moderated the effects of meditation, and we will offer interpretations of these in turn. First, spiritual meaning interacted with group such that those with higher levels of spiritual meaning experienced less benefit from meditation in terms of empathic accuracy. That is, individuals with lower levels of reported spiritual meaning in life experienced greater gains in empathic accuracy as a function of meditation. One possible explanation of this finding is that the SMS scale is tapping into a dichotomy between subjects who are steeped in an academic tradition and those coming from a more fundamentalist theological tradition(s). In fact, our participant population was recruited both from the upper-level (graduate and medical) schools at Emory University as well as from the greater Atlanta area. Polls consistently show that academics who believe in God are in the extreme minority, though it should be stressed that the questions on these polls usually ask about belief in a "personal god" (Larson and Witham 1998; Lynn et al. 2009). While the SMS scale was designed to correlate with rational thought processing (as opposed to close minded thinking) and to tap into aspects of spirituality that extend beyond the limits of belief in a personal god (Mascaro et al. 2004), it is likely that participants who belong to and heavily endorse more fundamentalist religions are the participants in our population that scored highly on this measure.

If it is true that participants who scored lower on the SMS tended to be those recruited from the academic setting, it may be that they were more open to learning a meditative practice. McMahan (2008) speaks of the image that characterizes modern Buddhism and Buddhist practices, particularly in the West, as scientifically rational and continuous with scientific knowledge. He notes that Buddhism is contrasted with other religions as being “largely free of superstition and irrational belief, and in basic harmony with science” (p. 67). This impression comes in large part from popularized Buddhist writers such as Allan Wallace (2007) and John Kabat-Zinn, who has said that “one might think of dharma as a sort of universal generative grammar, an innate set of empirically testable rules that govern and describe the generation of the inward, first person experiences of suffering and happiness in human beings (Kabat-Zinn 2003 p. 145). Similarly, the Dalai Lama has repeatedly stated that Buddhist tenets that are not in accord with scientific knowledge should be discarded (Hayward and Varela 1992). Thus, it is possible that those participants recruited from an academic setting, and who scored lower on the SMS scale, were more receptive to the modern notion of an empirically-validated meditation technique. This idea is consistent with Sarbacker’s (2005) suggestion that empiricism and “faith in science” have led many to a “religious flight” which characterizes many of the contexts in which meditation is practiced (p. 3). Related to this idea, it could be that those who scored higher on the SMS belong to more fundamentalist monotheistic religions and might feel more conflicted by the adoption of a meditative practice, even a secularized version. With respect to this idea, it is interesting that there was a negative correlation between the SMS and self exploration goals, suggesting that those who scored high on the SMS were less interested in learning to meditate in order to discover something about themselves.

Our hypothesis regarding the moderating effects of well-being on meditation outcomes was upheld. Specifically, those who had higher levels of baseline anxiety received less of a benefit of meditation in terms of increased empathic accuracy. At the same time, more anxious participants had more of an increase in brain activity in the right IFG due to meditation. It should be stressed that the anxiety subscale of the DASS reflects how frequently participants experienced panic-related symptoms over the previous week, suggesting that individuals prone to panic symptoms experience fewer gains from meditation, in terms of empathic accuracy. This, despite the fact that they receive more of an enhancement from meditation in terms of brain activity during the empathic accuracy task. To some extent, this is consistent with our findings from the Time 1 RtME study, in which anxiety levels were negatively correlated with empathic accuracy, but positively related to neural activity during the task (in the anterior paracingulate, supplementary motor and left fusiform gyrus). It is important to note that while the findings at Time 1 could reflect individuals' anxious feelings in the scanner interfering with task performance, the effect discussed here is an interaction effect, meaning that the interaction of group with anxiety levels predicted more variance than anxiety alone. Thus, not only do anxious participants work harder and perform worse on the task, but anxiety levels impact individual's level of benefit from meditation. It is also interesting to reflect on this finding with respect to a previous study conducted by our group which suggested that responsivity to a social stress task did *not* predict compassion meditation practice time (Pace et al. 2010). While we also found that panic-related symptoms were unrelated to subsequent practice time, these symptoms did interfere with the beneficial gains that came from meditation practice.

However, with respect to the fourth hypothesis, participants' goals did not moderate the effects of meditation, indicating that participants randomized to compassion meditation benefited from the course irrespective of why they entered the study or what they hoped to gain from meditation. Taken together these data suggest that while spiritual meaning and anxiety levels moderate the effects of meditation, the baseline goals with which one enters into meditation training do not moderate outcome. Thus our findings are in direct opposition to the statements of Kabat-Zinn: "I used to think that meditation practice was so powerful… that as long as you did it at all, you would see growth and change. But time has taught me that some kind of personal vision is also necessary." (Kabat-Zinn 1990 p. 46) It is worth emphasizing the fundamental differences that exist between meditation techniques and to suggest that further investigations should build upon the analyses done here in order to see if our findings truly characterize the relationship between meditation goals and outcomes.

Our fifth hypothesis, that brain activity during the empathy for pain tasks will predict practice time, yielded several interesting results. First, practice time was inversely correlated with activity in the left amygdala during self pain. Given the role of the amygdala in threat monitoring (Öhman 2005), this finding suggests that individuals who are more threatened by feeling pain are less able, or less likely, to engage in meditation. Conversely, the fact that practice time was positively related to empathy-related activity during the Other Pain task (both while watching others anticipate and receive pain) suggests that more empathic individuals engage more fully with compassion meditation. This result is particularly important given previous findings, based on cross-sectional studies, in which it was suggested that compassion meditation enhances activation in neural circuits important for empathy, including in the anterior insula (Lutz et al. 2008). In other words, it may be that high levels of empathy *cause* meditation engagement, rather than the inverse, highlighting the importance of longitudinal study designs for drawing causal associations between meditation and biological or cognitive measures of interest. Finally, these results are interesting in light of the traditional Tibetan works upon which our compassion protocol was based. In volume two of The Great Treatise on the Stages of the Path to Enlightenment, Tsong-Kha-Pa (2004) emphasized the importance of having compassion at the beginning of a practice, since one will not be moved to commit to being compassionate toward others if their compassion is weak to begin with. The fact that empathy-related brain activity predicted practice time suggests that this is true.

In conclusion, our analyses revealed that participants' underlying goals, beliefs and well-being interacted with meditation practice in unique ways that underscore the need for more nuanced investigations of meditation. While participants' goals and motivations for enrolling in the study predicted meditation participation, they did not moderate the effects of being randomized to the meditation group. However, the extent to which subjects report feeling personal distress at others' suffering predicted participants' participation in the compassion meditation group. Moreover, underlying personality variables, including levels of spiritual meaning and anxiety, proved to render meditation less effective for certain populations in our study. Finally, brain activity during Self and Other Pain predicted subsequent practice time in a way that suggested that individuals who are less responsive to their own pain but more empathic toward the pain of others engage most with compassion meditation. We are excited to see if results such as these form a consistent pattern among future meditation studies.

