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The neuroanatomical basis of empathy: is empathy impaired following damage to the ventromedial prefrontal cortex?

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THE NEUROANATOMICAL BASIS OF EMPATHY:

IS EMPATHY IMPAIRED FOLLOWING DAMAGE TO THE VENTROMEDIAL

PREFRONTAL CORTEX?

by

Janelle Nicole Beadle

An Abstract

Of a thesis submitted in partial fulfillment of the
requirements for the Doctor of Philosophy degree
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Thesis Supervisors: Professor Daniel Tranel
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ABSTRACT

Empathy plays a crucial role in our relationships with others and enhances personal well-being. The brain areas that are critical for the experience of on-line empathy and empathic behavior are not known. The current study investigated the neural substrates of empathy through the examination of whether the ventromedial prefrontal cortex (VMPC) is critical for empathy. For the first time, on-line empathic experience and behavior were measured in patients with brain damage to the VMPC.

Six patients with bilateral damage to the VMPC were case-matched on specific demographic and neuropsychological criteria to two comparison groups: a brain damage group and a healthy adult group. On-line empathy was induced in an ecologically-valid manner in which the participant experienced live the sorrow of another person. The participant thought they would be playing an economic game against two opponents. However, during the study the participant overheard their game opponent experience deep sadness, revealing that it was the anniversary of their son's death (empathic induction.) A comparison neutral induction involved the participant overhearing their opponent converse with the research assistant about a neutral topic. On-line empathic experience was measured by a questionnaire completed before and after the inductions. Empathic behavior was measured implicitly through an economic game. It was defined as the degree of behavioral change on the game as a result of the empathic induction (after accounting for baseline behavior.) The economic game used to measure empathic behavior was the Repeated Fixed Opponent variant of the well-validated Ultimatum Game. This particular variant had not been studied in participants of a similar age range to the patient sample (younger and older adults). Furthermore, there is evidence for some aging-related differences in behavior on economic games, providing additional rationale to examine the behavior of healthy younger and older adults on the game. Consequently, game behavior of younger and older adults was measured and then used to implement a model of healthy game behavior in the experiment that investigated empathy in patients with damage to the VMPC.

Patients with damage to the VMPC experienced poor on-line empathy and showed poor empathic behavior. Patients with brain damage to the VMPC reported significantly less on-line empathy than patients with brain damage to other regions. Empathic behavior was not shown by patients with damage to the VMPC as a result of the empathic induction and their behavior was significantly different from both the healthy and the brain damage comparison groups which showed increased empathic behavior due to the empathic induction. A specific role for the VMPC region in empathy was demonstrated by the finding that patients with damage to this region had less on-line empathy and empathic behavior than patients with brain damage to other regions. This study showed that the VMPC region of the brain is critical for empathy. Further research is needed to elucidate whether patients with brain damage to the VMPC show decreased empathic behavior in all domains or whether it is specific to monetary decision-making.

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PH.D. THESIS

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CHAPTER 1

BACKGROUND AND SIGNIFICANCE

Emotion, Social Emotion, and the Brain

Emotions are an enriching and integral part of human experience. Emotions can motivate our behavior in ways that are beneficial for our well-being and ultimately our evolutionary success. In mechanistic terms, emotional experience is a function of a feedback system between the physical environment, the body and the nervous system. As such, emotion is something we experience in our body as well as represent in our mind as a mental state. One possible evolutionary function of emotion is to promote the maintenance of social bonds that help us to survive in our environment. Emotions that are considered to be primal, or basic, exist across all cultures and include happiness, sadness, anger, fear, disgust, and surprise (Fridlund, Ekman, & Oster, 1987). The positive emotions, such as happiness, function in the maintenance of social bonds. These social bonds facilitate well-being by providing meaning as well as emotional and physical security. Emotions also serve to protect individuals from danger. For example, the signal of fear on another person's face warns us that danger is approaching.

During the experience of emotion, there is a physiological response in the body. This can take the form of an increased heart rate as well as a specific motor movement, for example a smile (Levenson, Ekman, & Friesen, 1990). The physiological and motor responses associated with each emotion are mediated by specific brain structures. The brain has a system that mediates emotional processing and responses in a social context. There are specific core structures thought to mediate emotion in the brain and these include the ventromedial prefrontal cortex, the amygdala, and the insula although many other parts of the brain play a role in this system. Each structure plays a particular role in the system. The amygdala serves as a ‘first-responder’ detecting low-level emotional stimuli in the environment such as threatening animal. Differently, the insula represents the bodily experience of emotion. Higher-order social and emotional processing is thought to occur in the ventromedial prefrontal cortex which receives information from both the amygdala and the insula. The ventromedial prefrontal cortex processes complex social emotions and functions in social decision-making. In particular, there is preliminary evidence that the ventromedial prefrontal cortex may play an important role in the social emotion of empathy. This thesis investigates whether the ventromedial prefrontal cortex plays a critical role in two types of empathic processing—on-line empathic experience and empathic behavior. Before this question can be investigated, it is first important to understand how the psychological construct of empathy is defined.

What is Empathy?

The Importance of Empathy

Social emotions have evolved to allow adaptation to the social environment. Empathy is a social emotion that has a critical impact on relationship quality and well-being. Empathy functions to connect people in a deep, meaningful way by allowing people to understand each other and share in each others’ thoughts and feelings. This function benefits both the self and the other as it enhances the well-being of both persons in the relationship. For instance, one’s ability to share an affective state with another person facilitates social behaviors that enhance personal well-being (Batson, Fultz, & Schoenrade, 1987). Empathy also serves to enhance the quality of interpersonal relationships. For example, in couples, high levels of empathy are associated with greater relationship satisfaction (Davis & Oathout, 1987). Alternatively, poor empathy can have an extremely negative impact on the quality of relationships and can lead to decreases in personal well-being as a consequence of isolation and feelings of loneliness (Kalliopuska, 1986). Impairments in empathy are found in a variety of neurological and psychiatric illnesses.

Poor empathy is a central clinical characteristic of patients who have acquired damage to the ventromedial prefrontal cortex (VMPC), and autism (Blair, 2008; Eslinger, 1998). More recently, researchers have found that other neurological and psychiatric populations experience poor empathy as well, including schizophrenia and frontotemporal dementia (Rankin et al., 2006; Shamay-Tsoory, Shur, Harari, & Levkovitz, 2007). Empathy has a direct impact on social rehabilitation efforts in these disorders. For instance, in patients with damage to the VMPC, empathy is one factor that affects rehabilitation outcome (Grattan & Eslinger, 1991). Following injury to the VMPC regions, normal levels of empathy are associated with a more positive social outcome (Grattan & Eslinger, 1991).

Defining Empathy

The construct of empathy first was described in German aesthetics in the early 1900's ("einfühlung"). However, it was the German psychologist Lipps that came to define "einfühlung" as the mental ability to project one's own mental state into that of an object (such as work of art) in order to understand and describe it in one's own fashion (Lipps, 1903). Later "einfühlung" was translated into the English word "empathy" by way of the greek word "empatheia" and this definition preserved the concept that part of the self is projected into an object as a means of understanding the object through one's own self concept and personal experiences (Titchener, 1909). Titchener believed that one mechanism that enabled this projection of the self into an object was through inner imitation processes which occurred "in the mind's muscle." He did not believe this process could be accomplished rationally by attempting to understand the mental states of others through a reasoning process. In the field of psychology from 1930 to 1960, the construct of empathy was widely utilized by clinical and social psychologists alike. For instance, Carl Rogers utilized the term empathy in the setting of therapy to point out that it was crucial for the therapist to adopt the experience of the client as a means of understanding them (Rogers, 1975). Within the field of social psychology, the study of a sub-discipline called person perception arose (Bruner & Tagiuri, 1954) and against this background empathy came to be thought of as a measure of predictive accuracy for the ability to detect the thoughts and feelings of others (Truax, 1967). From the 1960's to present day, empathy has primarily been studied in the fields of social and personality psychology. However, new disciplines related to the study of social psychology have emerged such as social neuroscience and social economic decision-making which have demonstrated a keen interest in the study of empathy. These disciplines have examined the neural correlates of empathy and the relationship between the function of empathy and fairness to others, among other relevant topics.

Through the examination of the mechanisms of empathy in social and personality psychology, researchers have demonstrated that empathy is composed of two components: cognitive empathy (the ability to take the perspective of others as a means of understanding their thoughts and feelings) and emotional or affective empathy (the ability to vicariously experience the emotions of others). A movement aimed at dissociating the two empathy constructs culminated with the development of scales measuring either cognitive or emotional empathy (Hogan, 1969; Mehrabian & Epstein, 1972). There has also been a movement to capture the multidimensional nature of empathy and an example of this is the Interpersonal Reactivity Index (Davis, 1980) which measures both cognitive and emotional empathy. To this day, new empathy scales are still produced and typically assess both components of empathy (Baron-Cohen & Wheelwright, 2004).

Components of Empathy

Empathy is currently understood as a term encompassing two components: cognitive and emotional. Cognitive empathy is a complex mental capacity whereby one adopts the perspective of another person in order to understand their mental state (Hogan, 1969). Emotional empathy is defined as a shared affective state between two individuals that is produced when observing and with the knowledge that another person is experiencing emotion (Mehrabian & Epstein, 1972).

Cognitive empathy involves the explicit, conscious process of perspective taking whereby one imagines the mental state of another based upon personal experience. In the current literature, the term cognitive empathy is frequently used interchangeably with theory of mind. Nonetheless, there are differences in the way the constructs of cognitive empathy and theory of mind are defined and measured. Consequently, there may be differences in their neural mechanisms. One difference between the two terms is that cognitive empathy is defined to include the process of perspective taking whereas theory of mind does not necessitate this process. Theory of mind is often defined as the capacity to predict the mental states (e.g. intentions) of others and therefore the definition focuses on the accuracy of prediction versus the process of perspective taking (Gallagher & Frith, 2003). Another difference between the two terms is that cognitive empathy encompasses understanding both the thoughts and feelings of others whereas theory of mind can entail understanding only the thoughts (and not feelings) of others.

There are differences in the way cognitive empathy and theory of mind have been measured. Cognitive empathy has primarily been assessed through self-report trait questionnaires of empathy that ask the participant to rate the frequency with which they are able to take the perspective of others and understand their thoughts and feelings in their daily lives (Baron-Cohen & Wheelwright, 2004; Davis, 1980). Another less frequently used method to assess cognitive empathy is through the experimental instruction to ‘adopt the mental perspective’ of a fictional character in photos or videos while undergoing functional neuroimaging (Decety & Chaminade, 2003). On the other hand, theory of mind is typically measured using behavioral responses whereby the participant is asked to infer the mental state of a fictional character in a story, a cartoon strip, or a movie and the accuracy of their performance is measured (Frith & Frith, 2005).

A second component of empathy—emotional empathy—measures the degree to which one is able to vicariously experience the emotions of others. Emotional empathy has been measured by self-report trait questionnaires of empathy and by on-line empathic inductions of empathy (Batson, O'Quin, Fultz, Vanderplas, & Isen, 1983; Davis, 1980; Mehrabian & Epstein, 1972). Through trait questionnaires of empathy, participants rate statements that assess the degree to which they take on the emotional states of others in their daily lives (Davis, 1980; Mehrabian & Epstein, 1972). Another way to measure empathy is through the induction of an empathic emotional state through seeing or hearing another person in distress followed by self-report state ratings of empathy (Batson et al., 1983). Physiological measures of emotional arousal are also often assessed during empathic inductions and include measurement of skin conductance response and heart rate, among other measures.

The Neuroanatomical Correlates of Empathy

Only within the last two decades has the topic of empathy been explicitly investigated within the field of neuroscience. Employing behavioral paradigms and experiential measures drawn from social and personality psychology, neuroscientists have created probes to measure the neural correlates of empathy. The majority of these studies have investigated the brain areas involved in the experience of empathy in healthy adults through functional neuroimaging tools. However, there have also been a small number of studies that have examined brain areas critical for the empathic experience through case studies and group studies of patients with brain damage to particular regions.

<u>Brain Areas Involved in Empathy:</u>

<u>Functional Neuroimaging Studies</u>

Functional neuroimaging studies of empathy have primarily examined empathy for another person's physical pain. These studies have hypothesized that the personal experience of pain and the recognition of pain in another person involve shared neural representations and as a consequence empathy for another person results from the simulation of that state in oneself. The methodology of these studies typically entails viewing photos or videos of others physically experiencing bodily harm (Jackson, Meltzoff, & Decety, 2005) or viewing facial expressions of physical pain (Botvinick et al., 2005; Saarela et al., 2007) while undergoing functional neuroimaging (BOLD fMRI). In an attempt to mimic a more realistic experience of pain, other researchers have given participants low level electric shock and then indicated that their romantic partner (who was present in the testing room) would also receive this same shock (Singer et al., 2004).

In general, these studies have emphasized the role for the anterior insula and the rostral and middle portions of the cingulate cortex in empathy (Botvinick et al., 2005; Jackson et al., 2005; Saarela et al., 2007; Singer et al., 2004). However, these studies also have found significant brain activity related to the empathic condition in other regions of the brain including the frontal cortex. For example, experiencing electric shock and knowing a loved one is receiving electric shock has produced increased activity bilaterally in the lateral orbitofrontal cortex (Singer et al., 2004). In another example, viewing another person experiencing bodily harm or facial expressions of emotional pain has produced activity in areas of the frontal cortex in general (Botvinick et al., 2005; Jackson et al., 2005; Saarela et al., 2007).

Summary

Functional neuroimaging studies of empathy have added to the understanding of the neural mechanisms for the personal experience of pain and the recognition of pain in others. These studies have provided evidence that the anterior insula, mid-cingulate, and regions of the frontal cortex (e.g. orbitofrontal cortex) may play a role in the personal experience of pain and viewing the pain of others. However, the neural correlates of the experience of pain in one’s own body and viewing others’ pain may not be the same as the experience of empathy for other emotions such as sadness and happiness. Consequently, further research is needed to elucidate the neural correlates of empathy for other types of emotion. Since previous studies have employed stimuli that represent various forms of the experience of pain, little is known about the neural correlates of other more complex empathic experiences that may occur in daily life. For example, the neural correlates of empathy when witnessing a person stubbing their toe may be very different from that of watching a person experience extreme sorrow due to the loss of a family member. Therefore a better understanding of the neural correlates of empathy for complex, real world emotional experiences of others is needed. Finally, although neuroimaging studies provide insight into the brain network involved in empathic processing, the methodology employed in these studies does not allow us to discern brain regions that are critical for empathic processing. As a complement to functional neuroimaging studies, lesion studies enable us to examine brain regions critical for empathic processing.

Critical Brain Regions for the Function of Empathy: the Lesion-Deficit Approach Reveals that Damage to the VMPC Impairs Empathy

Clinicians and neuropsychologists who have studied patients with brain damage to the ventromedial prefrontal cortex (VMPC) have reported that these patients show low levels of empathy. One of the earliest examples of a reduced empathic capacity as a consequence of damage to the VMPC is the case of Phineas Gage, a railroad worker living in the 1840's in New England. Before his brain injury, Phineas Gage was an industrious worker and a great leader—an integral part of his community. Due to an unfortunate accident while working on the railroad tracks, a tamping iron penetrated his brain just above his eye region, which was thought to result in damage to his frontal lobe.

At the time of the accident, there was insufficient technology available to discern the precise anatomical location of the brain damage. However since then, there have been several studies that have conjectured as to the location of the damage, and many believe that he incurred brain damage to the ventromedial prefrontal cortex among other regions (Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994). After the brain injury, Gage's physician, John Harlow, described several changes to Gage's personality that he believed were a consequence of the accident. One of the marked changes in Gage's personality was a decreased capacity for empathy. Harlow described this impairment: [Gage] "manifest[ed] but little deference for his fellows," (Harlow, 1868). Since this seminal case, further clinical and anecdotal evidence has accumulated that patients with damage to the VMPC may experience impaired empathy.

Experiential Measurement of Empathy: Self-report

Several studies have shown that patients with damage to the VMPC report low levels of empathy (Eslinger, 1998; Shamay-Tsoory, Tomer, Berger, & Aharon-Peretz, 2003; Shamay-Tsoory, Tomer, Goldsher, Berger, & Aharon-Peretz, 2004; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009). This impairment of empathy has been shown to be greater in patients with damage to the VMPC than patients with damage to posterior regions of the brain and healthy comparison participants (Shamay-Tsoory et al., 2003; Shamay-Tsoory et al., 2009). The specificity of damage to the ventromedial portion of the frontal lobe is questioned by another study showing that patients with damage to all regions of the frontal cortex report poorer empathy than those with parietal lesions or healthy comparison participants (Shamay-Tsoory et al., 2004).

Empathy has been measured in these studies through self-report questionnaires that measure empathy as a trait or a general tendency across one's lifetime. These questionnaires consist of a series of statements that describe empathic situations encountered in daily life. After reading the statements, the participant is often asked to rate the extent to which the statement describes them or the degree to which they disagree or agree with the statement. Some examples of the questionnaires used in these studies include: the Interpersonal Reactivity Index (Davis, 1980), the Empathy Scale (Hogan, 1969) and the Questionnaire Measure of Emotional Empathy (Mehrabian & Epstein, 1972). One of the primary limitations of using a self report measure of trait empathy with patients who have damage to the VMPC is that these patients may have intact social knowledge that they can use to determine the most socially desirable answer (Saver & Damasio, 1991).

Dissociation of the Components of Empathy through Self-reported Experience

A small number of studies have attempted to dissociate the brain areas critical for the two components of empathy: cognitive and emotional. In these studies cognitive empathy was assessed through the Hogan Empathy Scale (Eslinger, Grattan, Damasio, & Damasio, 1992; Eslinger, 1998). The construct of cognitive empathy has also been measured through the Perspective Taking and Fantasy subscales of the Interpersonal Reactivity Index (Shamay-Tsoory et al., 2003; Shamay-Tsoory et al., 2004; Shamay-Tsoory, Tomer, Berger, Goldsher, & Aharon-Peretz, 2005; Shamay-Tsoory et al., 2009). Some studies have combined the Perspective Taking and Fantasy subscales of the Interpersonal Reactivity Index to create a total cognitive empathy score (Shamay-Tsoory et al., 2003; Shamay-Tsoory et al., 2009). However, combining these two scales may not accurately measure the construct of cognitive empathy. For instance, it has been shown that the Fantasy subscale is actually more highly associated with the Empathic Concern subscale (a measure of emotional empathy) than the Perspective Taking subscale (Davis, 1980; Davis, 1983). Consequently, results regarding cognitive empathy based upon the combination of these two subscales should be interpreted with caution.

These studies have shown that patients with VMPC damage have low levels of cognitive empathy. Through the use of the Perspective Taking subscale of the IRI, it has been shown that patients with VMPC damage have more impaired cognitive empathy than patients with damage to posterior regions of the brain (Shamay-Tsoory et al., 2003) and healthy comparison participants (Shamay-Tsoory et al., 2003). Using the combined total of the Perspective Taking and Fantasy subscale, one study reported that patients with damage to the VMPC also had lower cognitive empathy than patients with damage to the inferior frontal gyrus (Shamay-Tsoory et al., 2009). Again, this finding should be interpreted with caution based upon the questionable nature of the construct validity when combining these two subscales.

