Cognitive Empathy Following Orbitofrontal Cortex and Dorsolateral Prefrontal Cortex Damage

By

Madeleine Shirley Goodkind

A dissertation submitted in partial satisfaction of the

requirements for the degree of

Doctor of Philosophy

in

Psychology

in the

Graduate Division

of the

University of California, Berkeley

Committee in charge:

Professor Robert W. Levenson, Chair
Professor Jodi Halpern
Professor Robert T. Knight
Professor Ann M. Kring

Fall 2011

Abstract

Cognitive Empathy Following Orbitofrontal Cortex and Dorsolateral Prefrontal Cortex Damage

By

Madeleine Shirley Goodkind

Doctor of Philosophy in Psychology

University of California, Berkeley

Professor Robert W. Levenson, Chair

Empathy is a multifaceted and complicated construct, encompassing several subprocesses and relying on diverse neural networks. In the current study, I focus on cognitive empathy, one facet of empathy that includes the process of taking another person's perspective and the ability to accurately identify his or her emotions. Frontal lobe regions underlie many social and emotional processes and may be critical for cognitive empathy. Specifically, injuries to the orbitofrontal cortex (OFC) result in wide-ranging emotional and behavioral disturbances that may in part reflect deficits in cognitive empathy. Additionally, the dorsolateral prefrontal cortex (DLPFC) is critical in emotion regulation and many higher-order cognitive processes, suggesting a contribution of this region to emotional functioning when cognitive abilities are implicated. In the current study, cognitive empathy was examined in six patients with OFC damage, six patients with DLPFC damage, and twelve control participants. Participants completed an extensive assessment of cognitive empathy, including self-report measures of the *process* of taking others' perspectives and performance-based measures of the *ability* to accurately identify others' emotions (also referred to as "empathic accuracy"). Additionally, relationships between cognitive empathy and neuropsychological performance on executive function measures were examined in patients. On self-report measures, both patient groups endorsed lower levels of cognitive empathy, but these scores were not associated with executive functioning. In all measures of empathic accuracy, OFC patients were indistinguishable from control participants, suggesting that socioemotional deficits seen in this patient group cannot be attributed to an inability to discern the emotions of others. However, DLPFC patients showed extensive impairments on empathic accuracy measures. Among patients, associations between neuropsychological performance and empathic accuracy were strongest on a task with static stimuli requiring patients to detect small changes in emotion. Results demonstrating preserved empathic accuracy in OFC patients are in contrast with previous work suggesting damage to this area results in extensive socioemotional deficits. Furthermore, these data suggest that understanding others' emotions relies on lateral frontal lobe regions, which are critical for tasks that require a blend of cognitive and emotional abilities.

Introduction

We live intrinsically social lives and our actions are often directed toward or in response to others. Empathy, which includes processes of perceiving, understanding, and responding to others' emotional signals has clear adaptive advantages and is especially important in the formation and maintenance of social relationships. As a complex and multifaceted construct, empathy is often divided into cognitive processes (knowing what others are feeling) and affective processes (feeling what others are feeling) and is thought to be related to prosocial behavior (behaving in a helpful manner towards others in need). In this dissertation I focus on processes and abilities related to cognitive empathy.

In general, neuroimaging and neuropsychological studies suggest that frontal lobe regions are critical in empathy and prosocial behavior and may be specifically important in cognitive empathy (George, Ketter, Gill, Haxby, Ungerleider, Herscovitch, & Post, 1993; Vuilleumier, Armony, Driver, & Dolan, 2001; Kringelbach & Rolls, 2004; Shamay-Tsoory, Tomer, Berger, Aharon-Peretz, 2003; Rankin, Gorno-Tempini, Allison, Stanley, Glenn, Weiner, et al., 2006; Heberlein, Padon, Gillihan, Farah, & Fellows, et al., 2008). One frontal lobe region, the orbitofrontal cortex (OFC) is thought to play roles in varied social and emotional tasks and damage to this region is associated with socioemotional deficits. However, precise contributions of the OFC to cognitive empathy remain unclear. Another frontal lobe region, the dorsolateral prefrontal cortex (DLPFC) has been correlated with emotional processes such as emotion regulation and is critical in a number of cognitive processes, but its role in cognitive empathy has not been systematically studied. Thus, the goal of the current study was to examine the impact of OFC or DLPFC damage in multiple aspects of cognitive empathy.

Component Parts of Empathy

Investigations of the components of empathy in developmental and social psychology provide a framework to study these subprocesses in patients with frontal lobe damage. Generally, empathy is considered to encompass processes related to perceiving, understanding, and attending to another's emotional state. Definitions vary greatly in terms of the scope and the type of processes included. Some researchers (e.g. Preston & de Waal, 2002) include a broad spectrum of processes ranging from agitation at another's distress (seen even in some non-human animals) to complete comprehension of their predicament. This spectrum approach places affective empathy as the starting point of empathy and complex, cognitive role-taking, or cognitive empathy as the pinnacle. Some researchers have proposed that the initial process of responding to another's emotions is critical to the downstream process and being able to understand another's emotions. According to this perspective, when we witness emotions in others, we automatically simulate those emotions in ourselves, and this facilitates understanding their emotions (Hess & Blairy, 2001; Carr et al., 2003). From this perspective, cognitive empathy is a top-down, phylogenetically-late perspective taking process whereas affective empathy is a bottom-up, phylogenetically-early process. Still others have described and studied empathy as a restricted set of distinct processes or constructs (e.g., Davis, 1983; Decety & Jackson, 2006; Blair, 2005). Descriptions of these sub-processes vary, but typically include a cognitive component ("I know what you feel") and an affective component ("I feel what you feel"; Decety & Jackson, 2006; Blair, 2005; Davis, 1983). These two components of empathy serve different purposes and show only moderate associations with each other. For example, cognitive empathy requires taking the perspective of another person and in doing so facilitates social interactions (Hoffman, 1990), while affective occurs through simulating the emotions of others in ourselves and is evolved to produce self-sacrificing, altruistic behavior. Furthermore, Davis found correlations between self-reported cognitive and self-reported affective empathy to be approximately .30 (Davis, 1983). Using this approach to study empathy does not exclude the possibility that different subprocesses are related to and may depend on each other. Distinguishing subprocesses of empathy in this way allows for the examination and comparison of different aspects of a complex construct that may be selectively impacted by different conditions. For example, various neurological and psychiatric conditions are thought to negatively impact empathy, but may have particular effects on *either* cognitive or affective empathy; in the current study, I examined cognitive empathy in patients with specific frontal lobe regions.

Cognitive Empathy

Cognitive empathy refers to knowing the emotions of another person and is often used interchangeably with terms such as “empathic accuracy” and “perspective taking”. Early definitions of cognitive empathy placed a large emphasis on the capacity to take the role of another person in order to understand his or her viewpoint (Mead, 1934). Later Ickes (1993) emphasized the concept of empathic accuracy, which refers to a person’s ability to accurately infer the specific content of another person’s thoughts and feelings. According to Decety and Jackson (2003) emotion regulation and self-other distinction are necessary for cognitive empathy to disentangle what is the other person’s emotions from one’s own.

Cognitive empathy can refer to either a process or an outcome. As a process, cognitive empathy is the tendency to take another person’s perspective (and will be referred to here as “perspective-taking”); this type of cognitive empathy is often measured through self-report measures. As an outcome, cognitive empathy can also refer to how accurately a person perceives another’s emotions (and will be referred to here as “empathic accuracy”). Various laboratory tasks are used to examine the accuracy with which a person is able to identify the emotions, thoughts, and intentions of others in photographs, sound clips, vignettes, or video clips. Despite the theoretical similarities between self-report measures of perspective-taking and objective, behavioral measures of empathic accuracy, these are often not strongly associated; multiple studies have failed to show a positive correlation between self- (or relative-) reported cognitive empathy and empathic accuracy in neurologically-normal adults (Ickes, Stinson, Bissonnette, & Garcia, 1990; Levenson & Ruef, 1992) and in patients with brain lesions (Shamay-Tsoory et al., 2003; Milders, Ietswaart, Crawford, & Currie, 2008).

Functional importance of cognitive empathy. Information in the social world is in large part communicated through people’s emotional cues in social interactions; understanding others’ emotional signals has clear adaptive advantages, providing clues about what others will think and do, and how we should behave. As such, cognitive empathy promotes social engagement, helping in the formation and maintenance of interpersonal relationships. Studies of control participants and patients with psychiatric or neurological disorders have examined the associations between cognitive empathy and functional ability as well as the functional implications of deficits in cognitive empathy. In a sample of 1200 college students, measures of perspective taking were positively related to self-reported measures of interpersonal functioning and of sensitivity to others (Davis, 1983); furthermore, insensitivity to emotional cues has been linked to poor social skills (Boice, 1983).

In patient studies, associations between cognitive empathy and functional outcome become more striking. Among patients with schizophrenia, empathic accuracy has been negatively correlated with community functioning (Couture, Penn, & Roberts, 2006), communication and occupational functioning (Hooker & Park, 2002), social competence (Mueser, Doonan, Penn, Blanchard, Bellack, Nishith, et al., 1996), and functional rehabilitation (Brekke, Hoe, Long, & Green, 2007). In fact, empathic accuracy ability mediates the relationship between cognitive skills and functional outcome in schizophrenia (Brekke et al., 2007). Mah and colleagues (Mah, Arnold, & Grafman, 2004) demonstrated that among patients with wide-ranging PFC lesions, deficits on an empathic accuracy task of interpersonal detection (e.g detecting lies and the degree of intimacy between people in videoclips) was negatively related to symptoms over time on a neurobehavioral rating scale (with worse performance associated with greater behavioral symptomatology).

Assessing cognitive empathy.

Self-reported cognitive empathy: perspective-taking. Based on a multidimensional approach to empathy, Davis developed a self-report scale that assesses the cognitive and affective aspects of empathy using individual subscales. This questionnaire, the Interpersonal Reactivity Index (IRI), is one of the most widely used scales for self-reported empathy and includes the following four subscales: perspective taking, fantasy, empathic concern, and personal distress. Most relevant to cognitive empathy, the perspective-taking scale measures the tendency to adopt the psychological point of view of others and includes items such as "When I'm upset at someone, I usually try to 'put myself in his shoes' for a while." Additionally, the fantasy subscale, which measures the tendency to imaginatively transpose oneself into fictional situations, is sometimes considered part of cognitive empathy. This scale includes items such as "I really get involved with the feelings of the characters in a novel". These two subscales measure the process of cognitive empathy, but not empathic accuracy (or how accurately a person reads others' feelings). In previous investigations, the fantasy scale and the perspective taking subscales have been combined to make a cognitive empathy composite (Hooker, Verosky, Germine, Knight, & D'Esposito, 2010; Shamay-Tsoory et al., 2004).