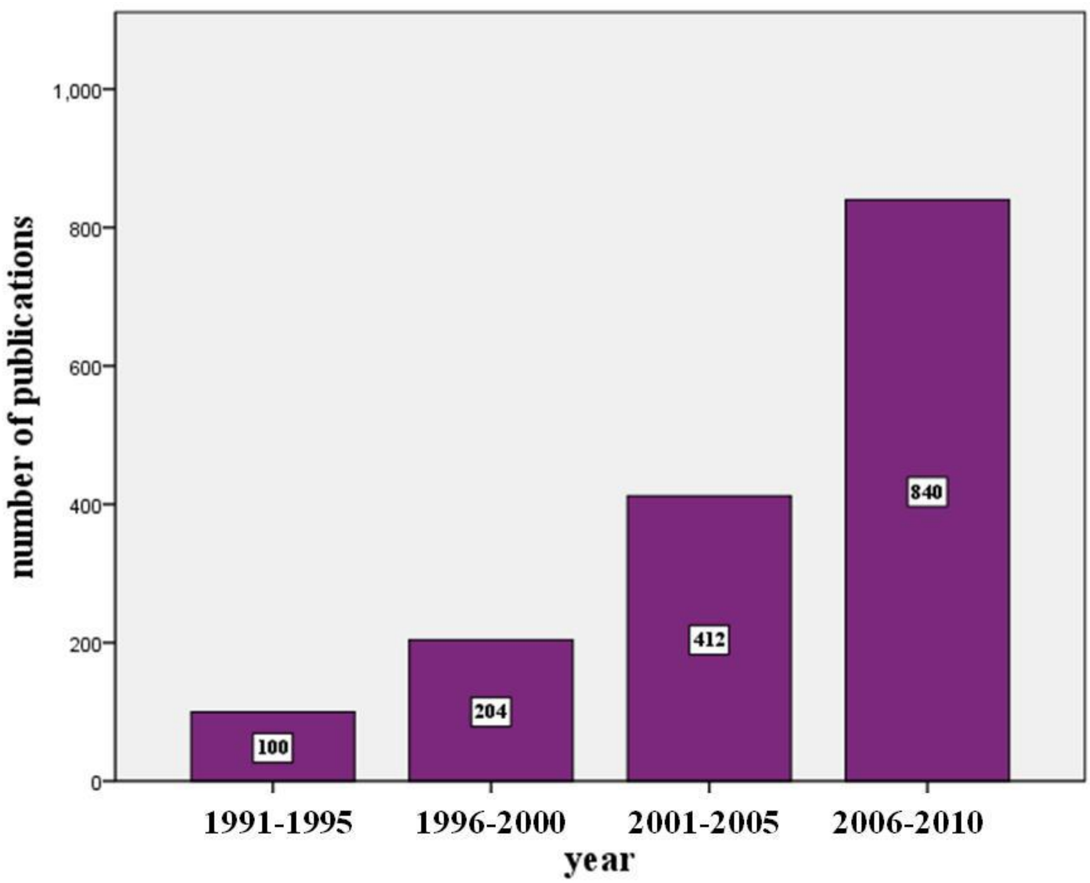

Figure 5-1: Results of PubMed review using the word "meditation" and broken up according to five-year spans.

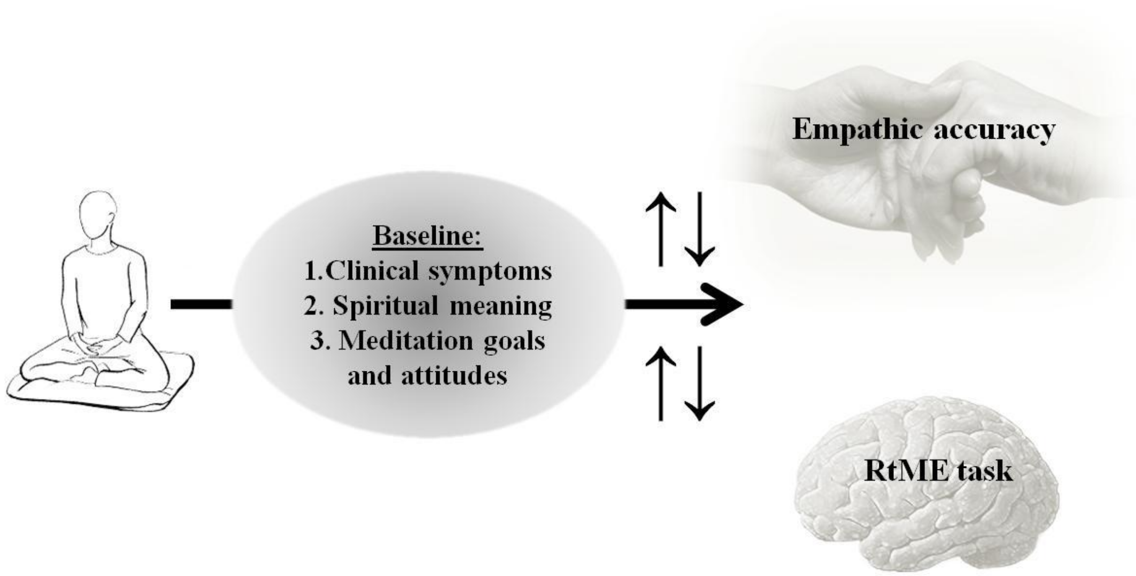

Figure 5-2: Schematic of the moderation effects that will be tested. We will test for an interaction effect between group and baseline levels of clinical symptomology, spiritual meaning, and meditation-related goals and attitudes, in order to investigate whether these variables render meditation more or less effective in terms of changes in empathic accuracy and brain activity.