Fewer studies have assessed the emotional component of empathy through trait questionnaires in patients with damage to the VMPC. It has been measured through a combined score of two subscales of the Interpersonal Reactivity Index: the Empathic Concern subscale and the Personal Distress subscale. Based upon the initial factor analysis of the Interpersonal Reactivity Index and subsequent research, there is evidence that these two subscales should not be combined when examining the construct of emotional empathy (Davis, 1980; Davis, 1983). In addition, the Personal Distress subscale has been shown to be a distinct construct from empathy (Davis, 1983). A study using the combined subscale in the IRI found that patients with inferior frontal gyrus lesions had poorer emotional empathy than patients with lesions to the VMPC (Shamay-Tsoory et al., 2009). When the study examined each subscale separately, patients with damage to the VMPC had the lowest mean score out of all of the groups on the Empathic Concern subscale. Because this difference did not reach statistical significance, it is unclear whether the VMPC group had lower empathy as measured by this scale. On a different scale—the Questionnaire Measure of Emotional Empathy—patients with damage to the general area of the prefrontal cortex showed poorer emotional empathy than patients with parietal lesions or healthy comparison participants (Shamay-Tsoory et al., 2004). This study provides preliminary evidence that there may be an impairment in emotional empathy in patients with damage to the general region of the prefrontal cortex.

The Role of the VMPC in Empathy is not Fully Understood

Currently, it is not known whether the VMPC is critical for all components of empathy. Previous studies have used self-report questionnaires to determine the degree to which patients report experiencing cognitive and emotional empathy in their daily life. Patients with damage to the VMPC report experiencing low levels of cognitive empathy. Yet what is missing from the current literature is an examination of *on-line empathic experience* in patients with damage to the VMPC. Self-report trait questionnaires of empathy are not able to assess on-line empathy because rather than asking the patients how they feel immediately after an empathic induction, instead they require patients to reflect back over the course of their lives and rate the degree to which they experience empathic thoughts and feelings. Measurement of empathy through off-line or trait questionnaires should be interpreted with caution because patients with damage to the VMPC have been shown to answer questionnaires in a socially desirable fashion (based upon their access to social knowledge before the injury) while they exhibit socially inappropriate behavior in real world settings. Consequently, measurement of on-line, momentary empathic experience through which the patients are asked to access currently experienced emotions (and are less able to rely on social knowledge) may more accurately measure their capacity for empathic experience. As empathy can be both experienced and shown outwardly with a specific behavioral choice, it is important to consider the effects of damage to the VMPC on empathic behavior. The behavior emerging as a consequence of empathy may have the most direct effect on family members and friends of the patient. Yet empathic behavior has not yet been examined in patients with damage to the VMPC. In order to measure on-line empathic experience and behavior, it is crucial to utilize experimental methodology that effectively elicits empathy. The aim of the current study is to measure on-line empathic experience and behavior through an ecologically valid empathic induction. To accomplish this goal, a novel, empathic induction was designed.

CHAPTER 2

SPECIFIC AIMS AND HYPOTHESES

Impairments in Empathy are a Significant Public Health Concern

The experience of poor empathy is an important public health concern because of its prevalence in a variety of neurological and psychiatric diseases and its negative impact on the well-being of both the patient and their family. Poor empathy is a symptom of a large number of clinical conditions including antisocial personality disorder, autism, schizophrenia, frontotemporal dementia, and brain damage to the ventromedial prefrontal cortex among others. Neuroscience research is in the early stages of understanding the brain basis of empathy. Consequently, there is an urgent need to further understand the neural mechanisms of empathy in order to develop targeted rehabilitation programs aimed at creating more fulfilling social lives in individuals with poor empathy as well as reducing the impact of poor empathy on their families. The few studies that have investigated the effectiveness of empathy rehabilitation have found that it is successful in improving empathic skills in some groups of healthy volunteers (students, parents) as well as criminals. However, more research is needed to fully understand which types of rehabilitation are most effective. Currently, there are no rehabilitation programs that have been shown to be effective in meeting the specific needs of individuals with neurological and psychiatric illness who suffer from poor empathy. One method that allows the investigation of brain regions critical for the function of empathy is the lesion method.

Investigation of the Brain Areas Critical for Empathy: Patients with Damage to the VMPC

Patients with lesions to the ventromedial prefrontal cortex serve as a useful model to examine the brain regions critical for empathic function. A carefully designed study that examines the components of empathic processing in patients with damage to the VMPC can determine whether the VMPC region of the brain is critical for empathy. The lesion method is useful to study the brain regions critical for empathy because it can determine which brain regions are necessary for a particular function in comparison to functional neuroimaging which is able to conclude which brain regions are involved in a particular function. Patients with focal damage to the VMPC serve as a logical starting point for the examination of brain regions critical for empathy because there is evidence that these patients report poor empathy in their daily lives. Patients with damage to the ventromedial prefrontal cortex report difficulty detecting the thoughts and feelings of others on trait measures of cognitive empathy and perform poorly on the detection of the feelings of others from written scenarios or cartoon drawings (on measures of theory of mind).

<u>Strengths and Limitations of Previous Studies of Patients with Damage to the VMPC</u>

Although previous studies provide evidence that patients with damage to the VMPC have difficulty detecting the feelings of others, little is known about their on-line experience of empathy or their ability to show empathic behaviors towards others. Through written scenarios of fictional characters, patients with damage to the VMPC have shown a clear impairment in detecting the feelings but not the thoughts of others. Several studies have utilized self-report measures of trait empathy as a means of investigating the patient's daily experience of empathy. However, the results from trait measures of empathy should be interpreted with caution due to evidence that patients with adult-onset damage to this region typically appear to be socially normal on these questionnaires because they have access to intact social knowledge whereas in real world settings these patients demonstrate socially inappropriate behaviors. Consequently, further research is needed to understand whether the VMPC is critical for empathy. In particular, there is a need to understand the on-line experience of empathy and empathic behavior in patients with damage to the VMPC.

The study of on-line empathic experience and empathic behavior in patients with VMPC damage is crucial because these two elements are most likely to impact the quality of life of patients and family members. In the psychological literature, empathic feelings are highly associated with exhibitions of empathic behavior towards others. Consequently, if patients with damage to the VMPC experience decreased empathic feelings, this may be accompanied with a decreased level of empathic behavior towards family members or friends. This seeming lack of empathy towards friends and family has the capacity to negatively impact the patient's relationships. Therefore it is important to study the degree of empathic behavior exhibited in these patients because of its potential effect on the well-being of both the patient and his/her family. Furthermore investigating empathy in patients with ventromedial prefrontal cortex damage through behavior serves as an effective way to measure the construct of empathy in an implicit fashion. Without explicit cues as to the purpose of the experiment, the patient will be less likely to access previously accumulated social knowledge and may be more likely to exhibit their actual empathic capacity.

Measurement of On-line Empathic Experience and

Behavior in Patients with Damage to the VMPC

This dissertation includes a series of experiments that measure on-line empathic experience and behavior in patients with damage to the ventromedial prefrontal cortex. In an attempt to measure empathy in an ecologically valid manner, the experiment employs a type of empathic induction that is reminiscent of a real world empathic experience, followed by the rating of the participant's on-line empathy and concludes with a measure of empathic behavior that is assessed through an economic game. The economic game that was used to measure empathic behavior had not been investigated in adults who were within the age range of our patient sample. Consequently, Chapter 3 (Experiment 1) describes a study that was conducted to produce normative data on this particular economic game of adults of a similar age to the patient sample. The data gained from Experiment 1 was then implemented in Experiment 2 which assessed on-line empathic experience and behavior in patients with brain damage to the ventromedial prefrontal cortex and two comparison groups (a brain damage comparison group and a healthy comparison group).

<u>Experiment 1: Study of an Economic Game Used to</u>

<u>Measure Empathic Behavior in a Sample of Healthy Adults</u>

Experiment 1 describes the study that examined how healthy adults of similar age to the patient sample played the economic game that was used in Experiment 2 to measure empathic behavior. Because the Repeated Fixed Opponent variant of the UG has rarely been studied, little is known about how healthy adults play this game. Consequently, there is currently no normative baseline with which the patients with brain damage to the VMPC can be compared. Chapter 3 (Experiment 1) addressed this issue by describing the behavior of healthy adults on the Repeated Fixed Opponent UG. Because the patients with damage to the VMPC in our sample consisted of younger and older adults, both age groups were examined on the Repeated Fixed Opponent Game. There is also evidence for aging-related differences in behavior on decision making games and consequently we investigated whether this was also the case in the Repeated Fixed Opponent UG.

Experiment 2: Investigation of On-line Empathic Experience and Behavior in Patients with Damage to the VMPC

Experiment 2 consisted of an on-line empathic induction, followed by on-line self report ratings of empathy and concluded with a measurement of empathic behavior through an economic game. The naturalistic induction of empathy was accomplished by the participant overhearing an empathy-inducing conversation between their opponent (who they would play in the economic game) and the Research Assistant. When the participant first arrived, the Research Assistant talked with them about their day. Following this conversation, the Research Assistant told the participant they would be asked to rate their current feelings on a questionnaire at four random time-points during the study. The first time point occurred after the conversation between the opponent and the Research Assistant and this served as a measure of the participant's baseline empathic state. Then the Research Assistant proceeded to the room of their opponent and in a similar manner talked with them about their day (actually an audio recording of the

Research Assistant and an actor). The Research Assistant then returned to the participant's room and asked them to rate their feelings a second time; this served as a measure of empathic feelings as a result of the neutral induction. Immediately after, the participant played the economic game against their first opponent. After the game concluded, the Research Assistant told the participant that they would play a second opponent in the game. Prior to game play, the participant overheard the Research Assistant talking to a second opponent about their day who revealed that day was the anniversary of their son's death and conveyed their deep sadness about this event which served as the empathic induction (actually a recording). Then the Research Assistant returned to the participant's room to rate their current feelings which assessed their feelings of empathy due to the empathic induction. Next the economic game was played against the second opponent to assess empathic behavior.

Empathic behavior was measured implicitly in patients through the Repeated Fixed Opponent UG. In the extant literature, the Ultimatum Game is thought to measure decision making behavior in a social context, as a pair of two people are asked to decide how to share a particular amount of money with each other. More specifically, one player decides how to share $10 with their opponent who can then either reject or accept the offer the participant gives them. In the current study, the Ultimatum Game was used to measure empathic behavior in an implicit manner by assessing the degree to which a participant is willing to give some of their own money to their opponent who they learn is deeply saddened by the recent death of their son. The empathic behavior of the participant on the Repeated Fixed Opponent UG was determined by the money given by the participant in the game (after the empathic induction) after accounting for their baseline giving behavior (their behavior after the neutral induction).

The Repeated Fixed Opponent variant of the Ultimatum Game was specifically selected to measure empathic behavior instead of the widely used 1-Shot variant of the UG because it enables an empathic induction to occur in a more effective and believable manner. In the commonly studied 1-Shot UG, a participant plays each round against a different opponent (typically around 15-20 opponents.) Differently, in the Repeated Fixed Opponent UG, the participant plays against one opponent for several consecutive rounds in a row. For a naturalistic empathy induction to be effective, the participant must believe it is real and it needs to occur over a long enough period of time for an emotional response to be evoked. In daily life, one typically encounters empathy inducing situations infrequently and these situations do not often occur in rapid succession, particularly in a laboratory setting. If the 1-Shot UG were used, it would be necessary for several empathic situations to occur in succession in order to obtain enough behavioral data. Inducing empathy in the participant several different times in a row may cause the participant to doubt the realism of the experiment. In addition, because the participant would be playing against several different opponents, the time that would be provided to induce empathy for each opponent would need to be of a short duration due to overall time constraints. Alternatively, in the Repeated Fixed Opponent UG, the participant would only need to play against two different opponents, each for twenty rounds, to determine the behavioral effect of a neutral state and an empathic state. In this way, only one empathic situation would need to occur, and thus the design would be more believable to the participant. Similarly, the empathic induction would be more effective because there would be enough time to sufficiently evoke an empathic state towards one person.

A Novel Measure of On-line Empathy and

Empathic Behavior in Patients with Damage to the VMPC

No studies have systematically examined the degree to which patients with damage to the VMPC experience on-line empathy, the capacity to feel empathy as an online emotional experience, or empathic behavior, behavior that is a product of an empathic state. In healthy adults, state empathy is thought to be what drives our ability to emotionally respond to other people through our words, emotional facial expressions or actions. In particular, state empathy has been shown to play an important role in motivating prosocial acts or empathic behavior towards others. Therefore it is essential to determine whether patients with damage to the VMPC have impairments in on-line empathic experience and empathic behavior. Anecdotal reports by family members strongly suggest that patients with damage to the VMPC experience little to no empathy and exhibit little empathic behavior in their everyday lives. Nonetheless experimental evidence for this phenomenon has not been attained. Therefore this will be the first study to investigate the capacity for on-line empathy and empathic behavior in patients with damage to the VMPC as well as to determine whether there is a predictive relationship between state empathy and empathic behavior in this population.

Future Directions

The ultimate goal of this research is to increase the understanding of empathy in order to develop targeted empathy rehabilitation programs for individuals with low empathy skills. To further this goal, this dissertation will help to advance the understanding of the capacity for empathy in a population of patients who are thought to suffer from low empathy. If state empathy is lower in patients with damage to the VMPC, one goal for rehabilitation will be to increase to a normal level the state empathy of the patients with VMPC damage. If empathic behavior is low in patients with damage to the VMPC, another goal for rehabilitation will be to increase their empathic behavior. If state empathy and empathic behavior are not related constructs in this specific population, it will be possible for rehabilitation efforts to focus on each construct separately. For example, if empathic behavior is unrelated to empathic states in this population, empathic behavior may be more effectively rehabilitated through behavioral modification rather than focusing on creating appropriate empathic states.

Description of Specific Aims and Hypotheses

Specific Aim 1

To develop an experimental paradigm to measure empathic behavior in healthy adults which would then be employed in a study examining empathic behavior in patients with brain damage to the ventromedial prefrontal cortex (VMPC).

Specific Aim 1 is addressed in Chapter 3: Experiment 1. The measure of implicit empathic behavior employed in this series of studies is an economic game called the Repeated Fixed Opponent UG. Because the Repeated Fixed Opponent Variant of the UG has rarely been studied, prior to this study the behavior of healthy, normal adults had not yet been characterized. Experiment 1 describes the behavior of healthy adults on the Repeated Fixed Opponent UG. The results from Experiment 1 are employed in the study examining on-line empathy and empathic behavior in patients with damage to the ventromedial prefrontal cortex to serve as normative baseline for the behavior of healthy adults on this particular economic game (Chapter 4: Experiment 2). Because the patients with damage to the VMPC in Experiment 2 range from early to late adulthood, to make the normative data comparable to the patient data, Experiment 1 included a sample of younger and older adults healthy adults. Due to evidence of age-related differences on other types of economic games, age-related differences were specifically examined in this sample.

Hypothesis 1

It was hypothesized that older adults would differ from younger adults in their empathic behavior as measured on the Repeated Fixed Opponent UG.

Specific Aim 2

To examine the degree to which patients who have incurred brain damage to the ventromedial prefrontal cortex (VMPFC) experience on-line empathy through a novel, naturalistic empathic induction paradigm.

Specific Aim 2 is investigated in Chapter 4: Experiment 2, Part B. The effectiveness of an on-line naturalistic induction of empathy is examined in healthy adults of similar ages to the patient sample in Chapter 4: Experiment 2, Part A. Chapter 4: Experiment 2, Part B consists of the description of the study that examines the on-line empathic experience and empathic behavior of patients with damage to the VMPC. The empathic experience of patients with damage to the VMPC is directly compared to two comparison groups: (1) a group of patients with brain damage to regions that do not include the VMPC or other areas thought to be related to empathy (e.g. amygdala, insula, inferior frontal gyrus) and (2) a group of healthy adults. Both comparison groups are matched to the patients with damage to the VMPC on age, education, sex, handedness and full scale IQ. On-line empathic experience was measured by self-report ratings of empathy immediately after the empathy induction occurred.

Hypothesis 2

It was hypothesized that patients with damage to the VMPC would report lower on-line empathy than the comparison groups (brain damage comparison, healthy comparison).

<u>Specific Aim 3</u>

To examine the degree to which patients who have incurred brain damage to the ventromedial prefrontal cortex (VMPFC) show empathic behavior.

Specific Aim 3 was described in Chapter 4: Experiment 2, Part B. Empathic behavior was measured by performance on the Repeated Fixed Opponent UG that occurred directly after the empathic induction (after accounting for baseline UG performance after the neutral induction.) Empathic behavior was determined by the amount of offers given in the game following the empathic induction after subtracting from this the amount the individual gave in the game immediately after the neutral induction. High levels of empathic behavior would constitute larger overall offer total in the game following the empathy induction than in the game following the neutral induction.

The performance of patients with damage to the VMPC was compared to a group of patients with damage to regions outside of the VMPC and other empathy-related areas and to a group of healthy adults (further described in Specific Aim 2).

Hypothesis 3

It was hypothesized that patients with damage to the VMPC would show less empathic behavior than the comparison groups (brain damage comparison and healthy comparison).

CHAPTER 3

EXPERIMENT 1: DEVELOPMENT OF A NEW MEASURE OF EMPATHIC BEHAVIOR—THE REPEATED FIXED OPPONENT ULTIMATUM GAME

This next section will describe a novel use of a tool to detect empathic behavior in sample of healthy adults and the plan for implementation of this tool in a sample of patients with damage to the VMPC. An social economic game was chosen to measure empathic behavior because it allows for structured social interaction that can be quantified by performance on the game. The tool that was chosen to measure empathic behavior was the Repeated Fixed Opponent version of an often-studied social economic decision making game called the Ultimatum Game. This particular economic game was chosen because it involves a straightforward monetary decision and is set in a social context. The monetary decision participants must make is simple: How would they like to split $10 with their opponent? The participant is able to give them as much money or little money as they would like within the context of a few constraints (e.g. the offer must range within $1-9 and add up to $10). Their opponent has a clear choice, if they reject the offer both people receive $0 but if they accept the offer both people receive the proposed division.

Empathic behavior can be measured in this game through the degree to which the participant gives more money to the other person than they take for themselves. Their baseline empathic behavior can be assessed by having them play the game after a neutral state induction (or even after no induction at all). Then after inducing an empathic state in the individual, empathic behavior can be assessed by measuring the change in the giving behavior from baseline. If a greater monetary amount is given after the empathic induction than at baseline, it would suggest that the person is exhibiting empathic behavior towards their opponent.

Although the original, 1-Shot form of the UG is well understood, less is known about the Repeated Fixed Opponent version of the UG which we chose to use in the current experiment. Consequently, in order to utilize this game as a measure of empathic behavior in the patient sample, first we examined this tool in a sample of healthy adults of similar ages to the patient sample. The purpose was to better understand how healthy adults behave in this game in order to determine whether the patient sample differed. The patient sample of interest included both younger and older adults. Since previous studies have found aging-related differences in economic game performance, it provided an impetus to examine whether there were aging-related differences in our sample as well.

The data from Experiment 1 was planned to be used for two purposes: (1) to determine the degree to which the Repeated Fixed Opponent Ultimatum Game can be used to measure empathic behavior in healthy younger and older adults, and (2) to employ this data to simulate a healthy individual's behavior on this game in the study that examines empathic experience and behavior in patients with damage to the VMPC (Experiment 2 Part B). In Experiment 2 Part B, instead of having the participant play against a real opponent, we experimentally controlled the behavior of the opponent so that each participant would be responded to in the same way. To achieve this goal, we used data from Experiment 1 to mimic the behavior of healthy opponent. We employed this data under the guise that the participant was actually playing a live person by linking our data-based response from Experiment 1 to voice clips of an actor.

In Experiment 1, first we investigated the behavior of healthy adults on the Repeated Fixed Opponent Ultimatum Game. Because the patients that took part in Experiment 2 Part B are a variety of ages, we wanted to determine whether there were age-related differences in game behavior. To investigate this question, we compared the behavior of younger and older healthy adults on the Repeated Fixed Opponent Ultimatum Game.