Laboratory measurements of performance-based cognitive empathy: empathic accuracy. Laboratory-based investigations of cognitive empathy, or empathic accuracy, use photographs, sound clips, vignettes, and videoclips to test participants' abilities to identify, decode, or describe the emotional state of another person. Facial expressions serve as important social cues about how another person feels and as such, presenting participants with photographs of emotional facial expressions is one of the most common methods for assessing empathic accuracy. Participants often view some or all of the basic emotions (anger, disgust, fear, happiness, sadness, and surprise; Ekman, 1992) and may see pure emotional facial expressions (e.g. anger; Bowers, Blonder, & Heilman, 1992), morphed images generated from two different emotional expressions (e.g. a blend of happiness and surprise; Blair & Cipolotti, 2000; Harmer, Thilo, Rothwell, & Goodwin, 2001), or cartoon drawings of socioemotional situations (Mah, Arnold, & Grafman, 2005). In another common empathic accuracy task, participants view photographs or a person's eyes with the task of inferring the emotional or cognitive state of the target (Baron-Cohen, Joliffe, Mortimore, & Robertson, 1997). These measures of empathic accuracy have been used with control participants (Calder et al., 2003; Malatesta, Izard, Ulver, & Nicolich, 1987), with psychiatric patients (in particular, patients autism or schizophrenia; e.g, Baron-Cohen at al., 1997; Harms, Martin, & Wallace, 2010; Brunë, 2005), and with neurodegenerative and traumatic brain injury populations (Fernandez-Duque & Black, 2005; Henry, Phillips, Crawford, Ietswaart, & Summers, 2006).

Many studies of empathic accuracy suffer from potentially limited ecological validity due to the use of static emotional stimuli that may not closely mimic the dynamic nature of emotional displays in the real world. To better understand how we decode others' real-world emotional displays, recent studies of empathic accuracy have employed more complex and ecologically-valid tasks, such as identifying the emotion of a character in a short film clip. McDonald and colleagues (2003) introduced the Awareness of Social Inference Test (TASIT) in which participants view videotaped vignettes of everyday social interactions and identify the primary emotion expressed by the main character. Select neuroscientific studies using this task have shown impairments in patients with nonspecific traumatic brain injuries (McDonald et al., 2003) and with patients who have undergone surgical removal of the anterior cingulate cortex (Ridout et al., 2007). Although these studies examine emotional signals as dynamic and contextually-based, they fail to capture the need to constantly update our judgments as others' emotions shift.

Emotions are short-lived phenomena (Levenson 2003) and successful real-world empathic accuracy requires evaluating and re-evaluating interpretations on the basis of changing information. A limited number of studies have made special effort to account for this aspect of emotions by examining repeated measures of empathic accuracy (Ickes, 1997; Levenson & Ruef, 1992). In these studies, participants typically use a rating dial to track the valence and the intensity of a film character's emotions. This task more closely mimics real-world empathic accuracy as it requires integrating information about the character's emotional displays with contextual cues on a continuous basis. In the past, the rating dial methodology has been used in the context of marital interactions (e.g. Levenson & Ruef, 1992). Recently, the neural correlates of this type of empathic accuracy have been examined in a functional imaging study (Zaki et al., 2009) and with patients with neurodegenerative disease (Goodkind et al., *in press*).

Socioemotional functioning and the frontal lobes

Socioemotional disturbances are frequently linked to frontal lobe dysfunction in various psychiatric disorders, such as schizophrenia and autism (Shur, Shamay-Tsoory, & Levkovitz, 2008; Abdi & Sharma, 2004) and in neurological conditions, including neurodegenerative diseases and brain injuries. For example, patients with frontotemporal dementia (FTD), a degenerative disease affecting the frontal and temporal lobes, are described as disinhibited, apathetic, socially inappropriate, and lacking empathy (Mendez, Lauterbach, and Sampson, 2008). Case reports of frontal lobe damage following traumatic brain injury, beginning with Phineas Gage, include many of the same symptoms as those described in FTD. Following an accident in which a large iron rod was driven through his head, Gage was described as "fitful, irreverent, indulging at times in the grossest profanity, impatient…when it comes to his desires" (Harlow, 1868); Blair and Cipolotti describe patient J.S., who sustained an injury to the right OFC after he collapsed at work presumably due to a seizure, as "reckless regarding others' personal safety" with a striking lack of remorse (Blair & Cipolotti, 2000). In both cases, the patients had suffered OFC damage leading to wide-ranging socioemotional difficulties. Patients with OFC damage often show striking behavioral symptoms that invite rich clinical descriptions of the bizarre and often difficult to categorize symptomatology. However, the data to carefully classify these symptoms is lacking and an overreliance on case reports may not elucidate the underlying processes that become disrupted following OFC injury.

Studies documenting emotional functioning following DLPFC injury are limited. In general, While OFC patients show more emotional and behavioral symptoms (e.g. insensitivity and social inappropriateness; Anderson, Barrash, Bechara, & Tranel, 2006), DLPFC patients are reported to have "less antisocial behavior" than non-DLPFC head injured patients (Bramham, Morris, Hornak, Bullock, & Polkey, 2009) and may have *preserved* emotional intelligence (Bar-On, Tranel, Denburg, & Bechara, 2003). In a study of patients with wide-ranging frontal lobe injuries, patients with DLPFC lesions were indistinguishable from control participants on measures of face and voice empathic accuracy, social behavior, and subjective emotional experience (Hornak et al., 2003). Furthermore, in a review of cases of early brain injury, children who had suffered DLPFC brain damage overall were much less severely impacted than those children suffering early OFC damage and generally showed normal social behavior in adulthood. However, some of these children did show social deficits that followed them into adulthood, particularly if the injury was in the right hemisphere. Symptoms in this group included "awkward emotional and pragmatic communication skills", indifference to others, and with a view of the social world that suggested more "confusion than alienation" (Eslinger, Flaherty-Craig, & Benton, 2004). These may be secondary to cognitive deficits that remain or due to lack of integration between cognitive and emotional processing. Taken together, clinical descriptions and caregiver ratings highlight the emotional and interpersonal disruptions that may arise following OFC or DLPFC damage. In either group, these disruptions may reflect difficulties taking the perspective of another and accurately identifying others' emotions; a comprehensive investigation of cognitive empathy may provide information about the underlying phenomenon and directions for intervention.

Cognitive Empathy and the Frontal Lobes: Previous Investigations

Perspective-taking. Across neuroimaging and patient studies, there is limited evidence for frontal lobe involvement in perspective-taking and empathic accuracy. In a functional imaging study, directed perspective-taking was associated with the insula and anterior cingulate cortex activation (Lamm, Batson, & Decety, 2007). Previous patient studies have described lower self-reported perspective taking in patients with OFC damage than control participants or patients with parietal or dorsolateral prefrontal cortex lesions (Shamay-Tsoory, Aharon-Peretz, & Perry, 2009; Shamay-Tsoory, Tomer, Berger, & Aharon-Peretz, 2003; Grattan et al., 1994). However, in another study, perspective-taking was lower in patients with DLPFC damage, and this deficit seemed to be related to cognitive deficits (Grattan et al., 1994). In sum, different frontal lobe regions may contribute to taking the perspective of other people.

Empathic accuracy. In functional imaging studies, ventrolateral and ventromedial regions are automatically activated when normal subjects view emotionally charged situations featuring one or two people (Kramer, et al., 2010) and recognizing emotions is associated with activation in various frontal lobe regions, including the inferior frontal gyri (George et al., 1993; Sprengelmeyer, et al., 1998), the OFC (Vuilleumier, Armony, Driver, & Dolan, 2001), and the ventral prefrontal cortex (Narumoto et al., 2000). Recently a study of dynamic empathic accuracy found temporal and frontal lobe regions were activated during a dynamic emotion tracking task (Zaki et al., 2009); more recently, we found that atrophy in the OFC was related to impairment on a dynamic emotion tracking task (Goodkind et al., *in press*). Select patient studies have documented that OFC injury may lead to deficits in empathic accuracy (Hornak et al., 1996; Heberlein et al., 2008), affective theory of mind (i.e. identifying social faux pas and irony; Shamay-Tsoory et al., 2010), and social intelligence (Mah, Grafman, & Arnold, 2005). However, other studies report deficits in both OFC and DLPFC patients in recognizing emotions in facial expressions (Shamay-Tsoory et al., 2003) and in the eyes (Geraci, Surian, Ferraro, & Cantagallo, 2010) and in using social cues to make interpersonal judgments (Mah et al., 2004). Contrary to those studies highlighting deficits in OFC patients, in a direct comparison of patients with medial and lateral lesions, Shamay-Tsoory and colleagues (2008) found that it was lateral patients (and not medial patients) who showed deficits in empathic accuracy) and that across all patients, damage in Brodmann area 44 was significantly more common in patients with empathic accuracy deficits.

Furthermore, DLPFC patients have been underrepresented in previous studies (e.g. Hornak et al., 1996) and a lack of statistically significant deficits may reflect an issue of statistical power more than it demonstrates preserved empathic accuracy in this patient population. Consistent with this notion, Mah and colleagues (Mah et al., 2005) found a trend for social knowledge deficits in DLPFC; in another study, problems detecting emotion from the eyes were most pronounced for a small group DLPFC patients compared to other frontal lobe patient groups (Shaw, Bramham, Lawrence, Morris, Baron-Cohen, & David, 2005). Taken together, across neuroimaging and patient studies, there is considerable evidence that frontal lobes play critical roles in perspective-taking and empathic accuracy; however, studies focusing on OFC and the DLPFC regions yield inconsistent and inconclusive results and have typically used single methods of cognitive empathy with limited ecological validity.

Theoretical basis for cognitive empathy and the frontal lobes. A number of theories that examine the functions of OFC and DLPFC regions are relevant to the study of cognitive empathy. In particular, two prominent theories, the somatic marker hypothesis and the reinforcement and reversal theory, propose mechanisms for the socioemotional deficits resulting from OFC damage described above and have implications for the role of the OFC in empathy. In terms of the DLPFC, one theory addresses the role this region plays in cognitive empathy by examining its role in cognitive processes generally. According to this theory, the DLPFC will be critical to cognitive empathy to the extent that cognitive processes are involved.

The somatic marker hypothesis. Damasio, Everitt, and Bishop (1996) developed the somatic marker hypothesis, which describes a mechanism by which emotional processes guide behavior. According to this hypothesis, reinforcing stimuli bring about physiological states; associations between the stimuli and the reinforcing physiological states are stored as somatic markers and are reactivated physiologically in future situations. As a result, physiological responses associated with previous experiences guide behavior toward advantageous decisions based on what was previously advantageous. The OFC provides the neural substrate for learning these associations between complex situations and emotional states associated with the situation. Consequently, OFC lesions impair a person's ability to respond emotionally to stimuli and use this response as information about his external world. As Carr (Carr et al., 2003) and others have suggested, the first step in understanding others' emotions may be having and understanding those emotions in ourselves. To the extent that understanding others' emotions relies on simulating those emotions in ourselves and acknowledging them, deficits in cognitive empathy may result from OFC damage.