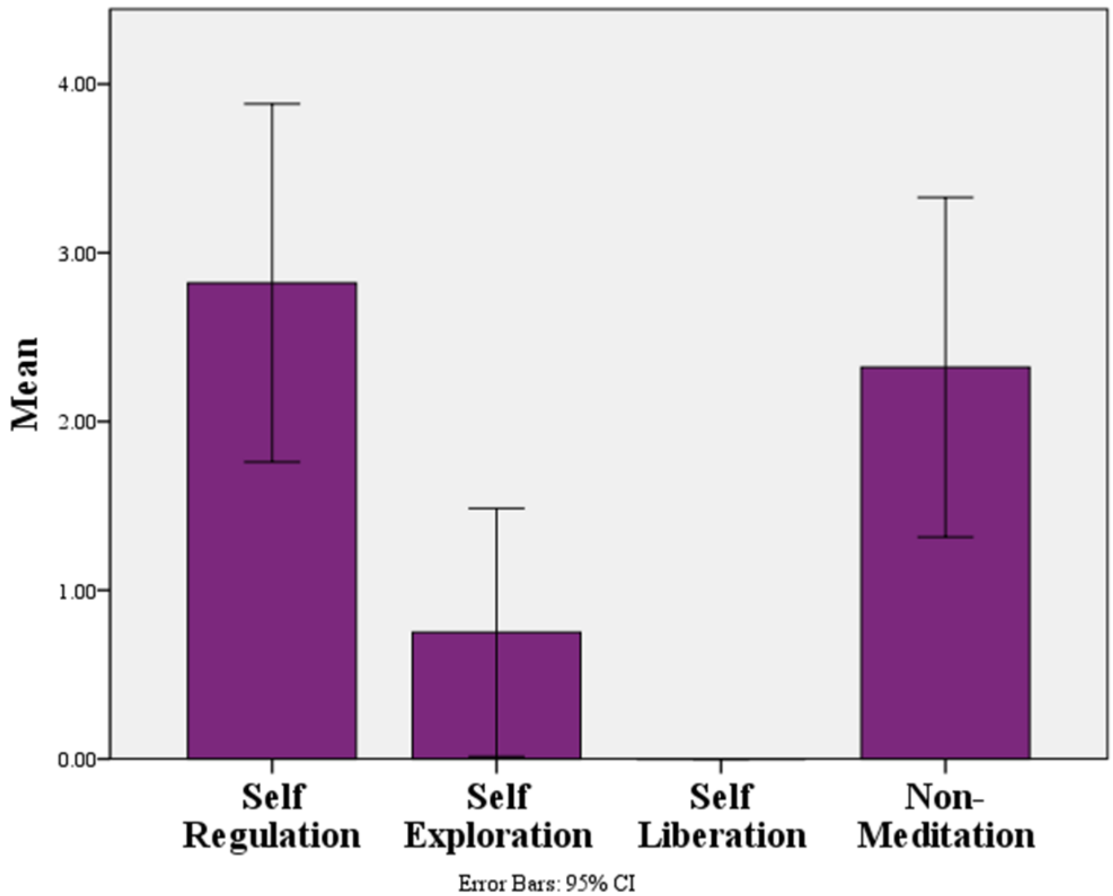

Figure 5-3: Plot of the mean intensity ratings (from 0-6) for the 4 possible goals: Self Regulation, Self Exploration, Self Liberation and Non-meditation related goals.

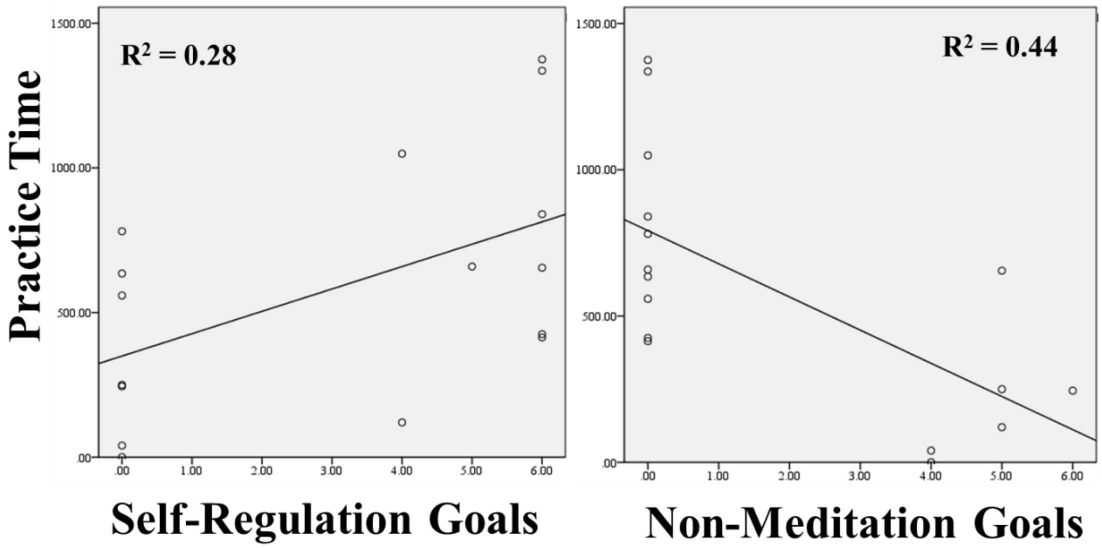

Figure 5-4: Plot of bivariate correlation analyses for the 16 participants randomized to compassion meditation looking at relationship between practice time and self-regulation (r (16) = 0.53, p = 0.04) and non-meditation goals (r (16) = 0.66, p = 0.01). Participants who endorsed more goals related to self-regulation tended to practice more, whereas participants who endorsed non-meditation goals practiced less.

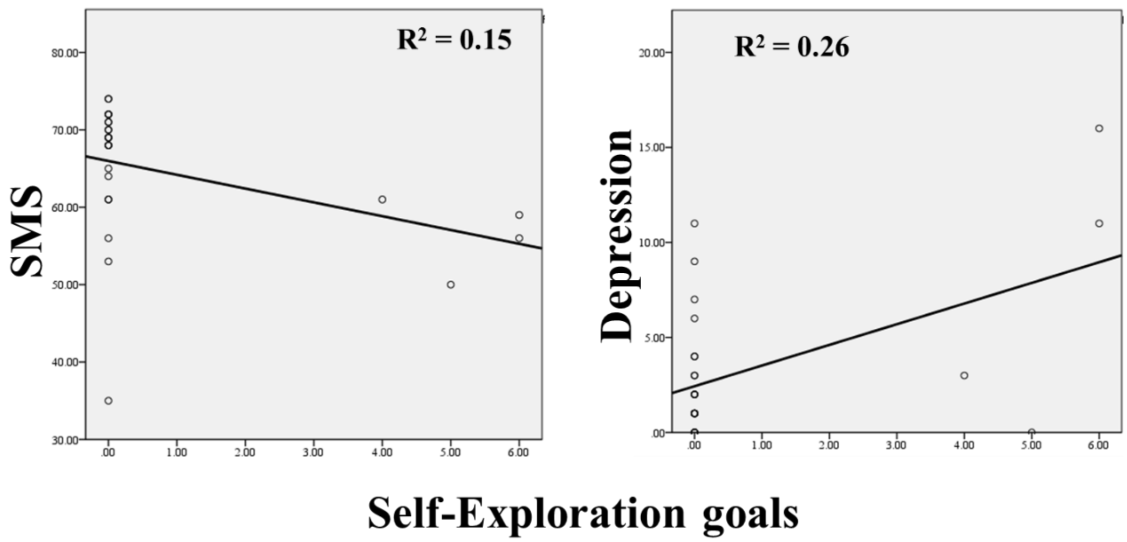

Figure 5-5: Plot of bivariate correlation analyses for all participants looking at the relationship between self-exploration goals and spiritual meaning (SMS) (r (26) = -.39, p = 0.05) and depression scores (r (28) = .51, p = 0.01). Participants who had higher levels of spiritual meaning reported fewer self-exploration goals, whereas participants who endorsed more symptoms of depression reported more self-exploration goals.

	group	N	Mean	Std. Deviation	Std. Error Mean	t	Sig. (2-tailed)
Fantasy	Drop-outs (D)	8	15.38	4.00	1.41	-1.40	0.17
	Complete (C)	21	18.38	5.50	1.20		
Perspective Taking	D	8	19.75	4.62	1.63	-0.62	0.54
	C	21	20.67	3.09	0.67		
Empathic Concern	D	8	20.75	4.56	1.61	0.22	0.83
	C	21	20.38	3.89	0.85		
Personal Distress	D	8	10.88	2.47	0.88	2.81	0.009*
	C	21	7.52	2.99	0.65		
PPI total	D	8	122.38	11.44	4.04	-0.13	0.90
	C	21	122.95	10.21	2.23		
SMS	D	8	67.25	8.41	2.97	1.00	0.33
	C	20	63.45	9.34	2.09		
Stress	D	8	5.25	3.88	1.37	-0.08	0.94
	C	21	5.38	4.21	0.92		
Anxiety	D	8	3.88	3.36	1.19	0.41	0.68
	C	21	3.33	3.07	0.67		
Depression	D	8	3.50	5.24	1.85	0.21	0.84
	C	21	3.14	3.58	0.78		
PPI Coldheart	D	8	14.75	4.17	1.47	-0.19	0.85
	C	21	15.05	3.65	0.80		
State Empathy Ratings	D	8	1.13	1.73	0.61	-0.03	0.98
	C	21	1.14	1.24	0.27		
RtME correct	D	8	17.50	5.04	1.78	-0.59	0.56
	C	21	18.48	3.54	0.77		
Gender	D	8	4 Males				
	C	21	12 Males				
Group	D	8	3 Meditators				
	C	21	13 Meditators				

Table 5-1: Descriptive statistics of personality variables based on dropout rates. Independent samples t-tests revealed that only the personal distress subscale of the IRI was significantly different according to group ($t(27) = 2.81$, $p = 0.01$).