Introduction

We regularly make financial decisions in a social context—e.g., haggling over the price of an item at a garage sale, bargaining with a salesperson over the final price of a car, or negotiating the purchase of a house. Poor financial decision making can have a negative impact on one's lifestyle and well-being. The impact of poor decision making may be even more pronounced in later life because there is less time to recover from the negative consequences of these decisions. The health and well-being of the aging population has become an increasingly important public health concern, and more research is needed to understand how social decision-making changes as a function of aging. One way to measure financial bargaining behavior in a controlled, experimental fashion is through an economic game. There is already extensive information about the behavior of young adults on such games (Guth, Schmittberger, & Schwarze, 1982; Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003), but little work has been done with older adults.

Distinct lines of research have shown that the aging process produces changes in social and emotional functioning as well as changes in decision making, making it plausible that social decision-making will also be affected by aging. For example, older adults have been shown to perceive and experience social and emotional information differently from younger adults (Gross et al., 1997; Slessor, Phillips, & Bull, 2008). There is also some evidence that the ability to make decisions undergoes aging-related changes, as seen, for example, in the disadvantageous financial behavior of a subgroup of older adults on the Iowa Gambling Task (Denburg, Tranel, & Bechara, 2005), or in the different strategies of decision making utilized by older compared to younger adults (Wood, Busemeyer, Koling, Cox, & Davis, 2005). A possible mechanism for these changes is the degeneration of specific brain structures (with prefrontal structures being most often implicated) due to the aging process (Denburg et al., 2007; West, 1996). But even the behavioral part of this story has yet to be pinned down, and accordingly, the study reported here investigates whether there are age-related differences between older and younger adults in their financial decision making in a social context.

A well established means of measuring decision making in the context of social interaction in a controlled, experimental setting is through an economic game called the Ultimatum Game (hereafter UG). In the UG, one player (the Proposer) splits a sum of money with another player (the Responder) who has the choice to either accept the offer (whereby both receive the proposed monetary division) or reject the offer (whereby neither person receives any money). While having a deceptive simplicity, the UG has proven to be very useful to explore many facets of social decision-making, and it has been used in contexts ranging from marketing to neuroscience (Kahneman, Knetsch, & Thaler, 1986; Koenigs & Tranel, 2007; Sanfey et al., 2003). The Repeated Fixed Opponent variant of the UG (where the Proposer and Respondent are fixed and play against each other for the entire game) investigates decision making during repeated social interaction with another person over time, and in some ways is reminiscent of building a relationship with someone.

In the UG, when Proposers make “low” offers, e.g., less than 20% of the total, Responders frequently reject the offer (Guth et al., 1982). On the other hand, offers of 50% of the total and greater are typically considered fair, and are rarely rejected (Fehr & Fischbacher, 2003). The rejection of low offers, which goes against the notion of a “rational actor” since some money is always better than no money, may be motivated by anger (Pillutla & Murnighan, 1996) which can result from the perception of being treated unfairly (Fehr & Fischbacher, 2003). This interpretation fits with findings from neuroscience, which have shown that this rejection behavior involves brain areas that subserve functions related to negative emotion, the insula (Sanfey et al., 2003) and emotion regulation, the ventromedial prefrontal cortex (Koenigs & Tranel, 2007). Interestingly, if a player is given that same (low) offer by a computer, the offer is rejected at a significantly lower rate (Sanfey et al., 2003), suggesting an important role for social context in eliciting emotion during decision making. Concerns for fairness are prevalent in many different cultures (Roth, Prasnikar, Masahiro, & Zamir, 1991). Fairness is thought to be driven by an implicit social norm which promotes group cooperation (Fehr & Fischbacher, 2003). Group cooperation is maintained by rewarding fair behavior and punishing unfair behavior (Fehr & Fischbacher, 2003). All in all, the social context of the UG appears to be an important determinant of behavior, as different responses occur when the game is played in a non-social context.

The current study examines a representative age sample of the adult population to investigate aging-related changes in social decision-making as measured by the Repeated

Fixed Opponent UG. A frequent concern regarding the extension of findings from economic games to real life decision making is that participants may not believe they are playing a real opponent because interaction often occurs through a computer interface. To facilitate the realism of social decision-making behavior in the current study, a novel methodology was employed which utilized a real-time voice communication system. Our study addressed the basic question of whether younger and older adults differ in the manner in which they perform a social decision-making task, the Repeated Fixed Opponent UG. We did not have an a priori directional prediction, but instead, went into the study with the goal of simply establishing whether (and if so, how) older adults differed from younger adults in their social decision-making behavior.

Method

Participants

The sample consisted of 80 healthy adults ranging in age from 24 to 81 years old (M = 48.9, SD = 19.6). There were 32 men and 48 women and 93.8% of the participants were of Caucasian ancestry. The sample was split into two groups based upon age (Table 1). The older age group consisted of participants between the ages of 55-81 years whereas the younger age group contained participants aged 24-45 years. The participant age distribution is shown in Figure 1. Studies of aging typically place participants aged 55 and older into an “older group” whereas participants below age 55 are designated as the “younger group” (Gunning-Dixon et al., 2003; Zamarian, Sinz, Bonatti, Gamboz, & Delazer, 2008), and we followed this convention. The two age groups were not significantly different in years of education [t (64.1) = 1.3, p = .2 (equal variances not assumed)]. Participants were from the Iowa City, Iowa community or nearby areas.

Recruitment occurred through the use of a normal adult registry that is a part of the Division of Behavioral Neurology and Cognitive Neuroscience of the Department of Neurology at the University of Iowa, and through the use of advertisements in a local community newspaper and through the University of Iowa Hospitals and Clinics newspaper, “Noon News.” During the recruitment phase, participants were notified of the inclusion and exclusion criteria before they decided whether to participate. Participants were included if they were normal, healthy adults between the ages of 24-85 years. Exclusionary criteria entailed history or current diagnosis of psychiatric illness or neurological disease based upon self report. Before beginning the study, each participant underwent an informed consent process. This study was conducted in accordance with Institutional and Federal Human Subjects regulations.

Design

During the experiment, the participant played an economic game against another participant. Participants played a version of the Ultimatum Game called the Repeated Fixed Opponent Ultimatum Game in which opponents remained paired together (“fixed”) for several consecutive rounds of game play. Prior to participation, participants were organized into pairs that would play each other during the game. In the Ultimatum Game, one participant (the Proposer) decided how to split $10 with another participant (the Responder), and the Responder then chose whether to ‘Accept’ or ‘Reject’ the offer. If the offer was accepted, both individuals earned the proposed division of money, whereas if it was rejected neither individual earned any money. This procedure of offer followed by response was repeated 20 times in a row within each participant pair. The same two participants remained paired throughout the 20 rounds and kept the same role assignment (either Proposer or Responder). After game play concluded, participants filled out a post-experimental questionnaire that assessed whether they believed they were playing a person "live" during the game. Following the post-experimental questionnaire, trait empathy was measured through the Interpersonal Reactivity Index (Davis, 1980).

Participants were told during the consent process that they would be paid $15 and would be given a parking voucher for their participation in the experiment, but would not be paid for their actual winnings in the Ultimatum Game. They were instructed to "Imagine as if you are playing this game for real money." The rationale for not using contingent incentives (monetary payment based upon performance in the game) was practical (helping to avoid inequity in participant compensation), and we note that such payoffs typically do not affect the mean offer amount given by Proposers or the acceptance thresholds of Responders in the Ultimatum Game (Camerer & Hogarth, 1999; Tompkinson & Bethwaite, 1995).

Previous studies in which participants interact either through a computer interface or by anonymous written note are somewhat artificial compared to what typically occurs during normal social interactions. To enhance the ecological validity of the game in our study, we used a naturalistic design while still controlling for relevant social variables that might have an impact on behavior. To promote enhanced realism in the game, the current study involved the exchange of offers and responses between two participants through an oral communication system. We administered a post-experimental questionnaire in which participants were asked to circle a response of 'yes' or 'no' to the statement: "Did you believe you were playing this game against a real person in another room?" In answer to this question, 100% (80/80) of the participants in the study responded ‘yes,’ indicating that our goal of having participants involved in a realistic interpersonal interaction was accomplished successfully.

In the context of the naturalistic design, we attempted to reduce the influence of other factors. The participants did not meet each other before or after the experiment thus precluding visual information about the participant that could lead to judgments of attractiveness, trustworthiness, and other such characteristics. In addition, participants were asked not to communicate with their game partner in any other way than simply to make an offer or respond to an offer. By preventing conversation, the participants did not learn information about their partner’s personality or biography through their verbal exchange.

Assignment of Participants to Pairs

Prior to the experiment, a research assistant determined which participants would be paired against each other during the Ultimatum Game. Participants were paired based on two criteria (1) current age and (2) schedule availability. Specifically, younger participants aged 24-45 years were matched with other participants within that age bracket, and older participants between the ages of 55-81 years were matched with other participants within that age bracket.

The variable of sex was not specifically controlled, and three different types of pairings emerged which included 24 male-female pairs, 12 female-female pairs, and 4 male-male pairs. Although the role of sex in bargaining behavior has been studied extensively, only a small number of studies have examined its specific role in the Ultimatum Game. Generally, men in the role of the Responder are given higher offers (Eckel & Grossman, 2001; Solnick & Schweitzer, 1999; Solnick, 2001) and are more likely to reject offers than women (Eckel & Grossman, 2001). There is mixed evidence about whether offers made by male or female Proposers are accepted more frequently (Eckel & Grossman, 2001; Solnick & Schweitzer, 1999). In our study, a majority of the participants were in male-female pairs (24), and within these pairs there were equal numbers of males and females in the role of the Proposer (12 male: 12 female) and the Responder (12 male: 12 female), thus decreasing any sex differences that may derive from behavior that is specific to playing a particular role. We might also note that the sex effects in the UG that are reported in previous studies are of small magnitude.

Procedure

When the pair arrived for the experiment, each participant was shown to a separate experimental testing room where they would play the Ultimatum Game against the other participant through a speakerphone system. They were notified in the informed consent document that audio recording would take place throughout the Ultimatum Game. This served as a way to obtain the participants' behavioral responses during the game in a manner that was not intrusive. The research assistant was not present in the experimental testing room during the Ultimatum Game. Each participant was randomly assigned to a role, either the Proposer or the Responder.

The participant in the Role of the Proposer decided how to split $10 with the participant in the other testing room. The Proposer followed four rules, which were presented orally to the participant: (1) No offers of $0 or $10 for the other participant were allowed; (2) Offers must be made in whole dollar amounts (i.e., not x dollars and y cents); (3) Offers (the proposed split) must add up to $10; and (4) Offers may be repeated over the course of the twenty trials. To communicate their offers, the Proposer spoke to their opponent through a hands-free speakerphone system. They were asked to word each offer using the following language: “You get $x, I get $y out of $10,” and were given a written script with this wording to serve as a reminder. The other participant served in the Role of the Responder. Their task was to decide whether to ‘Accept’ or ‘Reject’ each offer that was made to them. They were told that if they were to ‘Accept’ an offer, both people would get the proposed division for that round. For example, if the Proposer said, “You get $4, I get $6 out of $10,” the Responder would receive $4 and the Proposer would receive $6 for that round. On the other hand, if they were to ‘Reject’ an offer, both people would get $0 for that round. The Responder also made their response verbally through a hands-free speakerphone system. Their response was worded in the following manner: “I accept,” or “I reject,” (depending on their decision). This procedure of offer followed by response occurred 20 times in a row between the two participants in the pair.

Results

Age Differences in Behavior on the Repeated Fixed Opponent Ultimatum Game

To address the main question of the experiment, age differences in behavior on the Ultimatum Game were examined. The variables of interest in this analysis were age, offer type (i.e., how much money was offered), and rejection rate (i.e., how frequently various offer amounts were rejected). Typically, studies of the ultimatum game have examined how offer type can affect rejection rate (Koenigs & Tranel, 2007; Sanfey et al., 2003). To simplify the analysis, offers were binned as follows to create five levels of the Offer Type variable: $1&2, $3&4, $5, $6&7, and $8&9. A mixed ANOVA using Offer

Type (1&2, 3&4, 5, 6&7, 8&9) as a within-subjects factor and Age Group (Younger, Older) as a between-subjects factor was conducted to compare Rejection Rates (Figure 2).

In the ANOVA, there were significant effects for Age Group [F (1, 19) = 4.9, $p<.05$] and Offer Type [F (4, 76) = 42.7, $p<.01$]. The interaction between Age Group and Offer Type was not significant [F (4, 76) = 2.0, $p = .10$]. As the data in Figure 2 show, offers less than $5 led to much higher rejection rates (often exceeding 50% of the offers), whereas offers of $5 and greater had rejection rates that were barely above zero in most instances. In fact, the mean rejection rate for offers of $5 and greater was *M*=5.4% (*Mdn* = 0, *Mode* = 0, *SEM* = 2.1), whereas the mean rejection rate for offers less than $5 was *M*=64.6% (*Mdn* = 70, *Mode* = 100, *SEM*=5.6). This pattern, which was true of both the Younger and Older age groups (as shown in Figure 2), replicates a robust effect for the UG, which is that participants frequently reject offers that are less than half the total (so-called "unfair" offers) and rarely reject offers of 50% or more (Fehr & Fischbacher, 2003; Guth et al., 1982).

<u>Older Adults Reject Offers Less than $5 at</u>

<u>Higher Rates than Younger Adults</u>

The main effect of Age Group reflects the fact that the older participants tended to have higher rejection rates than the younger participants. As the data in Figure 2 show, this age-related difference appears to be especially pronounced for the lower, "unfair" offers. Specifically, for both the $1&2 offers (Older: *M*=83.5, *SEM*=9.6; Younger: *M*=65.5, *SEM*=11.8) and the $3&4 offers (Older: *M*=70.1, *SEM*=7.5; Younger: *M*= 48.6, *SEM*=8.9), the Older group had a much higher mean rejection rate than the Younger group. To explore this further, we collapsed across the low offer types (all offers less than \$5) and contrasted the Older and Younger groups (Figure 3). A statistical contrast of the data in Figure 3 yielded a large and statistically reliable difference, with the Older group showing a much higher rejection rate (*M*=75.0, *SEM*=7) than the Younger group (*M*=53.7, *SEM*=8.4), $t(37) = 1.9$, $p < .05$ (one-tailed), $d = .6$.

We next examined the relationship between age as a continuous variable and rejection rate. We conducted a Pearson product-moment correlation which determined whether there was an association between a Responder's rejection rate (of offers less than \$5) and their age in years. This analysis (Figure 4) revealed a positive association between age and rejection rate [r (39) = .3, $p < .05$ (two-tailed)], whereby higher rejection rates were associated with increasing age. The positive association between rejection rate (of offers less than \$5) and age remained after controlling for the type of offers (offer sum score) each participant was given [r (36) = .3, $p<.05$ (two-tailed).]

<u>Follow-up Analysis: Older Adults'</u>

<u>Behavior and Empathy</u>

Having found that older adults rejected lower offers at a higher rate than younger adults in the UG, we were naturally interested in what might be the cause of this behavioral difference. There are many potential factors that could be behind this, but one that seemed of particular intrigue, and for which we have relevant data, concerns the construct of "cognitive empathy." Cognitive empathy refers to the ability to take the perspective of another person in order to understand their thoughts and feelings, and previous studies have shown that cognitive empathy tends to be lower in older adults (Bailey, Henry, & Von Hippel, 2008). Consequently, we were curious to know whether the higher rejection rate in the Older group was related to a decreased level of cognitive empathy.

Cognitive empathy was measured as a trait through the Interpersonal Reactivity Index (IRI), a 28-item self-report questionnaire that assesses the multidimensional nature of empathy (Davis, 1980). The IRI includes four subscales which assess the perceived ability of the individual in each of these domains: Perspective Taking (adopting the mental perspective of another person), Empathic Concern (experiencing feelings of compassion for others), Fantasy (adopting the perspective of a fictional character in a book or movie), and Personal Distress (feeling unease or distress in the face of the physical or emotional harm of another person). In the current study, the Perspective Taking subscale of the IRI was used to index cognitive empathy. Similar to previous research, we found that older adults showed decreased cognitive empathy in comparison to younger adults (older: M=17.3, SD=3.2; younger: M=19.6, SD=3.1; t (38) = 2.3, p < .05 (two-tailed), d = .7). Moreover, taking age as a continuous variable, we found that age was reliably and negatively related to cognitive empathy, such that increasing age was associated with decreased cognitive empathy [r (40) = -.3, p < .05 (two-tailed)]. This outcome is consistent with previous findings (Bailey et al., 2008).

Now, turning to the key question of whether decreased cognitive empathy might be related to UG behavior, we investigated the correlation between cognitive empathy and rejection rate (of offers less than $5) in the UG. The results are presented in Figure 5. Cognitive empathy was reliably and negatively related to rejection rate, such that increasing rejection rate was associated with decreased levels of cognitive empathy [r (39) = -.3, p < .05 (two-tailed)]. Thus, these two findings might help explain the UG behavior of older adults: (1) Older adults have lower cognitive empathy than younger adults; and (2) Lower cognitive empathy is related to higher rejection rates for unfair offers in the UG.

Discussion

The current study examined whether younger and older adults differ when making financial decisions in a social context. We found that in the Repeated Fixed Opponent UG, when the offers were “fair” (offers of 50% of the total or greater), both older and younger adults rejected very few offers. This outcome is consistent with previous research on the Ultimatum Game, which has shown that participants rarely reject offers of 50% of the total or greater (Fehr & Fischbacher, 2003). However, for the lower, “unfair” offers (offers less than 50% of the total) we found that rejection was frequent. This rejection of unfair offers was especially pronounced in the older group. In fact, older participants rejected a majority of the lower offers, 75% to be exact, whereas younger participants rejected about half of the lower offers (just over 50%). In sum, there was a notable difference in the behavior of older and younger adults in the Repeated Fixed Opponent UG, whereby older participants had significantly higher rejection rates for low (“unfair”) offers, compared to younger participants. This is the first study to our knowledge to use the Repeated Fixed Opponent UG to examine age-related differences in financial decision making in a social context. Through the use of a novel verbal communication system, believability was enhanced such that 100% of participants thought they were playing another person ‘live.’ This type of methodology enabled us to ensure that participants believed this game was taking place in a social context.

In general, the maintenance of fairness may serve as a strong motivator of behavior in the Ultimatum Game. In the Repeated Fixed Opponent UG, there is a clear, sharp distinction between behavior on the “fair” offers (which are rarely rejected) and “unfair” offers (which are often rejected). This corroborates previous studies of the Ultimatum Game, which have also shown a distinction between behavior towards fair versus unfair offers (Koenigs & Tranel, 2007; Sanfey et al., 2003). The motivation to promote fairness in the Ultimatum Game is thought to be driven by a social norm for fairness that exists in many cultures (Roth et al., 1991). Evolutionarily, it is thought that this norm developed to promote cooperation between groups (Fehr & Fischbacher, 2003). To maintain fairness in situations where an individual acts unfairly, altruistic punishment may come into play (Fehr & Fischbacher, 2003). Altruistic punishment involves the punishment of an unfair act in order to promote fair and cooperative behavior in the future (Fehr & Fischbacher, 2003), at some personal cost to the agent doing the punishing. In the context of the Ultimatum Game, rejection of “unfair” offers is a form of altruistic punishment that may be used to promote more equitable behavior in subsequent interactions. There is evidence that inequitable offers elicit anger in Responders as measured by self-report (Pillutla & Murnighan, 1996). Moreover, functional imaging (Sanfey et al., 2003) and lesion (Koenigs & Tranel, 2007) studies have shown that responses to perceived inequitable treatment during the UG are linked to neuroanatomical regions that are part of the brain’s emotion circuitry, including the insular cortex and ventromedial prefrontal cortex. Clearly, negative emotion is a common response to inequitable behavior on the Ultimatum Game.