Two types of patient studies provide evidence for this theory. First, a series of studies that use a risky gambling task have examined the relationship between physiological responding and decision-making. Over the course of the task, control participants and patients with damage to non-OFC regions begin to gamble in a way that is less risky and that maximizes winnings; changes in behavior follow increased physiological reactions that occur in anticipation of making a risky gamble. Patients with OFC damage do not adopt an optimal gambling strategy and do not show the anticipatory physiological reaction (e.g. Bechara, Damasio, Tranel, & Damasio, 1997). According to the somatic marker hypothesis, OFC patients' failures to adopt optimal strategies occur because they lack the physiological responses to guide them towards advantageous decisions and away from disadvantageous ones. Additionally, in response to less complex stimuli, patients with OFC damage show smaller physiological reactions when passively viewing emotionally-evocative scenes and faces (Damasio, Tranel, & Damasio, 1990, Damasio et al., 1991; Blair & Cipolotti, 2000), in the context of normal physiological responses to orienting stimuli and loud noises. A number of criticisms have been raised about the somatic marker hypothesis, in particular regarding consistency, efficiency, and necessity of physiological responses for guiding decisions (cf., Dunn et al., 2006). Despite these criticisms, this hypothesis provides a model for the influence of emotional and physiological information on decision-making. Supporting evidence for the somatic marker hypothesis suggests that OFC damage may negatively impact abilities to process and respond to emotional stimuli and may be expressed as cognitive empathy deficits.

Reinforcement and reversal theory. Another perspective on the role of the OFC in emotion focuses on reinforcement and reversal processes. According to this theory, reward and punishment values based on environmental factors are computed by the OFC (Kringelbach & Rolls, 2004) which is involved in continually updating these values to allow for quickly relearning, modifying, and reversing associations between stimuli and reward or punishment value. Determining the reward or punishment value of stimuli helps people decide when behaviors should be increased or decreased. With respect to emotional behavior, Rolls (2004) suggested that OFC damage causes deficits in decoding and updating the value of emotional stimuli. In social environments, others' emotional displays often serve as rewarding and punishing stimuli and as cues about how to act and when to modify our behavior. A failure to accurately and continually decode these displays may result in misinterpretation of other people's feelings and be expressed as a lack of cognitive empathy.

A number of studies have shown reversal deficits following OFC damage. Non-human primates with lesions including the OFC show impairment at extinguishing or switching responses from a previously rewarded stimulus (Meunier, Bachevalier, & Mishkin, 1997). Human patients with OFC damage show impairment reversing and changing their behaviors when contingencies change and previously rewarded behavior becomes disadvantageous or punishing (Rolls et al., 1994; Kringelbach & Rolls, 2004). In a task simulating reward or loss of money, patients with OFC lesions made financially disadvantageous decisions because they failed to reverse their behavior when cues alerted them to changing conditions (Hornak et al., 2004). In a functional imaging study using emotionally-relevant stimuli, Kringelbach and Rolls (2003) demonstrated that the OFC is activated when participants view emotional facial expressions that cue a change in behavior is necessary. Thus, it appears that the OFC is critical for determining the significance of incoming information and that deficits in cognitive empathy in OFC patients may be the result of an inability to adapt to others' changing emotional cues.

Cognition and cognitive empathy. In the laboratory, cognitive and emotional abilities are often assessed separately. However, in the real world, successful socioemotional functioning is typically a blend of cognitive and emotional processes. Both taking another's perspective and correctly identifying his emotions seem to rely on higher cognitive functions. Among the necessary cognitive tasks and skills, cognitive empathy requires maintaining attention, detecting details, considering and integrating different types of information, inhibiting irrelevant information, and shifting between and updating ideas. Together, these constitute many areas of executive functioning (EF). A range of cognitive abilities fall under the umbrella of EF and different ones may have unique associations with cognitive empathy. For example, working memory, or the ability to keep information in mind, and sustained attention are both necessary for processing multiple cues at once and over time in a social context. Secondly, inhibition is required in cognitive empathy to tune out irrelevant information in order to focus on the other person's emotions and perspectives. Finally, cognitive flexibility is necessary for monitoring incoming information, considering alternate perspectives, and adjusting perceptions as situation demands change. Intact EF may be are necessary for taking others' perspectives and identifying their emotions in real-world social situations. Consistent with this notion, developmentally, the acquisition of the ability to take another's perspective coincides with the development of executive control (Perner & Lang, 1999); by extension, it is hypothesized that conditions that interfere with executive functioning may too interfere with cognitive empathy.

Associations between EF and cognitive empathy have been demonstrated in normal aging control participants, in psychiatric populations, and in neurological populations. In a normal aging sample, spanning eight decades, detecting facial emotional expressions of fear and anger was associated with working memory and happiness recognition was correlated with working memory and sustained attention/vigilance (Mathersul, Palmer, Gur, Gur, Cooper, Gordon et al., 2008). In patients with schizophrenia, deficits in neuropsychological performance have been associated with deficits in both self-reported cognitive empathy (Shamay-Tsoory, Shur, Harari, & Levkovitz, 2007) and empathic accuracy (Bora, Gokcen, & Vednezdaroglu, 2008). According to Bryson, Bell, and Lysaker (1997), these empathic accuracy deficits can be attributed to basic neuropsychological impairments, particularly within the domains of executive functioning. In fact, in separate studies, neuropsychological test performance accounted for between .30 and .56 of the variance on empathic accuracy tests and fully mediated the relationship between empathic accuracy and functional impairment (Bryson et al., 1997; Fiszdon & Johannesen, 2010).

Among brain-injured patients, self-reported cognitive empathy has been associated with neuropsychological performance, and in particular with measures of cognitive flexibility (Grattan et al., 1994; Shamay-Tsoory et al., 2003; Rankin et al., 2005) and perseveration (Grattan & Eslinger, 1989). Additionally, Mah and colleagues (2004) demonstrated that impairments detecting lies and in general interpreting socioemotional cues were associated with performance on working memory and reversal tasks in patients with frontal lobe lesions. Mah and colleagues (2004) suggest that poor performance in patients with DLPFC lesions may be interpreted as reflecting deficits in sociocognitive skills necessary for these types of tasks. EF has been linked to the integrity of the DLPFC (Miller & Cummings, 2007) and deficits in this domain have been documented in patients with DLPFC damage (Anderson, Damasio, Jones, & Tranel, 1991; Stuss, Bisschop, Alexander, Levine, Katz, & Izukawa, 2001; Troyer, Moscovitch, Winocur, Leach, Freedman, 1998). Cognitive deficits are thought to outweigh emotional ones in DLPFC patients. However, to the extent that cognitive empathy relies on EF, DLPFC patients may exhibit cognitive empathy deficits. Along these lines, Carberry & Burd (1986) proposed that "cognitive rigidity of brain injured patients manifests itself socially as egocentric and limited empathic responses in interpersonal relationships".

Limited evidence has documented that the relationship between EF and perspective-taking is present in patients with lateral frontal lobe lesions and not for patients with other lesions, but who have cognitive empathy deficits (Grattan et al., 1994; Eslinger, 1998; Shamay-Tsoory et al., 2003). These data highlight the equifinality of cognitive empathy deficits, suggesting that multiple problems may result in deficits in this area. Of note, Geraci and colleagues (2010) found that the association between performance-based cognitive empathy and executive functioning (as measured by a perseveration task) was significant in both OFC and DLPFC participants. Among patients with lateral frontal lobe injuries in particular, emotional difficulties may come secondarily to cognitive deficits.

Current Study

Taken together, theories described above have been put forth to explain the clinical striking social and emotional problems experiences by patients with frontal lobe injury. These theories suggest that OFC or DLPFC lesions may impair a person's ability to take the perspective of another and accurately identify his emotions. However, prior investigations of cognitive empathy in these patient groups have been limited by the types and number of cognitive empathy measures used. The purpose of this investigation was two-fold: first, OFC and DLPFC patients were examined using a comprehensive investigation of cognitive empathy, including self-report measures of perspective-taking and static and dynamic measures of empathic accuracy. Second, associations between cognitive empathy and neuropsychological performance were examined.

Methods

Participants

Six individuals with bilateral damage to the OFC and six individuals with damage to the left or right DLPFC were recruited from the San Francisco General Hospital Neurology Clinic and the Northern California Veterans Administration Health Care System, Martinez, CA. OFC lesions were due to traumatic brain injury or tumor resection; DLPFC patients had suffered strokes. See Figure 1. Twelve control participants were recruited to match each patient on age, education, and gender. All participants were paid $20/hour for participation in the study. There were no differences among the groups in years of age ($F(2,21) = 1.00$, *ns*), education ($F(2,21) = 1.09$, *ns*) or sex ($\chi^2(2, N = 24) = .34$, *ns*). Means and standard deviations along with additional demographic data are presented in Table 1.

General Procedure

The laboratory assessment of cognitive empathy was conducted at the Berkeley Psychophysiology Laboratory at the University of California, Berkeley. Upon arrival, an experimenter explained the procedure and each participant signed a consent form (approved by the Committee for the Protection of Human Subjects [CPHS] at the University of California, Berkeley) that described the experimental tasks. An additional consent form regarding the future use of the videotapes was presented at the beginning of the day and signed at the end of the day so that all participants knew exactly what had been recorded. Physiological data were recorded throughout the day. Although those data will not be explored here, the rating dial measurements (discussed below in "Emotion tracking task") were collected using the same computer used to record physiological data. In a separate session, a trained staff member at the Helen Wills Neuroscience Institute collected neuropsychological data using standard neuropsychological testing procedures.

Self-reported cognitive empathy. To measure self-reported trait cognitive empathy, participants completed the Davis Interpersonal Reactivity Index (IRI). The IRI consists of four 7-item subscales, which are reduced to total scores on each of the four subscales. It has been used in previous studies of patients with neurodegenerative diseases (including those that primarily affect the frontal and temporal lobes; Rankin et al., 2006; Rankin, Kramer, & Miller, 2005) and with brain-injured patients (Shamay-Tsoory et al., 2003, 2004). The perspective taking (PT) and fantasy (FS) scale were used as a measure of self-reported cognitive empathy. Each participant received a total score for self-reported trait perspective taking (PT) and trait fantasy scale (FS).

Empathic accuracy.

The Eyes Test (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). Participants were presented with 35 photographs of actors, featuring just the eye regions. In each item, the picture was flanked by 4 choices (the correct answer and three foils) presented as text. Participants were asked to choose the answer that best fit what the actor was thinking or feeling. Participants were provided with a glossary of definitions of all of the terms. This test has been described as an advanced theory of mind test and assesses the ability to decode emotional facial expressions using minimal information. Performance was based on the total number answered correctly. Additionally, performance on subsets of eyes (male vs. female and positive vs. negative) were examined.