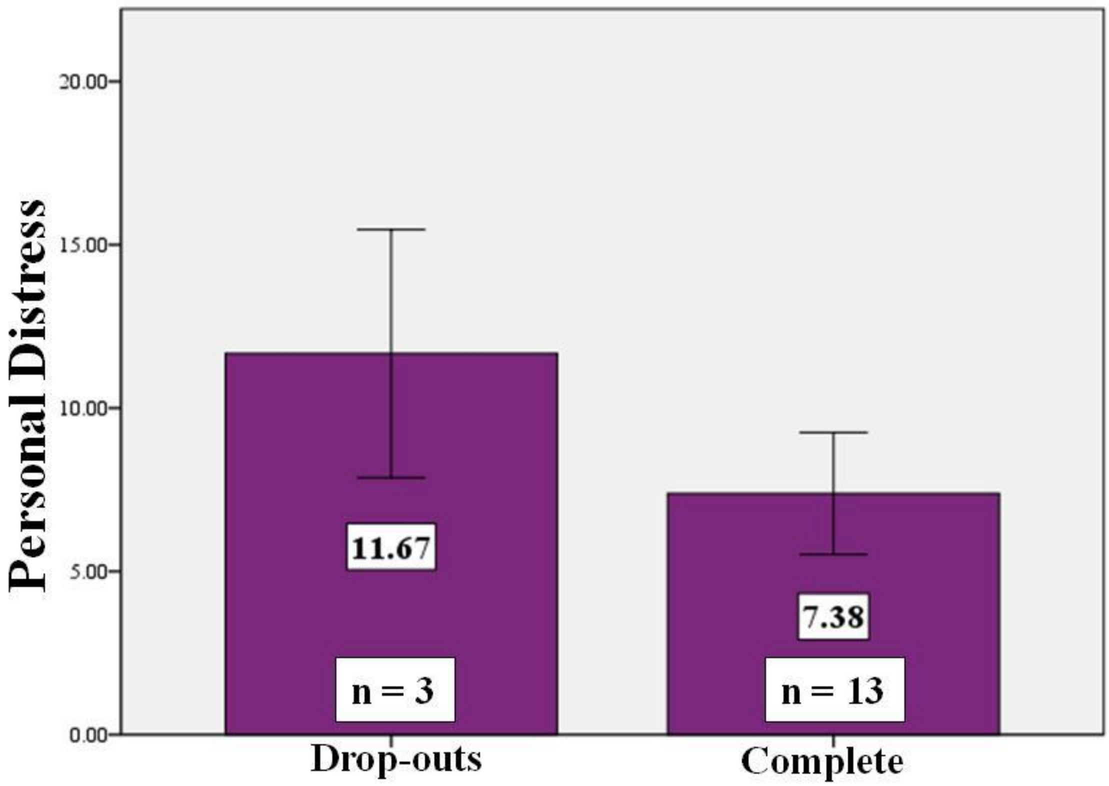

Figure 5-6: Plot of mean scores on the Personal Distress subscale of the IRI in those randomized to compassion meditation, broken up according to those who dropped out and those who completed the study (t(14) = 2.29, p = 0.04).

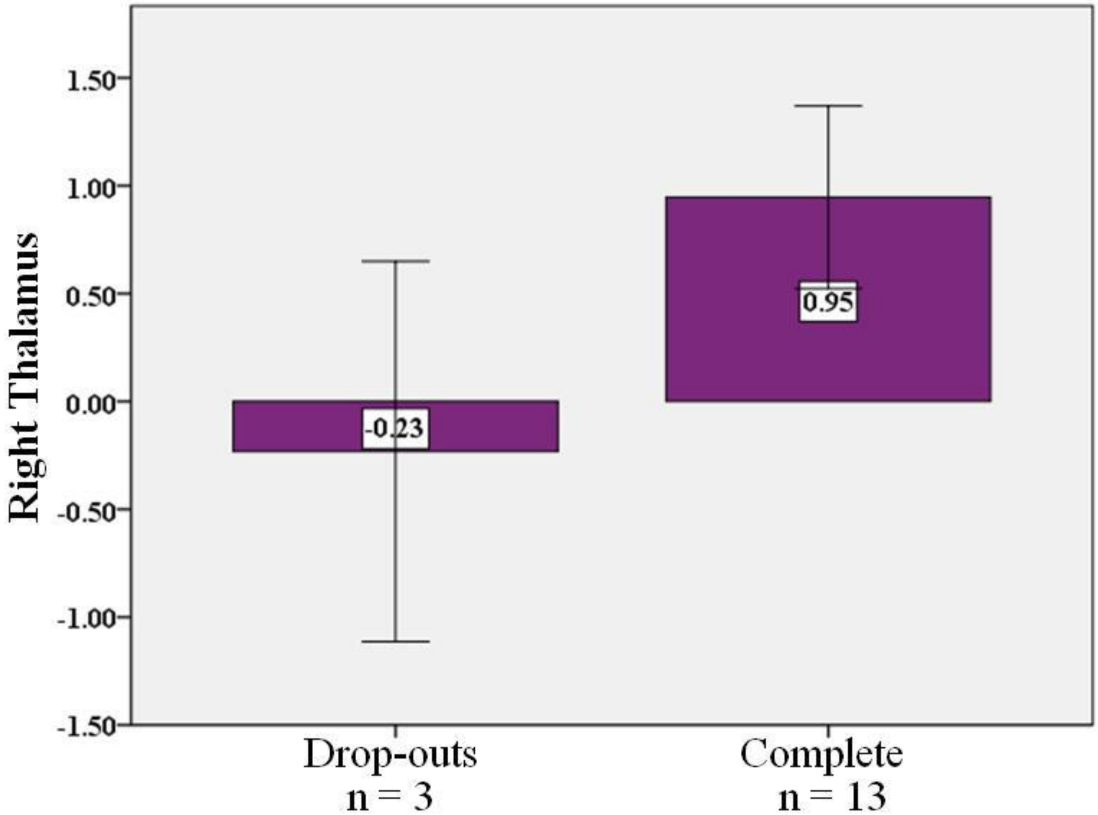

Figure 5-7: Plot of the mean beta contrast value in the Other Pain task [Pain – NoPain] in the right thalamus in drop-outs compared to those who completed meditation training (t (14) = 2.79, p = 0.02).