Returning to the current study, the question can be posed as to why we found age-related differences in behavior in response to “unfair” offers in the Repeated Fixed Opponent UG, and whether emotion-related factors could be contributing to this finding. Current research on older adults suggests that aging leads to a decrease in negative emotion, or a “positivity” effect (Carstensen & Mikels, 2005). There is evidence that negative emotions are less frequent and less intense in older adults (Birditt & Fingerman, 2003; Gross et al., 1997). Moreover, fMRI studies have revealed that stimuli with negative valence produce less activation in older adults than younger adults in so-called “limbic system” structures, which play an important role in emotion processing (Iidaka et al., 2002; Mather et al., 2004).

In light of this evidence, one might expect that a decrease in negative emotion would lead to *lower* rejection of “unfair” offers in the UG, since responders would, for example, feel less anger, resentment, and so on, from unfair treatment. Accordingly, if older adults have less negative emotion, and if negative emotion is part of the reason why people reject unfair offers in the UG, it would be expected that older adults would reject fewer low offers in the UG. But this is not what happened in our study—in fact, we found exactly the opposite result. This outcome suggests that the story is more complex than simply the notion that negative emotion leads to higher rejection rates in the UG. One parsimonious account of our findings is that in older adults the fairness response may be accentuated. The older adults may simply be “tough” players: they are not willing to put up with unfair treatment, and they are more inclined to send an immediate and direct message back to their playing partner to the effect of, “that was not fair; make me a better offer.” This might not have anything to do with negative emotion, per se, but simply with the basic tenets of fair treatment—reminiscent of the sentiment that “right is right, wrong is wrong.” It will be interesting in future studies to collect feedback from the players regarding their strategies, feelings, and so on during the game, to get a better handle on what could be accounting for their behavior, and especially the high rejection rates for low offers.

In addition to changes that affect basic emotions, older adults also show changes in their ability to engage in complex interpersonal emotions such as empathy and theory of mind (Bailey et al., 2008; Maylor, Moulson, Muncer, & Taylor, 2002; Sullivan & Ruffman, 2004). Cognitive empathy is defined as mentally taking the perspective of another person, or in other words, attempting to put oneself in the shoes of another person (Davis, 1980). Cognitive empathy has been shown to be decreased in older adults (Bailey et al., 2008). There is also evidence that older adults show a decrease in a related construct, known as “theory of mind” (or mentalizing)—specifically, the ability to predict and understand the mental states (beliefs, intentions) of others (Gallagher & Frith, 2003). Older adults have more difficulty than younger adults in recognizing the mental states of others from written scenarios (Maylor et al., 2002) and videos (Sullivan & Ruffman, 2004). Functional imaging studies have shown that theory of mind involves the medial prefrontal cortex as well as the temporal pole and posterior superior temporal sulcus (Singer, 2006). A lesion study has shown that cognitive empathy (as measured through self report questionnaire) is decreased in patients with damage to the ventromedial prefrontal cortex (Shamay-Tsoory et al., 2009). Since the frontal lobes have been shown to play a role in both theory of mind and cognitive empathy, degeneration of this brain region as a consequence of aging (Raz & Rodrigue, 2006) may produce decreased functioning in older adults.

In looking for possible explanations of the age-related difference in UG behavior, we had data regarding cognitive empathy which we were able to bring to bear on the findings. Specifically, measurements of cognitive empathy were available, and we found that (1) cognitive empathy was reduced in the older participants, and (2) cognitive empathy was negatively related to rejection rates for low offers. To put the second finding another way, lower cognitive empathy was associated with higher rejection rates for low offers. Together, these findings raise the interesting possibility that reduced cognitive empathy in older individuals could be a contributing factor in their higher tendency to reject “unfair” offers in the Ultimatum Game.

One additional factor that should be noted is the nature of the UG. We used a Repeated Fixed Opponent version, where the playing partners remained paired throughout 20 rounds of the game. This is different from the more widely used, 1-Shot version of the UG, where the Proposer changes on every round (i.e., the Responder receives and responds to offers from 20 different Proposers across the 20 trials of the game). The Repeated Fixed Opponent UG has not been studied very extensively (Slembeck, 1999), and much less is known about the nuances of this version compared to the 1-Shot version. Thus, it is possible that the age-related effect we obtained might not extend to the 1-Shot version of the UG, and this is an empirical question that can be answered in future research. In any event, in the Repeated Fixed Opponent version that we utilized in the current study, it seems clear that older adults have a very strong proclivity to reject low offers, compared to younger adults. Given the relationship between lower cognitive empathy and higher rejection rates, it is possible that the lower cognitive empathy in older adults is a contributing factor to this phenomenon.

In closing, we would like to mention that these findings, albeit in need of replication and extension in further research, could have very important implications for understanding social decision-making behavior in the context of aging. For example, taking the current findings at face value, it would appear that when negotiating a financial arrangement with an older person, one would be well advised to start out with a “fair” offer. Offers that appear unfair may be rejected outright, ending the bargaining process before it even gets started. This could have many important implications for the manner in which various business persons, financial institutions, and other financial brokers approach their deal-making interactions with older persons.

Table 1. Experiment 1: Fixed Opponent Repeated UG Sample Demographics

	# of Pairs (Participants)	# of Males/ Females	Age in years *M* *(SD)*	Education in years *M* *(SD)*
Younger Adult Pairs	20 (40)	15/25	30.8 (6.5)	16.5 (1.6)
Older Adult Pairs	20 (40)	17/23	67 (7.9)	15.8 (2.7)

Figure 1. Experiment 1: Frequency Distribution of Participant Age

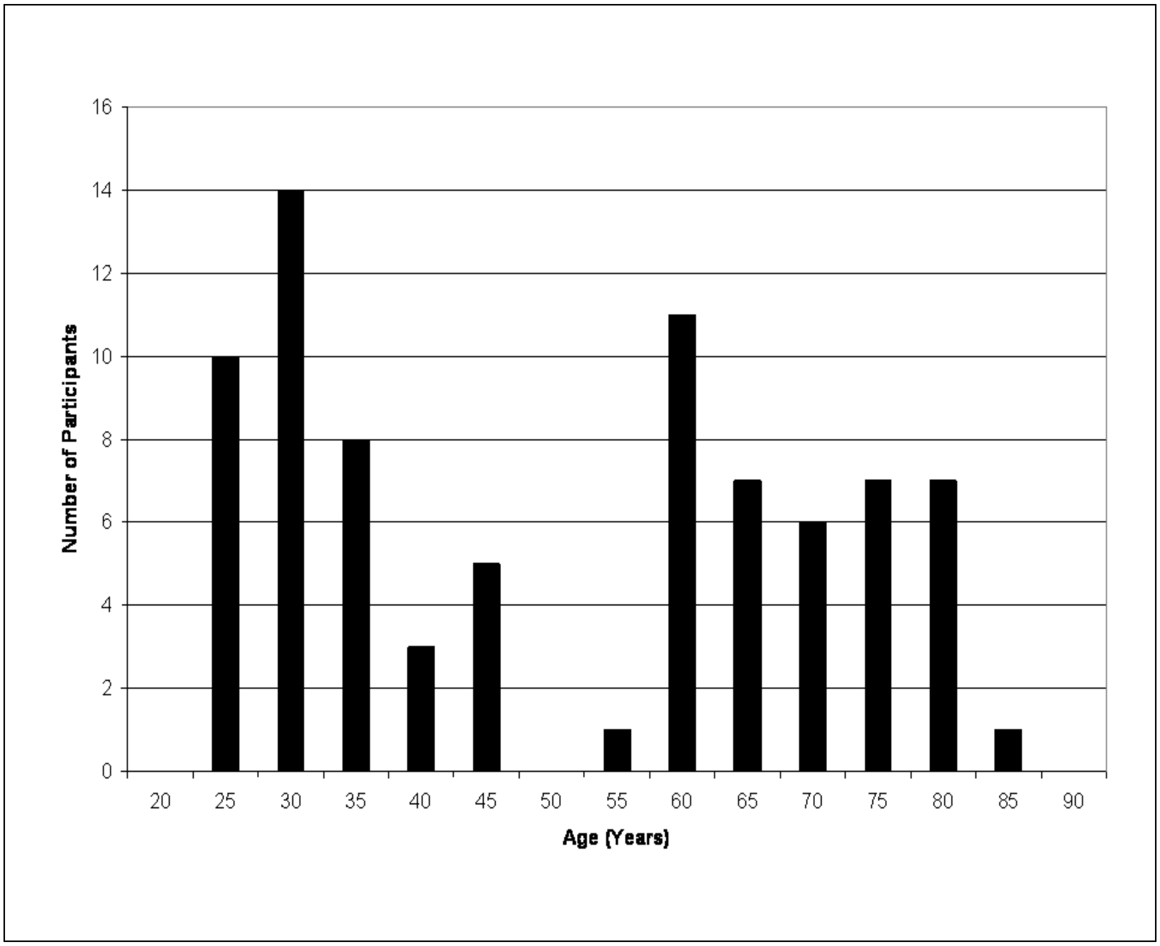


Figure 2. Experiment 1: Age Differences in Behavior on the Repeated Fixed Opponent Ultimatum Game (UG.) Rejection rate (%) was contrasted as a function of Offer Type ($1&2, 3&4, 5, 6&7, 8&9) and Age Group (Younger, Older). Error bars indicate standard error of the mean.

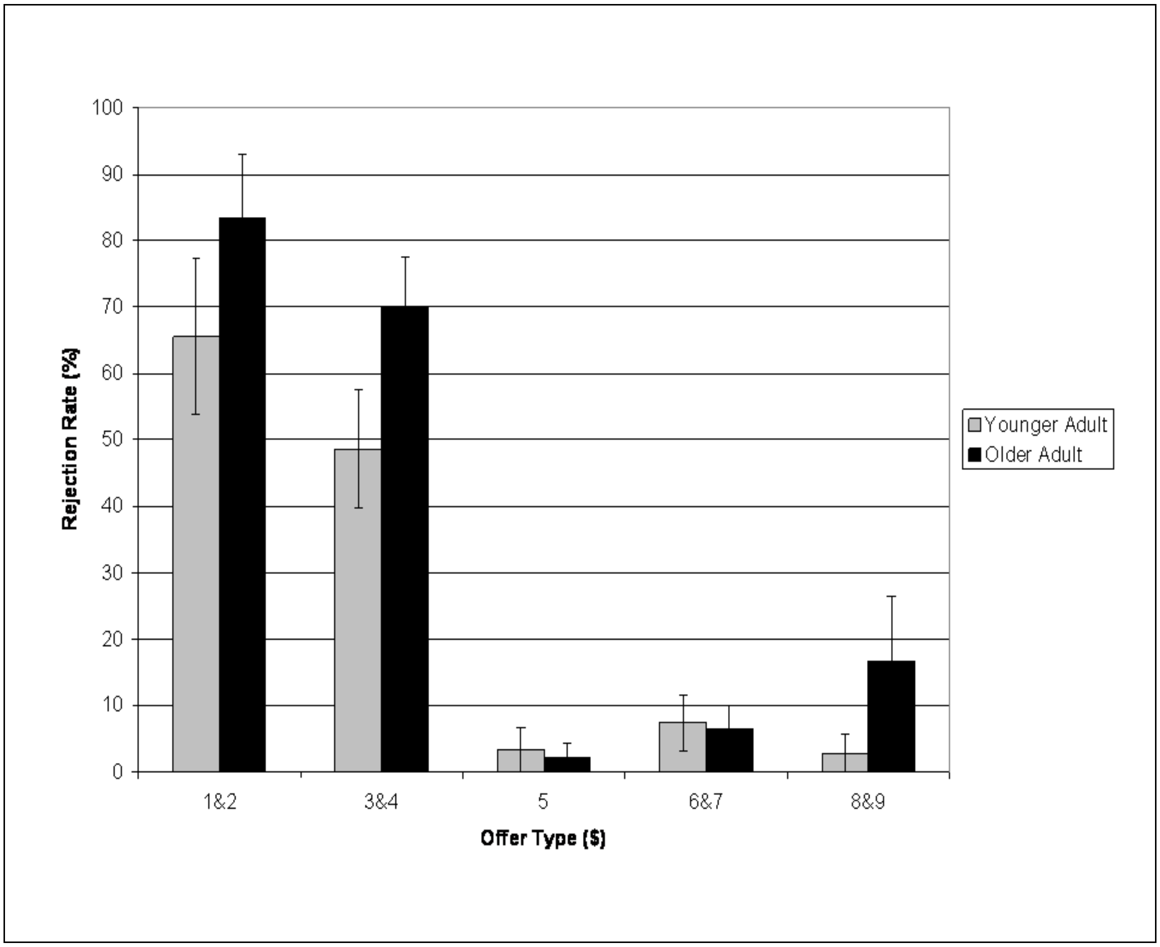


Figure 3. Experiment 1: Rejection Rates for All Offers Less than $5 (“unfair” offers) on the UG as a Function of Age Group (Younger, Older).

Error bars reflect standard error of the mean.

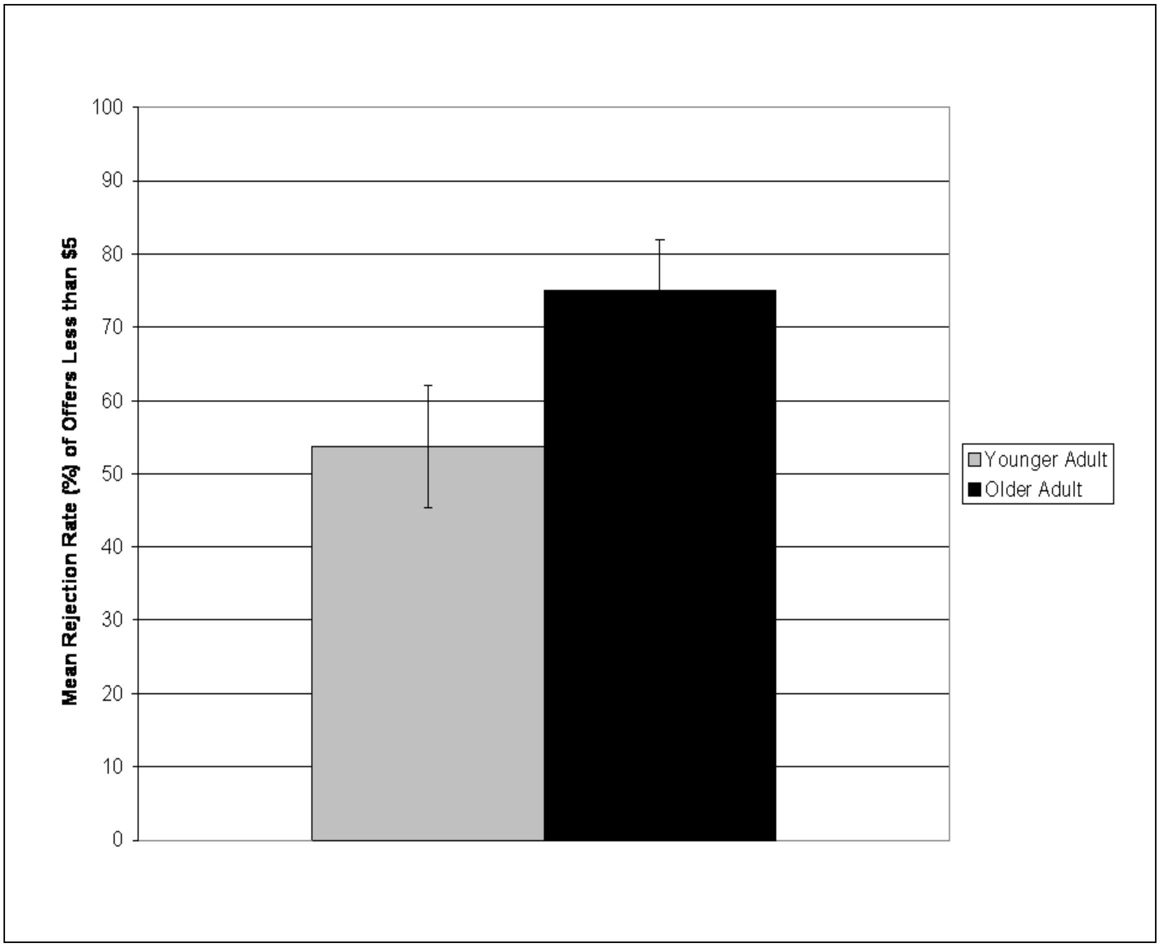


Figure 4. Experiment 1: Responder Rejection Rate (of offers less than $5) on the UG is Positively Associated with Age, such that Higher Rejection Rates are Related to Increased Age