Morphing Test. Using photographs of emotional facial expressions of one woman, 16 linear morphs were created between a neutral expression and a fully-posed emotional expression for each of five basic emotions: anger, disgust, fear, sadness, and happiness. Participants viewed photographs of the basic emotions at each linear stage between levels 2 and 12 (i.e. from 6% to 75% of the full expression) for five emotions (anger, disgust, fear, happiness, and sadness) as well as a neutral expression in a pseudorandomized order. In total, participants viewed 168 photos (3 x 11 stages of the emotion x 5 emotions + 3 neutral emotions). Participants chose from six options (anger, disgust, fear, sadness, happiness, and neutral) on each slide and said answers aloud. The purpose of this test was to assess empathic accuracy of basic emotions in static stimuli using a sensitive task.

Each participant received a total correct score (out of 168) and total scores for each individual emotion. Additionally, a measure of empathic accuracy sensitivity was calculated by determining for each participant for each emotion the first morphing level (between 2 and 12) when a participant gave ≥ 2 of 3 correct responses (and continued to give ≥ 2 of 3 correct for all subsequent levels). For each score, the sensitivity level was subtracted from 12 (essentially reverse scored) so that higher scores indicated greater sensitivity. These two measures, total correct and sensitivity, were combined to create a composite for each emotion (for each participant).

Film clip empathic accuracy task. Participants viewed six film clips extracted from full-length commercial movies, each depicting a target character strongly displaying one of six emotions: enthusiasm, calm, pride, fear, sadness, and embarrassment. In each valence category (positive and negative), one high-arousal emotion (enthusiasm and fear), one low-arousal emotion (calm and sadness) and one self-conscious emotion (pride and embarrassment) were selected. The enthusiasm clip was taken from a scene of the movie, “My Best Friend’s Wedding,” depicting a woman (target character) greeting two friends, hugging them, and saying how excited she is to meet them in a high, giggly voice. The fear clip was from the movie, “Pirates of the Caribbean,” and included a scene depicting a woman (target character) running away from a pirate ghost, getting caught, and screaming several times during the chase. The calm clip was from the movie, “The Graduate,” and depicted a man (target character) lounging on a float in a swimming pool, wearing sunglasses, smiling, and drinking a beer as pleasant music plays in the background. The sadness clip was a scene from the movie, "Playing by Heart," depicting two women sitting on chairs at a cemetery. Both women are crying as one woman (target character) tells the other how much she will miss the man whose funeral they had just attended. The pride clip was a scene from the movie, "The Karate Kid," depicting the end of a karate competition. The winner is being held up on his teammates' shoulders as they all cheer and a man (target character) watches and nods, with a slight smile, while uplifting music plays in the background. The embarrassment clip was a scene from the movie, "The Princess Diaries," depicting a teenage girl (target character) seated in a classroom full of students. Another girl interrupts the lesson to point out that the target character is wearing a hat in class, violating the dress code. The teacher instructs the target character to take her hat off. As she does so, the other students laugh at her and tease her and she shrinks in her seat.

Each clip was preceded by a 60-second baseline period, during which a black "X" was presented in the middle of a white screen; during this time, participants were instructed to relax and watch the "X". After the baseline period and before the 30-second clip began, participants were shown a still image of the target character displaying a neutral expression and instructed to pay attention to that character's feelings. After viewing each empathy stimulus, participants chose from a list the emotion the target character in the film was feeling most strongly. Eight distractor emotion terms (for each film, the target emotions from the other five clips plus angry, disgusted, and contemptuous) were included on the list. In pilot testing, undergraduate students reliably identified the target emotion more often than the other emotion choices for each of the films selected; this task is currently being used in a large study of patients with diverse neurodegenerative disorders. The purpose of this task was to assess empathic accuracy for basic and self-conscious emotions that occur in dynamic stimuli.

Each participant received a score for the total number correct out of six. To examine performance for different types of emotional films, total scores on positive films (calm and enthusiastic), negative films (sad and afraid), and self-conscious films (embarrassed and proud) were also calculated.

Emotion tracking task. This task is based on a procedure developed and used in studies with neurologically-normal adults (e.g. Levenson & Ruef, 1992) and patients with diverse neurodegenerative diseases (Goodkind et al., *in press*). Stimuli for this task was taken from another study of marriage across the life-span (Levenson, Carstensen, & Gottman, 1994). Participants viewed six three-minute film clips of conversations about important marital topics between spouses. The clips were recorded in a split-screen format, with the husband on the left and the wife on the right. Participants viewed two older couples (ages 60-70), two middle-aged couples (ages 40-50) and two younger couples (ages 20-30). For each clip, one of the members of the couple was designated as the target person (with one husband and one wife designated as the target person in each age group). Participants were instructed to continuously indicate how they thought the target person was feeling during the interaction. To do this, participants adjusted a rating dial so that it always indicated how positive or negative the target was feeling at that moment. The rating dial traversed a 180 degree path with the dial pointer moving over a nine-point scale anchored by the legends "extremely negative" and "extremely positive", with "neutral" in the middle.

The purpose of this task is to assess empathic accuracy using a dynamic task that closely mimics the way that emotional information is typically decoded in others.

For each marital interaction film clip, an accuracy criterion was established by averaging the ratings of two research assistants who had been trained in emotional behavior coding. To establish a gold standard, any discrepancies between the two raters were discussed and resolved. Two measures of accuracy were computed. First, a deviation score for each participant in this study was derived by computing the deviation from the criterion for each second and summing the absolute deviations. This measure was then reverse-scored so that lower scores indicated more impairment and lower empathic accuracy. Additionally, a cross-correlation score was computed by calculating cross correlations between the criterion score and the participant's rating for each clip. A Fisher's r-to-z transformation was performed on each score to convert the Pearson's r to a normally-distributed value z. Total scores averaging across the six films were calculated as well as total score for male and female targets separately and for young targets, middle-aged targets, and old targets.

Neuropsychological performance. OFC and DLPFC participants were tested on various standard measures of neuropsychological performance through a battery of computer-based and paper-and-pencil tasks. Although a more comprehensive battery of tests was given, only those falling into the following three categories will be reported and described here: working memory/sustained attention, inhibition, and cognitive flexibility.

Working memory and sustained attention. To assess working memory and sustained attention, three neuropsychological tests were used: the n-back, dot counting, and WAIS-Digit Symbol. On the n-back task, participants viewed a series of shapes (e.g. squares) on the computer screen and compared the location of the current one to the shape that was presented two before (i.e. on each trial, participants responded if the current shape was in the same location as the one that had appeared two ago). Performance was measured as the total number answered correctly. The dot counting task required participants to view a series of images containing different shapes in different colors (e.g. blue circles, green circles, and blue squares) on the computer screen. Participants had to count the number of blue squares presented across multiple slides. Performance was measured as the total number answered correctly. Finally, the Digit Symbol subtest of the WAIS required participants to write the symbols that correspond to a string of digits as indicated by a key at the top of the page; performance is enhanced if the person learns the corresponding symbol and does not have to consult the key as frequently. Performance was measured as the total correct completed in 120 seconds. To create a working memory/attention composite score, the three tests were z-scored and averaged.

Inhibition. Three neuropsychological tests were used to measure inhibition performance: the continuous performance task (CPT), the Stroop task, and the Flanker task. On the CPT, participants were presented with different shapes on a computer screen. When a 5-pointed star was presented, they were instructed to press a button, but if any other shape was presented, they were instructed to refrain from pressing any button. Performance was measured as the average time per trial between shape presentation and button press, with higher numbers indicating worse inhibition. This measure was then reverse-scored. The Stroop task consisted of two trials in which participants viewed a sheet that contained columns of letter strings in different ink colors (e.g. red, blue, and green). On the first trial, the letter strings said "XXXX" and on the second trial, they said a word that was incongruent with the ink color (e.g. the word "red" printed in green ink). In both trials, the participant's task was to name the ink color for as many items as possible in 60 seconds. The first trial measured speeded color naming (and acted as a control task) whereas the second trial required participants to ignore the word and just name the color of the ink. Performance was measured as the total number named on the incongruent trial. To control for individual differences in color naming speed, a Stroop inhibition score was created by multiplying the incongruent score by the ratio of incongruent to congruent score. Higher scores indicated better inhibition. Finally, on the flanker task, participants viewed a series of arrows on the computer screen pointing to the left or to the right. Participants had to determine the direction of the middle arrow. The arrows flanking the middle arrow either faced the same or opposite direction as the middle arrow. Performance was measured as the average time per trial, with higher numbers indicating worse inhibition. This measure was then reverse-scored. To create an inhibition composite the three tests were z-scored and averaged.

Cognitive flexibility. Two types of tasks were used: fluency tasks and a set shift task. Four fluency tasks were used, including two verbal fluency and two visual fluency tests taken from the Delis Kaplan Executive Function System (DKEFS; Delis, Kaplan, & Kramer, 2001). For letter (or phonemic) fluency, on separate one-minute trials, participants were asked to generate words that began with the letters F and then A (excluding proper nouns and not repeating the same word with different suffixes). Verbal fluency was calculated as the total number of correct words produced across the two trials. For category fluency, on two separate one-minute trials, participants were required to generate as many words as possible that belonged to particular categories (animals and then vegetables). Category fluency was calculated as the total number of correct words produced across the two trials. On both tasks, more words indicated better fluency. Visual fluency was assessed with the two components of the design fluency tasks of the DKEFS: empty dots and switching dots. In both tasks, participants were presented with sheets that had a series of squares, each with 10 dots in them (5 filled dots and 5 empty dots). On the empty dots tasks, participants were instructed to make a different design in each square by connecting empty dots only and using four straight lines. On the switch dots task, participants were instructed to again make a design in each square using four straight lines, but to alternate between empty and filled dots with each straight line. Participants could lift the pen from the page; that is, the designs did not have to be made with one, continuous stroke. The lines could cross each other and the participants did not have to use all the dots. On both trials, fluency score was calculated as the total number of non-repeated designs completed in one minute. The final cognitive flexibility task was the set shifting task. For this task, on each trial participants saw a picture in the middle of the computer screen and they had to use arrow keys to indicate either what shape it was (square or triangle) or what color it was (blue or red). A word at the bottom of the screen indicated for each item if they should be matching on shape or color. Performance was measured as the average time per trial, with higher numbers indicating worse inhibition. This measure was then reverse-scored. To create an cognitive flexibility composite the five tests were z-scored and averaged.

Results

Group comparisons

Demographic data are presented in Table 1. OFC patients, DLPFC patients, and control participants did not differ significantly in terms of age (F = 1.00, p = .38) or education (F = 1.09, p = .35). A chi-square test showed no differences between the groups in terms of gender distribution ($\chi^2(2, N = 24) = .69$, p = .88). See Table 1.