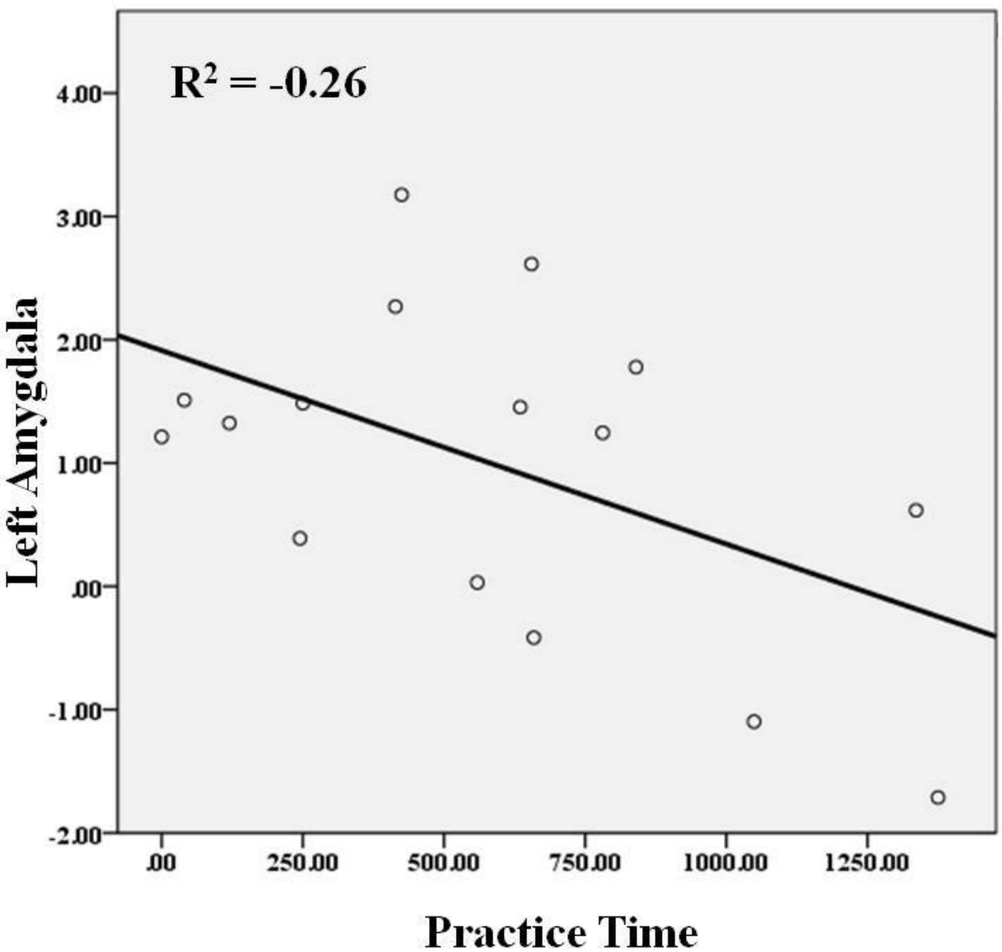

Figure 5-8: Plot of bivariate correlations for practice time with beta contrast values in the Self Pain task [Pain – NoPain] in the left amygdala (r(16) = -0.51; p = 0.05).

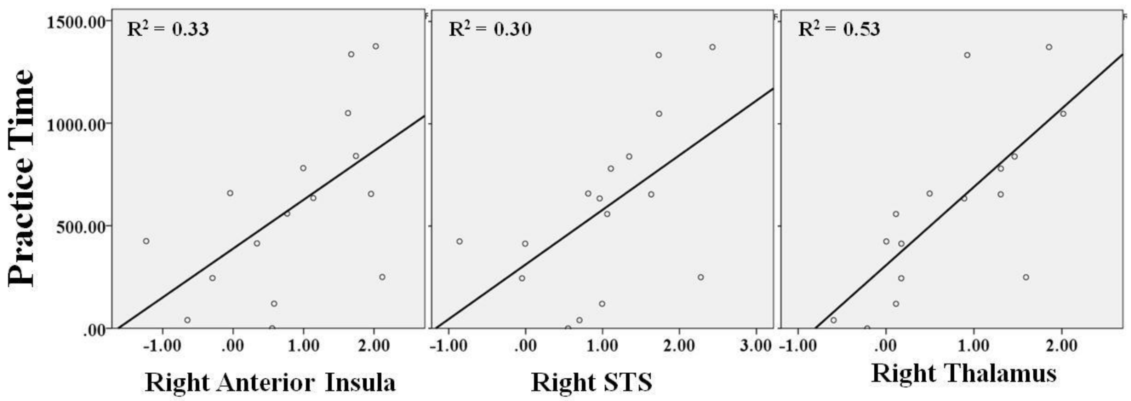

Figure 5-9: Plot of bivariate correlations for practice time with beta contrast values in the Other Pain task [Pain – NoPain] in the right anterior insula (r(16) = 0.58; p = 0.02), right STS (r(16) = 0.55; p = 0.03), and right thalamus (r(16) = 0.73; p < 0.01).

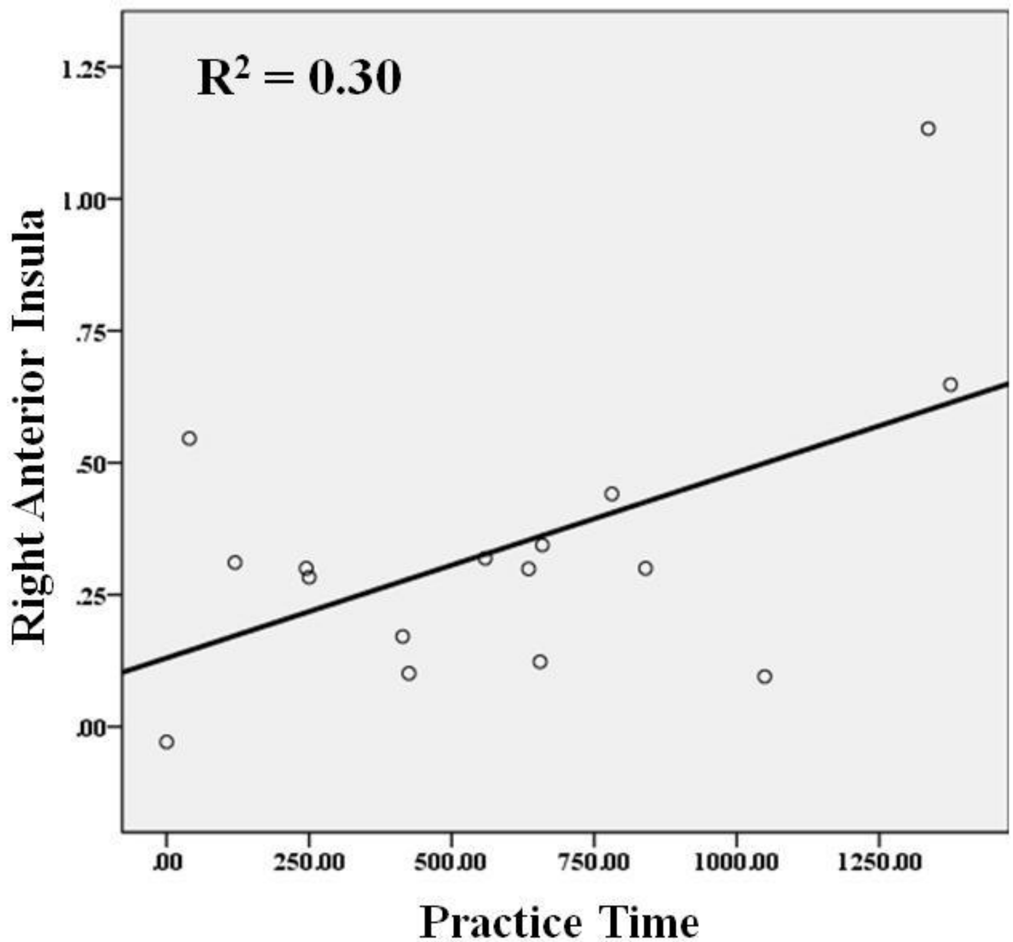

Figure 5-10: Plot of bivariate correlations for practice time with beta contrast values in the Other Pain task [Pain Antic – NoPain Antic] in the right anterior insula (r(16) = 0.54; p = 0.03).