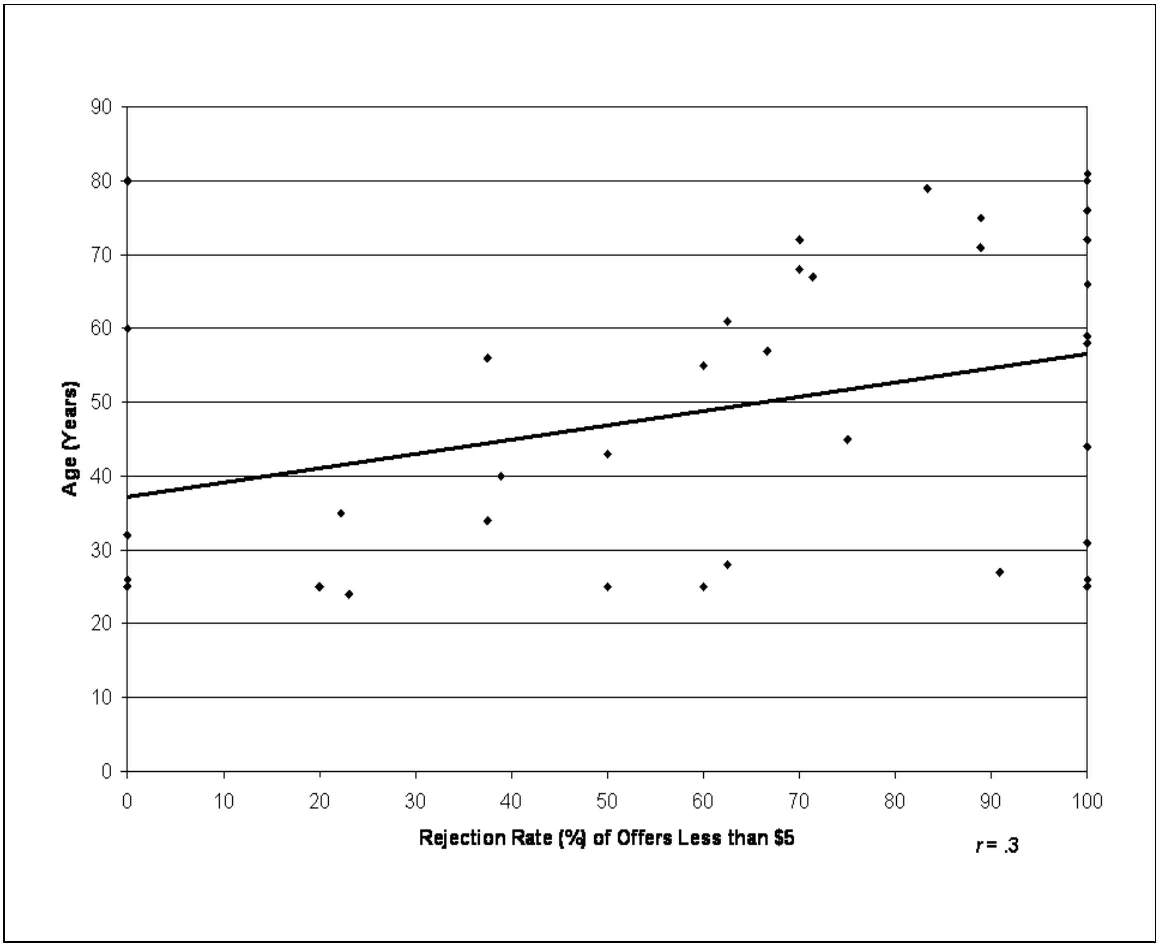
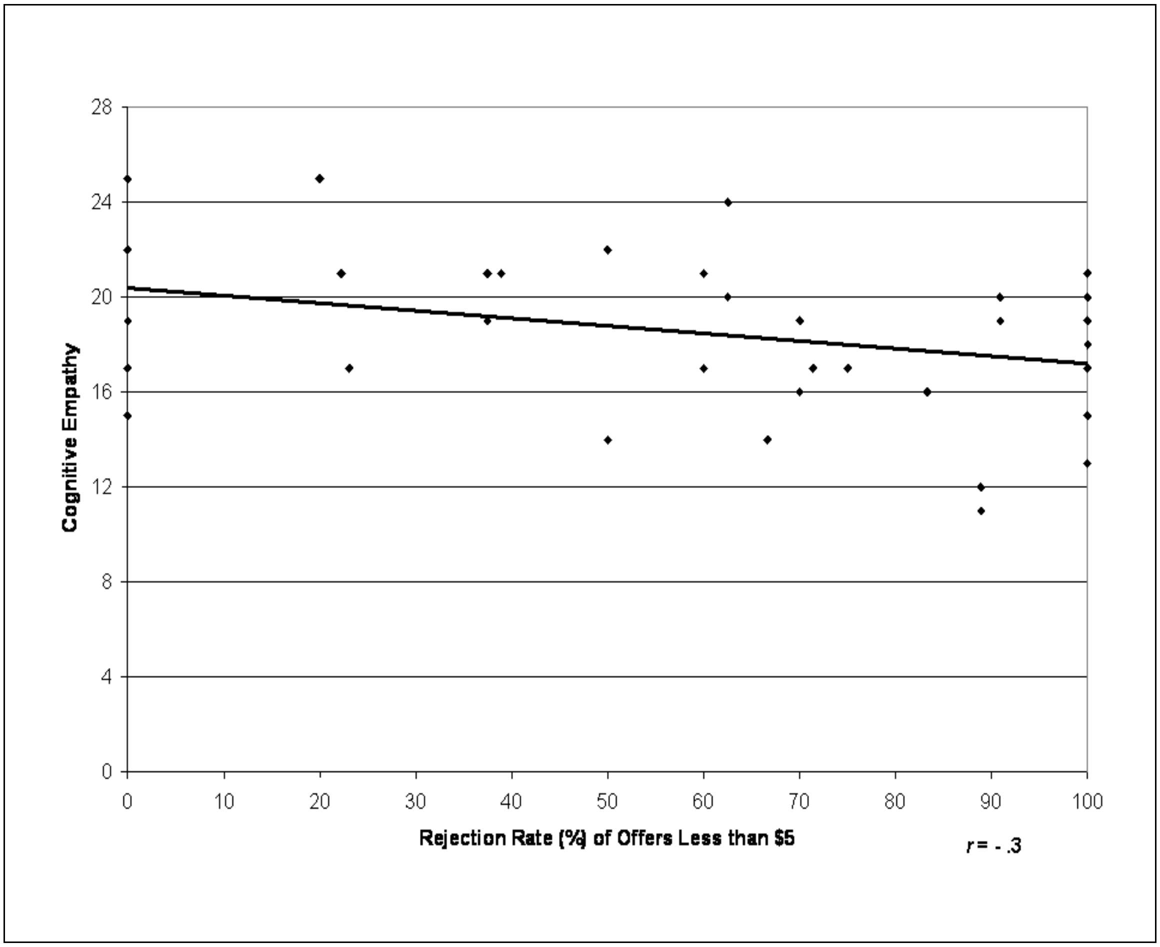


Figure 5. Experiment 1: Responder Rejection Rate (of offers less than $5) on the UG is Negatively Associated with Cognitive Empathy, such that Higher Rejection Rates are Related to a Decreased Level of Cognitive Empathy



CHAPTER 4

EXPERIMENT 2: INVESTIGATION OF EMPATHIC EXPERIENCE AND BEHAVIOR IN PATIENTS WITH DAMAGE TO THE VENTROMEDIAL PREFRONTAL CORTEX

Part 1: Pilot Study Examining the Effectiveness of a Novel Empathic Induction in Healthy Adults

Participants

Twelve healthy adults ranging in age from 25-62 years from the Iowa City, IA community or nearby areas participated in this study. Inclusionary criteria entailed healthy volunteers from communities nearby Iowa City, IA who were between the ages of 25-85 years. Participants were excluded if they had a history of or current diagnosis of neurological or psychiatric illness based upon self report.

Recruitment

Recruitment occurred through the use of a normal adult registry that is a part of the Division of Behavioral Neurology and Cognitive Neuroscience of the Department of Neurology at the University of Iowa. Additional recruitment was conducted through the use of advertisements in a local community newspaper and through the University of Iowa Hospitals and Clinics newspaper, “Noon News.” During the recruitment phase, participants were notified of the inclusion and exclusion criteria before they chose to participate.

Design

This experiment measured the effectiveness of a novel, empathic induction in healthy adults. During the experiment, participants underwent an experimental induction of an empathic and a neutral state. On-line empathic experience as a result of the two inductions was measured through a self-report questionnaire which will be further described in the section below entitled, 'Questionnaire Measure of On-line Empathy.' The empathic and neutral states were induced through audio recordings. In order to prevent interference effects between the two inductions, another audio recording that consisted of white noise (4 ½ minutes long) occurred between the two inductions. The order of the inductions was as follows: the neutral induction, followed by the white noise recording, and finally the empathic induction. The neutral recording consisted of a male participant in his mid 50's and female research assistant who was conducting the experiment in her 20's discussing the events of their day. The empathy-induction recording consisted of the same female research assistant and a different male research participant in his 50's who begins the conversation by talking about his day and then reveals his deep sorrow over the death of his son of whose anniversary of his death is that day.

Questionnaire Measure of On-line Empathy

A self-report questionnaire assessed on-line empathy during the experiment. It was given immediately before and immediately after each induction type (neutral, empathy.) In the course of the experiment the questionnaire was given four times: Baseline 1 (immediately before the neutral induction), Neutral Induction (immediately after the neutral induction), Baseline 2 (immediately before the empathy induction), and

Empathy Induction (immediately after the empathy induction.) The white noise recording took place after the Neutral Induction but before the Empathic Induction.

On-line empathy was measured by a questionnaire which assessed the participants current feeling state through a series of emotion adjectives. Specifically, participants were asked to rate a series of emotion words based upon these instructions: 'Indicate to what extent you feel this way right now, that is, at the present moment.' Participants rated the emotion adjectives based upon this scale: 1 'Very slightly or not at all,' 2 'a little,' 3 'moderately,' 4 'quite a bit,' and 5 'extremely.' This rating scale was drawn from the instructions for the Positive and Negative Affective Schedule—PANAS—which is often used to assess mood state (Watson & Clark, 1994).

The questionnaire items measured emotional empathy as well as other emotions to assess divergent validity. The items were drawn from two different questionnaires: the Positive and Negative Affective Schedule (Watson & Clark, 1994) and the Emotional Responsiveness scale (Batson, Duncan, Ackerman, Buckley, & Birch, 1981). The sadness subscale of the PANAS was used to measure emotional empathy. Emotional empathy has been defined as a sharing or matching of emotions between the person experiencing the emotion and the person observing them. During the empathic induction, the man describes how he feels about his son's death, clearly revealing the anguish and sadness he is currently experiencing. Consequently, a direct emotional match to these emotions would be the experience of sadness in the participant. From the PANAS, the two items that were thought to most clearly measure sadness were selected and included the terms 'sad' and 'downhearted.' To provide an assessment of the specificity of the negative emotion the participant was experiencing, two items from another negative emotion subscale, the hostility subscale, were used and included the terms ‘hostile’ and ‘angry.’ Lastly for divergent validity, two items from a positive emotion subscale, the joviality subscale, were selected and included ‘happy’ and ‘joyful.’ This questionnaire also assessed the participant’s empathic concern or feelings of sympathy towards the other person. Empathic concern was assessed through two items most representative of this construct from the Emotional Responsivity Questionnaire (Batson et al., 1981).

Design of Experimental Inductions

The empathy and neutral inductions were specifically created for this dissertation to produce realistic, natural, and effective inductions that were constrained by relevant experimental parameters. The recordings involve a female in her 20’s and two different actors, one who performs the neutral conversation and another who performs the empathic conversation. I played the role of the female research assistant in the recordings and served as the research assistant for this experiment. First, the criteria for actor selection was decided. Because there is some evidence that similarity enhances one’s ability to induce empathy, we selected actors from an age range that is most similar to the majority of our participants (50-60 years). We also considered the effect of the sex of the actor on empathy induction. We chose to include only male actors because there is some evidence that when males play the Ultimatum Game they treat both sexes similarly whereas females show preferential behavior to males (Eckel & Grossman, 2001; Solnick & Schweitzer, 1999; Solnick, 2001). This was important because the empathy induction is employed within the context of the Ultimatum Game for Experiment 2.

Next we determined the content of the conversations in the neutral and empathic induction. These decisions were made by consensus selection of a panel of six researchers from the current laboratory. For the neutral induction, we selected a number of conversation topics thought to induce a neutral experience. It was decided that the topic of the neutral conversation would be a non-emotional discussion of the activities that take place during a typical day of a person between 50-60 years. Specifically, the neutral conversation included a discussion of such things as what they had to eat for breakfast, the specifics of their game of bridge, and reading the newspaper, among others. To select the topic for the empathic induction, we again composed a list of several possible topics and then made a consensus decision based upon the realism and the effectiveness of the induction. We decided that the empathic recordings would include a conversation of a father talking about his feelings about the death of his college-aged son.

After deciding upon the content of the recordings, we selected the experimental parameters we wanted to control within the recordings. To enhance believability, one parameter we chose to control was the time of day that the recording took place. Since the testing of most participants for the current study would occur in the late morning or early afternoon, the actors in the recordings only referenced daily activities that could have realistically happened during the morning. For example, the actors talk about what they had for breakfast and reading the newspaper. The length of the conversations in the recordings was another parameter that was controlled. Conversations were limited to 4 ½ minutes. This specific length of time was chosen based upon the time constraints of the experiment as well as extensive piloting that revealed that this length of time is necessary to induce a realistic empathic response.

After parameter selection was finalized, we began a pilot process to select the most effective actors and recordings. An advertisement was sent by email to the various community theaters in Iowa City, IA and surrounding areas. Four actors were selected over the phone based upon age and sex criteria as well as years of theatrical experience. The actors were told that they would be given $30 as compensation for the time it would take to make the recordings. Then the actors were sent a word document containing the empathic and neutral scenarios as well as the other relevant parameters (time of day, length of recording). Each of the four actors was asked to come to a sound studio where they would make the recordings. Once they arrived, the actors practiced the scenario with the Research Assistant about 3-4 times. The Research Assistant and the actors discussed various ways to make the scenario as believable as possible. Finally, the actor performed both the neutral and empathy recordings six times, each time with a slight variation of performance. Then out of the 12 recordings from each actor we selected the most effective two actors and recordings. The panel of researchers listened to all versions of the recordings and rated the degree to which each recording was effective. Based on the group ratings, two of the actors were chosen each of whom performed in either the neutral or empathic induction.

Results

This experiment tested the degree to which the empathy induction was able to produce an empathic state in the participant as measured by a self report questionnaire of emotional ratings. First, the affect of each induction (neutral, empathy) on the self report ratings of emotion was assessed per subscale (sadness, empathic concern, hostility, and joviality; see Figure 6). For the empathy induction condition, mean ratings of sadness (M=2.75, SD=1.27) were higher than in the neutral induction (M=1.17, SD=0.39) or the two baseline conditions (Baseline 1: M=1.33, SD=0.75; Baseline 2: M=1.29, SD=0.45.)

Due to the empathic induction, a mean rating of sadness of 2.75 is representative of feelings of ‘moderate’ sadness according to the scale. In the empathic induction condition, the mean of the empathic concern ratings was 3.58 (*SD*=1.22) which was higher than in the neutral induction condition (*M*=1.96, *SD*=0.78) or either of the two baseline conditions (Baseline 1: *M*=1.96, *SD*=1.18; Baseline 2: *M*=1.38, *SD*=0.64). The mean empathic concern ratings of 3.58 during the empathy induction indicate that the participants were feeling ‘quite a bit’ of empathic concern on average.

Next, the degree to which each induction (neutral, empathy) condition caused a change from one’s baseline emotional state (Baseline 1, Baseline 2) was calculated. More specifically the baseline ratings that occurred immediately before each induction were subtracted from the ratings that occurred immediately after each induction. For example, the calculation to determine the degree to which the neutral induction caused a change from baseline state was calculated by: ‘Emotional Ratings after Neutral Induction’ – ‘Emotional Ratings before Neutral Induction (i.e. Baseline 1). Similarly, to assess the change in emotional ratings due to the empathic induction we performed this calculation: (Emotional Ratings after Empathic Induction – Emotional Ratings before Empathic Induction, Baseline 2). These calculations were computed separately for each subscale (sadness, empathic concern, hostility, and joviality) and per participant. Based upon this calculation, a Neutral Change Score and an Empathy Change Score was created for each participant. Then the mean of the Neutral Change score and Empathy Change Score across participants was calculated. Due to the empathic induction the change from Baseline 2 resulted in an increase in sadness (*M*=1.46, *SD*=1.01) and empathic concern (*M*=2.21, *SD*=1.03). Both hostility (*M*= -0.13, *SD*=.38) and joviality (*M*= -0.29, *SD*=1.1) showed a slight decrease due to the empathic induction from the ratings at Baseline 2 (see Figure 7).

Next we assessed the degree to which the empathic induction produced empathic feelings that were greater than those produced in the neutral and baseline conditions. To investigate this question, for each participant and for each emotional rating subscale the Neutral Change Score was subtracted from the Empathy Change Score (Empathy Change Score – Neutral Change Score) in order to determine the emotional ratings that were specific to the Empathic Induction condition. Once this score was computed, we determined the mean for each emotional rating subscale across the group of participants. Specific to the empathic induction, participants showed the greatest increase from the neutral condition in their emotional ratings of sadness (M = 1.63, SD = 1.28) and empathic concern (M = 2.2, SD = 1.39), see Figure 8. There was also a slight decrease in their feelings of hostility (M = -0.17, SD = 0.44) as a consequence of the empathic induction.

Conclusions

The results suggest that the empathy induction was effective in producing an increase in empathy as measured by ratings of sadness and empathic concern. When examining the raw scores of the emotional ratings due to the empathic induction, we found that participants felt 'moderate' feelings of sadness and experienced 'quite a bit' of empathic concern. After accounting for the effect of both the neutral induction and the baseline conditions on emotional ratings, it was found that as a consequence of the empathic induction specifically, only emotional empathy and empathic concern increased. In addition, there was a slight decrease in feelings of hostility whereas feelings of joviality did not change. These results suggest that the empathic induction effectively increased on-line empathy in healthy adults.

Figure 6. Experiment 2 Part 1: Effect of Induction of Empathy through Recordings on Emotion Ratings (Sadness, Empathic Concern, Hostility, Joviality) at Baseline 1, after the Neutral Induction, Baseline 2, and after the Empathy Induction

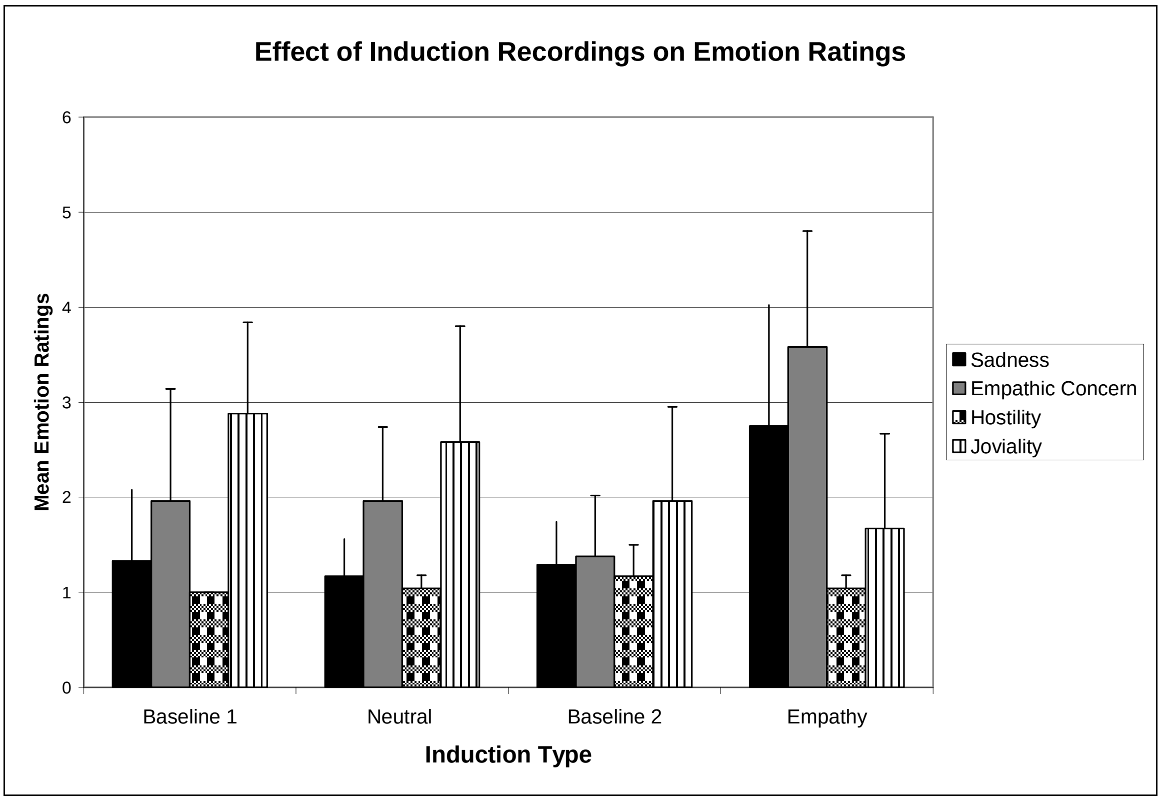
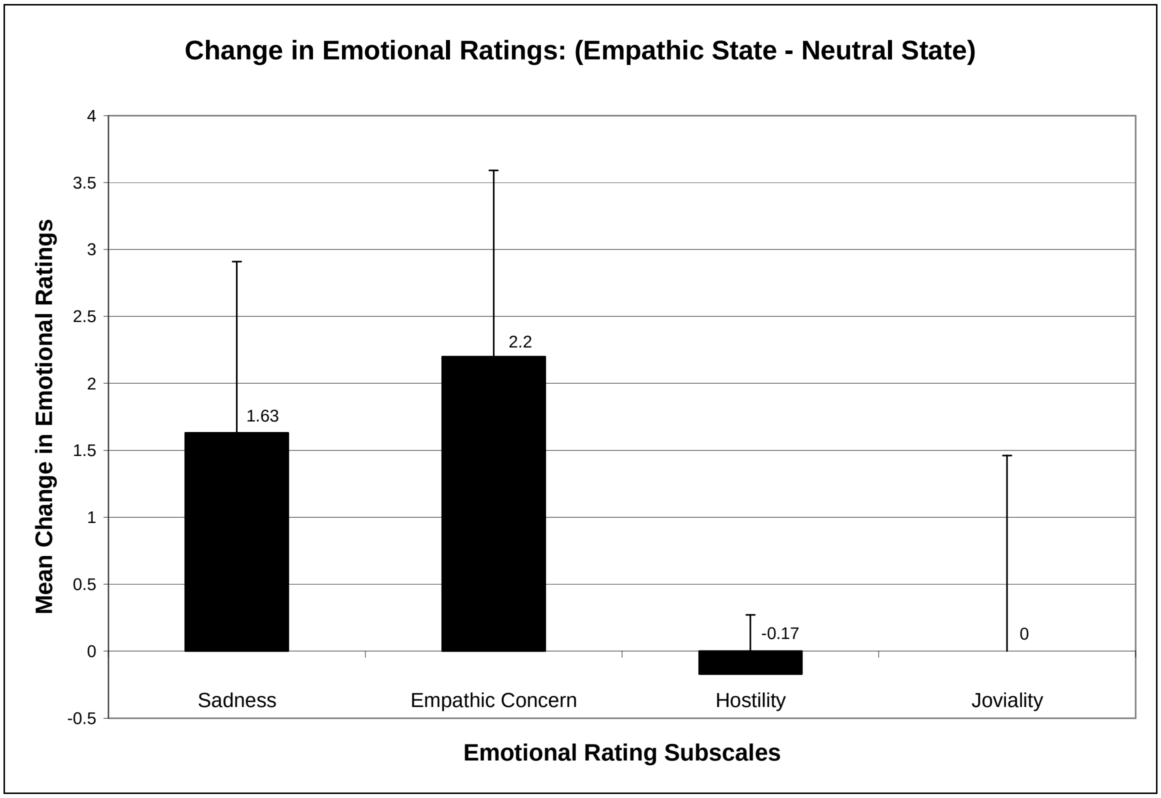


Table 2. Experiment 2 Part 1: Emotional Change from Baseline due to either the Neutral or Empathic Induction

Emotion Ratings	Neutral Induction *M* *(SD)*	Empathic Induction *M* *(SD)*
Sadness	-0.17 (0.62)	1.46 (1.01)
Empathic Concern	0 (1.02)	2.21 (1.03)
Hostility	0.04 (0.14)	-0.13 (0.38)
Joviality	-0.29 (0.96)	-0.29 (1.1)

Figure 7. Experiment 2 Part 1: Emotional Change due to the Empathic Induction after Accounting for Emotions Produced by Neutral Induction



Part 2: Examination of Empathic Experience and Behavior in Patients with Damage to the Ventromedial Prefrontal Cortex

<u>Participants</u>

Target Group: Patients with Bilateral Brain Damage to the VMPC region

This group included six patients with chronic, focal, bilateral damage to the VMPC region of the brain. Damage to the VMPC region of the brain is defined as a focal lesion extending into both hemispheres of the VMPC that includes the medial half of the orbital surface as well as the medial surface of the prefrontal cortex that is located at or below the genu of the corpus callosum (and includes the associated white matter.)