Cognitive empathy analyses

To assess differences in cognitive empathy between OFC patients, DLPFC patients, and control participants, general linear model (GLM) analyses were conducted with diagnostic group as the predictor variable, cognitive empathy performance as the dependent variable, and age included as a covariate. Despite the lack of significant group differences, age was included as a covariate because of the wide variability in age (with patients ranging in age from 28 to 72) and because of documented age-differences in cognitive empathy (Richter & Kunzmann, 2010). Partial eta squares representing the portion of explained variance in the dependent variable are reported for each significant effect. The following eta squares (η^2) correspond with small (.10), medium (.25), and large (.40) effect sizes (f) respectively: $\eta^2 = .01$, $\eta^2 = .06$, $\eta^2 = .14$ (Cohen, 1988).

IRI – PT and FS. In a GLM, the overall effect of the perspective taking and fantasy scale composite was significant ($F = 4.18$, $p = .03$, $\eta^2 = .30$); pairwise comparisons showed that the control participants reported significantly higher IRI scores than OFC patients ($p = .02$) and DLPFC patients ($p = .05$). There were no differences between OFC patients and DLPFC patients ($p = .71$). An examination of the individual IRI scales showed a main effect of group for the fantasy scale ($F = 4.72$, $p = .02$, $\eta^2 = .32$, again with OFC and DLPFC patients reporting lower fantasy scale scores than control participants, $p = .03$ and DLPFC patients, $p = .02$). There was no main effect of group for the perspective-taking scale ($F = 1.11$, $p = .35$, $\eta^2 = .10$). See Table 2.

The Eyes Test. In a GLM, with diagnostic group (OFC, DLPFC, NC) as the predictor and age included as a covariate, the overall effect of diagnosis was at trend level ($F = 2.70$, $p = .09$, $\eta^2 = .21$). Pairwise comparisons show that DLPFC patients performed worse than control participants ($p = .03$); OFC patients did not differ from control participants ($p = .53$) or DLPFC patients ($p = .17$). In a follow-up analysis, examining performance for male eyes and female eyes separately, a significant group effect for recognizing male eyes was significant ($F = 3.93$, $p = .04$, $\eta^2 = .28$) with DLPFC patients worse than control participants at $p = .01$, but OFC patients not differing from DLPFC patients or control participants). There was no difference for recognizing female eyes ($F = 1.30$, $p = .29$, $\eta^2 = .12$). Furthermore, there were no significant differences among the three groups for recognizing positive ($F = 1.52$, $p = .24$, $\eta^2 = .13$) or negative ($F = 1.69$, $p = .21$, $\eta^2 = .14$) eyes. See Table 3.

Morphing Test. In a GLM, with diagnostic group (OFC, DLPFC, NC) as the predictor and age included as a covariate, the overall effect of diagnosis was significant ($F = 5.25$, $p = .02$, $\eta^2 = .34$). Follow-up pairwise comparisons revealed that DLPFC patients were once again worse than control participants ($p < .01$) and OFC patients did not differ significantly from control participants ($p = .12$) or DLPFC patients ($p = .20$). In a repeated 5 X 3 measures analysis with emotion type (anger, disgust, fear, sad, and happy) entered as the within-subject variable and diagnostic group entered as a between subjects factor, there was a significant interaction between morph emotion and diagnosis ($F = 4.22$, $p < .001$, $\eta^2 = .30$). There was no significant effect of morph ($F < 1$) and the effect of diagnosis remained significant. See Table 3.

Based on the significant interaction between morph and diagnosis, follow-up GLM analyses of each emotion were performed. For anger, there was a trend level effect ($F = 2.94$, $p = .08$, $\eta^2 = .28$), with DLPFC patients performing worse than control participants ($p = .03$) and marginally worse than OFC patients ($p = .10$). There were no differences between OFC patients and control participants ($p = .75$). For disgust, the effect of diagnosis was significant ($F = 8.66$, $p = .002$, $\eta^2 = .46$). DLPFC patients were worse than control participants ($p < .001$) and OFC patients ($p = .02$); OFC patients did not differ from control participants ($p = .25$). For fear, the main effect of diagnosis was at trend level ($F = 3.23$, $p = .06$, eta = .24), with DLPFC patients worse than control participants ($p = .02$) and no differences between OFC patients and controls ($p = .38$) or DLPFC patients ($p = .18$). For sad, the main effect of diagnosis was significant ($F = 9.55$, $p = .001$, eta = .49), with DLPFC patients performing worse than both control participants ($p < .001$) and OFC patients ($p = .01$). Finally for happy, the main effect of diagnosis was marginal ($F = 2.61$, $p = .10$, eta = .21). Pairwise comparisons showed that the only significant difference was that OFC patients were *worse* than DLPFC patients ($p = .03$); the control group did not differ significantly from DLPFC patients ($p = .23$) or OFC patients ($p = .16$). Given the pattern of worse performance among DLPFC patients on negative emotions, the four negative emotions (anger, disgust, fear, and sad) were averaged into a negative emotion composite and an additional 2x3 repeated measures GLM was performed, with negative and positive emotion score entered as within subjects variables and diagnosis as the between subjects measure. The interaction between morph emotion and diagnosis was significant ($F = 8.55$, $p = .001$, $\eta^2 = .46$). In a follow-up GLM of the negative emotion composite, the main effect of diagnosis was significant ($F = 13.83$, $p < .001$, $\eta^2 = .58$), with DLPFC patients worse than both control participants ($p < .001$) and OFC patients, ($p = .003$). Again, the main effect of happy was at trend level ($F = 2.61$, $p = .10$, $\eta^2 = .21$)

Empathic Accuracy Film Task. In a GLM with diagnostic group as the predictor and age included as a covariate, there were no significant differences between groups ($F = 1.07$, $p = .36$, $\eta^2 = .10$). Variability on this task was minimal: OFC patients made no errors on negative or self-conscious films and among all participants across six films, only eight errors were made (out of 144 trials). Additionally, only one participant responded correctly on more than one film. Due to the lack of variability on this task, associations with neuropsychological performance will not be explored. See Table 3.

Emotion tracking task. In a GLM, looking at a composite of cross correlations and deviation score, there was a significant main effect of age ($F = 4.21$, $p = .03$, $\eta^2 = .30$) with DLPFC patients showing impairment compared to control participants ($p = .03$) and OFC patients ($p = .01$). OFC patients did not significantly differ from control participants ($p = .43$). Repeated measures GLMs were also examined, exploring differences for rating male versus female targets and differences for rating young, middle, or old targets. In a 2X3 repeated measures GLM, the interaction between diagnosis and target gender was not significant ($F = 1.43$, $p = .26$, $\eta^2 = .13$); furthermore in a 3X3 repeated measures GLM, the interaction between diagnosis and target age was not significant ($F < 1$, $\eta^2 = .06$).

GLMs exploring total cross correlation scores and total deviation scores were also explored separately. For cross correlation scores, the main effect of group was marginally significant ($F = 2.99$, $p = .07$, $\eta^2 = .23$); again for the deviation total score, the main effect of group was marginally significant ($F = 3.10$, $p = .07$, $\eta^2 = .24$). See Table 3.

Relationships with Neuropsychological Performance

Neuropsychological data were available for 5 (of 6) OFC patients and 5 (of 6) DLPFC patients. To explore associations between cognitive empathy and neuropsychological performance, partial correlations (controlling for age) across these 10 participants were conducted.

Self-reported cognitive empathy.

Working memory/sustained attention. In partial correlations, controlling for age, the perspective-taking and fantasy-scale IRI composite was not significantly associated with the working memory composite or any of the individual working memory measures (all p's > .05). Similarly, the individual PT and FS were not significantly associated with the working memory composite, although the PT scale was marginally associated with the digit symbol task (r = .47, p = .10) and the FS scale was marginally associated with the n-back task (r = .56, p = .06).

Inhibition. In partial correlations, controlling for age, the IRI composite was not significantly associated with the inhibition composite or any of the individual measures of inhibition (all p's > .05). Similarly, the individual PT and FS were not significantly associated with the inhibition composite, although the PT scale was marginally associated with the flanker task (r = .47, p = .10).

Cognitive flexibility. In partial correlations, controlling for age, the IRI cognitive empathy composite was not significantly associated with the cognitive flexibility composite or any of the individual measures (all p's > .05). Similarly, the individual PT and FS were not significantly associated with the inhibition composite, although the FS scale was marginally associated with category fluency (r = .54, p = .07). Taken together, measures of self-reported cognitive empathy were not strongly or consistently associated with neuropsychological measures. See Table 4.

The Eyes Test.

Working memory/sustained attention. In partial correlations, controlling for age, total score on the Eyes Test was marginally associated with the working memory composite (r = .49, p = .09). Among individual working memory tests, Eyes Test score was associated with the dot counting (r= .58, p = .05) and digit symbol tasks (r = .57, p = .05).

Inhibition. In partial correlations, controlling for age, total score on the Eyes Test was marginally associated with the inhibition composite (r = .57, p = .06) as well as the CPT (r = .49, p = .10) and the Stroop task (r = .56, p = .06).

Cognitive flexibility. In partial correlations, the Eyes Test total score was significantly related to the cognitive flexibility composite (r = .76, p = .01) as well as the following individual measures of cognitive flexibility: category fluency (r = .70, p = .02), design fluency empty dots (r = .67, p = .02), and design fluency switch dots (r = .60, p = .04). Taken together, the Eyes Test showed marginal to strong correlations with neuropsychological variables, especially those measuring cognitive flexibility. See Table 5.

Morphing Test.

Working memory/sustained attention. In partial correlations, controlling for age, total score on the morphs was associated with the working memory composite (r = .61, p= .04) as well as individually, the digit symbol task (r = .82, p = .004). Similarly, total score for negative emotions was marginally associated with the working memory composite (r = .55, p = .07) and significantly associated with the digit symbol task (r = .70, p= .02). Performance for happy did not correlate with the composite or any individual measures of working memory/attention (all p's > .05).

Inhibition. In partial correlations, controlling for age, total score on the morphs task was associated with the inhibition composite (r = .71, p = .02) as well as the following individual measures: CPT (r = .56, p = .06), Stroop task (r = .65, p = .03), and the flanker task (r = .47, p = .10). Total score for negative emotions was associated with the inhibition composite (r = .64, p = .03) and with the Stroop task (r = .87, p = .001), but not significantly associated with the CPT or flanker tasks (p's > .05). Performance for happy morphs was marginally associated with the

CPT (r = .51, p = .08) but not the inhibition composite or other individual inhibition measures (p's > .05).

