5-2-2018

The Relationship between Executive Function and Empathy: An fMRI Investigation in Healthy Adults

Zinat Taiwo

Follow this and additional works at: https://scholarworks.gsu.edu/psych_theses

Recommended Citation
https://scholarworks.gsu.edu/psych_theses/184

This Thesis is brought to you for free and open access by the Department of Psychology at ScholarWorks @ Georgia State University. It has been accepted for inclusion in Psychology Theses by an authorized administrator of ScholarWorks @ Georgia State University. For more information, please contact scholarworks@gsu.edu.
THE RELATIONSHIP BETWEEN EXECUTIVE FUNCTION AND EMPATHY: AN FMRI INVESTIGATION IN HEALTHY ADULTS.

by

ZINAT TAIWO

Under the Direction of Sharee N. Light, PhD

ABSTRACT

Theoretical models propose that executive function may play a role in empathy (to “share in” the emotion of another); however, the specific contribution of executive function to emotional empathic processing remains unclear. This study utilized neuroimaging and neuropsychological measures to examine the relationship between individual differences in executive function abilities (working memory, inhibition, cognitive flexibility, verbal fluency) and empathic responding during an empathy induction paradigm in 20 healthy participants. fMRI analyses revealed that prefrontal brain regions may be important for empathic responding, with empathy for positive emotions recruiting a greater number of prefrontal regions. Prefrontal activation was associated with working memory, but not with other executive function abilities. Findings suggest that working memory abilities contribute to affective empathic responding.

INDEX WORDS: empathy, executive function, prefrontal cortex, working memory, inhibition, cognitive flexibility, verbal fluency
THE RELATIONSHIP BETWEEN EXECUTIVE FUNCTION AND EMPATHY: AN FMRI INVESTIGATION IN HEALTHY ADULTS.

by

ZINAT TAIWO

A Thesis Proposal Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Arts in the College of Arts and Sciences Georgia State University 2017
THE RELATIONSHIP BETWEEN EXECUTIVE FUNCTION AND EMPATHY: AN FMRI INVESTIGATION IN HEALTHY ADULTS.

by

ZINAT TAIWO

Committee Chair: Sharee N. Light

Committee: Erin Tone
Jessica Turner

Electronic Version Approved:

Office of Graduate Studies
College of Arts and Sciences
Georgia State University
May 2018
DEDICATION

I would like to dedicate this thesis to my grandmother who gave everything to educate her children and create a better future for all subsequent generations. I am eternally grateful.
ACKNOWLEDGEMENTS

Firstly, I would like to express my deepest appreciation to my committee chair and academic advisor, Dr. Sharee Light, for her guidance and support throughout this process. I would also like to thank Drs. Erin Tone and Jessica Turner for their feedback and guidance. Finally, I would like to thank Dr. Matt Bezdek who provided immeasurable guidance and training in fMRI analysis. This work was supported by a CABI seed grant Research Scholar Grant, awarded to Dr. Sharee Light and a GSU 2CI Neuroimaging Fellowship awarded to Zinat Taiwo.
# TABLE OF CONTENTS

ACKNOWLEDGEMENTS ................................................................................................. v

LIST OF TABLES ........................................................................................................... viii

LIST OF FIGURES ......................................................................................................... ix

LIST OF ABBREVIATIONS ........................................................................................... x

1 INTRODUCTION ......................................................................................................... 1

1.1 The Construct of Empathy ...................................................................................... 3

1.1.1 Empathy Subtypes ......................................................................................... 7

1.2 Executive Function and Empathy ........................................................................... 10

1.2.1 The Role of the Prefrontal Cortex .................................................................. 12

1.3 Specific Aims and Hypotheses ............................................................................. 15

1.3.1 Specific Aim 1 ............................................................................................... 15

1.3.2 Specific Aim 2 ............................................................................................... 16

2 METHODS ................................................................................................................ 17

2.1 Participants and Procedure .................................................................................... 17

2.2 Measures ............................................................................................................... 18

2.2.1 Empathy Induction Paradigm ....................................................................... 18

2.2.2 Executive function measures ........................................................................ 20

2.3 Image Acquisition and Parameters .................................................................... 22

2.4 Neuroimaging Processing Steps ......................................................................... 23
2.4.1 Preprocessing of fMRI data ................................................................. 23
2.4.2 Individual level processing of fMRI data ........................................... 23
2.4.3 Group Level processing of fMRI data ................................................. 24
2.5 SPSS statistical analysis ......................................................................... 26

3 RESULTS ........................................................................................................ 26
3.1 Demographic Information ........................................................................ 26
3.2 Data Preparation and Preliminary Analyses ............................................. 27
3.3 Specific Aim 1 ............................................................................................ 28
3.4 Specific Aim 2 ............................................................................................ 31

4 DISCUSSION .................................................................................................... 37

REFERENCES ................................................................................................... 46

APPENDICES ..................................................................................................... 61
Appendix A ........................................................................................................ 61
Appendix B ........................................................................................................ 63
LIST OF TABLES

Table 2.1 Average empathy ratings (N=20) ........................................................................... 20

Table 3.1 Regression analyses for cognitive measures performance predicting BOLD response in the SFG (BA 10) ........................................................................................................ 30

Table 3.2 Locations and MNI coordinated of peak clusters of BOLD activity in prefrontal brain regions ........................................................................................................................................... 33

Table 3.3 Regression analyses for cognitive performance predicting BOLD response in the differentially activated prefrontal brain regions.......................................................... 35

Table 3.4 Regression analyses for cognitive performance predicting state empathic response during the empathy induction paradigm................................................................. 36
LIST OF FIGURES

Figure 1.1 Social Neuroscience Model of Empathy (Decety & Lamm, 2006) ............... 5

Figure 2.1 Schematic diagram of an experimental run of the empathy induction paradigm ................................................................. 19

Figure 2.2 State empathy rating scales .................................................................................. 20

Figure 3.1 Commonly Activated Brain Regions .................................................................... 29

Figure 3.2 Working memory performance is associated with BOLD response in SFG (BA 10) ............................................................................................................ 31

Figure 3.3 Prefrontal brain regions with greater BOLD response during empathic happiness eliciting video clip ..................................................................................... 32

Figure 3.4 Working memory performance is associated with BOLD response in SFG (BA 8) during empathic happiness eliciting video clips ............................................ 34

Figure 3.5 Category fluency performance is associated with mean self-report empathic concern during the empathy induction paradigm ......................................................... 37
# LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC</td>
<td>Anterior cingulate cortex</td>
</tr>
<tr>
<td>AI</td>
<td>Anterior Insula</td>
</tr>
<tr>
<td>BCa</td>
<td>Bias corrected and accelerated</td>
</tr>
<tr>
<td>BOLD</td>
<td>Blood oxygenation level dependent</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>DLPFC</td>
<td>Dorsolateral prefrontal cortex</td>
</tr>
<tr>
<td>DMPFC</td>
<td>Dorsomedial prefrontal cortex</td>
</tr>
<tr>
<td>fMRI</td>
<td>Functional magnetic resonance imaging</td>
</tr>
<tr>
<td>FPC</td>
<td>Frontopolar cortex</td>
</tr>
<tr>
<td>MPFC</td>
<td>Medial prefrontal cortex</td>
</tr>
<tr>
<td>PFC</td>
<td>Prefrontal cortex</td>
</tr>
<tr>
<td>VLPFC</td>
<td>Ventrolateral prefrontal cortex</td>
</tr>
<tr>
<td>VMPFC</td>
<td>Ventromedial prefrontal cortex</td>
</tr>
</tbody>
</table>
1 INTRODUCTION

Executive function encompasses the higher-level processes necessary to coordinate, control, and modify goal-directed behavior (Diamond, 2013). Historically, research has focused on understanding the mechanisms that support executive functions (e.g., attention and working memory). Recently, however, there has been increased focus on the interplay of executive function and emotion (Gray, Braver, & Raichle, 2002). It is theorized that this higher-level ability is particularly necessary for the inhibition, reappraisal, and regulation of emotionally evocative information (Mueller, 2011). Neurobiological research has provided support for an integrative relationship between emotion and cognition, with evidence suggesting that brain structures responsible for both reasoning and emotion are interconnected and work in concert to facilitate social decision-making (Beauchamp & Anderson, 2010). While most studies have focused on the influence of emotion on executive function, there is utility in understanding how executive function influences emotional processes (Schmeichel & Tang, 2015).

Emotion regulation, the process by which emotional responses are evaluated and modified (Koole, 2009), has been shown to be associated with several core executive functions (e.g., inhibition of responses, attentional control) that become engaged in emotionally demanding contexts (Tottenham, Hare, & Casey, 2011). For example, von Hippel and Gonsalkorale (2005) reported that inhibition, the ability to suppress task-irrelevant information, was associated with the suppression of socially inappropriate expressions of emotions. In this study, non-Asian participants were asked by a Chinese experimenter to taste a chicken foot, which was stated to be a national
dish of China. Participants who performed better on the Stroop task, a measure of inhibitory ability, made fewer negative facial and verbal responses. This finding suggests that higher inhibitory control related to better ability to regulate emotion (i.e., suppress aversion).

Further, findings from neuroimaging studies indicate that enhanced frontostriatal connectivity is associated with executive function performance, particularly subserving emotion regulation skill. Specifically, self-reported regulation “success” (i.e., an individual’s perception of their ability to successfully down-regulate negative emotion when instructed) is associated with both relative increases in nucleus accumbens/ventral striatum-ventrolateral prefrontal cortex activity, and decreases in amygdala-ventrolateral prefrontal cortex activity, during regulation periods (Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). Thus, brain regions typically involved in personal positive and negative affect, the nucleus accumbens/ventral striatum and amygdala, respectively, are known to also be involved in cognitively mediated emotion change.