A lesion overlap map of the six patients with damage to the VMPC was created to examine brain regions where there were the greatest number of patients with lesions. Based upon the lesion overlap map, the VMPC was found to be one of the regions of greatest overlap (see Figure 8.)

Participants were included if they had chronic, focal brain damage to the VMPC region in both hemispheres. The chronic period of brain damage was defined as 3 months or longer after onset of brain damage. Patients were only included if the brain damage was a consequence of cerebrovascular accident, herpes simplex encephalitis, anoxia/ischemia, or surgical ablation. Patients who had brain damage to regions outside of the VMPC were excluded. Other exclusionary criteria consisted of full scale IQ, executive function or memory scores below the normal range, current or history of psychiatric illness, alcohol or drug abuse, uncorrected visual impairment, or hearing problems. Because the study involved completing written questionnaires and listening to auditory stimuli, it was necessary to ensure that participants had intact vision and hearing.

Full scale IQ was determined through neuropsychological testing using the WAIS-III or WAIS-R. Participants were screened for psychiatric illness through clinical interview and were not included in the study if they were currently experiencing psychiatric disease. Further details about the demographic and neuropsychological characteristics of the participant groups can be found in Table 3.

Recruitment occurred through the Patient Registry that is a part of the Division of Behavioral Neurology and Cognitive Neuroscience of the Department of Neurology at the University of Iowa. Patient inclusion in this registry follows a strict induction process. Patients are not included if they have mental retardation, dementia, psychiatric disease, or alcohol or drug abuse. To be included in the registry, patients must have brain damage in the chronic epoch (i.e. three months or more after the accident) and the damage must be focal and circumscribed. Brain damage may be caused by cerebrovascular accident, herpes simplex encephalitis, surgical ablation, anoxia/ischemia, and in some cases cerebral contusion (Traumatic Brain Injury).

Comparison Group 1: Patients with Focal Damage to Brain Regions that do not include the VMPC or other Regions Related to Empathy

Six patients with chronic, focal brain damage were included in this comparison group. The comparison patients were case-matched to the patients with damage to the VMPC on the following variables: age, sex, handedness, education, and Full Scale IQ. Full Scale IQ was also assessed through the WAIS-3 or WAIS-R. Those with a current psychiatric illness (as determined by clinical interview) were excluded from the study.

Participants were included if they had chronic, focal damage to brain regions that do not include the VMPC or other regions thought to be involved in empathy including the amygdala, the insula, and the inferior frontal gyrus. Participants with damage to the VMPC, amygdala, and insula were excluded from this group. Participants who had full scale IQ, executive function or memory below the normal range were also excluded. Other exclusionary criteria consisted of current or history of psychiatric illness, alcohol or drug abuse, uncorrected visual impairment, or hearing problems. Recruitment occurred through the same procedure that was used to recruit participants in the group with brain damage to the VMPC.

Comparison Group 2: Healthy Individuals

This group included six healthy, normal individuals that were screened for neurological and psychiatric illness. The healthy comparisons were case-matched to the patients with damage to the VMPC on age, sex, handedness, education, and full scale IQ.

Healthy, normal participants that did not have a history of neurological or psychiatric illness were included in the study. Participants were excluded if they had full scale IQ scores, executive function or memory scores below the normal range. Participants with current or history of neurological or psychiatric illness, alcohol or drug abuse, uncorrected visual impairment, or hearing problems were excluded.

Psychiatric disorders were screened through the use of an interview that utilized a modified version of the Structured Clinical Interview for DSM Axis I Disorders (SCID). This version of the SCID assessed Major Depression, Schizophrenia, Dysthymic Disorder, Mania/bipolar Disorder, Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Post Traumatic Stress Disorder, and Panic disorder, Somatoform Disorders, and Eating Disorders. Neuropsychological testing was conducted to assess neuropsychological status. Full Scale IQ was assessed through the Wechsler Abbreviated Scale of Intelligence (WASI). Memory and executive function was assessed through the Rey Auditory Verbal Learning Test (RAVLT), and the Rey Complex Figure Test, and the Wisconsin Card Sorting Task (WCST).

Participants were recruited from a sample used in a previous study conducted in Dr. Sergio Paradiso’s laboratory that measured emotional functioning in normal, healthy adults and patients with depression entitled, ‘Thoughts and Emotions in Depression’ (HawkIRB # 200306053). Neurological, psychiatric, and neuropsychological assessment of participants occurred at the time of participation in the, ‘Thoughts and Emotions in Depression study.’ This study has been taking place from November 2005 to the present. I am a research team member on the ‘Thoughts and Emotions in Depression’ IRB as well as the current project, ‘Decision Making in Patient and Aging Populations’ (HawkIRB # 200701714). The protocol for the current project explicitly stated that I would recruit participants for my study from the sample of individuals who had participated in the ‘Thoughts and Emotions in Depression’ study. The normal, healthy adults that participated in this experiment did not overlap with those in Experiment 1 or Experiment 2 Part A.

Recruitment for the current study entailed calling participants from the ‘Thoughts and Emotions in Depression’ Study. Through the use of an IRB approved phone script, I asked participants if they were interested in participating and then I went through a list of screening questions. The screening process included an assessment of whether the participant met the inclusionary and exclusionary criteria.

Original recruitment for the ‘Thoughts and Emotions in Depression’ study occurred through the use of newspaper advertisements in the local newspapers and university hospital, brochures, posters, a registry, and a website. Specifically, the websites used to recruit participants was: http://www.uihealthcare.com/depts/med/psychiatry/research/lateonsetdepression.html and http://www.uihealthcare.com/depts/clinicaltrials/volunteer.html. In addition, some participants were selected from the "Seniors Together in Aging Research" (STAR) registry developed by the University of Iowa Center on Aging. Recruitment brochures and presentations about this study were given at various UIHC and VAMC clinics/clinicians, such as Family Practice/General Practitioners, Internal Medicine, and Adult Psychiatry.

Design

Case-based Matching of Participant Groups

Each patient with brain damage to the ventromedial prefrontal cortex (N=6) was matched in a case-based fashion to a comparison participant with brain damage to regions outside of the VMPC region (and other empathy-related regions) and a healthy comparison participant). The criteria for the case-based matching included age, sex, handedness, education, and full scale IQ. The demographic and neuropsychological information of the 6 pairs can be found in Table 3.

Experimental Overview

During Experiment 2 Part B, a naturalistic empathy induction occurred whereby on-line empathy was evoked and measured through self-report questionnaire and behavior on an economic game. Participants were told that the study would consist of playing an economic game against two different opponents. Unbeknownst to the participant, during the course of the experiment empathy was induced by having one of the opponents experience deep sorrow. The specifics of the empathic induction are discussed in further detail below. On-line empathy was measured through the self-report questionnaire that was described in Experiment 2 Part A. Empathic behavior was measured through the Repeated Fixed Opponent Ultimatum Game (UG) which was described in more detail in Experiment 1.

Experimental Premise:

an Economic Decision-Making Game

Participants were led to believe that the experiment solely consisted of playing an economic decision making game against a series of two opponents through an intercom system. However, the participants were not aware that this economic decision making game was actually designed to measure their empathic behavior towards their opponents. In addition, the participants were not told that the study would entail the experimental induction of a neutral and an empathic state. Rather, the experimental inductions occurred implicitly in a manner designed to be reminiscent of experiencing empathy during daily life.

Experimental Inductions of

Neutral and Empathic States

Each induction occurred as a function of the participant overhearing their opponent speak with the Research Assistant either about a neutral or empathic topic. As a means of enhancing realism, the Research Assistant had a conversation with the participant of the similar duration and content to the conversations that occurred in the recordings. However, it was made clear to the participant that their game opponent was not in the other testing room while the participant and the Research Assistant were having the conversation.

The neutral induction consisted of the participant overhearing through the intercom a conversation between the first opponent and the Research Assistant who then gave further instructions about the experiment (actually an audio recording). In this conversation, the Research Assistant asked the first opponent about their day and the opponent responded by describing their morning (e.g. their breakfast, the contents of the paper, etc.) The neutral induction is described in more detail in the section on Experiment 2 Part A. During the empathic induction, the participant overheard their second opponent experiencing overwhelming sadness. Empathy was evoked through a conversation between the second opponent and the Research Assistant (actually a recording). In this conversation, the second opponent began by talking about the events of their day but then related that it was the anniversary of their son's death today and revealed that they were experiencing deep sorrow. At the end of this conversation, the opponent made it clear that they would like to continue with the experiment as a means of 'getting their mind off things.' Further details about this recording are also described in the section on Experiment 2 Part A. The inductions were pre-recorded in order to prevent bias that may result due to the idiosyncrasy of people's interactions with the Research Assistant and their behavior on the economic game. For example, if the responses were not pre-taped, the opponent's mood, personality or other variables may affect the participant's offers in the game.

Measurement of On-line Empathy

through Self-report Questionnaire

On-line empathy was measured as a function of both the neutral and empathic inductions through a self-report questionnaire. Since the participants are led to believe that the experiment is about playing an economic game, the Research Assistant told the participants that the questionnaire was used to assess their feelings at random intervals throughout the experiment. The questionnaire assessed on-line empathy through a series of emotional adjectives that measured sadness and empathic concern as well as other unrelated emotional states (e.g. hostility and joviality) to assess the specificity of the effect. This questionnaire was described in further detail in Experiment 2 Part A. This questionnaire was given at four time points during the experiment: at Baseline 1 (immediately before the neutral induction takes place), after the neutral induction, at Baseline 2 (immediately before the empathic induction), and then directly after the empathic induction. The measurement of on-line empathy at the four time-points allows for an assessment of the degree of on-line empathy produced specifically by the empathic induction in comparison to the neutral induction and comparison to two other baselines.

Measurement of Empathic Behavior

Empathic behavior was measured through the Repeated Fixed Opponent Ultimatum Game (UG). Empathic behavior was defined as behavior on the UG exhibited immediately following the empathic induction. Baseline or normal behavior for each participant was defined as their behavior immediately following the neutral induction. To determine game behavior that was specific to the empathic induction, game behavior following the empathic induction was examined after accounting for baseline game behavior following the neutral induction.

The Ultimatum Game is a widely used social economic decision making game that was described in detail in Experiment 1. The Repeated Fixed Opponent version of the UG that was used in Experiment 2 Part B was also used in Experiment 1. However, there are some methodological differences in the way the game was employed in Experiment 2 Part B. The primary difference is that in Experiment 1, two people played a live game against each other whereas in Experiment 2 Part B, the participant played against the recording of an opponent (although this fact is not made known to the participant).

In Experiment 2 Part B, the participant played the role of the Proposer, or the person who decided how to split $10 with their opponent. The two opponents (actually voice recordings) played in the role of the Responder, or the person who decided whether to accept or reject the offer. The two opponents were recordings of the two male actors who performed in the empathy and neutral induction recordings. If the offer was rejected by the Responder, neither player received any money, whereas if the offer was accepted, the players each received their share of the proposed division. This procedure of offer followed by response occurred twenty consecutive times against the same opponent. Later, the participant played the same game against a second opponent for twenty consecutive rounds. The participants were made aware at the beginning of the experiment that three random offer and response pairs (rounds) would be chosen and the money they earned on those rounds would be added to their total payment for the experiment. Their payment would be sent in check form approximately a month after the experiment.

Offers and responses were made verbally by the participant and their opponents through an intercom system. These offers were audio recorded by a small digital tape recorder placed on the edge of the table. At the beginning of the experiment, participants were informed to make their answers orally and were asked not to write their answers. Participants made their offers orally using specific language (a script) in order to ensure that their offers were understood by their opponent. The script for the participant consisted of: “You get $x, I get $y, out of $10.” The Research Assistant told the

Responder (in the recording) to make their response using this language: either, “I Accept” or “I Reject.” The participant was given these instructions orally as well as through a written script that was placed on the table in front of them. The scripted response that was employed in the current study is very similar to the standard response that appears on the monitor in computerized forms of the UG where the participant serves only in the role of the Responder: “Sally gets $x. You get $y,” (Koenigs & Tranel, 2007; Sanfey et al., 2003).

Before the game began, the participants were instructed about the rules of the game. These rules are based upon the rules utilized in previous studies of the ultimatum game, as a means of later comparisons across studies (Koenigs & Tranel, 2007; Pillutla & Murnighan, 1996; Sanfey et al., 2003). These rules were explained orally by the experimenter and were also given to the participant in written format that were able to peruse during the experiment if they forgot. The rules included (1) the offer division must add up to $10, (2) offers must range between $1 to $9, thus no offers of $0 or $10 were allowed (3) offers must be made in whole dollar amounts rather than dividing the total into dollars and cents (4) offers may be repeated. This last rule was included to make the participant aware that they would run out of offers to give ranging between $1 to $9 because they would be giving twenty offers in row.

Since the two opponents were actually recordings rather than two persons live, there was a need for the recording to mimic how a normal person in the role of the Responder would typically play the Repeated Fixed Opponent UG. To achieve this goal, results based upon Experiment 1 were employed. In Experiment 1, a large sample of healthy individuals of similar ages to the patients were investigated on the Repeated

Fixed Opponent UG. Based upon the normative data from the two age groups, it was revealed that on average offers of $4 and greater were typically accepted whereas offers of $3 and below were typically rejected. Consequently this rule was applied in Experiment 2 Part B. During the experiment, we waited for the participant to make their offer and then based upon what type of offer they made, we responded with a recording that either said ‘I accept’ or ‘I reject.’ The recordings were done by the same actors who did the neutral and empathic induction recordings. In these voice files, the voice of the actor is recorded saying “I Accept” or “I Reject.” The actors were asked to vary the way they said these phrases slightly each time in order to make the voice files believable as a whole based upon the assumption that during daily life people tend to naturally vary the way they say things.

Procedure

Arrival and Instructions

The experiment took approximately 2 hours. First, the participant was shown to the experimental testing room by a Research Assistant who was 22 years old and underwent the consent process. Following the consent process, a 26-year old female Research Assistant entered the testing room and conversed with the participant for approximately 4 ½ minutes. The Research Assistant made conversation with the participant to enhance the believability of the recordings that the participants would later hear that involve the Research Assistant making conversation in a similar manner with the participant’s opponents in the Ultimatum game. The content of this conversation with the participant was designed to be neutral and consequently the Research Assistant asked the participant such things as, “How are you doing?” and, “How is your day going?”

Next, the Research Assistant reviewed the instructions of the experiment in more detail with the participant.

The Research Assistant explained to the participant that the experiment would involve playing an economic decision making game against two different opponents (one at a time) through an intercom system. The participants were informed that they would receive $10 compensation for their participation in the study. In addition, they were told that they could obtain additional money depending on how they played on three randomly selected trials of the Ultimatum Game. They were told that they would be informed of their total pay at the end of the experiment and that a check would be mailed to their residence approximately one month after the experiment had completed.

The participant was told that they would be making their offers orally through an intercom system. Following this, the participant was taught how to use the intercom to communicate with their opponent during the Ultimatum Game. The intercom was 'hands-free' so the participant did not need to press any buttons but rather simply speak their offers aloud at the normal level with which they speak. The participant's offers were audio-recorded by a small, discrete tape recorder located within the testing room. In this way, the data was collected in a naturalistic fashion without the need to have the Research Assistant present in the testing room.

The participants were told that the Feelings Questionnaire would assess their emotions at several random points during the experiment. However, the participant was not told that the Feelings Questionnaire would actually measure their empathic feelings at baseline and then again after the neutral and the empathic induction. The participant was told that they would be informed by the Research Assistant about the time points when they would need to fill out the questionnaire. Next the Research Assistant mentioned that she needed to meet the first opponent at the waiting room and then set them up to play the game. Once the opponent was set up, the game would begin. The Research Assistant asked the participant to fill out the first page of the Feelings questionnaire while they would go set up the first opponent. The participant was asked to wait to fill out the Feelings questionnaire until the experimenter had left the room. The participant was given 1 ½ minutes to fill out the Feelings Questionnaire, a time length which has been shown to be a sufficient for completion of the questionnaire through a piloting process that took place prior to the experiment. While the participant was filling out the Feelings Questionnaire, the Research Assistant was no longer in the testing room because they had left to set up the first opponent. Similarly, throughout the experiment the Research Assistant was not present while the participant was filling out the questionnaire or playing the Ultimatum Game in order to alleviate participant concerns for social desirability.

Research Assistant Sets up First Opponent

After completing the Feelings Questionnaire, the participant overheard (through the intercom) the Research Assistant making conversation with their first opponent for approximately 4 ½ minutes as she prepared them for the experiment. The content of this conversation was neutral and involved the Research Assistant asking the opponent about the activities of his day. The opponent responded by describing some common daily activities such as eating breakfast, reading the paper, and playing bridge. Although the participant was not aware, the conversation between the Research Assistant and the opponent was not live but actually a pre-taped audio recording. After the Research

Assistant finished giving the experimental instructions to the opponent, she returned to the participant's room and asked them to fill out the Feelings Questionnaire again. Once the questionnaire was completed, the Ultimatum game began.