Cognitive flexibility. In partial correlations controlling for age, total score on the morphing test was strongly related to the cognitive flexibility composite (r = .88, p = .001) as well as individually all of the fluency variables: letter (r = .53, p = .07), category (r = .57, p = .06), design fluency empty dots (r = .72, p = .01), and design fluency switch dots (r = .65, p = .03). Additionally, the total negative emotion score was significantly correlated with all measures of cognitive flexibility: composite (r = .91, p < .001), letter fluency (r = .63, p = .03), category fluency (r = .58, p = .03), design fluency empty dots (r = .62, p = .04), design fluency switch dots (r = .54, p = .07), and the set shift task (r = .60, p = .05). No cognitive flexibility variables were significantly associated with the happy score on the morphing test. Taken together, performance on the morphing test was highly correlated with many neuropsychological measures; most notably, performance on negative emotion morphs showed strong associations with measures of cognitive flexibility. See Table 5.

Emotion tracking task.

Working memory/sustained attention. In partial correlations controlling for age, the total score on the emotion tracking task (a composite of cross correlation and deviation performance) was marginally related to the working memory composite (r = .51, p = .08) as well as the n-back task (r = .59, p = .05). Associations between the different accuracy measurements for the emotion tracking task (cross correlations and deviations) and the neuropsychological variables were also examined separately. The total cross correlation score on the emotion tracking task was associated with the working memory composite (r = .69, p = .02), the n-back (r = .60, p = .04), and the digit symbol task (r = .49, p = .09). The total deviation score on the emotion tracking task was not significantly associated with the working memory composite, but was marginally associated with the n-back task (r = .51, p = .08).

Inhibition. In partial correlations controlling for age, the total score on the emotion tracking task was not significantly related to the inhibition composite and among individual inhibition measures, was only related to the Stroop task (r = .67, p = .02). The total cross correlation score on the emotion tracking task was significantly associated with the inhibition composites (r = .62; p = .04) and with the Stroop task (r = .88, p = .001) but not other measures of inhibition. The total deviation score on the emotion tracking task was marginally associated with the Stroop task (r = .47, p = .10) but not the composite or other individual measures of inhibition.

Cognitive flexibility. In partial correlations controlling for age, the total score on the emotion tracking task was marginally associated with the cognitive flexibility composite (r = .46, p = .10). No associations with individual fluency measures were significant, but the relationship with the set shift task was marginally significant (r = .54, p = .07). In other partial correlations controlling for age, the total cross correlation score on the emotion tracking task again was associated with the cognitive flexibility composite (r = .72, p = .02). This measure was also associated with the set shift task (r = .60, p = .04) and marginally associated with the letter fluency (r = .56, p = .06) and the design fluency empty dots (r = .45, p= .06). In partial correlations controlling for age, the total deviation score on the emotion tracking task was not significantly associated with the cognitive flexibility composite, but was marginally associated with the set shift task (r = .47, p = .10). Taken together, cognitive flexibility measures showed some associations with the tracking task and these associations were strongest when examining the cross-correlation measure. See Table 6.

Neuropsychological Performance as an Explanation of Group Differences

Overall, empathic accuracy performance was related to group membership with DLPFC patients showing deficits and OFC patients showing preserved abilities. Across patient groups, associations with neuropsychological variables were seen for empathic accuracy tasks. Given these sets of results, I explored whether neuropsychological performance explained the relationship between diagnostic group and empathic accuracy. These analyses were performed only for the morphing test and the emotion tracking task, those in which OFC patients significantly differed from DLPFC patients. First I established that this diagnostic difference existed between the two patients groups (in addition to when looking at all three groups in one analysis). Then I examined if any significant effects became non-significant after including neuropsychological variables as additional covariates. These analyses consisted of first a GLM with diagnosis (OFC or DLPFC) as the predictor and age included as a covariate. In follow-up analyses, neuropsychological performance was included as a second covariate to examine if its inclusion reduced of the diagnosis effect below a significant level.

Morphing test. In a repeated measures GLM with patient status (OFC or DLPFC) as the predictor, 2 levels of morphed empathic accuracy (negative vs positive faces) as the dependent measure, and age included as a covariate, there was a significant group by morph interaction ($F = 8.54$, $p = .02$, $\eta^2 = .55$). Follow-up GLMs revealed that there were no differences between the groups for happy morphs ($F = 2.18$, $p = .18$, $\eta^2 = .24$), but a significant effect for negative emotions ($F = 10.21$, $p = .02$, $\eta^2 = .59$), with OFC patients showing better performance than DLPFC patients. Based on these results, analyses between diagnostic group and negative empathic accuracy additionally controlling for neuropsychological performance were explored.

Working memory tasks. With the working memory composite included as a covariate, the effect diagnostic group was reduced to a level just below significance ($F = 5.70$, $p = .054$, $\eta^2 = .48$). Examining individual working memory measures, no individual test caused the significant effect of diagnosis to become non-significant (all p's remained below .05 with n-back, dot counting, and digit symbol individually included as covariates).

Inhibition. With the inhibition composite included as a covariate, diagnostic group remained significant ($F = 6.49$, $p = .04$, $\eta^2 = .52$). However, looking at individual inhibition measures, including Stroop as a covariate caused the main effect to fall above significance ($F < 1$, $\eta^2 = .01$). Neither the flanker nor the CPT task caused the main effect of diagnosis to become non-significant.

Cognitive flexibility. Including the cognitive flexibility as a covariate completely mediated the relationship between diagnostic group and negative emotion empathic accuracy such that with this covariate, the effect of diagnosis was non-significant ($F < 1$, $\eta^2 = .10$). Examining individual cognitive flexibility measures, phonemic fluency mediated the relationship resulting in $F = 3.43$, $p = .11$, $\eta^2 = .36$, but category fluency did not and the effect of diagnosis remained significant with this covariate, $F = 7.71$, $p = .03$, $\eta^2 = .56$. With design fluency included as a covariate, the effect of diagnostic group dropped above significant, $F = 5.30$, $p = .06$, $\eta^2 = .47$. Finally, the set shift measure also mediated this relationship, causing it to become non-significant, $F = 3.64$, $p = .11$, $\eta^2 = .38$.

Emotion tracking task. In a repeated measures GLM with patient status (OFC or DLPFC) as the predictor and 2 levels of the rating dial films (male and female) and age included as a covariate, there was a significant main effect of diagnosis ($F = 13.47$, $p = .01$, $\eta^2 = .66$), but no significant group by stimuli gender ($F < 1$, $\eta^2 = .01$). Furthermore, running a similar repeated measures GLM with patient status as the predictor, age as a covariate, and 3 levels of rating dial films (young, middle, and old), there was again no significant diagnosis X film effect ($F < 1$, $\eta^2 = .03$). As such, in the following mediation analyses, I examine only the total score across all rating dial films.

Working memory tasks. After including the working memory composite as a covariate, the effect of diagnosis remained significant, $F = 7.60$, $p = .03$, $\eta^2 = .56$ (although the effect size was decreased somewhat). Examining individual working memory measures, no single working memory measure caused the effect of diagnosis to become non-significant.

Inhibition. After including the inhibition composite as a covariate, the effect of diagnosis remained significant ($F = 9.27$, $p = .02$, $\eta^2 = .61$). Examining individual inhibition measures, none caused the effect of diagnosis to become non-significant except the Stroop task ($F = 4.11$, $p = .09$, $\eta^2 = .41$).

Cognitive flexibility. After including the cognitive flexibility composite as a covariate, the effect of diagnosis remained significant, $F = 8.47$, $p = .03$, $\eta^2 = .59$. Examining individual cognitive flexibility measures showed that only the set shift variable caused a drop in significance of diagnostic effect (down to $F = 6.2$, $p = .05$, $\eta^2 = .51$).

Associations with Lesion Size and Duration of Injury

To explore whether cognitive empathy performance was related to the size of lesion or duration of injury, partial correlations (controlling for age) were conducted across OFC and DLPFC patients. In terms of self-reported cognitive empathy, the perspective-taking and fantasy-scale IRI composite was not significantly associated with lesion size, but was negatively associated with time since injury ($r = -.62$, $p = .03$), with higher empathy scores associated with a shorter duration of injury. In terms of measures of empathic accuracy, total score on the Eyes Test was not associated with either the lesion size or duration of injury. Total score on the morphing task was marginally associated with lesion size ($r = .54$, $p = .06$), however this was in the unexpected direction with larger lesion size predicting better performance on this task. Total score on the morphing task was not associated with time since injury; total score for negative emotions was not associated with either lesion size or time since injury. Performance on the emotion tracking task was not associated with lesion size, but was marginally associated with the time since injury ($r = .51$, $p = .06$) with better emotion tracking related to a greater number of months since sustaining the injury. Across patients, there was a wide variability in terms of lesion size and duration of injury: lesions ranged from 30.76cc to 375.75cc; duration of injury ranged from 8 to 480 months.

Discussion

Cognitive empathy, which includes both taking other people's perspectives and accurately identifying their emotions, is critical for successful interpersonal interactions and at least in part reliant on frontal lobe functioning. However, the frontal lobes play wide-ranging roles in social and emotional behavior and precise associations between specific areas and cognitive empathy are unclear. Anecdotal and clinical descriptions of patients with OFC damage portray them as having diffuse, interpersonally-disruptive social and emotional deficits, often in the context of preserved cognitive abilities. Patients with DLPFC injuries often have documented cognitive deficits, but the clinical picture of their social and emotional functioning is not well established. In the current study, a comprehensive battery was used to assess cognitive empathy in OFC and DLPFC patients compared to neurologically-normal control participants. Additionally, relationships between cognitive empathy and executive functioning were examined. Cognitive empathy measures included those assessing self-reported perspective taking and performance-based empathic accuracy. Empathic accuracy abilities were assessed with multiple measures, including those with static or dynamic stimuli and those requiring single responses or continuous responding.

Group Differences in Self-reported Cognitive Empathy—A Patient Effect

Patients and control participants rated their own empathy levels with the Interpersonal Reactivity Index (IRI), which includes two subscales thought to tap into cognitive empathy and in particular, the tendency to take on others' perspectives. Using a composite of the two IRI scales, both OFC and DLPFC patients reported lower levels of cognitive empathy than control participants. These results are consistent with those of Shamay-Tsoory and colleagues (Shamay-Tsoory et al., 2003) who found that a similar IRI-composite was lower in a group of patients with mixed PFC lesions than control participants and than patients with parietal lesions. However, these authors found that self-reported cognitive empathy levels were even lower for OFC patients than for DLPFC patients (Shamay-Tsoory et al., 2004), whereas in the current study both patient groups reported nearly identical levels of cognitive empathy.