Failures to adaptively regulate emotional responses are a feature of common neurological and psychiatric disorders (e.g. Major Depressive Disorder), and can lead to difficulties in interpersonal engagement and social interaction (Gross & Muñoz, 1995; Kimhy et al., 2012; Levenson, Sturm, & Haase, 2014). In other words, deficits in empathy are common in populations with these conditions and can result in socially maladaptive behaviors (Decety & Moriguchi, 2007; Derntl et al., 2009; Eslinger, Moore, Anderson, & Grossman, 2011; Schreiter, Pijnenborg, & Aan Het Rot, 2013; Yeh & Tsai, 2014). For example, when faced with another’s negative emotion, individuals with
internalizing disorders can have a maladaptive self-oriented response (i.e., personal distress) rather than an adaptive other-oriented empathic response, characterized by poor emotion regulation, which can lead to over-arousal and ultimately social withdrawal and isolation (Tone & Tully, 2014). In fact, Eisenberg (2000) suggests that the ability to effectively regulate one’s emotions distinguishes between appropriate (i.e., empathic concern) and maladaptive empathic responding (i.e., personal distress). Individuals who effectively regulate their emotional arousal in response to the perceived distress of another do not experience personal distress but rather tend to experience empathic concern and exhibit prosocial behavior. Such individual differences in empathic response based on emotion regulation makes empathy an ideal behavior to study in relation to the interaction between cognition and emotion.

1.1 The Construct of Empathy

Empathy plays a critical role in human interpersonal engagement and social behavior. The ability to share in the emotional state of another enables one to better understand the feelings and motivations of others during social interaction and ultimately strengthens social bonds. Empathy is considered a multifaceted, multidimensional construct (Zaki & Ochsner, 2011) that generally refers to the ability to vicariously share in the emotional life of others resulting from the contemplation of their emotional state (Light et al., 2009). There is general consensus among modern researchers that distinct, yet interrelated, mechanisms contribute to the experience of affective (i.e., feelings) and cognitive (i.e., thoughts) aspects of empathy: a) affective sharing, b) self-awareness, c) mental flexibility/perspective taking, and d) regulatory
processes (de Vignemont & Singer, 2006; Decety & Moriguchi, 2007; Goubert, Craig, & Buysse, 2011).

In their social neuroscience model of empathy (Figure 1.1), Decety and Lamm (2006) propose that top-down regulation, through executive function, modulates automatically activated affective sharing, which allows for flexible responding and leads to an appropriate empathic response in reaction to others’ affective states. They suggest that the cognitive capacity for, and emotion regulation of, empathy may depend on executive function. Evolutionary accounts suggest that the impulse for empathic responding to offspring is adaptive and contributes to genetic fitness (Decety, Norman, Berntson, & Cacioppo, 2012). However, the generalization of this empathic response to any target has advanced over the generations and is no longer necessarily tied a biological drive to nurture one’s young. Decety and Lamm suggest that this advanced level of social cognition may have emerged due to the progressive parallel evolution of executive function and prefrontal cortex.
Although modern definitions of empathy incorporate both bottom-up and top-down processing, early models solely attributed empathy (particularly empathy for physical pain) to more automatic processes. For example, according to the perception-action model (Preston & de Waal, 2002), the representation of another’s emotional state is automatically activated (e.g., perceptual coupling), given that the empathizer focuses attention on the other person. This representation results from the association of a specific stimulus with an internal representation (e.g., a sad face equates to feeling sad); therefore, once the stimulus is perceived, it automatically triggers the associated autonomic and somatic responses, leading to an empathic experience. However, contemporary research suggests that although empathy might seem to occur automatically, outside of conscious and effortful processing, it can be inhibited,
controlled, and modulated by top-down mechanisms (Bufalari & Ionta, 2013; Zaki, 2014).

Empirical findings provide evidence for a role of executive function in empathy (Eslinger, 1998; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009). One early lesion study reported an inverse relationship between empathy scores and cognitive inflexibility, indexed by perseverative errors on the Wisconsin Card Sorting task (Grattan & Eslinger, 1989). This study provided early support for the idea that flexible thinking may be an important underlying cognitive skill involved in empathy. Since then, cognitive flexibility, the ability to adjust thinking, behavior and/or attention in order to perceive and process changing goals and environmental stimuli (Scott, 1962), has been implicated as a necessary component of empathy (Bernhardt & Singer, 2012; Gonzalez-Lienres, Shamay-Tsoory, & Brune, 2013; Lamm & Majdandzic, 2015).

Further support for this hypothesis comes from research studies that show that empathy can be influenced by altering attentional demands. For example, Gu & Han (2007) found blunted neural response in the anterior cingulate cortex (ACC), anterior insula (AI), and the lateral frontal cortex when participants performed a counting task while viewing pictures of hands in painful situations relative to simply focusing attention on the intensity of the other’s pain. They interpreted this finding as evidence that empathy for physical pain is weakened when attentional demands are increased. Similarly, Morelli and Lieberman (2013) also reported diminished activation in empathy-related brain regions under enhanced attentional load conditions, remembering an 8-digit number while looking at emotionally-evocative images. Taken together, these results suggest that increasing cognitive demands may disrupt empathic responding.
Models of executive function posit that higher-order processing depends on the demands of the task. Specifically, once automatic processes are no longer sufficient, executive function kicks in to modify and guide goal-directed behavior (Miller & Wallis, 2009). Consequently, in line with theoretical accounts, it is reasonable to expect that executive function processes would contribute the most to more evolutionarily complex empathic responses, i.e., empathy for increasingly abstract emotions likely follow the evolution of the evolution of prefrontal regions - such as emotional pain versus physical pain, and empathy for positive emotions.

Despite theoretical models and empirical results suggesting a role for higher-level executive control in empathic processing, the nature of the role of executive function in empathic processing remains unclear. Decety & Lamm's (2006) model suggests that executive function broadly plays a role in empathic responding. For example, an essential aspect of empathy, maintaining a clear distinction between the self and another may rely on working memory, an executive function (Goodkind, 2010). Further, adopting the perspective of another and limiting over-arousal may be associated with executive inhibition (Decety & Hodges, 2006). However, these ideas have not been systematically tested. Therefore, within this social neuroscience framework of empathy, the current study examined the relationship between executive function abilities and empathic responding.

1.1.1 Empathy Subtypes

Individuals can experience empathy for a wide variety of emotional states such as pain, fear, sadness, happiness, or lust (Perry, Hendler, & Shamay-Tsoory, 2012; Singer, 2006). Light and Zahn-Waxler (2011) emphasized the heterogeneity of
empathy, proposing the existence of negative and positive valence empathy. They made a distinction between empathic concern and empathic happiness, two subtypes of empathy. Empathic concern is defined as the ability to vicariously share someone else’s negative emotions (e.g., pain, sadness) while empathic happiness is sharing in the positive emotions of others (e.g., happiness, joy). Both empathic happiness and empathic concern are associated with feelings of goodwill, and may lead to prosocial behavior.

Although few studies have focused on empathy for both positive and negative emotions within the same study, some physiological and imaging studies provide evidence that they are neurally distinguishable processes. For example, Light and colleagues (2015) identified distinct electromyographical signatures for empathic concern and empathic happiness.

In an fMRI study, Morelli, Rameson, and Lieberman (2014) found that empathy for physical pain, relative to happiness, resulted in increased activity in regions such as the anterior insula (AI), that have been associated with personal negative affect (Lindquist, Satpute, Wager, Weber, & Barrett, 2016). In contrast, empathy for happiness, relative to physical pain, involved greater activation in regions linked to mentalizing (i.e., MPFC and DMPFC), and the VMPFC-which is associated with personal positive affect (Roy, Shohamy, & Wager, 2012). Notably, this study did not report ACC and AI activations, which are considered core empathy regions, during empathy for positive emotion. Research suggests that overlapping brain regions are activated when an individual experiences an emotion and when observing another experience the same emotion (Singer et al., 2004), which might explain the affective
congruence evident in the aforementioned studies. Additionally, the differential prefrontal activation observed in the few studies conducted to date across empathy for positive emotion versus physical pain may lend support to the premise that empathy for physical pain has a stronger evolutionary adaptive value (Jackson, Meltzoff, & Decety, 2005). Empathy for positive emotion, in contrast, is evolutionarily newer and thus requires additional contextual processing to be understood, resulting in broader engagement of prefrontal regions (Zaki, Weber, Bolger, & Ochsner, 2009).

The Neural Basis of Empathy

Neuroimaging studies examining brain regions essential for empathy for physical pain (by far the most well studied form of empathy) suggest an important role for the anterior insula (AI) and the anterior cingulate cortex/midcingulate cortex (ACC/MCC). In a meta-analysis, Fan and colleagues (2011) identified the dorsal ACC (dACC)/anterior MCC (aMCC) and the bilateral AI extending to the inferior frontal gyrus (IFG), as core brain regions involved in empathy for physical pain. Notably, studies based on empathy for other’s negative affective states, such as anxiety, disgust, and social exclusion, have consistently reported AI and ACC/MCC activations (Jabbi, Bastiaansen, & Keysers, 2008; Masten, Morelli, & Eisenberger, 2011; Prehn-Kristensen et al., 2009). In contrast, a study examining neural correlates of empathy for positive emotions did not find AI or dACC activations; rather they identified significant activation in the ventromedial prefrontal cortex (Mobbs et al., 2009).