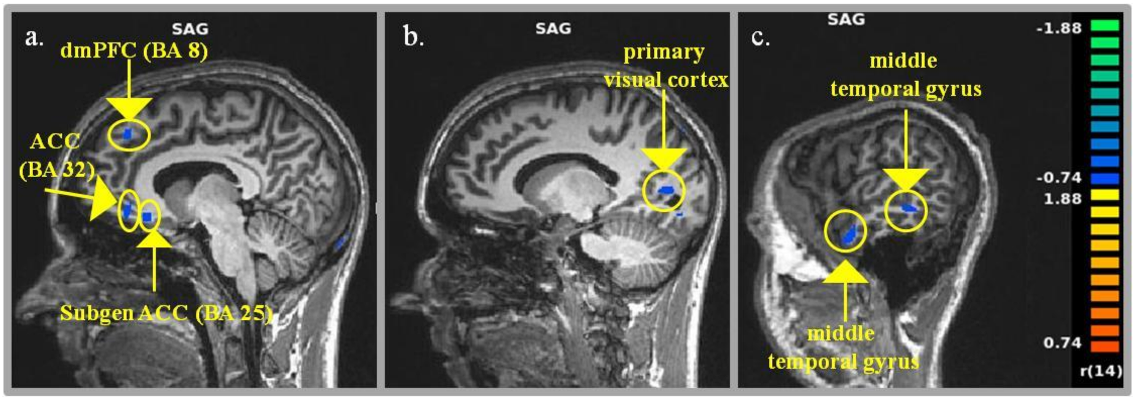

Figure 5-11: Areas of activation during Other Pain Anticipation that are inversely correlated with practice time in meditators (n = 16); threshold at p < 0.001. (a.) x = -6; activations in dmPFC (BA 8) and ACC (b.) x = -55; (c.) activations in middle temporal gyrus.

Chapter 6

Conclusion

Summary of findings

The Reading the Mind in the Eyes task was used as a task of empathic accuracy and findings related to its use are as follows:

1. Females scored significantly higher on the emotion task, but not on the gender task.

2. There was a negative relationship between anxiety and accuracy for the emotion task.

3. The emotion task (compared to the gender control task) activated the temporal poles, right STS, inferior frontal gyrus bilaterally, dmPFC, anterior paracingulate cortex (BA 32) and left amygdala.

4. Activity in the anterior paracingulate, supplementary motor cortex, left fusiform gyrus, anterior insula and dorsal ACC was positively correlated with anxiety scores.

With respect to the empathy for pain task, findings included:

5. Participants reported that the painful condition was more aversive than the nonpainful for both self and other, though they found self pain more aversive than other pain.

6. The Self Pain task [Pain – NoPain] robustly activated neural regions related to the experience of pain (S1, posterior insula, anterior insula, dorsal and mid cingulate cortex and amygdala), and female participants had more activation in the right amygdala.

7. The Other Pain task [Pain – NoPain] revealed activations thought to be important for empathizing with others in pain, including in the anterior insula, mid cingulate cortex, inferior frontal gyrus, posterior STS and dmPFC.

8. Activation in the right amygdala during Other Pain was negatively related to depression scores.

9. Anticipation of Pain in the Other [Pain Anticipation – NoPain Anticipation] activated the anterior insula bilaterally, and this activation was positively related to state empathy ratings and negatively related to scores on the coldheartedness subscale of the PPI.

The longitudinal investigation of the effects of compassion meditation training revealed that:

10. The meditation group did not increase, compared to the control group, in self-reported state or trait empathy.

11. The meditation group endorsed a greater increase, compared to the control group, in symptoms of stress (generalized anxiety) and a strong trend for symptoms of depression.

12. The meditation group did not differ from the control group in terms of the amount of money donated during the compassion induction.

13. Participants randomized to meditation had significantly higher odds of increasing their empathic accuracy.

14. The meditation group did not exhibit changes, with respect to the control group, in neural activity induced by the Self Pain task, although there was a trend suggesting that meditators had decreased activity in the right amygdala compared to the control group.

15. The meditation group did not exhibit enhanced neural activity, with respect to the control group, induced by the Other Pain task. However, the meditation group did have significant decreased activation, compared to the control group, in areas in the inferior temporal gyrus and superior temporal sulcus.

16. The meditation group had significant increases in neural activity, compared to the control group, during the Reading the Mind in the Eyes task in the inferior frontal gyrus bilaterally and the right caudate nucleus. There were trends in the same direction for activations in the left posterior STS and left fusiform gyrus.

17. Change in activity in the left IFG accounted for a significant amount of the change in empathic accuracy scores, and there was a trend for the right IFG. Changes in brain activity in the dmPFC, left posterior STS and right temporal pole also accounted for a significant amount of the change in empathic accuracy scores.

The investigation of the relationship between underlying personality variables and engagement with, and efficacy of, meditation revealed that:

18. The majority of participants (n = 16) reported enrolling in the study for non-meditation related goals. Only 3 participants solely reported meditation-related goals and 9 participants reported having both non-meditation and meditation-related goals.

19. None of the participants reported having any goals related to self-liberation (e.g. to increase compassion, spiritual gains). Fifteen participants reported goals related to self-regulation, 4 mentioned self-exploration goals and 13 reported non-meditation related goals (e.g. to promote and support health research).

20. Practice time was positively correlated with self-regulatory goals and negatively correlated with non-meditation related goals.

21. Self-exploration goals were negatively related to spiritual meaning scores, but positively correlated with depression scores.

22. Of those randomized to compassion meditation, those who dropped out scored significantly higher on the personal distress subscale of the IRI.

23. Spiritual meaning and personal distress were negatively related to class attendance.

24. Self-regulation goals accounted for a significant amount of the changes in empathic accuracy scores.

25. Non-meditation related goals were associated with lower empathic accuracy scores at Time 1.

26. Baseline levels of spiritual meaning moderated the effects of meditation on empathic accuracy, such that those who reported higher levels of spiritual meaning had less of a meditation-related increase in empathic accuracy.

27. Baseline levels of anxiety moderated the effects of meditation on empathic accuracy and brain activity during the empathic accuracy task, such that those who reported higher levels of anxiety had less of a meditation-related increase in empathic accuracy but more of a meditation-related increase in brain activity in the inferior frontal gyrus during the task.

28. Baseline brain activity in the left amygdala during Self Pain was inversely related to subsequent practice time.

29. Baseline brain activity in the right anterior insula during both Other Pain and during Other Pain Anticipation was positively related to subsequent practice time.