A closer examination of the IRI data for the current study showed that both patient groups endorsed lower levels on the fantasy subscale but that patients and control participants reported similar levels on the perspective-taking scale. The fantasy subscale of the IRI examines how easily a person relates to fictional characters, such as those in a novel or a movie and is intended to tap into a type of vicarious emotional experience. Fantasy scores are thought to relate to verbal intelligence (Shamay-Tsoory et al., 2004) and cognitive flexibility (Rankin et al., 2005). However, in previous investigations the fantasy scale was the only IRI scale that showed no relationship to frontal lobe behavioral traits (Spinella, 2005) and the only one that did not change following the onset of frontotemporal dementia (Lough et al., 2006). These studies suggest that the fantasy scale may be more sensitive to cognitive changes than it is to emotional symptoms. The perspective-taking scale taps responding to people in real-life situations and is more commonly used, often in isolation, to assess self-reported cognitive empathy.
Based on data from the current study, OFC and DLPFC patients did not view themselves as less able or likely to take the perspective of another person in real-life. To the degree that patients and controls can accurately capture their own perspective-taking tendencies, OFC and DLPFC lesions did not seem to impact this component of cognitive empathy. However, drawing firm conclusions from these data is difficult because of potential limitations in understanding the meaning of taking others' perspective and judging one's own ability to do so.

Associations with neuropsychological performance. Among OFC and DLPFC patients, self-reported cognitive empathy scores were not significantly associated with any of the neuropsychological measures of cognitive performance. Specifically, the composite score of the perspective taking and fantasy scales of the IRI was not associated (even at a trend level) with any neuropsychological measures; the individual scales each showed a few weak relationships with limited neuropsychological measures but without any apparent pattern. Thus, these data are not consistent with previous investigations showing associations between self- and relative-rated cognitive empathy and cognitive flexibility (Grattan et al., 1994; Shamay-Tsoory et al., 2003; Rankin et al., 2005) or perseveration (Eslinger and Grattan, 1989). The discrepancy in findings cannot be attributed to the type of cognitive-empathy measure used, because many of these studies used versions of the IRI. However, the number of patients in the current study may not have been sufficient to show a significant relationship and limited the type of analyses that could be performed. Previous studies have shown that the relationship between self-reported cognitive empathy and neuropsychological performance may be strongest among patients with lateral frontal lobe damage (Grattan et al., 1994; Eslinger, 1998; Shamay-Tsoory et al., 2003). In the current study, the association between self-reported cognitive empathy and neuropsychological performance was examined across DLPFC and OFC patients (because there were only ten patients with neuropsychological data). However, including OFC patients in this analysis may have obscured a relationship that would exist for DLPFC patients alone.

Additionally, issues regarding the use of self-report scales, particularly with patients with frontal lobe injuries, should be considered when interpreting all self-reported cognitive empathy results. First, despite the theoretical similarity between self-reported tendencies to take another's perspective and performance-based indications of how well others' emotions are detected, measurements of perspective-taking and empathic accuracy tend to show weak correlations. In studies of control participants, self-reported and performance-based cognitive empathy measures were not significantly correlated (Ickes, Stinson, Bissonnette, & Garcia, 1990; Levenson & Ruef, 1992) and these correlations were lower among patients with frontal lobe damage (Shamay-Tsoory et al., 2004). Second, earlier studies of neurological and psychiatric populations demonstrated discrepancies between how patients rated themselves and how caregivers rated them on measures of empathy and personality traits (Rankin et al., 2005; Bora et al., 2008). Specifically, patients with frontal lobe damage may accurately describe how they were pre-morbidly, but fail to update ideas about themselves to reflect the changes that occur after the onset of illness.

Group Differences in Empathic Accuracy

Across measurements of empathic accuracy, a clear trend emerged in which OFC patients performed similarly to control participants, but DLPFC patients showed pervasive deficits. First, on two tasks measuring empathic accuracy using static stimuli, DLPFC patients showed moderate to severe impairment. On the Eyes Test, DLPFC patients performed at a borderline impaired level compared to control participants and OFC patients. On the morphing test, in which participants viewed a full face and had to identify small changes in emotional expression, the DLPFC patients showed an overall impairment in identifying emotions. Both of these tasks select for and reward the ability to detect small details in others' emotional signals in order to correctly identify the emotion. It is important to note that impairments were less pronounced for the Eyes Test, which is more verbally mediated (each item included a different set of 4 word choices and they tended to be more complicated words, such as "dispirited" and "despondent", than the morphing test, which included the same set of six words that were all basic emotion terms). Additionally, on a dynamic task requiring participants to track continually the emotions of the target in a film clip, DLPFC patients again showed impairment compared to both control participants and OFC patients. This task required participants to monitor continuously and to respond to ongoing fluctuations in another person's emotions. Taken together, DLPFC patients were impaired on multiple measures of empathic accuracy that spanned a range of stimuli format and response requirements, suggesting that the deficit in DLPFC patients is a global one of empathic accuracy. DLPFC patients were unimpaired on one empathic accuracy measure in which they had to identify the main emotion shown by a character in a film clip. However, few errors were made across all participants and this finding resulted from the lack of variability.

OFC patients did not show impairment on any measures of empathic accuracy, suggesting that socioemotional deficits often described in patients with OFC damage should not be attributed to an overall inability to understand others' emotions. Importantly, the lack of impairment among OFC patients did not reflect an issue of power as the effect sizes between OFC and control participants were consistently quite small and on the emotion tracking task, performance scores were actually higher for OFC patients than control participants (although this difference was not significant).

Preserved empathic accuracy in OFC patients. Despite theories and limited previous investigations predicting deficits in OFC patients, on all measures of empathic accuracy in the current study, this patient group was indiscriminable from control participants and in most cases, significantly better than DLPFC patients. These results have a number of important implications. First, these data are important to consider in the context of clinical descriptions of OFC patients, who are often described as interpersonally inappropriate and lacking concern for social rules (e.g. Blair & Cipolotti, 2000). Eslinger and Damasio (1985) describe a patient who, following surgery for an orbitofrontal meningioma, showed changes in social and emotional behavior leading to two divorces and financially costly business decisions. Furthermore, clinical descriptions suggest that OFC patients fail to respond appropriately to others' emotional signals. For example, Blair and Cipolotti (2000) report an OFC patient who was "reckless regarding others' personal safety" and once "continued to push around a wheelchair bound patient despite her screams in terror" (pg. 1124).

In order to reconcile results of the current study with clinical descriptions of OFC patients, differences between responding correctly on empathic accuracy tasks in the laboratory and performing similar tasks in the real world must be considered. The empathic accuracy tasks used in the current study were selected explicitly for their ecological-validity. For example, the emotion tracking task seems to capture many aspects of identifying others' emotions in the real world—participants were required to integrate the dynamically-changing visual and auditory emotional cues of the target. However, this and other empathic accuracy tasks fail to capture an important aspect of real-world emotion detection: participants were seated alone in a laboratory and not in the midst of an interaction with another person. OFC patients may be able to interpret correctly emotional information when removed from the interaction by one step, but unable to do so online in an interpersonal situation in which they are involved. Consistent with this interpretation, OFC patients provide appropriate responses on a moral judgment interview (Saver and Damasio, 1991) but may not make these same judgments when applied to their own behavior in the real world.

The reinforcement and reversal theory and the somatic marker hypothesis attempt to explain the role of the OFC in social situations. According to the reversal theory, the OFC is responsible for flexibly processing the value of environmental stimuli and adapting behaviors with the changing contingencies of the environment; according to the somatic marker hypothesis, our responses are based on previous experiences and these responses guide our behavior. In both cases, the role of the OFC is a) processing environmental information and b) *using this information* to guide future behavior. Tasks used in the current study tap the former ability; it may be that deficits in OFC patients arise at the level of the latter. For OFC patients, a breakdown may occur after coming to a correct interpretation of another person's emotions but before the execution of a behavioral response.

These results suggest the need for explorations of other aspects of emotional functioning that may be impaired in OFC patients and may have negative consequences for emotional and interpersonal functioning. First, a thorough investigation of affective empathy is warranted. Responding to others emotional signals in an emotional way is thought to co-occur with or lead to compassion, warmth and prosocial behavior (Hoffman, 2000; Eisenberg & Miller, 1987; Batson & Moran, 1999). Conversely, a lack of affective empathy may impede OFC patients' ability to connect with others and respond compassionately. Patients with OFC damage show reduced physiological responding to emotional stimuli (Blair & Cipolotti, 2000; Damasio, Tranel, & Damasio, 1990), suggesting that OFC damage may lead to reductions in affective empathy. Second, studying emotion regulation performance in OFC patients may shed light on their reported socioemotional deficits. It may be that aggressive, impulsive, and inappropriate behaviors that have been reported following OFC damage (cf, Blair & Cipolotti, 2000) result from difficulties modifying behaviors in the moment to fit the demands of current situations.

Taken together, results of the current study suggest that socioemotional behavioral abnormalities in OFC patients cannot be attributed to an inability to detect and track emotional signals in others; further research of affective empathy and emotion regulation may elucidate the basis for interpersonal difficulties in this patient group.

Impaired empathic accuracy in DLPFC patients. In contrast to OFC patients, DLPFC patients were impaired across measures of empathic accuracy; these deficits pervaded tasks with static and dynamic stimuli, suggesting that impairments were not due to type or level of difficulty of stimuli. These findings were somewhat surprising given the lack of emotional difficulties that are typically reported in DLPFC patients, particularly in comparison to OFC patients. However Eslinger (1998) proposed that in DLPFC patients, cognitive abilities interfere with perceiving and adaptively interacting with others. Furthermore, a small number of previous studies have established a precedent for empathic accuracy deficits in DLPFC patients. For example, Geraci and colleagues (Geraci et al., 2010) found that DLPFC patients were as impaired as OFC patients on the Eyes Test. In another study, Shamay-Tsoory and colleagues (2008) found that patients with lateral lesions and not those with medial lesions were impaired on measures of empathic accuracy.

Empathic accuracy and cognitive performance. Theory and supporting data suggest that empathic accuracy is associated with and relies on cognitive processes. Across psychiatric, neurological, and healthy populations, performance on empathic accuracy tasks has correlated positively with cognitive functioning, particularly in the domains of executive functioning (Bryson, Bell, & Lysaker, 1997; Mah et al., 2004; Mathersul et al., 2008). From this perspective, the ability to decode the emotions of others relies heavily on underlying cognitive processes, including focusing and maintaining attention, blocking out irrelevant information, and adjusting interpretations as the situations change. In the current study, measures in each of these domains were associated to varying degrees with empathic accuracy. On the Eyes Test, which taps the ability to infer the cognitive and emotional states of others using minimal information around the eyes, performance was most strongly associated with visual and verbal measures of cognitive flexibility. On this task, it may be necessary to consider and compare different possibilities simultaneously in order to arrive efficiently at the correct answer. More modest associations were found between the Eyes Test and other areas of cognitive functioning, including working memory and to a smaller extent, inhibition.