A recent meta-analysis of neuroimaging studies on vicarious reward (i.e., empathy for positive events) reported common AI and dACC activations, but more consistently found activation in prefrontal regions associated with mentalizing - the
ability to infer the mental states of others (Morelli, Sacchet, & Zaki, 2015). An earlier study by Morelli and colleagues (2013) suggested a core role of prefrontal regions in empathy for both positive and negative emotions. Overall, evidence from the literature suggests an empathy neural circuit that involves both cortical (e.g., prefrontal cortex) and subcortical (e.g., insula, amygdala) regions.

To better understand the neural regions essential for higher-order empathic processing, the current study sought to address these discrepancies by studying both empathy for positive and negative emotions (but not physical pain) utilizing an ecologically valid empathy induction paradigm consisting of video clips, which included both visual and contextual stimuli.

1.2 Executive Function and Empathy

Executive functions are a set of inter-related abilities responsible for goal-directed behavior (Banich, 2009). In their review, Best, Miller, and Jones (2009) argue that executive function primarily includes inhibition, working memory, shifting and planning (e.g., problem solving). Similarly, one prominent theory, derived through latent factor analyses, posits that executive function can be characterized by at least three factors: a) a switching or shifting factor (e.g., shifting between different tasks and representations), b) an inhibition factor (e.g., inhibiting prepotent responses) and c) an updating factor (e.g., working memory operations such as maintenance and updating of relevant information) (Miyake et al., 2000). Using these theories as a framework, this study considered and measured working memory, inhibition and cognitive flexibility as core executive function processes.
Working memory is the ability to temporarily hold and manipulate information for a short period of time (Baddeley, 2012). Social interaction is guided by the ability to maintain and update information as social cues change (Meyer, Spunt, Berkman, Taylor, & Lieberman, 2012), suggesting a critical role of working memory in empathic processing. Tasks of working memory were included in this study, given the potential necessity of working memory for maintaining/manipulating the internal representation of one’s own and the target’s emotional state on an ongoing basis during the successful empathic process. Inhibition, the ability to suppress task-irrelevant information (Friedman & Miyake, 2004), supports flexible and goal-directed behavior in social environments (Verbruggen, Best, Bowditch, Stevens, & McLaren, 2014). Inhibition tasks were included to capture the influence of the potential role of suppressing one’s own perspective in favor of the target’s perspective as it relates to successful empathic processing. Cognitive flexibility, the ability to switch between mental processes to generate appropriate behavioral responses (Dajani & Uddin, 2015), is important for monitoring incoming information, considering others’ perspectives and adjusting perception as situational demands change (Ionescu, 2012). Tasks of cognitive flexibility were included in this study to test the idea that empathic processing involves an ability to switch between thinking about one’s own feelings or emotional state and that of the target’s.

Decety and Svetlova (2012) stressed the importance of complex forms of cognitive abilities such as language in the evolution of empathy. Infants’ ability to attend to another’s affect, an early precursor of empathic responding, is related to later language abilities (Hutman, Rozga, DeLaurentis, Sigman, & Dapretto, 2012; Soto-Icaza,
Aboitiz, & Billeke, 2015). Other work has shown that verbal ability is associated with emotion recognition and understanding skills (De Stasio, Fiorilli, & Di Chiacchio, 2014; Reed & Steed, 2015), and may be related to empathic abilities (Jolliffe & Farrington, 2006).

Verbal fluency is the ability to generate words quickly based on specified criteria, whether phonemic (by letter) or semantic (by categories). Measures are verbal fluency tests that capture both verbal ability and executive functioning skill. Particularly, phonemic fluency is considered more of an executive task, requiring a number of executive abilities, such as working memory, inhibition, and generation of ideas; while semantic fluency is more of a measure of language skills (Baldo, Schwartz, Wilkins, & Dronkers, 2006). Thus, verbal fluency was included in this study to capture the influence of executive aspects of language generation on empathic processing.

1.2.1 The Role of the Prefrontal Cortex

Researchers propose that executive function relies on a collection of anatomically independent yet functionally interacting brain regions (e.g., parietal cortex and subcortical regions), with the prefrontal cortex playing a central role (Alvarez & Emory, 2006; Lovstad et al., 2012; Stuss & Alexander, 2007). The prefrontal cortex (PFC), the anterior portion of the frontal lobe, has reciprocal connections with major sensory and motor cortical systems, as well as subcortical regions, which enables it to play a role in the integration of diverse information, and modulation of lower-order processes needed to guide goal-directed behavior (Miller & Cohen, 2001). Functional interactions among these regions allow for the use of executive function processes in
the evaluation, modification, and execution of socio-emotional behaviors, such as empathy (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004).

The dorsolateral prefrontal cortex (DLPFC; BA 9, 46), is implicated in attentional control, retrieval and manipulation of relevant information (TANJI & HOSHI, 2008), active maintenance of information in working memory (GILBERT & BURGESS, 2008; MULLER & KNIGHT, 2006), maintenance and shifting of sets/task switching (BUNGE, 2004), verbal and design fluency, and planning and problem solving (DUKE & KASZNIAK, 2000; HEDDEN & GABRIELI, 2010; LEH, PETRIDES, & STRAFELLA, 2010). In short, the DLPFC is a core prefrontal region associated with executive function. Researchers have found that patients with DLPFC damage have difficulties with perspective taking (Grattan, Bloomer, Archambault, & Eslinger, 1994), recognizing emotions from facial expressions (Shamary-Tsoory, Tomer, Berger, & Aharon-Peretz, 2003) and using social cues to make interpersonal judgements (Mah, Arnold, & Grafman, 2004). In addition, Shamay-Tsoory and colleagues (2009) found that DLPFC lesions were associated with decreased empathic accuracy. Clearly, the DLPFC appears to be an important prefrontal region that may subserve executive involvement in empathy.

The ventrolateral prefrontal cortex (i.e. VLPFC, IFG; BA 46/47) has been associated with working memory, emotion regulation (Ochsner et al., 2012), inhibition, and anhedonia (see LIGHT et al., 2011). This region becomes active when a pre-potent response must be inhibited, such as when down-regulating negative emotion, and greater activity in this region is associated with greater pleasure capacity in individuals who are depressed.
The frontopolar prefrontal cortex (i.e. FPC; BA 10), the anterior-most portion of the prefrontal cortex, has been found to be related to the updating process of working memory (Van der Linden et al., 1999), the coordination of two simultaneously ongoing tasks (Braver & Bongiolatti, 2002; Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999), task-switching and attentional set-shifting (Braver, Reynolds, & Donaldson, 2003; Pollmann, 2001). In a review, Christoff and Gabrieli (2000) suggests that in contrast to the DLPFC, which is associated with externally generated information, the FPC may underlie the active processing and monitoring of internally generated information. This region may thus be especially important for updating working memory operations during empathic processing because individuals must continuously compare new and prior information in order to maintain appropriate information in working memory (Collette et al., 2005). Koechlin and Hyafil (2007) posit that the lateral prefrontal cortex and frontopolar cortex functionally interact via reciprocal connections, with the DLPFC and VLPFC actively representing the ongoing task-set and selecting the appropriate task rules to execute the task at hand, while the FPC enables previously selected task sets to be maintained in a pending state for subsequent automatic retrieval and execution upon completion of the ongoing one.

Each of these prefrontal regions was of particular interest in the current study. The core hypothesis was that empathic happiness would relate to a broad swathe of prefrontal activation (i.e. more, and higher-order, prefrontal regions would be involved) given later evolutionary development, whereas empathy for emotional pain would relate to a more circumscribed region or set of regions of prefrontal activation given its likely earlier evolutionary emergence.
1.3 Specific Aims and Hypotheses

Despite research implicating top-down processing in empathy, questions remain regarding the specific executive mechanisms associated with vicarious affective processing. The current study addressed this gap in the literature by examining the relationship between executive function abilities and affective empathic responding, measured by brain activation and self-report, during an empathy induction paradigm. Given all of the above considerations, this study addressed two main questions: 1) Are executive function abilities related to empathic responding? 2) Does executive function explain differences in prefrontal activation across empathy subtypes?

1.3.1 Specific Aim 1

The first aim of this study was to investigate how performance on executive function measures was related to commonly activated brain regions across empathy subtypes, during an empathy induction paradigm. First, brain regions commonly activated across empathy subtypes during the empathy induction paradigm were determined. Next, the relationship between executive function abilities and BOLD response in identified prefrontal brain region(s) was examined.

Aim 1 Hypothesis A – Conjunction Analysis

We expected common BOLD activation in certain prefrontal regions, such as the DLPFC, during both empathic concern and empathic happiness conditions of the empathy induction paradigm.

Aim 1 Hypothesis B – Common BOLD Activation and Executive Function
In line with Decety and Lamm’s theoretical model, we expected that better performance on measures of executive function would be associated with greater BOLD activation in prefrontal regions identified in the conjunction analysis.

1.3.2 Specific Aim 2

The second aim of this study was to examine the relationship between executive function abilities and each empathy subtype individually, measured by both BOLD activation and self-report during the empathy induction paradigm. First, the current study examined differential patterns of prefrontal BOLD activation across empathy subtypes during the empathy induction paradigm. Next, we investigated the relationship between each uniquely activated prefrontal brain region and executive function, to test whether executive function would explain the differential prefrontal BOLD activation across empathy subtypes. Finally, the relationship between executive function abilities and self-reported empathic concern and empathic happiness during the empathy induction paradigm was examined.

**Aim 2 Hypothesis A: Differential Prefrontal Activation**

It was expected that there would be a significant difference in BOLD activation in certain prefrontal regions, specifically the FPC and VLPFC, with empathic happiness conditions eliciting greater response in these prefrontal regions relative to empathic concern conditions.