Participant Plays Ultimatum Game Against

First Opponent

Before the participant made each offer, he/she waited to hear a beep which signaled them to make their offer. Once the offer was completed, another beep sounded which cued the opponent to make their response. The game was set up in this manner in order to cue the players to make their offer/response. This same procedure of offer followed by response continued until the participant had made a total of twenty offers. The participant made their responses in the format, "You get x $ out of $10." The opponent made their responses in the format of either, "I accept" or "I reject."

The responses of the opponent were based upon results from Experiment 1 which indicated that offers $4 and up were to be accepted whereas offers $3 and below were to be rejected. Based upon the offer either an "I accept" or an "I reject" voice file was played spoken by the particular actor that was involved in the conversation preceding the game. This oral response played through the intercom to the participant.

Waiting Period for Setup of Second Opponent

Once the first session of the game was over, the Research Assistant entered the room of the participant and asked them to fill out the Feelings Questionnaire again. Then the Research Assistant left the participant's room to set up the second opponent, while the participant filled out the Feelings Questionnaire again. Once the participant had completed the Feelings Questionnaire, he/she overheard through the intercom the

Research Assistant making conversation with the second opponent. This conversation was designed to evoke empathy in the participant. In the recording, the opponent told the Research Assistant that it was the anniversary of his son's death today. He then reflected upon his memories of his son and talks about the loss he has felt. Because of the emotional nature of the conversation, the Research Assistant asked the opponent if he feels ready to continue the experiment or if he would like to re-schedule. The opponent told the Research Assistant that he would like to continue because he is feeling fine and that it would help to keep his mind off these thoughts. Once the Research Assistant ensured that the opponent was feeling fine, she continued with the experimental instructions. She then returned to the room of the participant and asked them to fill out the Feelings Questionnaire again. Once the participant finished filling out the questionnaire, the Ultimatum Game against the second opponent began.

Participant Plays Ultimatum Game Against Second Opponent

The participant followed the same procedure as in Step 2. He/she made twenty, consecutive verbal offers and their opponent responded to them. Once the game was completed, the Research Assistant returned to the participant's room and asked them to fill out the Feelings Questionnaire for the final time.

Assessment of Induction Effectiveness and Debriefing

Once the participant completed the Feelings Questionnaire, the Research Assistant asked them to fill out additional questionnaires which assessed their thoughts and opinions about the experiment. More specifically, the participants were asked questions about the believability of the experiment such as whether they thought they were playing a live person or a recording.

After the experiment concluded, the Research Assistant verbally explained the rationale for the experiment as well as the aspects of deception that were employed such as using audio recordings instead of live participants. In addition to receiving $10 compensation for participating, the participants were told they would receive payment based upon how they played during three randomly selected trials of the Ultimatum Game. The debriefing form stated the amount of money they earned from the three randomly selected trials of the experiment. The specific amount they had accumulated was pointed out and they were asked for their signature to convey understanding that they would receive this specific amount. A copy of this form was given to the subject. A payment voucher was then be filled out by the participant containing information about how much money they would receive and their contact information. The participant was sent a check in the mail for the specified amount. Finally, the participant was given a parking voucher.

Results

First, we assessed participant believability about the realism of the experimental induction process. In particular, we were interested to determine whether the participant thought the two conversations they overheard during the experiment were real. The first conversation the participants overheard during the experiment was the neutral induction whereas the second conversation the participant overheard was the empathic induction. After the experiment was over, we asked the participants if they believed that they had overheard a conversation between the Research Assistant in the study and one of their opponents on the ultimatum game (separately for the neutral and empathic inductions). We measured believability through a dichotomous yes/no response (e.g. yes= I believed; no= I did not believe.) Based on this categorization, we examined the frequency of participants in each group that believed they had overheard a conversation between the Research Assistant and another participant in the game for the Neutral and Empathic conditions (see Figure 9). The results indicated that all participants believed the neutral induction was a real conversation (18 out of 18 participants). For the empathic induction, the majority of the participants in each group (VMPC, BDC, Healthy Comparison) believed it was real (15 out of 18 participants). It was also found that the groups were similar in their ratings of believability during the empathic condition (number of participants who believed: VMPC=4, BDC=6, Healthy Comparison= 5).

Next we investigated the believability regarding whether the participants thought they were playing the ultimatum game against a real participant (see Figure 10). This was assessed through a dichotomous yes/no response on the questionnaire. The results of this analysis were the same as mentioned in the previous believability analysis regarding the realism of the conversations. More specifically, all participants believed they played the game against a real person after the neutral induction (18 out of 18 participants.) For the game that took place immediately after the empathy induction, the majority of the participants believed they were playing against a real participant (15 out of 18 participants.) The participant groups were very similar in their believability ratings regarding the belief that they played against a real person after the empathic induction (number of participants who believed: VMPC=4, BDC=6, HC=5). Taken together, the results of these two analyses suggest that as a whole, participants in the experiment believed that they were playing the ultimatum game against two real participants in the study (opponents in the game) and through the course of the experiment they overheard these opponents participate in conversations with the Research Assistant.

Next we examined the on-line empathic experience of patients with damage to the ventromedial prefrontal cortex and two comparison groups (brain damage comparison, healthy comparison). To do this, we examined ratings of on-line empathy, after the neutral induction and after the empathic induction for each participant group. On-line empathy was measured by self-report state ratings of feelings of 'sympathy' and 'compassion' that occurred immediately after the neutral induction and directly after the empathic induction. On average, all groups reported experiencing higher empathy after the empathic induction than after the neutral induction (see Figure 11). At a mean level, the two comparison groups, reported higher empathy after the empathic induction than patients with damage to the VMPC. We were particularly interested in empathic feelings that were evoked due to the empathic induction (rather than baseline level empathy evoked by the neutral induction) because of our interest in whether on-line empathy is experienced by patients with damage to the ventromedial prefrontal cortex due to empathic situations in real-world settings. Consequently, we next conducted an analysis that examined the change in empathic feelings from the neutral induction to the empathic induction in each participant group.

This change in on-line empathy was examined as a function of participant group (VMPC, BDC, Healthy Comparison). Because the comparison participants were case-matched to a patient with VMPC damage, we conducted pair-wise t-tests. Patients with bilateral damage to the VMPC reported less on-line empathy than their case-matched brain damage comparison participants [see Figure 12; t (5)=4.5, p<.01 (2-tailed)]. Patients with damage to the bilateral VMPC did not differ from the healthy comparison participants in their experience of on-line empathy [t (5)=1.98, p=.11 (2-tailed)]. Patients with brain damage outside of the VMPC region did not differ from the healthy comparison participants [t (5)=1.12, p=.31 (2-tailed)]. These results indicate that patients with brain damage to the VMPC report lower on-line empathy than patients with brain damage to regions outside of the VMPC (and other empathy-related regions.)

Next we examined whether patients with brain damage to the VMPC showed lower empathic behavior on the ultimatum game than the two comparison groups. The patients with damage to the VMPC showed little empathic behavior, behaving similarly on the UG after the neutral and after the empathic inductions (see Figure 13). In contrast, the two comparison groups (brain damage comparison and healthy comparison), showed increased empathic behavior after the empathic induction, giving more money on the UG after the empathy induction than after the neutral induction. In order to examine the specific effect of the experimental empathic induction of UG behavior, we next examined the change in behavior on the UG from the neutral induction to the empathic induction.

We compared change in empathic behavior from the game after the neutral induction to the game after the empathic induction in each group. Because the comparison participants were case-matched to the patients with damage to the VMPC, we conducted pair-wise t-tests. Empathic behavior was defined as the difference between the sum offer given on the UG after the neutral induction and the sum offer given on the UG after the empathic induction (Empathy game – Neutral Game.) Greater empathic behavior was indicated by an increase in the sum of the offers given in the empathic game (after the empathic induction). First, we found that patients with bilateral damage to the VMPC showed less empathic behavior than their case-matched brain damage comparison participants [see Figure 14; t (5)=2.61, p <.05 (2-tailed)]. The second comparison revealed that patients with bilateral damage to the VMPC also showed less empathic behavior than their healthy case-matched comparison participants [(t (5)=3.11, p<.05 (2-tailed).] The brain damage comparison participants and healthy comparison participants that were case-matched to the patients with bilateral damage to the VMPC did not differ from each other in their empathic behavior [t (5)=.96, p=.38 (2-tailed)].

Discussion

In this study, we examined the degree to which the ventromedial prefrontal cortex is critical for empathy as measured by behavior and an on-line experience. We found that the ventromedial prefrontal cortex is critical for one form of empathic behavior. We measured empathic behavior as the difference in baseline monetary giving behavior as a consequence of experiencing on-line empathy. Patients with brain damage to the ventromedial prefrontal cortex showed little difference in their giving behavior as a result of the induction of on-line empathy. This effect was not a general consequence of brain damage but was instead found to be specific to the ventromedial prefrontal cortex region. This was determined by a comparison that showed that patients with damage to the ventromedial prefrontal cortex showed less empathic behavior than patients with brain damage to regions outside of the ventromedial prefrontal cortex (and other empathy-related regions.) The empathic behavior of patients with brain damage to the ventromedial prefrontal cortex was also lower than that of healthy adults of similar demographic characteristics.

The on-line empathic experience of patients with damage to the VMPC was found to be lower than patients with brain damage to regions outside of the VMPC (and other empathy-related regions.) This suggests that the dampening of on-line empathic experience is specific to patients with brain damage to the VMPC and not a general effect of brain damage. We did not find a significant difference between the reported on-line empathic experience of patients with brain damage to the VMPC and case-matched healthy comparison participants. At a mean level, the ratings of on-line empathic experience of the healthy comparison participants are greater than that of the group of patients with damage to the VMPC. However, the lack of statistical difference may be due to the small sample size of the study and future research will re-examine this question with a larger sample size.

The findings from this study add to the understanding of the neural correlates of empathy. Previous studies have suggested that empathy may be impaired in patients with brain damage to the ventromedial prefrontal cortex through anecdotal reports and self-report trait questionnaires measuring empathy as a general tendency (Shamay-Tsoory et al., 2003; Shamay-Tsoory et al., 2004; Shamay-Tsoory et al., 2009). However, prior to the present study, on-line empathic experience and empathic behavior had not yet been measured in patients with brain damage to the ventromedial prefrontal cortex. This study provides strong evidence that empathic behavior is decreased in patients with ventromedial prefrontal cortex damage not only in comparison to healthy adults but also in comparison to patients with damage to other regions of the brain (outside of the VMPC and other empathy-related regions). This suggests that the VMPC region may be critical for empathic behavior. This study also shows that the VMPC may be a critical region for on-line empathic experience because the experience of these patients is dampened in comparison to patients with brain damage to other regions of the brain.

The study's findings suggest that there is a need to examine the specific role of the VMPC in functional neuroimaging studies of empathy in healthy adults. The study of empathy through functional neuroimaging technology has primarily used paradigms that examine the personal experience of pain and the observation of pain in another person (Jackson et al., 2005; Saarela et al., 2007; Singer et al., 2004). These studies have primarily focused on findings that implicate the anterior insula and mid-cingulate region in the function of empathy (Jackson et al., 2005; Saarela et al., 2007; Singer et al., 2004). Although regions of the frontal cortex have been found to be involved in empathy in these studies, these results are typically not highlighted. Consequently, little emphasis has been given to the ventromedial prefrontal cortex in functional neuroimaging studies of empathy to date. This may in part be due to the type of induction paradigms utilized to evoke empathy in the previous studies in comparison to the present study. Previous studies have evoked empathy for the pain of another primarily through viewing others in pain, either through actual physical depictions of their pain (e.g. a severed finger) or emotional facial expressions of pain (Jackson et al., 2005; Saarela et al., 2007). This may employ a simpler empathic process than is needed for complex empathy inducing situations (similar to the current experiment) whereby the physical pain of the other is simply mapped onto the feelings of pain in the self through a somatotopic mapping in the insula. Due to the content of the empathic induction in the current experiment (empathizing with the emotional pain of another person whose son has died), the experience of empathy in the present study may have involved higher order empathic processing that is not directly tied to a physical sensation such as pain. It is this difference which may be one of the reasons the ventromedial prefrontal cortex is typically not robustly activated in experiments on empathy for the physical pain of another.

The present study provides the first piece of experimental evidence that the ventromedial prefrontal cortex is critical for empathic behavior. In particular, results from the present study indicate that the ventromedial prefrontal cortex is critical for empathic behavior as measured by monetary generosity during an economic game. Further research is needed to examine whether the ventromedial prefrontal cortex is critical for all forms of empathic behavior. Results from previous functional neuroimaging studies of empathy suggest that the anterior insula and mid-cingulate may be involved in the neural system for empathy. A future lesion study is needed to examine whether these regions are critical for empathy.

Figure 8. Experiment 2 Part 2: Overlap of Lesion Location of Six Patients with Brain Damage to the Bilateral Ventromedial Prefrontal Cortex. The color band on the legend depicts the number of patients with brain damage to a particular region of the brain, ranging from 0 to 6 patients. On this scale, cooler (blue) colors indicate a fewer number of patients with brain damage to a particular region while warmer (red) colors indicate a greater number of patients with damage to that region.

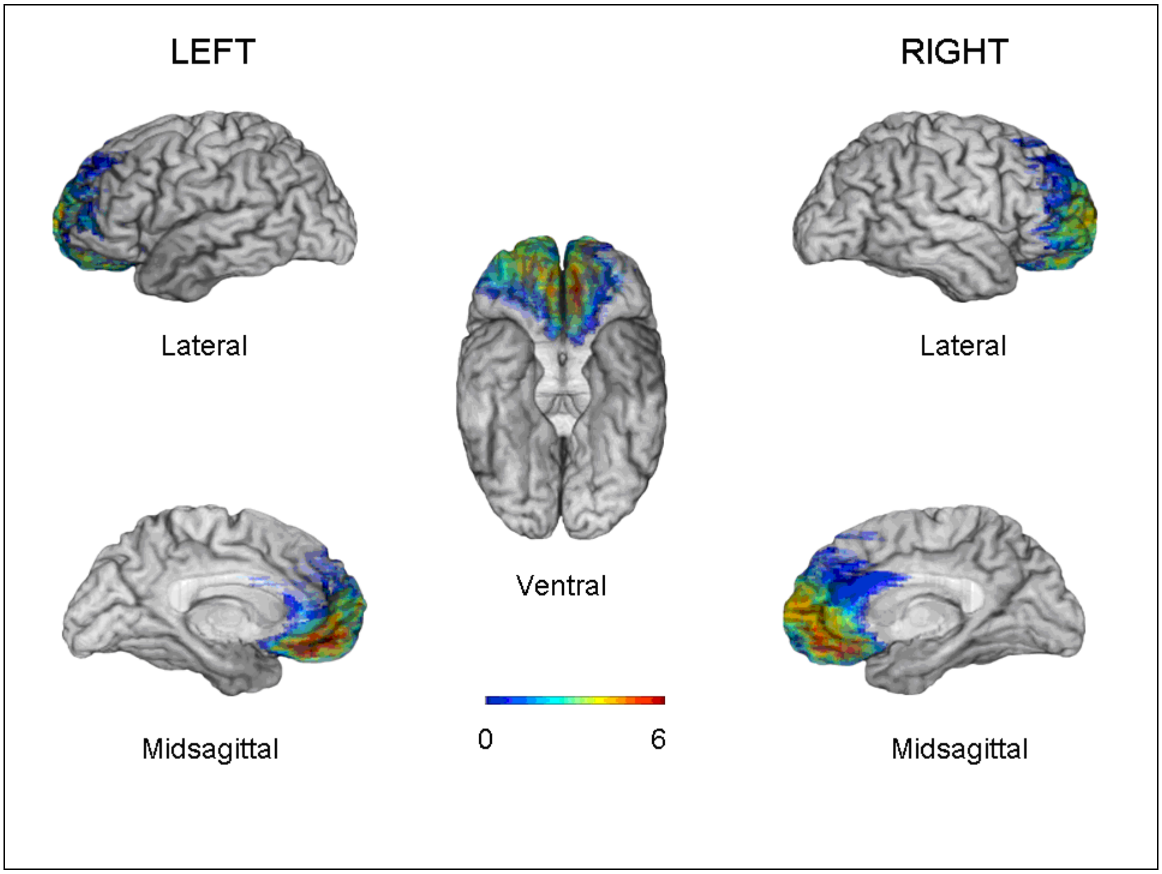


Table 3. Experiment 2 Part 2: Six Patients with Brain Damage to the Ventromedial Prefrontal Cortex (VMPC) were Matched Pair-wise to Two Comparison Groups: a Brain Damage Comparison Group (BDC) and a Healthy Comparison Group (HC)

PAIR #	GROUP	AGE (years)	SEX	HAND	EDU (years)	FSIQ
Pair 1	VMPC	69	M	R	14	143
	BDC	46	M	R	16	129
	HC	79	M	R	20	126
Pair 2	VMPC	68	F	R	16	108
	BDC	75	F	R	12	107
	HC	69	F	R	16	107
Pair 3	VMPC	46	F	R	13	108
	BDC	46	F	R	12	102
	HC	58	F	L	18	113
Pair 4	VMPC	61	F	R	14	106
	BDC	64	F	R	18	113
	HC	66	F	R	18	114
Pair 5	VMPC	63	F	R	13	109
	BDC	67	F	R	13	99
	HC	65	F	R	16	122
Pair 6	VMPC	70	M	R	12	84
	BDC	69	M	R	11	97
	HC	74	M	R	13	107

Note: The matching criteria included age in years (AGE), sex (SEX), handedness (HAND), education in years (EDU), and full-scale IQ (FSIQ).