Significance

Importance for Anthropology

Social Production of Health: As stated in the introduction to this dissertation, one of the motivations for this research was to investigate the extreme variation in our ability to empathize with, and willingness to help, others. Questions such as these have spurred explorations within social psychology and social cognitive neuroscience into the contextual factors that impact empathy, compassion and altruism. However, another type of exploration has, up to now, largely been absent from the discussion of empathy and compassion. That is, very few investigations have asked how cultural factors and behaviors create variation in empathy and compassion, both across individuals (i.e. why do individual differ from one another?) as well as within a single individual (i.e. why does an individual behave differently in certain contexts or across time?). Given anthropology's expertise in this type of inquiry, the understanding of empathy and compassion will benefit from the introduction of an anthropological perspective.

Within anthropology, there has been a call for investigations into the ways in which culture impacts well-being, as Levin and Browner (2005) have urged anthropologists to study the "social production of human health"; that is, to "identify social conditions and practices that have contributed to positive physiological and psychological states in particular cultures, times and across time" (p. 746). While we are cautious not to characterize ours as a direct investigation of the ways in which a Tibetan meditation practice has affected (in the past) and currently affect Tibetan practitioners, we believe that it may inform such questions. More to the point, it is a study of the ways that a Tibetan meditation practice has been incorporated into an American context, and how it affects practitioners within such a context. As McMahan (2008) notes: "This "taking up" of selected elements of a tradition in the context of another tradition is how religions develop, adapt, change, and come to occupy different ideological niches from the ones they evolved in" (p. 116). For this reason, this investigation may prove all the more important as Buddhist meditation practices are increasingly incorporated into clinical, secular and religious settings in the United States.

Neuroanthropology: Recent reports have documented the rise of *neuroanthropology*, defined as "the study of the experiential and neurobiological aspects of cultural activity" (Domínguez Duque et al. 2010 p. 140). Dias (2010) discusses the unique niche that neuroanthropology holds:

> "The first thing that is important to bear in mind is that the authority of new fields of research relies on the premise that they introduce new lines of research, which cannot be perfectly characterized within the epistemological structure of a previously established field of research. Many anthropologists conduct research within natural science frameworks, such as social and evolutionary neuroscience, and up to this point there was no clear reason to consider that these works represent new epistemological traditions, since these studies are all committed to the questions, methods, and theories that are dear to the natural sciences. Hence, it follows that the emergence of neuroanthropology as a concept announcing something new implies that these studies introduce methods and questions of interest to the social sciences…" (p. 1).

While some of the hypotheses tested within this dissertation could clearly be tested in existing traditions of social cognitive neuroscience, a neuroanthropological framework opens up new questions to the study of meditation, such as: Who engages with meditation? What personality factors render meditation more or less beneficial? How important are preexisting goals and attitudes in meditation outcomes? That these questions are not being addressed in other studies of meditation imply that they are the subject matter of a new field: neuroanthropology.

What is more, with respect to the study of neuroanthropology, Campbell and Garcia (2009) note that cultural anthropology has resisted "reductionist" neuroscience, but document increasing explorations of "the brain processes underlying those capacities for culture that seem uniquely human" (p. 4) They point to the investigation of 'embodiment' as a lens through which neuroscience can deepen our understanding of the ways in which culture works on the brain to influence personal experience. They highlight the integral role of embodiment processes in cultural practices, specifically interoceptive processes related to activity in the anterior insula. It has been argued that interoception is a uniquely human cognitive ability (Craig 2003), and Campbell and Garcia posit that it "deserves special focus from neuroscientists and anthropologists alike" (p. 2) This dissertation contributes to this discussion, as it has investigated the ways in which a cultural behavior (meditation) modulates and is modulated by activity in interoceptive neural networks, as well as the ways in which these networks are related to human social cognition.

Importance for Social Cognitive Neuroscience

The research described in this dissertation contributes in several ways to the inquiries that engage the field of Social Cognitive Neuroscience. First, these data suggest that the use of dynamic, high quality video stimuli for investigations of empathy for pain yield a more nuanced and complete understanding, particularly with respect to anticipating another individual suffering a painful event. What is more, based on our study it appears that the brain activity related to the anticipation of pain may be a more sensitive indicator of trait and state empathy. Second, the empathy for pain study revealed that differences in neural activity are associated with variation in non-clinical levels of psychopathic personality traits. Third, the longitudinal investigation of compassion meditation revealed the ways in which a compassion-based meditative practice differentially affects aspects of the empathic response. Recent reviews have asked not only whether people can be trained to become more empathic, but also how individual differences in personality interact with training (e.g. Singer and Lamm 2009). To the best of our knowledge, ours is the first direct investigation of both of these questions and the results presented herein suggest that the compassion practice increases empathic accuracy, and that this benefit is greater for those who begin the practice in a less anxious state.

Importance for the study of meditation

This investigation demonstrates the importance of a longitudinal and controlled study design. First, the majority of the effects described here were identified with mixed design analyses, which are only possible with the study design employed here. In other words, had we not included a control group we likely would not have recognized many of the effects of compassion meditation training and practice. In addition, the longitudinal design allowed for the investigation of predictors of engagement with meditation, which revealed that empathy-related brain activity predicted practice time. It also enabled us to investigate how baseline personality variables as well as goals and attitudes moderated the effects of meditation training, and ours is the first study to show that baseline levels of anxiety render meditation less effective, in this case, with respect to changes in empathic accuracy.

Problems encountered

As with any large study, we encountered several unforeseen factors that introduced unwanted variability into this investigation and partially compromised our ability to draw definitive conclusions**.** Each will be discussed in turn.

Problems with qualitative assessment

The qualitative assessment that was used was derived from a previous study that investigated the goals of meditators attending a meditation retreat. However, in our study design we administered the instrument during the time 1 assessments, before subjects were informed of the group that they were randomized to. For this reason, some subjects expressed confusion as to how to answer the probe, “please talk about what specifically you hope to gain from the course you are about to take.” In hindsight, it may have been better to administer this instrument just prior to the first class when subjects had been made aware of their course assignment and had a chance to think about the course that they would take. In addition, it would have been fruitful to administer a follow-up questionnaire in which we asked subjects what they gained from the meditation course. This would have allowed us to better investigate how baseline personality features related to outcomes.

Problems with RtME task

High Pass Filter for RtME task: During fMRI pre-processing, it is common to employ one or two filters in order to increase the signal-to-noise ratio. A temporal high-pass filter (filters out signals with a frequency below the high pass setting) is often used to remove low-frequency drift, which can be caused by physiological noise as well as scanner-related noise. The BrainVoyager support documentation calls high-pass filtering both “one of the most important preprocessing steps” and “one of the more “dangerous” ones,” and the study design described within this dissertation is illustrative of both of these warnings (http://support.brainvoyager.com/functional-analysis-statistics/35-glm-modelling-a-single-study/23-users-guide-high-pass-filtering-of-design-matrix.html). Our lab traditionally used a high pass filter setting of 3 cycles, which means that any signal that occurs fewer than 3 times during a voxel's timecourse will be filtered out. This is thought to be a good setting because it removes signals that occur at a low frequency, such that only the high frequency events (i.e. stimulus –related signals) remain. This is the recommended cycle length for removing low-frequency physiological and scanner drift, and is particularly suited for an event-related design such as the one used for the Self pain and Other pain tasks. However, a block design such as the one used for the RtME task essentially produces one event for each block (albeit, a robust event). As such, if a study design employs three or fewer blocks of a single task, a high pass filter may remove some or all of the task-related signal. What is worse, if one uses three blocks of a control task and three blocks of the task of interest, the signal that is common to both tasks will remain (as it will essentially occur 6 times) while the signal that is unique to the task of interest will be filtered out. This is the reason that the Brainvoyager support documentation highly recommends that block designs include far more than 3 blocks of each task.