**Aim 2 Hypothesis B: Differential Prefrontal Activation and Executive Function**

It was expected that greater BOLD activation in prefrontal regions, such as the FPC and VLPFC, during empathic happiness conditions relative to empathic concern conditions would relate to executive function performance.
Aim 2 Hypothesis C: Self-report Empathic Response and Executive Function

It was expected that there would be a positive relationship between better executive function task performance and self-reported empathic happiness or empathic concern. However, we expected the relationship to be stronger for empathic happiness relative to empathic concern.

2 METHODS

2.1 Participants and Procedure

Participants were recruited primarily using advertisements that included a short study description and brief eligibility criteria. Interested individuals were asked to contact the lab via an email address. Upon contacting the lab, potential participants were provided a detailed explanation of the study (i.e., they will undergo fMRI to study how the brain processes emotion while watching video clips and complete neuropsychological assessments to test their cognitive abilities) and informed about the compensation of $25 per hour. A member of the research team completed a study eligibility screening form, medical history questionnaire, and MRI safety screening form with each participant over the phone. Participants were included if they were 18 years or older, right-handed, had normal or corrected to normal vision and were native English-speakers. Individuals who were not free of neurological and psychiatric disorders and at risk for undergoing an MRI were excluded. A total of 20 individuals participated in the study.

All procedures were reviewed and approved by the Center for Advanced Brain Imaging (CABI) Institutional Review Board. Participants completed all study procedures
in one visit, lasting no longer than 3 hours, at the Georgia State University/Georgia Institute of Technology Center for Advanced Brain Imaging. Upon each participant’s arrival, a graduate student explained the study procedures and obtained informed consent. Participants were informed that the study was voluntary and they could withdraw at any time without penalties. Next, the participants were administered a battery of neuropsychological tests and had an MRI scan while they completed an empathy induction paradigm. Following the scan, participants were debriefed and compensated.

2.2 Measures

2.2.1 Empathy Induction Paradigm

This study utilized a previously validated MRI-based empathy induction paradigm (Light et al., 2015) consisting of video clips from an episode of the television show *Extreme Makeover: Home Edition*. This episode depicts an African–American woman, Alice, and her family whose home was ruined by a devastating and rare flood. The beginning of the episode shows the viewer why the family needs a remodeled home. This first half of the episode elicits peak negative emotions such as sadness (i.e., empathic concern). In the second portion of the show, the design team reveals the remodeled home to the family. This last half elicits peak happiness and joy (i.e., empathic happiness). A neutral clip is embedded between the empathic concern and empathic happiness eliciting video clips. All video clips are presented in sequential order to maintain the integrity of the story, strengthening the ecological validity. The paradigm was administered using Psychopy software and imaging data was collected using a Siemens 3T MRI scanner. Each run during the empathy paradigm consisted of
a fixation screen, then the empathy inducing or neutral video clip, followed by the empathy rating scales (Figure 2.1).

![Schematic diagram of an experimental run of the empathy induction paradigm](image)

**Figure 2.1 Schematic diagram of an experimental run of the empathy induction paradigm**

*State Empathy Ratings.* Participants were asked to rate their emotional reactivity immediately following each video clip to determine the subjective degree to which each video clip evoked an empathic emotional response. Participants were instructed to respond by pressing the corresponding button on the a MRI-compatible button box. The participants rated the presence or absence of empathic concern and empathic happiness on a continuous scale from 1 to 4 (Figure 2.2) with higher ratings indicating greater empathic response. Empathic concern and empathic happiness ratings following the video clips were used as regressors of interest in fMRI data analysis. For fMRI analysis, the two video clips with the highest empathic response ratings during each condition were concatenated (see Table 2.1). For statistical analyses, a mean
empathic concern and mean empathic happiness score were derived and used as dependent variables.

Figure 2.2 State empathy rating scales

Table 2.1 Average empathy ratings (N=20)

<table>
<thead>
<tr>
<th>Clip type</th>
<th>Empathic concern</th>
<th>Empathic happiness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>SD</td>
</tr>
<tr>
<td>Empathic Concern</td>
<td>2.15</td>
<td>1.14</td>
</tr>
<tr>
<td>Empathic Concern</td>
<td>3.00</td>
<td>1.17</td>
</tr>
<tr>
<td>Neutral</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Empathic Happiness</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Empathic Happiness</td>
<td>1.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

2.2.2 Executive function measures

Working memory. The digit span subtest of the Wechsler Adult Intelligence Scale, 4th edition (WAIS-IV) is an untimed measure consisting of three conditions, digit span forward, backwards and sequencing. The internal consistency of this measure is .84 (Wechsler, 2008). Age-normed digit backward scores, derived from the normative sample of the WAIS-IV, was used as a measure of working memory and as an independent variable in statistical analyses. In the digit span backward condition, a
sequence of numbers of increasing length were read aloud to the participants. Participants were asked to repeat the sequence in reverse order. The task got progressively more difficult as the length of the number sequence increased across trials. Performance was based on the total number of accurate sequences repeated backwards.

**Inhibition.** The Delis-Kaplan Executive Functioning System, D-KEFS, (Delis, Kaplan, & Kramer, 2001) Color Word Interference Test (CWIT) is a timed task, based on the popular Stroop task, which consists of four conditions: color naming, word reading, inhibition, and inhibition/switching. This measure has demonstrated a split-half reliability of .62–.86 (Delis et al., 2001). Age-normed inhibition condition scores, derived from the normative sample of the DKEFS, were used as a measure of inhibition and an independent variable in statistical analyses. In the inhibition condition, a page with incongruent ink colors and words was presented and participants were asked to name the color of the ink the words were printed in rather than read the words. Performance on this task was based on the completion time.

**Cognitive Flexibility.** The category switching condition of the DKEFS verbal fluency test was used as a measure of cognitive flexibility and an independent variable in this study. The category switching condition required participants to alternate between two semantic categories (fruit and piece of furniture). This condition assesses the extent to which individuals can flexibly shift between or alternate between thinking about and generating responses from two different semantic categories. The DKEFS category switching condition has a split-half reliability of .37 - .68 (depending on age).
Verbal Fluency. The letter fluency and category fluency conditions of the DKEFS verbal fluency task was used to measure phonemic and semantic fluency, respectively. Letter fluency subtest has a split-half reliability of .68 - .90 (depending on age) and a test-retest reliability of .80. Category Fluency subtest has a split-half reliability of .37-.68 (depending on age) and a test retest reliability of .79 (Homack et al., 2005). In the letter fluency condition, participants were asked to name as many words as quickly as possible that begin with a specified letter, with three separate letter conditions (F,A,S). Phonemic (letter) fluency assesses the ability to conduct a strategic search through lexical/phonological memory. In the category fluency condition, participants had to generate as many different words as possible from specified semantic categories (animals and boy’s names). Semantic (category) fluency requires a search through conceptual or semantic memory. Age-normed letter and category scores were each derived from the normative sample of the DKEFS and were used as independent variables in statistical analyses. Performance was based on the number of words generated in a 60 second period.

2.3 Image Acquisition and Parameters

All MRI data was acquired on a Siemens 3T Magnetom Trio MRI scanner. Participants were outfitted with protective earplugs to reduce scanner noise. A high-resolution T1 structural scan (3D MPRAGE, TI = 850 ms, field of view= 256ms, flip angle = 9°, 1 mm isotropic resolution) was acquired before the start of the paradigm, and was used for anatomical registration. Functional images were obtained using a
whole-brain echo-planar imaging sequence sensitive to blood oxygenation level-dependent (BOLD) signals (transverse orientation, TR = 2,000 ms, TE = 30 ms, flip angle = 90°, field of view = 204 mm) of 37 interleaved slices with 3 mm isotropic resolution and a 17% gap.

2.4 Neuroimaging Processing Steps

fMRI data analysis was conducted using the Analysis of Functional Neuroimages (AFNI) software from the National Institutes of Health, http://afni.nimh.nih.gov/afni, (Cox, 1996). Neuroimaging processing consisted of three separate steps: preprocessing, individual level, and group-level processing, which are outlined below in detail.

2.4.1 Preprocessing of fMRI data

The following preprocessing steps were applied to the data using the AFNI proc program: 1) truncated spikes in each voxel’s time series, 2) slice timing corrections were made to the EPI images, 3) aligned EPI to anatomical anatomy, 4) warped anatomy to MNI standard space, 5) spatial smoothing was completed with a 6 mm full-width half-maximum three-dimensional Gaussian filter to account for small variations in signal due to movement and vascular effects (i.e., noise), 4) masking, 5) scaling, and 6) motion correction was completed using six head motion parameters as nuisance regressors.

2.4.2 Individual level processing of fMRI data

Single-subject general linear model (GLM) analysis was conducted on the preprocessed data for each participant using the AFNI 3dDeconvolve program (Ward, 2002) to contrast brain activation during the empathic concern, empathic happiness and
neutral video clips. The two video clips with the highest empathic response ratings during each condition were concatenated (refer to Table 2.1). To quantify neural activity corresponding to empathic processing, regressors of interest were constructed using self-reported empathic response ratings following the video clips. The durations of the video clips were also included as parametric modulators. Six head movement parameters, and constant, linear, and quadratic trends were included as nuisance regressors. These regressors were convolved with a gamma variate function to approximate the temporal course of the blood-oxygen-level dependent (BOLD) hemodynamic response function. The neutral video clip embedded within the two empathy conditions was used to create contrasts. For each participant, a whole brain statistical parametric map ($\beta$-map) was generated associated with four contrasts of interest: Concern>Neutral, Happiness>Neutral, Concern>Happiness and Happiness>Concern.