Figure 9. Experiment 2 Part 2: Frequency Distribution of Participants who Believed the Experimental Induction was a Real Conversation

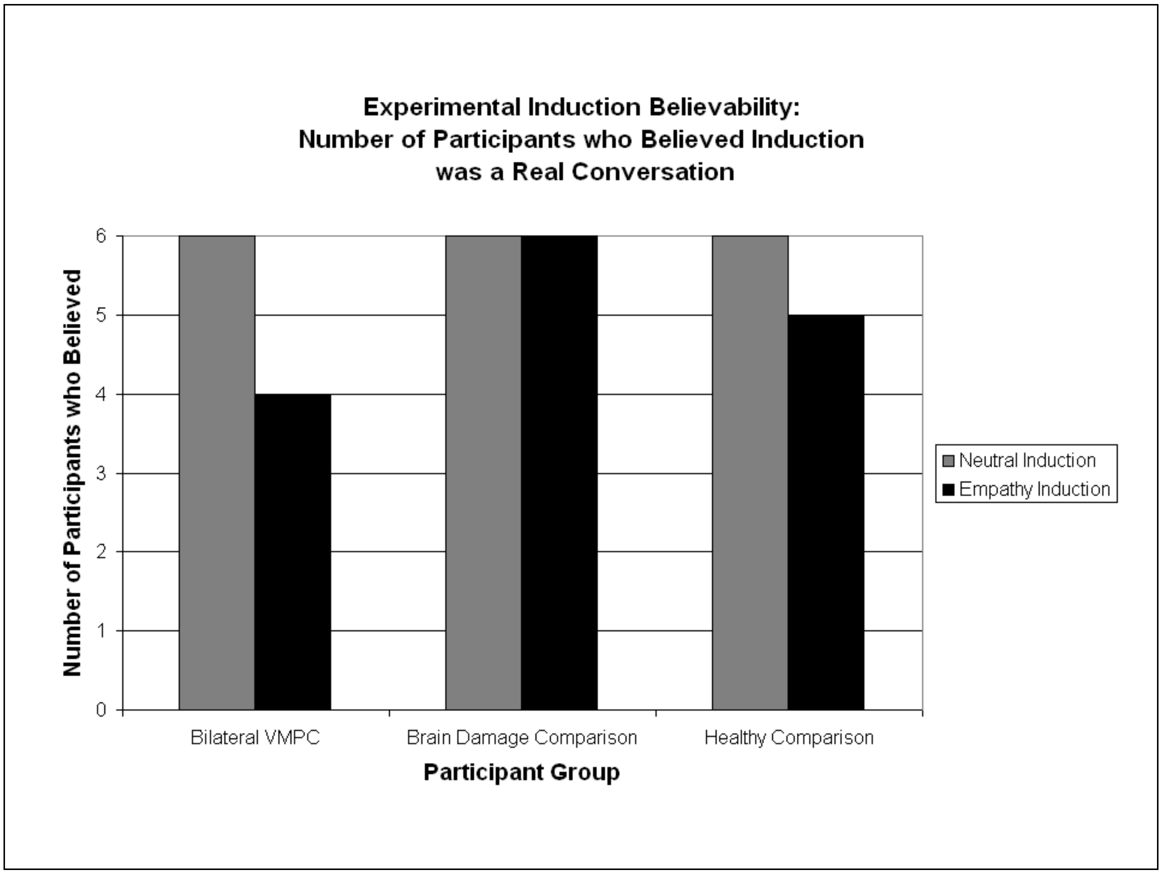


Figure 10. Experiment 2 Part 2: Frequency Distribution of Participants who Believed the Ultimatum Game was Played Against a Real Opponent

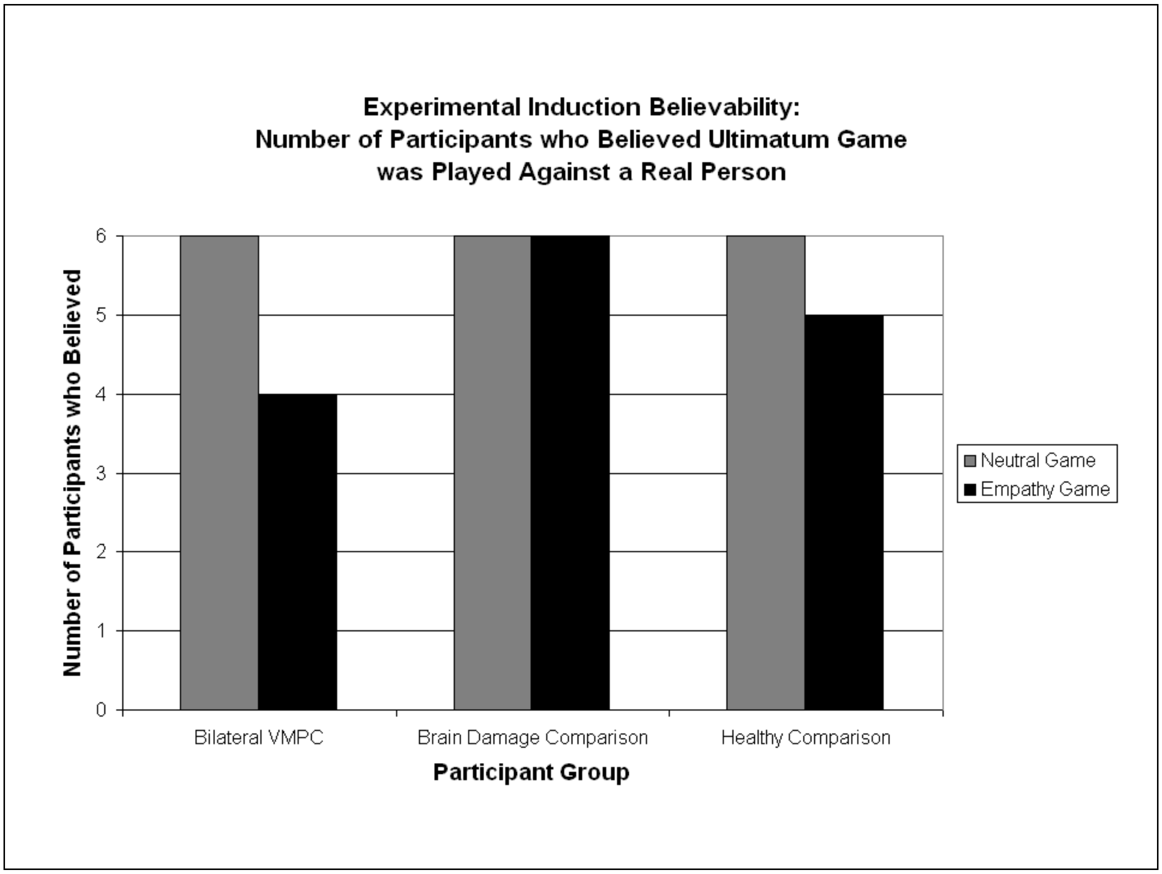


Figure 11. Experiment 2 Part 2: On-line Empathic Experience of Patients with Brain Damage to the VMPC and Two Comparison Groups (Brain Damage Comparison, Healthy Comparison) as a Function of the Experimental Induction (Neutral, Empathy)

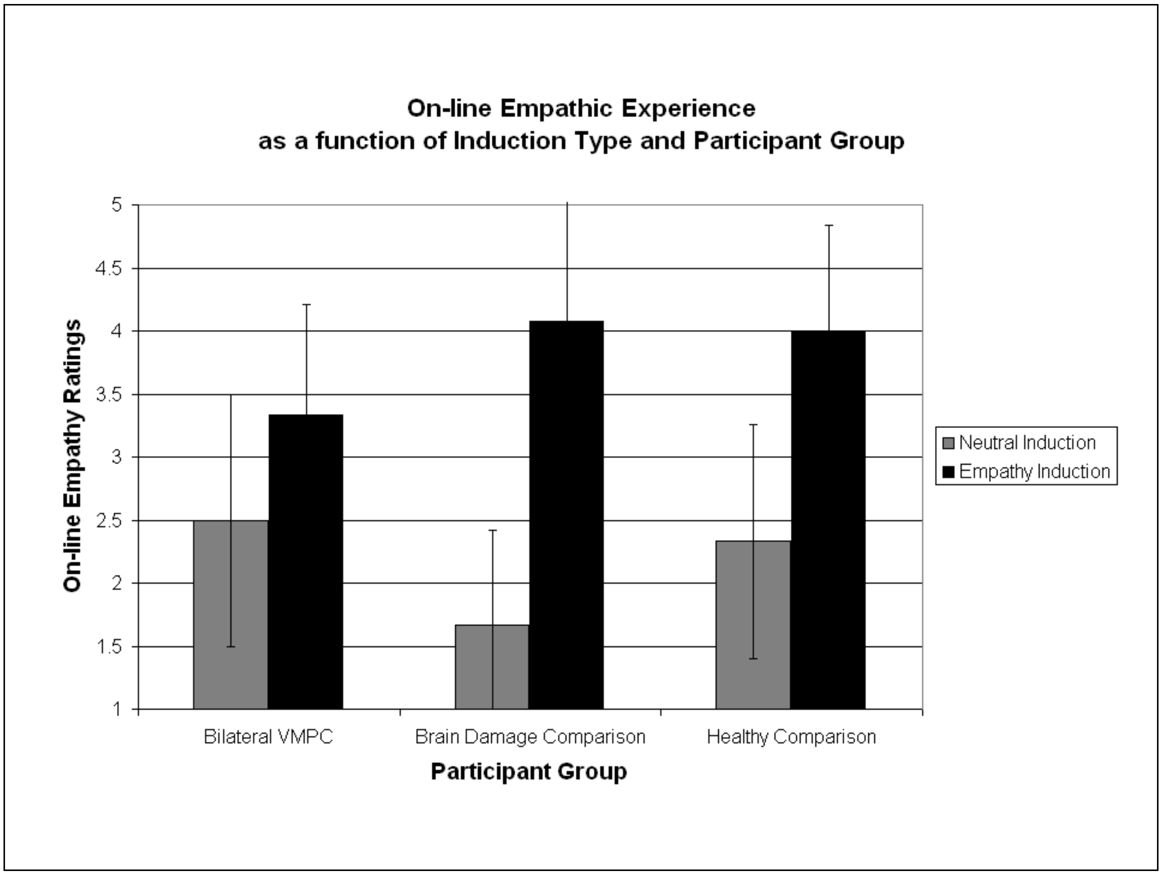


Figure 12. Experiment 2 Part 2: Pair-wise Comparison of On-line Empathic Experience in Patients with Bilateral Damage to the VMPC and Case-matched Comparison Participants (Brain Damage Comparison, Healthy Comparison). On-line empathy specific to the empathic induction, after accounting for the emotional response to the neutral induction, is depicted (Empathic Induction – Neutral Induction). The results of paired t-tests between the groups are illustrated on the graph [* p<.05 (2-tailed); ** p<.01 (2-tailed).]

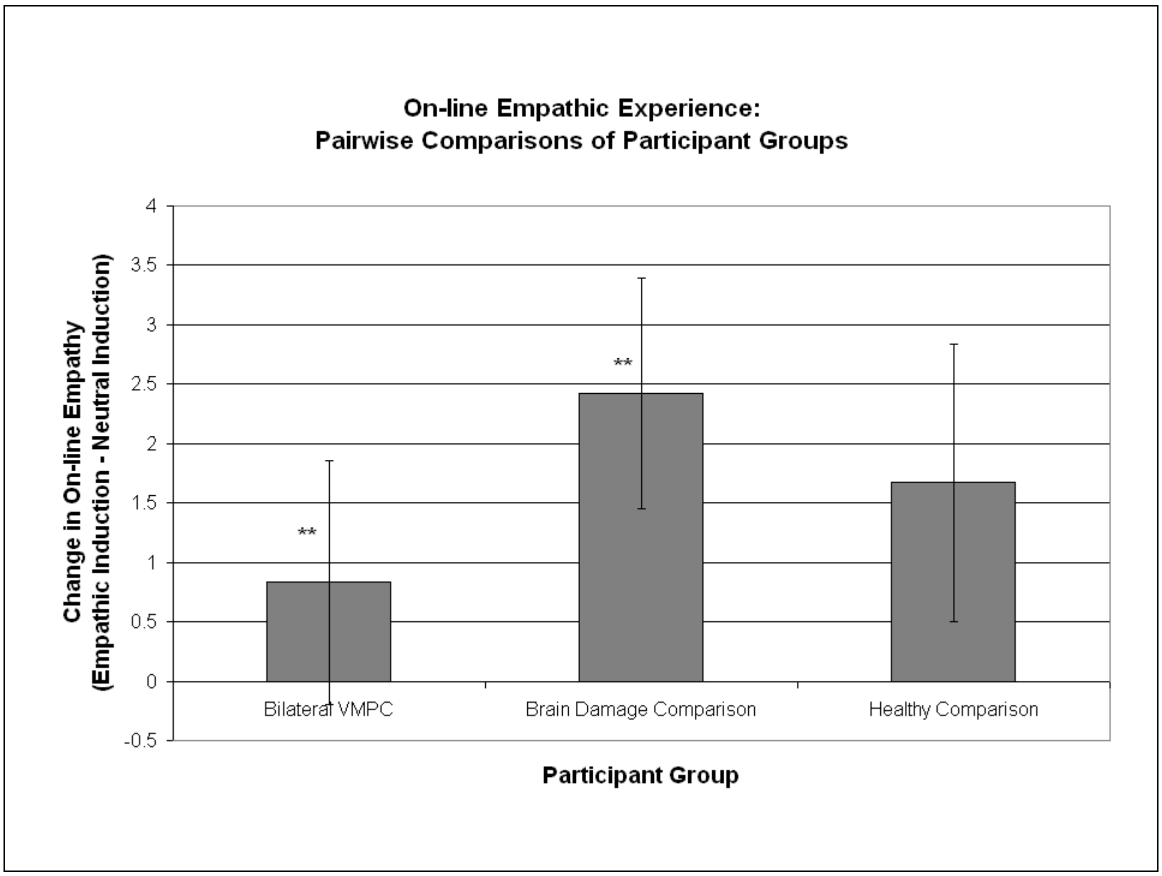


Figure 13. Experiment 2 Part 2: Empathic Behavior Exhibited on the UG in Patients with Brain Damage to the VMPC and Two Comparison Groups (Brain Damage Comparison, Healthy Comparison) as a Function of the Experimental Induction (Neutral, Empathy). Empathic behavior is measured by the sum offer ($) given during the Ultimatum Game during each condition. Empathic behavior is indicated by giving a greater sum of money ($) during the ultimatum game after the empathic induction than after the neutral induction.

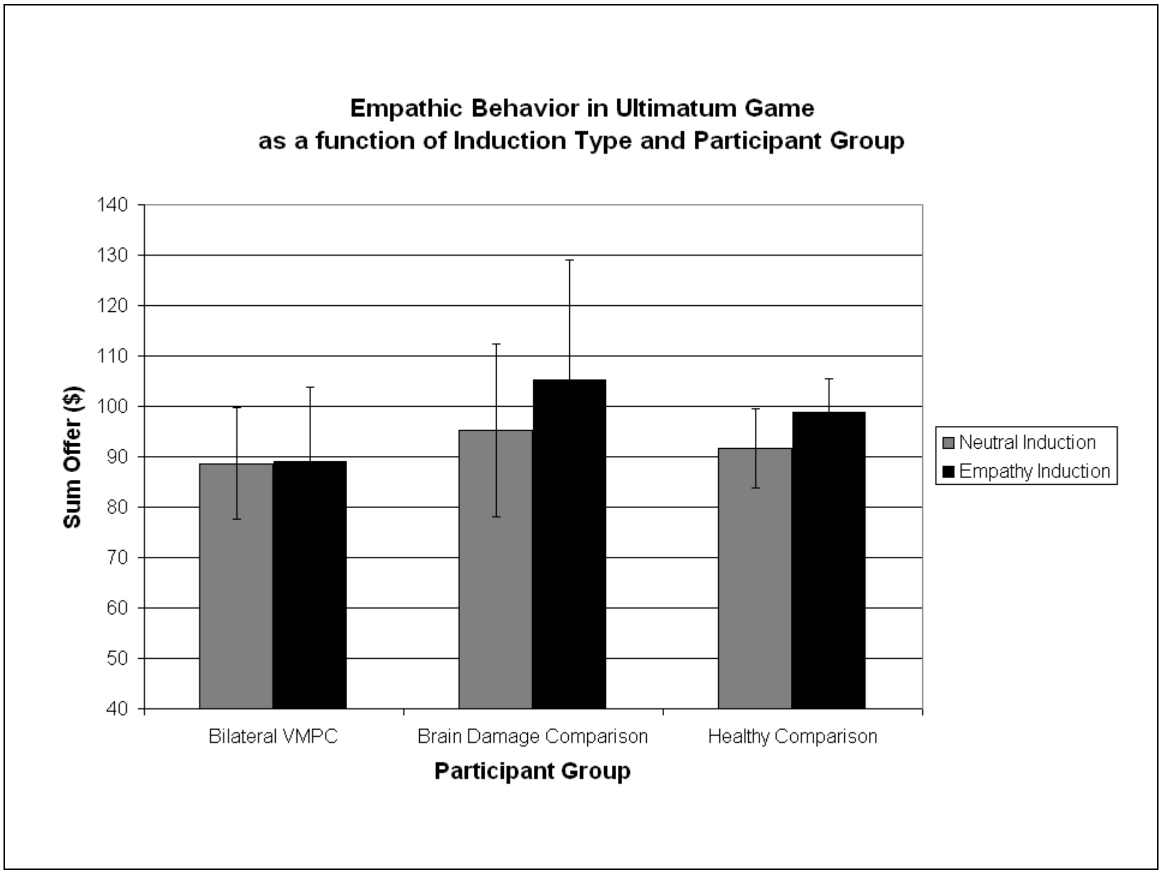
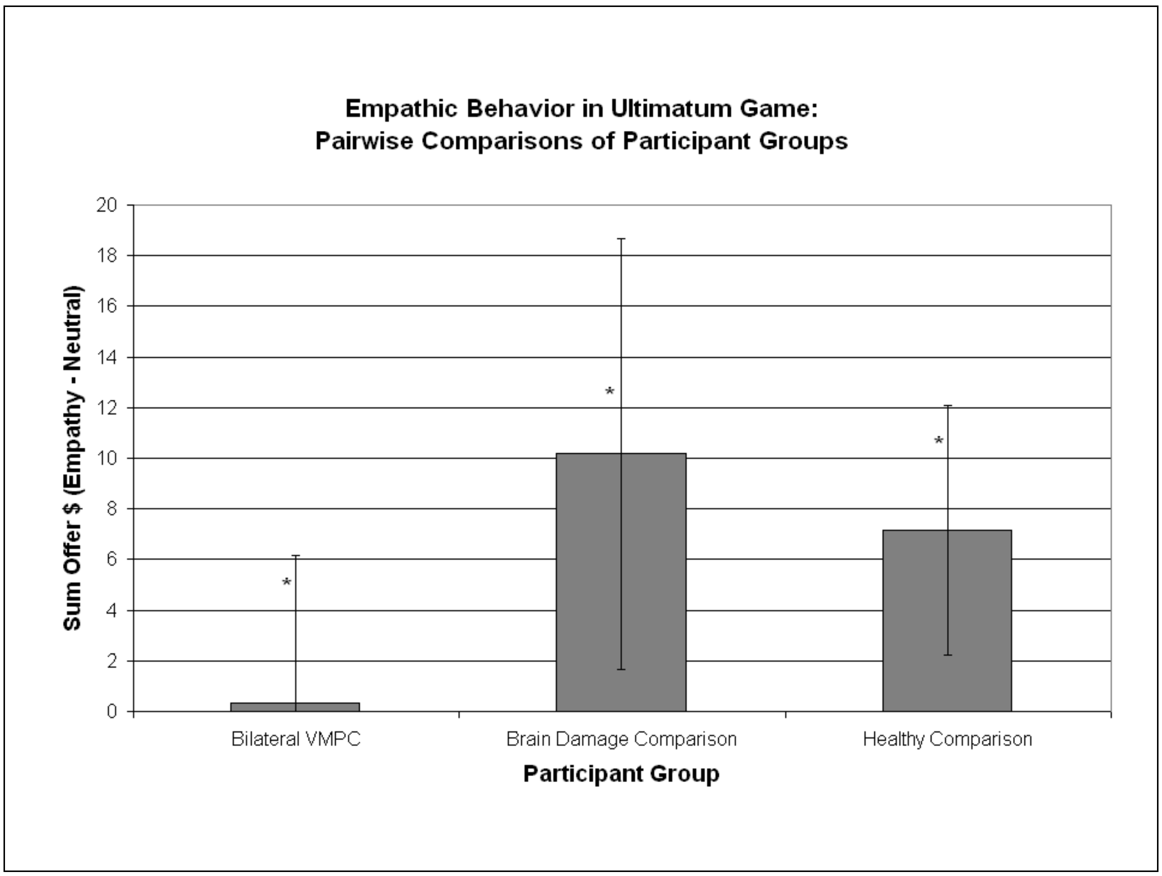


Figure 14. Experiment 2 Part 2: Pair-wise Comparison of Empathic Behavior in Patients with Bilateral Damage to the VMPC and Case-matched Comparison Participants (Brain Damage Comparison, Healthy Comparison). Empathic behavior was defined as the difference between the sum offer given on the UG after the neutral induction and the sum offer given on the UG after the empathic induction (Empathy game – Neutral Game.) Greater empathic behavior was indicated by giving a greater sum of money in the empathic condition than in the neutral condition. The results of pair-wise t-test between the groups are indicated by [* p<.05 (2-tailed); ** p<.01 (2-tailed).]



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