Given this, we employed a 2-cycle HPF which yielded results consistent with previous findings; however, qualitative assessments suggest that this setting rendered the final data far noisier, and it is possible that this less than optimal signal-to-noise ratio may have led to Type 2 errors.

Difference in task difficulty: As mentioned previously, we used a variation of the RtME task that has been used previously in the scanner. That is, in order to preserve the difficulty of the original, non-scanner task, we left the emotion task as a multiple-choice task with 4 choices rather than 2 as others have done (. In retrospect, this was a good decision as it is likely that this prevented a ceiling effect and allowed us to discover the trend for the interaction effect (group x time) suggesting that meditators performed more accurately after training.

However, our results would be more robust had we better matched the task difficulty for the control task. Instead, we kept the control task the same as has been used previously, and this meant that subjects only had to read two word choices (male and female) for each item. Moreover, while we varied the order of the gender choices so that subjects had to at least briefly read them, the control task required far less lexical processing than the emotion task. Not surprisingly, the results reflect this: subjects complete the control task significantly faster, and the strongest brain activations with the contrast [emotion – gender] are in left hemispheric language-related areas.

We recognized that this was a potential problem while designing the study, but could not think of an alternate control task that would best preserve all elements of the emotion task except for the cognitive empathy component. One alternative that may have yielded better results would have been a control task in which the subject was asked to judge the age of the person in the photographs. We could have given them 4 age words (spelled out to match semantic processing demands of emotion words) and these words would have been different for each item so that the subject always had to read all of the answer choices. Should we employ the RtME task in the future, I would pilot it using this control task.

Problems with empathy for pain task

Should have had them doing something: Upon asking subjects about their experiences in the scanner after they were done with the task, many subjects reported that it was difficult to stay alert during the empathy for pain task. Given the length of the task as well as the fact that the same stimuli were shown at times 1 and 2, it is quite understandable that their attention would wax and wane, particularly in the scanner environment where many people have trouble staying awake. This is another factor that we considered during study design, and decided that this was exactly the type of individual variation that we were trying to assess. In other words, we surmised that less empathic people would be more likely to become bored while watching others receiving painful stimulations, and that compassion meditation might moderate this effect. Moreover, we wanted this task to be one of implicit empathy rather than one in which the subject is prompted or primed to be empathic.

However, in hindsight the decision to use a passive, implicit empathy task may have introduced unintended variation simply because subjects likely had differing levels of arousal upon entering the scanner. For example, a subject who was sleep deprived may have had more trouble staying alert and thus paid less attention to the stimuli. For this reason, the task may have benefited from the introduction of some sort of required response from the subjects. For example, we could have had them push a button every time they saw a fixation cross. While this would not overtly prompt subjects to empathize (as would the request that they push a button every time they saw someone receive a pain stimulus, for example), it would have aided in helping subjects maintain attention throughout the task, as well as given us a metric of their attention. We contemplated doing this from the outset, but the scanner set-up made it extremely difficult to record button presses while playing a video and we opted to forgo this option. In hindsight, it may have been prefereable to include it..

Problems with state empathy rating: The state empathy ratings used in our task were modified from that used in Singer (Singer et al. 2004), which used a 5 point scale. Upon looking at the data, it appears that there is little variation due to such a small scale and it is possible that our results would have been more robust had we used a bigger scale (e.g. a ten point scale). Moreover, we used only one rating, which occurred after both the self and other pain tasks were complete. Had we have asked them throughout the task we would have acquired more data points, which may have resulted in more variation and thus more robust findings.

Where to go from here

There are several additional hypotheses that we would like to test with the existing data set from this study. First, we plan to do morphometric analyses using the structural scans from the 21 subjects who completed the entire study. With these analyses, we can determine whether subjects randomized to meditation show an increase in gray matter. In particular, we will look in the regions that show increased activation in the RtME task as a function of group, including the inferior frontal gyri and caudate. We will also do a whole brain, exploratory analysis to investigate whether any other areas change as a result of practicing compassion meditation. Diffusion weighted scans (DTI) were collected at Times 1 and 2 in order to look for changes in white matter that may result from meditation practice, but unfortunately the correct type of gradient field map was not acquired in the first cohort of subjects. Because only one average was collected, it will be important to correct for inhomogeneities using the field map, and thus, the DTI scans from the first cohort are likely not usable. Unfortunately, there is likely not enough power to definitively test our hypotheses with the remaining sample.

In addition to morphometric analyses, we also plan to incorporate data from other study collaborators. In particular, each subject in this study also wore an electronic audio recorder (EAR) for one weekend, which randomly recorded 50 seconds of ambient audio every 9 minutes. These data will be coded and quantified in terms of 1. Amount of laughter, 2. Amount of time spent with other people as opposed to alone, 3. Amount of we/us speech as opposed to I/me speech, and 4. Amount of compassionate language. With these data, we plan to ask two questions:

1. At time one (n=29), are laughter, sociality and prosocial speech related to a. differences in brain activity during the EFP and RtME tasks, b. differences in gray matter in areas thought to be related to social cognition (e.g. dmPFC, amygdala, or IFG)?
2. In the meditation group compared to the control group, do changes in laughter, sociality and prosocial speech correlate with changes in brain activity during the RtME task or to changes in gray matter?

To the best of our knowledge, this would be among the first studies to incorporate such ecologically valid, real-world behavioral data into a neuroimaging study.

We are also directly testing the hypothesis that changes to the oxytocin (OT) system are meditating the affects of meditation presented in this dissertation, specifically, the effects on empathic accuracy. While peripheral plasma OT levels are not perfectly correlated with levels in the central nervous system (Landgraf and Neumann 2004), plasma OT levels have frequently been shown to be related to behavior (Heinrichs et al. 2009). Thus, we will analyze plasma levels of OT collected both before and after the behavioral interventions, and we will use a correlation analysis to investigate whether changes in OT were related to changes in empathic accuracy or in brain activity during the RtME task.

Finally, it is worth speculating on how one could build upon this study in future studies. First, although we identified some interesting changes in participants randomized to the meditation group compared to the control group, our sample size may not have been adequate to find all changes that would result. With regards to the RtME task, we are currently administering the task to more participants (both meditation and control participants) in order to see whether our results will be strengthened with additional power. We are not administering this in the scanner, so we will not have fMRI data to go along with these empathic accuracy data. While we recognize that these participants are performing the task in a different environment than those described in this dissertation (in a hospital testing room rather than in the scanner), we feel that these results can be combined with our existing data since we are most interested in changes in scores.

Second, a follow-up study might compare the effects of compassion meditation to another type of meditation, for example, a non-analytical style such as mindfulness meditation. This would allow one to investigate whether the effects reported within this dissertation are related to specific aspects of compassion meditation or whether they are related to non-specific aspects of meditation. In fact, we are currently also administering the RtME task to a group of participants who have been randomized to a mindfulness and attention-based meditation practice, and it will be quite interesting to see if these participants show increased empathic accuracy compared to our control group.

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