2.4.3 Group Level processing of fMRI data

First to summarize the results from the individual level processing, group level one-sample t-tests were performed on each contrast (Concern>Neutral, Happiness>Neutral, Concern>Happiness and Happiness>Concern) which yielded a statistical parametric map of the t-statistic.

Conjunction analysis

To identify commonly recruited brain regions that were activated for both empathic happiness- and empathic concern-eliciting video clips, a conjunction analysis (Nichols, Brett, Andersson, Wager, & Poline, 2005) was conducted. The generated statistical maps for the Concern>Neutral and the Happiness>Neutral contrast were
overlayed using the AFNI 3dcalc program set to a voxel-wise threshold of $p = 0.05$, corresponding with a t-statistic threshold of 2.093. Conservative cluster-wise thresholding was used to correct for multiple comparisons (family-wise error). First, the AFNI 3dFWHMx program was used to estimate smoothness based on the spatial autocorrelation function to give an accurate false positive rate (FPR) control (Cox, Reynolds, & Taylor, 2016). Next, the AFNI 3dClustSim program was used to estimate a minimum cluster size of 18.5 contiguous voxels corresponding to an uncorrected $p$-value of 0.001 and a corrected $p$-value of 0.05. A conjunction mask of commonly activated brain regions was generated and parameter estimates ($\beta$-values) were extracted for each participant and used as dependent variable in statistical analyses in SPSS. Locations and corresponding Brodman areas of all peaks were determined using Talairach Daemon Atlases in AFNI, NIH Neurosynth platform and BioImage Suite.

**Differential Prefrontal Brain Activation across Empathy Subtypes**

To determine differential prefrontal brain activations across empathy subtypes, the group level statistical maps of the contrasts Concern$>$Happiness and Happiness$>$Concern were used. These statistical maps were corrected for multiple comparison using the same method and programs detailed above. Cluster-wise correction using an uncorrected $p$-value of 0.001 and corrected $p$-value of 0.05 yielded a minimum cluster size of 24 for the Concern$>$Happiness contrast and 25 for the Happiness$>$Concern contrast. Prefrontal regions with greater BOLD activity during one empathy subtype relative to the other were identified. To confirm the differential activation in these prefrontal regions, mean BOLD responses in prefrontal brain regions
with greater activity were entered into paired t-tests \((p < 0.05)\). A mask of BOLD activity in the prefrontal regions was created and parameter estimates were extracted for each participant and used as dependent variables in statistical analyses in SPSS.

### 2.5 SPSS statistical analysis

**Specific Aim 1.** To examine the relationship between executive function and BOLD response in prefrontal regions commonly activated during the empathy induction paradigm, a series of linear regression analyses were conducted. Each executive function and verbal fluency measure was individually entered as an independent variable and BOLD response was the dependent variable.

**Specific Aim 2.** To examine whether executive function was associated with differential prefrontal activity during the empathic concern condition relative to the empathic happiness condition, a series of simple linear regressions were conducted, with each executive function and verbal fluency measure individually entered as independent variables and BOLD response entered as the dependent variable.

Linear regressions were also used to examine the relationship between mean self-reported empathic response and executive function abilities. In this case, executive function and verbal fluency measures were individually entered as independent variables and mean empathic response was entered as the dependent variable.

### 3 RESULTS

#### 3.1 Demographic Information

A total of 20 participants enrolled and completed all aspects of the study and were included in the analyses. Demographic characteristics are listed in Table 2.
Participants were between 18- and 48-years-old ($M_{age} = 22.65$, $SD = 6.85$), and 60% were female. Ethnicity in the sample was as follows: 35% non-Hispanic white, 30% black, 25% Hispanic, and 10% Asian. With regard to education, most participants had attained at least some college education (85%), 10% had a college degree, and 5% had a graduate degree.

### 3.2 Data Preparation and Preliminary Analyses

In preparation for regression analyses, all executive function task scores were converted from scaled scores to z-scores. Higher scores on the measure correspond to better performance. Also, participant ratings following each video clip were averaged across each condition, resulting in a mean empathic concern score and a mean empathic happiness score for each participant.

All variables were examined for missing values, and outliers. Outliers were defined using the outlier labeling rule, employing a multiplier of 2.2 (Hoaglin & Iglewicz, 1987). Outlier analysis revealed univariate outliers: five participants across three video clips had intense BOLD responses during the empathic happiness conditions (i.e. Z-scores of 2.45, 2.53, 2.45, 2.53 and 2.70), and one participant had an outlying mean empathic happiness rating (Z-score of -0.44), along with an outlying inhibition score (Z-score of -3.11) and an outlying letter fluency score (Z-score of -2.51). In order to maintain the already small sample, minimize bias, and ensure enough power, a robust nonparametric technique, bootstrapping was used to estimate bias corrected (BCa) confidence intervals (Poldrack, 2012).

Due to the small sample size ($N = 20$), it was important to consider confidence intervals in addition to the significance level ($p < .05$) to ensure that a lack of statistical
power was not the main driving force explaining results. Robust nonparametric methodology, the bootstrap method, was used. The bootstrap method, a nonparametric technique is not dependent on a priori assumptions that limit parametric methods of analysis (Ong, 2014). In this method, the sampling distribution is estimated nonparametrically by sampling with replacement. The resulting distribution is used to generate bias-corrected 95% confidence intervals. A bootstrapped confidence interval (5000 iterations of the entire sample) that does not include zero was considered statistically significant. In other words, if $p$ was less than 0.05 but the confidence interval included zero, the test was considered nonsignificant.

**Preliminary Analyses.** Correlation analysis was conducted to identify potential demographic variables (i.e., age, gender, education) that were correlated with both the independent (executive function measures) and dependent (each frontal brain region) variables. Education was the only variable found to be correlated with inhibition and letter fluency measures; however, education was not related to any dependent variables. As such, no covariates were included in subsequent regression analyses.

### 3.3 Specific Aim 1

**Conjunction Analysis.** First to identify regions that were commonly activated across empathic concern- and empathic happiness-eliciting video clips, a conjunction analysis was run with a cluster-threshold of 18.5 voxels. The conjunction analysis revealed overlapping activity in the left superior frontal gyrus extending medially (SFG, BA 10) during empathic concern- and empathic-happiness eliciting video clips (see Table 3.2). Other regions activated by both types of empathy included the precuneus, bilateral occipital gyri and cerebellum. Lowering the voxel extent ($k = 13$) did reveal
overlapping activity in the anterior cingulate cortex ($x = -12$, $y = 42$, $z = 9$); however, it did not pass the conservative cluster-wise threshold used for this analysis. Significant clusters can be seen on Figure 3.1. Table A.1, in Appendix A, lists the locations and peak MNI coordinates of all significant clusters across the whole brain. Figure B.1 in Appendix B displays the time course (across all 18 runs) for BA 10.

![Figure 3.1 Commonly Activated Brain Regions](image)

Regions were significant at a cluster threshold of 18.5 contiguous voxels at an uncorrected $p$-value of 0.001 and corrected $p$-value of 0.05

**Executive Function and Common Prefrontal Activity.** To examine the relationship between commonly activated frontal regions and core executive functions, a series of linear regressions was conducted. In each model, the z-scores of each executive function measure (i.e., inhibition, working memory, cognitive flexibility) were individually regressed onto the BOLD response ($\beta$ weights) in the SFG (BA 10). BOLD response was entered as the outcome variable, while executive function scores were entered as a predictor variable. Results revealed that working memory was positively associated with BOLD response in the SFG (BA 10) during both empathic happiness- ($r = .54$, $p < .05$) and empathic concern- ($r = .50$, $p < .05$) eliciting video clips. Regression analyses are reported in Table 3.1. Figure 3.2 shows the relationship between working
memory and SFG (BA 10) activity during both empathic happiness- and empathic concern-eliciting video clips.

Activity in this frontal region during empathic concern eliciting video clips was also significantly associated with inhibition ($r = .45, p < .05$), however, the bootstrapped BCa confidence interval (-.02 -.10) included zero, suggesting this finding must be interpreted with caution. There were no other significant relationships between BOLD response in SFG (BA 10) and performance on other core executive function and verbal fluency measures.

Table 3.1 Regression analyses for cognitive measures performance predicting BOLD response in the SFG (BA 10)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>$R$</th>
<th>$R^2$</th>
<th>$\beta$</th>
<th>$B$</th>
<th>$SE$</th>
<th>$p$</th>
<th>BCa CI Lower</th>
<th>BCa CI Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superior Frontal Gyrus (BA 10)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Empathic Concern</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.45</td>
<td>.20</td>
<td>.45</td>
<td>.07</td>
<td>.03</td>
<td>.048</td>
<td>-.02</td>
<td>.10</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.50</td>
<td>.25</td>
<td>.50</td>
<td>.06</td>
<td>.02</td>
<td>.03</td>
<td>.02</td>
<td>.10</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.18</td>
<td>.03</td>
<td>-.18</td>
<td>-.02</td>
<td>.02</td>
<td>.45</td>
<td>-.06</td>
<td>.04</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.19</td>
<td>.04</td>
<td>.19</td>
<td>.02</td>
<td>.03</td>
<td>.42</td>
<td>-.03</td>
<td>.11</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.09</td>
<td>.01</td>
<td>-.09</td>
<td>-.01</td>
<td>.02</td>
<td>.71</td>
<td>-.05</td>
<td>.02</td>
</tr>
<tr>
<td><strong>Empathic Happiness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.05</td>
<td>.00</td>
<td>.05</td>
<td>.01</td>
<td>.03</td>
<td>.84</td>
<td>-.06</td>
<td>.04</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.54</td>
<td>.29</td>
<td>.54</td>
<td>.06</td>
<td>.02</td>
<td>.02</td>
<td>.00</td>
<td>.11</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.08</td>
<td>.01</td>
<td>-.08</td>
<td>-.01</td>
<td>.02</td>
<td>.75</td>
<td>-.03</td>
<td>.03</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.15</td>
<td>.02</td>
<td>.15</td>
<td>.01</td>
<td>.02</td>
<td>.65</td>
<td>-.03</td>
<td>.12</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.08</td>
<td>.01</td>
<td>.08</td>
<td>.01</td>
<td>.02</td>
<td>.73</td>
<td>-.03</td>
<td>.03</td>
</tr>
</tbody>
</table>

Note. Each predictor was individually entered into a simple linear regression. BCa CI = Bias corrected confidence interval
Specific Aim 2

Dissociation of activity across empathy subtypes. One-sample t-test revealed regions with greater BOLD response in the right superior frontal gyrus (SFG, BA 8), a region implicated in mentalizing; right middle frontal gyrus (MFG, BA 9) extending to dorsolateral prefrontal cortex (DLPFC) and bilateral ventrolateral prefrontal cortex (VLPFC) during empathic happiness- relative to empathic concern-eliciting video clips (see Figure 3.3). Other regions included angular and supramarginal gyri and the hippocampus. There were no frontal regions with greater BOLD activity during empathic concern- relative to empathic happiness- eliciting video clips. Paired sample t-tests were used to confirm differential activations. Table A.2, in Appendix A, lists the locations and peak MNI coordinates for all differentially activated brain regions across empathy.
subtypes. Locations of the peak MNI coordinates in the significant frontal clusters are listed in Table 3.2.

Results suggest that both empathic concern- and empathic happiness-eliciting video clips result in significant BOLD response in a common prefrontal region, BA 10, but as predicted, empathic happiness-eliciting video clips resulted in greater BOLD response in several prefrontal regions, including the FPC, DLPFC, VLPFC, and prefrontal regions typically found to be active during mentalizing or “theory of mind” tasks (i.e. BA 8/9).

Figure 3.3 Prefrontal brain regions with greater BOLD response during empathic happiness eliciting video clip

Regions were significant at a cluster threshold of 25 contiguous voxels at an uncorrected p-value of 0.001 and corrected p-value of 0.05. (A) Superior frontal gyrus, BA 8 (B) Middle frontal gyrus BA 10/46 and 9 (C) Superior frontal gyrus, BA 6 (D) Inferior frontal gyrus BA 46
Table 3.2 Locations and MNI co-ordinates of peak clusters of BOLD activity in prefrontal brain regions

<table>
<thead>
<tr>
<th>Area</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Empathic Happiness &amp; Empathic Concern</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left superior frontal gyrus</td>
<td>10</td>
<td>-21</td>
<td>54</td>
<td>12</td>
<td>58</td>
</tr>
<tr>
<td><strong>Empathic Happiness &gt; Empathic Concern</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right superior frontal gyrus</td>
<td>8</td>
<td>3.18</td>
<td>15</td>
<td>36</td>
<td>48</td>
</tr>
<tr>
<td>Right middle frontal gyrus ext. to the inferior frontal gyrus</td>
<td>10,46</td>
<td>3.32</td>
<td>39</td>
<td>45</td>
<td>12</td>
</tr>
<tr>
<td>Right middle frontal gyrus</td>
<td>9</td>
<td>3.31</td>
<td>39</td>
<td>36</td>
<td>39</td>
</tr>
<tr>
<td>Left Inferior frontal gyrus</td>
<td>46</td>
<td>2.93</td>
<td>-45</td>
<td>45</td>
<td>3</td>
</tr>
<tr>
<td>Right precentral gyrus/inferior frontal gyrus</td>
<td>6,44</td>
<td>2.68</td>
<td>48</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>Left superior frontal gyrus</td>
<td>6</td>
<td>3.48</td>
<td>-15</td>
<td>24</td>
<td>63</td>
</tr>
</tbody>
</table>

Note. BA = putative Brodmann’s Area; x,y,z are in MNI coordinates; k = cluster size

**Executive Function and Differential Prefrontal Activation.** Working memory was positively associated with BOLD response in the SFG (BA 8) during empathic happiness eliciting video clips ($r = .50$, $p < .05$). Figure 7 shows the relationship between working memory and activity in the SFG (BA 8) during empathic happiness-eliciting video clips. No other significant associations were found. Regression analyses are reported in Table 3.3.
Figure 3.4 Working memory performance is associated with BOLD response in SFG (BA 8) during empathic happiness eliciting video clips
Table 3.3 Regression analyses for cognitive performance predicting BOLD response in the differentially activated prefrontal brain regions

<table>
<thead>
<tr>
<th>Predictor</th>
<th>$R$</th>
<th>$R^2$</th>
<th>$\beta$</th>
<th>$B$</th>
<th>$SE$</th>
<th>$p$</th>
<th>BCa CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superior Frontal Gyrus (BA 8)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.22</td>
<td>.05</td>
<td>.03</td>
<td>.22</td>
<td>.03</td>
<td>.37</td>
<td>.04 - .06</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.50</td>
<td>.25</td>
<td>.05</td>
<td>.50</td>
<td>.02</td>
<td>.03</td>
<td>.01 - .09</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.32</td>
<td>.10</td>
<td>-.03</td>
<td>-.32</td>
<td>.02</td>
<td>.17</td>
<td>-.06 - .01</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.17</td>
<td>.03</td>
<td>.17</td>
<td>.02</td>
<td>.02</td>
<td>.46</td>
<td>-.02 - .06</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.34</td>
<td>.11</td>
<td>-.34</td>
<td>-.03</td>
<td>.02</td>
<td>.15</td>
<td>-.08 - .02</td>
</tr>
<tr>
<td><strong>Middle Frontal Gyrus (10,46)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.15</td>
<td>.02</td>
<td>.03</td>
<td>.15</td>
<td>.08</td>
<td>.53</td>
<td>-.18 - .15</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.02</td>
<td>.00</td>
<td>.00</td>
<td>-.02</td>
<td>.04</td>
<td>.92</td>
<td>-.11 - .11</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.12</td>
<td>.01</td>
<td>-.02</td>
<td>-.02</td>
<td>.03</td>
<td>.61</td>
<td>-.09 - .03</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.04</td>
<td>.00</td>
<td>.04</td>
<td>.01</td>
<td>.04</td>
<td>.85</td>
<td>-.09 - .04</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.01</td>
<td>.00</td>
<td>.01</td>
<td>.00</td>
<td>.02</td>
<td>.96</td>
<td>-.03 - .04</td>
</tr>
<tr>
<td><strong>Middle Frontal Gyrus (9)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.28</td>
<td>.08</td>
<td>.04</td>
<td>.28</td>
<td>.05</td>
<td>.24</td>
<td>-.07 - .10</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.32</td>
<td>.10</td>
<td>.04</td>
<td>.32</td>
<td>.03</td>
<td>.18</td>
<td>-.01 - .09</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.19</td>
<td>.04</td>
<td>-.02</td>
<td>-.19</td>
<td>.02</td>
<td>.42</td>
<td>-.06 - .04</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.11</td>
<td>.01</td>
<td>.11</td>
<td>.01</td>
<td>.02</td>
<td>.63</td>
<td>-.04 - .04</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.09</td>
<td>.01</td>
<td>-.09</td>
<td>-.01</td>
<td>.03</td>
<td>.70</td>
<td>-.07 - .04</td>
</tr>
<tr>
<td><strong>Inferior Frontal Gyrus (46)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.28</td>
<td>.08</td>
<td>.05</td>
<td>.28</td>
<td>.06</td>
<td>.23</td>
<td>-.04 - .16</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.27</td>
<td>.07</td>
<td>.04</td>
<td>.27</td>
<td>.04</td>
<td>.25</td>
<td>-.03 - .15</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.16</td>
<td>.03</td>
<td>-.02</td>
<td>-.16</td>
<td>.02</td>
<td>.50</td>
<td>-.08 - .06</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.02</td>
<td>.00</td>
<td>.02</td>
<td>.00</td>
<td>.03</td>
<td>.94</td>
<td>-.05 - .05</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.03</td>
<td>.99</td>
<td>-.07 - .07</td>
</tr>
<tr>
<td><strong>Inferior Frontal Gyrus (6,44)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.02</td>
<td>.00</td>
<td>.00</td>
<td>.02</td>
<td>.07</td>
<td>.94</td>
<td>-.11 - .11</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.08</td>
<td>.01</td>
<td>.08</td>
<td>.01</td>
<td>.04</td>
<td>.74</td>
<td>-.08 - .12</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.12</td>
<td>.01</td>
<td>.02</td>
<td>.12</td>
<td>.02</td>
<td>.61</td>
<td>-.04 - .06</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.03</td>
<td>.00</td>
<td>-.03</td>
<td>.00</td>
<td>.03</td>
<td>.90</td>
<td>-.09 - .03</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.16</td>
<td>.03</td>
<td>.16</td>
<td>.02</td>
<td>.03</td>
<td>.50</td>
<td>-.04 - .07</td>
</tr>
<tr>
<td><strong>Superior Frontal Gyrus (BA 6)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.19</td>
<td>.04</td>
<td>-.04</td>
<td>-.19</td>
<td>.06</td>
<td>.42</td>
<td>-.21 - .01</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.24</td>
<td>.06</td>
<td>.04</td>
<td>.24</td>
<td>.04</td>
<td>.32</td>
<td>-.05 - .13</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.03</td>
<td>.00</td>
<td>.00</td>
<td>-.03</td>
<td>.03</td>
<td>.90</td>
<td>-.06 - .08</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.25</td>
<td>.06</td>
<td>.25</td>
<td>.04</td>
<td>.04</td>
<td>.28</td>
<td>-.02 - .13</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.15</td>
<td>.02</td>
<td>-.15</td>
<td>-.02</td>
<td>.03</td>
<td>.52</td>
<td>-.08 - .03</td>
</tr>
</tbody>
</table>

Note. Each predictor was individually entered into a simple linear regression. BCa CI = Bias corrected confidence interval.
Executive Function and Self-Reported Empathic Response. Participant empathic response ratings following each video clip were averaged across each condition resulting in a mean empathic concern score and a mean empathic happiness score for each participant. State empathic concern and empathic happiness scores were not significantly associated with performance on core executive function measures (i.e. inhibition, working memory, or cognitive flexibility) or letter fluency. However, category fluency was positively associated with mean state empathic concern score \((r = .45, p < .05)\), but not mean state empathic happiness. Figure 3.5 displays the relationship between category fluency and state empathic concern. Regression analyses are reported in Table 3.4.

Table 3.4 Regression analyses for cognitive performance predicting state empathic response during the empathy induction paradigm

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Mean empathic concern</th>
<th>Mean empathic happiness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(R)</td>
<td>(R^2)</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Mean empathic concern</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.12</td>
<td>.01</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.16</td>
<td>.03</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.35</td>
<td>.13</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.05</td>
<td>.00</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.45</td>
<td>.21</td>
</tr>
<tr>
<td><strong>Mean empathic happiness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.08</td>
<td>.01</td>
</tr>
<tr>
<td>Working Memory</td>
<td>.13</td>
<td>.02</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>.23</td>
<td>.05</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>.11</td>
<td>.01</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>.07</td>
<td>.01</td>
</tr>
</tbody>
</table>
4 DISCUSSION

The purpose of the current study was to examine the relationship between executive function and empathic response across empathy subtypes. We measured neural response during a positive and negative vicarious emotion induction task, and identified prefrontal regions central to both positively and negatively valenced empathic processing. Furthermore, we confirmed our prediction that executive function relates to affective empathy, with working memory and inhibition abilities particularly playing a role. Our results provide evidence to support theoretical models of empathy that posit the involvement of executive processes in empathy.

**Overlapping brain regions across empathic subtype**

Both empathic happiness- and empathic concern-eliciting video clips engaged the superior frontal gyrus extending medially, consistent with Brodmann area 10 of the
frontopolar cortex extending medially. This rostral region which is greatly expanded in humans relative to other animals has been found to play a critical role in higher-order cognition and emotional processing (Amodio & Frith, 2006; Koechlin et al., 1999; Koechlin, Corrado, Pietrini, & Grafman, 2000; Ochsner & Gross, 2005; Ramnani & Owen, 2004). Common activity in this region across empathy subtype suggests that vicarious emotion requires attending, mentalizing, and monitoring one’s own feelings and thoughts (Burgess, Scott, & Frith, 2003; Raposo, Vicens, Clithero, Dobbins, & Huettel, 2010) making inferences about the mental/emotional states of others (Isoda & Noritake, 2013), and maintaining concurrent processing of internally- and externally-generated representations of both (Braver & Bongiolatti, 2002; Christoff & Gabrieli, 2000).

Our findings suggest that the anterior prefrontal cortex may be a common neural region essential for higher-order empathic processing regardless of emotional valence. Although we found overlapping activity in BA 10 across empathy subtypes, we did not find overlapping activity in the dorsal anterior cingulate cortex and insula, which have been considered core empathy-related regions (Fan et al., 2011). This discrepant finding may indicate that the ACC and insula are more related to empathy for physical pain as seen in several studies. Our results are consistent with prior work that suggests the essential role of the prefrontal cortex in higher-order empathic processing (Light et al., 2015).

As predicted, activity in this same anterior prefrontal cortex region during both empathic concern- and empathic happiness-inducing video clips was associated with working memory performance. This suggests that both types of empathic responding
rely on working memory abilities centered on maintenance and manipulation of self-other mental representations and processing. These results build on previous findings that show that holding in mind the emotions of others and one’s own emotions is associated with activity in working memory-related frontal regions (Smith et al., 2017; Xin & Lei, 2015).

Thus, we have established the existence of a relationship between affective empathy and working memory using separate neuroimaging and neuropsychological methodology, which extends prior work demonstrating a relationship between cognitive empathy (i.e., theory-of-mind) and executive function. However, although theoretical models and prior research has hypothesized the importance of cognitive flexibility in empathy (Grattan & Eslinger 1989, Decety & Jackson 2004), we did not find a relationship between prefrontal activity across empathy subtypes and our measure of cognitive flexibility. Although it makes sense that switching flexibly between representations may play a role in empathy, our results suggest that at least for affective empathy, the ability to hold and manipulate mental/emotional state representations in mind may be more essential, while other executive functions may play a greater role in cognitive empathy processes.

Interestingly, activity in this same prefrontal region during empathic concern-eliciting video clips was also associated with better inhibition. This hints that the ability to relate to the negative emotions of someone else may uniquely require the ability to inhibit one’s own mental state representation in order to focus on the mental status of the target. Notably, the conservative nonparametric statistical confidence interval
approach used in this study calls into question this association; thus, further studies are needed to confirm this result.

Differences in prefrontal cortex activity during empathic happiness- versus empathic concern-eliciting video clips

We also predicted differential prefrontal activity across empathy subtypes. Essentially, we predicted that greater control, operationalized as greater prefrontal engagement and better executive function task performance across a wider spectrum of tests, would be evident in relation to empathic happiness-eliciting video clips relative to empathic concern-eliciting video clips. When comparing empathic happiness- and empathic concern-eliciting video clips, whole-brain contrasts did reveal greater engagement of various prefrontal cortex regions during empathic happiness-eliciting video clips relative to empathic concern-eliciting video clips. In addition to the shared activation of BA 10 across empathy subtypes, and that region’s relationship to working memory performance, empathic happiness was additionally and uniquely associated with greater engagement of the superior frontal gyrus (BA 8), a region implicated in mentalizing/cognitive empathy (Frith & Frith, 2006). Furthermore, activity in this region during the elicitation of empathic happiness related to better working memory performance, bolstering the view that empathic happiness may require more extensive executive skills than empathic concern for emotional pain.

Evolutionary explanations for empathy argue that empathy for physical pain had adaptive value, particularly in the context of parental attachment and care for young (Tucker, Luu, & Derryberry, 2005); with empathic concern supporting specific actions that promoted survival and fostered social connection. However, empathic capacity
likely naturally evolved over time. For example, Barrett et al (2003) explain that advanced social cognitive ability emerged due to advances in executive functioning and the ongoing evolutionary development of prefrontal regions. Our results align with this framework, showing that empathic happiness, which emerges later in development than empathy for physical pain, relates to greater engagement of collective prefrontal cortex regions often engaged during both affective and cognitive empathy; whereas empathic concern involves more circumscribed prefrontal cortex activation relative to empathic happiness. Given the widespread involvement of prefrontal cortex in empathic happiness, and the particular regions of prefrontal cortex specifically implicated in empathic happiness (i.e. ventrolateral/dorsolateral/frontopolar PFC and medial BA 8 & 9 of the PFC), this may suggest that empathic happiness evolved intermediately between empathic concern and theory of mind.

Specifically, regarding the evolution of empathy for physical pain to empathy for emotional pain (and the hypothesized later emergence of empathy for emotional pain and happiness) results from prior studies suggest that some overlap between the functioning of the “emotional pain” system and the “physical pain” system, with both being affected by the opioid analgesia system. For example, studies have shown that Tylenol™ alleviates physical and social pain by acting on the partially overlapping pain centers in the brain. However, we do believe our findings—when combined with the literature on empathy for physical pain—provide evidence that there are some key differences between the ways we empathize with physical versus emotional pain. Namely, based on Ledoux and Brown’s (2017) “Higher Order Theory of Emotional Consciousness,” empathic concern for emotional pain should theoretically involve the
“higher-order representation” (HOR) of an emotional state whereas empathic concern for physical pain should only involve the “first-order representation” of a sensory state. We suggest here that our findings support this view, our findings suggest that empathy for emotional pain draws upon more complex (i.e. higher-order prefrontal cortex) regions of the brain than the literature suggests for empathy for physical pain. Similarly, as empathic happiness also requires the higher-order representation of emotional states—again—this should call upon activity in higher-order prefrontal regions such as frontopolar PFC, which our findings reveal.

Finally, regarding the ventrolateral prefrontal cortex aspect of activation during empathic happiness but not during empathic concern, we draw upon previous emotion regulation studies showing a relationship between activity in this region and emotion change; with increased activity in VLPFC relating to successful emotion regulation. In the current study, increased activity in this region was associated with greater empathic happiness, possibly suggesting that successful shifts away from self-focused joy toward vicarious happiness is also tracked by activity in this region.

**Category fluency predicts self-reported empathic concern during empathic concern-eliciting video clips**

We observed a relationship between category fluency (but not letter fluency) and state empathic concern during empathic concern-eliciting video clips. This is an interesting finding given neuroimaging studies that have clearly implicated the temporal lobe during performance of the category fluency task (Baldo et al., 2006). Essentially, it suggests that the medial temporal lobe may contribute to empathic processing for emotional pain, which is in line with Light & Zahn-Waxler (2011). Overall, this would
suggest that empathic concern is an evolutionarily older process, and may be a developmental process that comes online earlier in life than empathic happiness (Light & Zahn-Waxler, 2011) Specifically, Sheldon & Moscovitch (2012) propose that the medial temporal lobe is specifically recruited during category fluency tasks that require accessing autobiographical memories. This would seem particularly relevant in the context of empathy, as the empathizer would likely benefit from calling up/simulating past emotional states that are relevant for interpreting the current situation they are trying to empathize with. Thus, when combined with this prior literature, this finding is an indicator that empathic concern for emotional pain is likely based in fronto-limbic circuitry.

**Limitations and Strengths**

A potential limitation of the current study design is the lack of randomization of emotion states in the empathy paradigm, with the empathic concern condition always preceding the empathic happiness condition. To maintain the integrity and ecological validity of the story, we believe it was important to present the video clips sequentially which required the empathic concern clips to precede the empathic happiness clips. It is important to note that a neutral clip was included to separate empathic concern and empathic happiness video clips. Emotional reactivity ratings showed appropriate low empathic concern and empathic happiness ratings during the neutral clip and a subsequent increase in mean empathic happiness and decrease in mean empathic concern rating during the first empathic happiness video clip. Nevertheless, it is possible that an order effect may affect empathic happiness reactivity ratings in the second half of the paradigm. However, we do not find a linear increase in empathic happiness video
clip reactivity rating across the empathic happiness condition, which would be expected if earlier clips were priming greater empathic responses. Together these results suggest that participants were appropriately responding to the content of the video clips during the empathy paradigm.

Also, the current study may have been limited by the relatively small sample size, which may result in limited power. To remedy this, we utilized robust statistical methodology, including bootstrapped confidence intervals, to verify significant associations.

A key strength of this study is that it is the first to connect working memory abilities to neurally measured affective empathic response. Our results provide solid support for theoretical claims that empathy is not automatic, but rather engages higher-order processes. While other studies have reported prefrontal engagement in empathic processing, we show that activity in these prefrontal regions are related to working memory abilities, providing specific support for Decety and Lamm’s social neuroscience model of empathy. Importantly, our study provides evidence of prefrontal and executive function involvement in empathy in a normative sample which may be used to better understand empathic processing in clinical populations. With an understanding of normal function, we can formulate more accurate hypotheses to address social cognitive deficits in clinical populations. Taken together, this study makes methodological, theoretical, and empirical contributions to our current understanding of empathy. We have demonstrated an association between a specific type of executive function (working memory) and prefrontal brain activity during empathy. As more data emerges, clinicians may be better able to characterize social cognitive deficits in patient
populations. Specifically, interventions targeting working memory, or increased engagement of the anterior prefrontal cortex, may aid in improving empathic abilities.

Conclusions

Taken together, our results suggest a role of executive processes in affective empathy of positive and negative valence. Our results bolster Decety and Lamm’s social neuroscience model by presenting normative evidence for the relationship between working memory and affective empathy. We show that the anterior prefrontal cortex is essential to empathic responding across empathy subtype and relates to working memory abilities. We further show that empathic happiness engages additional executive related prefrontal brain regions relative to empathic concern. As such, working memory deficits are likely to impact empathic abilities in clinical populations. This relationship deserves continued attention for better understanding empathy deficits across neurological and psychiatric populations. On a broader scale, our findings contribute to a body of work on the interaction of emotion and cognition. This complex interaction helps us navigate and likely facilitates our everyday social interactions.
REFERENCES


10.1176/jnp.23.1.jnp74


Ong, D. C. (2014). A Primer to Bootstrapping; and an Overview of doBootstrap.

*Department of Psychology, Stanford University, Palo Alto.*


APPENDICES

Appendix A

MNI and peak locations of BOLD activation

Table A. 1 Commonly Activated Brain Regions

<table>
<thead>
<tr>
<th>Area</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior frontal gyrus (Left)</td>
<td>10</td>
<td>-21</td>
<td>54</td>
<td>12</td>
<td>58</td>
</tr>
<tr>
<td>Parietal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Precuneus</td>
<td>7</td>
<td>-12</td>
<td>-51</td>
<td>51</td>
<td>40</td>
</tr>
<tr>
<td>Occipital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Occipital Gyrus</td>
<td>18</td>
<td>-39</td>
<td>-81</td>
<td>0</td>
<td>503</td>
</tr>
<tr>
<td>Right Occipital Gyrus</td>
<td>18/19</td>
<td>36</td>
<td>-75</td>
<td>3</td>
<td>337</td>
</tr>
<tr>
<td>Right Occipital Gyrus</td>
<td>19</td>
<td>9</td>
<td>-90</td>
<td>36</td>
<td>19</td>
</tr>
<tr>
<td>Cerebellum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Cerebellum</td>
<td>--</td>
<td>-27</td>
<td>-54</td>
<td>-18</td>
<td>258</td>
</tr>
<tr>
<td>Right Cerebellum</td>
<td>--</td>
<td>33</td>
<td>-54</td>
<td>-18</td>
<td>173</td>
</tr>
</tbody>
</table>

Note. BA = putative Brodmann’s Area; x, y, z are MNI coordinates; k = cluster size
# Table A. 2 Locations and MNI coordinates of peak clusters of greater BOLD activity

<table>
<thead>
<tr>
<th>Area</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>k</th>
<th>Area</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CORTICAL REGIONS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>CORTICAL REGIONS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Frontal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Frontal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>8</td>
<td>15</td>
<td>36</td>
<td>48</td>
<td>87</td>
<td>Superior frontal gyrus</td>
<td>6</td>
<td>-15</td>
<td>24</td>
<td>63</td>
<td>25</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>6</td>
<td>-15</td>
<td>24</td>
<td>63</td>
<td>25</td>
<td>Superior frontal gyrus</td>
<td>9</td>
<td>39</td>
<td>36</td>
<td>39</td>
<td>35</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>10,46</td>
<td>39</td>
<td>45</td>
<td>12</td>
<td>48</td>
<td>Middle frontal gyrus</td>
<td>46</td>
<td>-45</td>
<td>45</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>6,44</td>
<td>48</td>
<td>6</td>
<td>27</td>
<td>27</td>
<td>Inferior frontal gyrus</td>
<td>46</td>
<td>-45</td>
<td>45</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td><strong>Parietal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Parietal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precuneus</td>
<td>7</td>
<td>-18</td>
<td>-54</td>
<td>57</td>
<td>559</td>
<td>Angular gyrus</td>
<td>39</td>
<td>45</td>
<td>-48</td>
<td>36</td>
<td>244</td>
</tr>
<tr>
<td>Angiular gyrus</td>
<td>39</td>
<td>-57</td>
<td>-60</td>
<td>6</td>
<td>114</td>
<td>Supramarginal gyrus</td>
<td>40</td>
<td>-48</td>
<td>-36</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td><strong>Temporal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Occipital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital gyrus</td>
<td>19</td>
<td>-12</td>
<td>-63</td>
<td>0</td>
<td>86</td>
<td>Occipital gyrus</td>
<td>18</td>
<td>-6</td>
<td>-105</td>
<td>21</td>
<td>256</td>
</tr>
<tr>
<td>Occipital gyrus</td>
<td>19</td>
<td>15</td>
<td>-54</td>
<td>0</td>
<td>49</td>
<td>Occipital gyrus</td>
<td>18</td>
<td>18</td>
<td>-78</td>
<td>9</td>
<td>197</td>
</tr>
<tr>
<td><strong>Occupital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Temporal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial temporal gyrus</td>
<td>21/38</td>
<td>-60</td>
<td>-3</td>
<td>-21</td>
<td>44</td>
<td>Superior temporal gyrus</td>
<td>22</td>
<td>-51</td>
<td>-42</td>
<td>12</td>
<td>69</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>--</td>
<td>27</td>
<td>-54</td>
<td>-39</td>
<td>181</td>
<td>Cerebellum</td>
<td>--</td>
<td>27</td>
<td>-54</td>
<td>-39</td>
<td>181</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>--</td>
<td>24</td>
<td>-75</td>
<td>-39</td>
<td>53</td>
<td>Cerebellum</td>
<td>--</td>
<td>24</td>
<td>-75</td>
<td>-39</td>
<td>53</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>--</td>
<td>18</td>
<td>-90</td>
<td>-33</td>
<td>34</td>
<td>Cerebellum</td>
<td>--</td>
<td>18</td>
<td>-90</td>
<td>-33</td>
<td>34</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>--</td>
<td>-21</td>
<td>-75</td>
<td>-48</td>
<td>32</td>
<td>Cerebellum</td>
<td>--</td>
<td>-21</td>
<td>-75</td>
<td>-48</td>
<td>32</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>--</td>
<td>-33</td>
<td>-45</td>
<td>-48</td>
<td>28</td>
<td>Cerebellum</td>
<td>--</td>
<td>-33</td>
<td>-45</td>
<td>-48</td>
<td>28</td>
</tr>
</tbody>
</table>

Note. BA = putative Brodmann’s Area; x,y,z are MNI coordinates; k = cluster size
Appendix B

Figure B.1 Time course (across all runs) of commonly activated BA 10 during the empathy induction paradigm.

A mean trial time course (across voxels and participants) of BOLD responses (β-weight) during the empathy induction paradigm. For fMRI analyses, runs 2 and 4 were used to quantify brain activation during the empathic concern condition, runs 16 and 18 for the empathic happiness condition, and run 9 for neutral.
Figure B.2 Time course across all runs of differentially activated BA 10/46 during the empathy induction paradigm.

A mean trial time course (across voxels and participants) of BOLD responses (β-weight) during the empathy induction paradigm. For fMRI analyses, runs 2 and 4 were used to quantify brain activation during the empathic concern condition, runs 16 and 18 for the empathic happiness condition, and run 9 for neutral.