On the morphing test, performance was significantly associated with all measured domains of executive functioning, and in particular with cognitive flexibility. Specifically, identifying negative emotions (anger, disgust, fear, sad) was strongly correlated with the composite and all individual measures of cognitive flexibility. Additionally, performance on cognitive flexibility measures accounted for the group difference between OFC and DLPFC patients on the morphing test. OFC patients performed significantly better than DLPFC patients' for negative emotions on the morphing test but this difference was eliminated when cognitive flexibility was included as a covariate. Select working memory/attention and inhibition measures were associated with empathic accuracy but did not account for the patient group differences. Interestingly, no significant associations were found between the ability to recognize happy morphs (the only positive emotion) and neuropsychological performance. This finding parallels that for the Eyes Test: performance for recognizing negatively-valenced eyes correlated significantly with composite scores in each neuropsychological domain; performance on positively-valenced eyes correlated with none of the neuropsychological scores. These results suggest that recognizing negative emotions is more cognitively-mediated than recognizing positive emotions.

In general, performance on the emotion tracking task was moderately associated with neuropsychological performance, although these associations varied depending on the type of rating accuracy score used and tended to be less pronounced than those with static empathic accuracy measures. Tracking accuracy was computed in multiple ways: a cross-correlation score reflected how well the participant captured the gross wave-form of the conversation and a deviation score captured how precisely the participant detected moment-to-moment fluctuations. Tracking performance based on a composite of these two types of accuracy scores was moderately associated with neuropsychological performance in each domain, especially the n-back and Stroop tasks. Interesting relationships emerged when examining the cross-correlation and deviation scores separately. Cross-correlation performance was associated with composite scores within each neuropsychological domain, suggesting that the ability to follow the general wave-form of the conversation relies on being able to focus attention, tune out irrelevant information, and think flexibly with changing incoming information. However, deviation scores did not correlate strongly with any measures of neuropsychological function, suggesting that being able to identify precisely specific moment-to-moment fluctuations in the conversations did not depend on the cognitive abilities examined here. Importantly, despite divergent associations with neuropsychological variables, both cross correlation and deviation scores produced similar patterns across patient groups, with DLPFC patients, and not OFC patients, showing impairment. Unlike in the morphing task, associations with neuropsychological measures did not explain the difference between OFC and DLPFC patients on the emotion tracking task, suggesting that impairments among DLPFC patients could not be exclusively attributed to deficits in cognitive abilities examined in the current study. Further investigation is warranted to understand the other aspects of empathic accuracy that are affected by DLPFC damage but not attributable to the cognitive measures examined here.

Methodological Considerations in Cognitive Empathy Studies

The current study employed both self-reported and performance-based measures of cognitive empathy. Additionally, multiple methods of performance-based cognitive empathy, or empathic accuracy, were included. Accordingly, this study differs from others of cognitive empathy that have relied exclusively on self- or caregiver-rated cognitive empathy or single, simple measures of empathic accuracy. Tests of empathic accuracy vary widely, with individual measures offering certain advantages and disadvantages. For example, many studies of empathic accuracy require participants to identify the basic emotions in photographs of emotional facial expressions. This type of task enables detecting deficits for recognizing specific emotions (such as selective fear recognition deficits following amygdala damage [Adolphs et al., 1994] and selective disgust recognition deficits following insula damage [Calder, et al., 2000]). However, because we do not often encounter snapshots of specific and static emotions in others, this type of measure lacks ecological-validity. The dynamic emotion tracking task used in the current study maintains some of this ecological-validity lost in many empathic accuracy studies by mirroring the process of identifying others' emotions in the real world. Participants were required to make continual judgments of another person's emotions as the target was embedded in contextual information. However, the diverse components of this task and the varied and multiple skills necessary to perform it well make drawing conclusions difficult about the origin and the meaning of deficits. Investigations of cognitive empathy (as with the study of most emotional processes) must strike a balance between using tasks that are ecologically-valid and those in which performance can be carefully measured and interpreted. Additionally, this and other studies failed to capture a critical component of real-world cognitive empathy (an element that may shed light on difficulties reported in OFC patients). Specifically, once effective perspective taking has occurred and a person has correctly identified another's emotion, how this information is used becomes critically important. Investigations are needed to understand processes by which we use others' emotions (once we have identified them) to guide our subsequent behavior and the circumstances that cause these processes to go awry.

Limitations and Future Directions

As with any research, certain limitations exist. First, our study suffered from limited power due to the small numbers of patients in each group. Because of the small sample size, associations between empathic accuracy and neuropsychological performance could not be examined separately in OFC and DLPFC patients. In previous studies, measures of empathy have been related to neuropsychological performance in patients with lateral frontal lesions and not in patients with medial lesions (Grattan et al., 1994). Second, this study used a patient design in which associations were examined between brain lesion and impaired task performance. A patient model for studying brain-behavior relationships has certain advantages over activation-based studies. For example, conclusions can be drawn regarding the necessity of a certain neural regions that avoid issues of co-activation found in functional imaging studies. However, this method also presents certain disadvantages and thus does not replace studies examining associations between performance on a particular task and the attendant pattern of neural activation. Furthermore, additional investigations are needed to explore the contributions of the OFC and the DLPFC to constructs related to cognitive empathy; empathic accuracy is just one aspect of emotional functioning and that other aspects (reactivity, regulation, emotional empathy, prosocial behavior) would all be of interest in understanding the specific emotional deficits in these patients. such as affective empathy and prosocial responding. Finally, this study would be enhanced by including assessments of functional outcome. OFC patients are thought to have more pronounced and overt social deficits but in this study, DLPFC patients showed difficulties on empathic accuracy tasks. It would be helpful to compare this pattern of results to real-world socioemotional functioning.

Conclusion

Results of the current study showed preserved empathic accuracy performance in OFC patients and impaired performance in DLPFC patients, a pattern that was consistent over static and dynamic measures. The lack of deficits in OFC patients was in contrast with many prevailing views suggesting that damage to this region results in extensive socioemotional and interpersonal problems. Across both patient groups, accurately identifying others' emotions showed variable relationships with working memory/attention, inhibition, and cognitive flexibility. Relationships with neuropsychological performance were strongest on measures requiring participants to detect small emotional details in static stimuli and were not as pronounced on a dynamic test of continuous emotion recognition. Previous studies have linked empathic accuracy abilities with functional outcomes, including overall behavioral symptomatology (Mah, Arnold, & Grafman), occupational functioning (Hooker & Park, 2002), social competence (Mueser et al., 1996). Remediation of empathic accuracy skills may lead to improvements in daily life and offer the next step of this type of research.

References

Abdi, Z., & Sharma, T. (2004). Social Cognition and Its Neural Correlates in Schizophrenia and Autism. *CNS Spectrums. Vol 9(5), 9*, 335-343.

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature*, *372*(6507), 669-672.

Anderson, S. W., Damasio, H., Jones, R. D., & Tranel, D. (1991). Wisconsin Card Sorting Test performance as a measure of frontal lobe damage. *Journal of Clinical and Experimental Neuropsychology*, *13*(6), 909-922.

Anderson, S. W., Barrash, J., Bechara, A., & Tranel, D. (2006). Impairments of emotion and real-world complex behavior following childhood- or adult-onset damage to ventromedial prefrontal cortex. *Journal of the International Neuropsychological Society: JINS*, *12*(2), 224-235. doi:10.1017/S1355617706060346

Bar-On, R., Tranel, D., Denburg, N. L., & Bechara, A. (2003). Exploring the neurological substrate of emotional and social intelligence. *Brain: A Journal of Neurology*, *126*(Pt 8), 1790-1800. doi:10.1093/brain/awg177

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "Reading the mind in the eyes" Test revised version: A study with normal adults, and adults with Asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry*, *42*(2), 241-251.

Batson, C. D., & Moran, T. (1999). Empathy-induced altruism in a prisoner's dilemma. *European Journal of Social Psychology*, *29*(7), 909-924.

Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1997). Deciding advantageously before knowing the advantageous strategy. *Science (New York, N.Y.)*, *275*(5304), 1293-1295.

Blair, R. J., & Cipolotti, L. (2000). Impaired social response reversal. A case of 'acquired sociopathy'. *Brain : a journal of neurology*, *123 (Pt 6)*(Pt 6), 1122-1141.

Blair, R. J. R. (2005). Responding to the emotions of others: Dissociating forms of empathy through the study of typical and psychiatric populations. *Consciousness and Cognition: An International Journal.Special Issue: The Brain and Its Self*, *14*(4), 698-718.

Boice, R. (1983). Observational skills. *Psychological Bulletin. Vol 93(1)*, *93*(1983), 3-29.

Bora, E., Gökçen, S., & Veznedaroglu, B. (2008). Empathic abilities in people with schizophrenia. *Psychiatry Research*, *160*(1), 23-29. doi:10.1016/j.psychres.2007.05.017

Bowers, D., Blonder, L., & Heilman, K. M. (1992). *The Florida Affect Battery*. Gainesville, FL: Center for Neuropsychological Studies, University of Florida.

Bramham, J., Morris, R. G., Hornak, J., Bullock, P., & Polkey, C. E. (2009). Social and emotional functioning following bilateral and unilateral neurosurgical prefrontal cortex lesions. *Journal of Neuropsychology*, *3*(Pt 1), 125-143. doi:10.1348/174866408X293994

Brekke, J. S., Hoe, M., Long, J., & Green, M. F. (2007). How neurocognition and social cognition influence functional change during community-based psychosocial rehabilitation for individuals with schizophrenia. *Schizophrenia Bulletin*, *33*(5), 1247-1256. doi:10.1093/schbul/sbl072

Brüne, M. (2005). Emotion recognition, 'theory of mind,' and social behavior in schizophrenia. *Psychiatry Research. Vol 133(2-3)*, *133*, 135-147.

Bryson, G., Bell, M., & Lysaker, P. (1997). Affect recognition in schizophrenia: a function of global impairment or a specific cognitive deficit. *Psychiatry Research*, *71*(2), 105-113.

Calder, A. J., Keane, J., Manes, F., Antoun, N., & Young, A. W. (2000). Impaired recognition and experience of disgust following brain injury. *Nat Neurosci*, *3*(11), 1077-1078. doi:10.1038/80586

Calder, A. J., Keane, J., Manly, T., Sprengelmeyer, R., Scott, S., Nimmo-Smith, I., & Young, A. W. (2003). Facial expression recognition across the adult life span. *Neuropsychologia*, *41*(2), 195-202. doi:10.1016/S0028-3932(02)00149-5

Carberry, H., & Burd, B. (1986). Individual psychotherapy with the brain injured adult. *Cognitive Rehabilitation. Vol 4(4)*, *4*, 22-24.

Carr, L., Iacoboni, M., Dubeau, M., Mazziotta, J. C., & Lenzi, G. L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *Proceedings of the National Academy of Sciences of the United States of America*, *100*(9), 5497-5502. doi:10.1073/pnas.0935845100

Couture, S. M., Penn, D. L., & Roberts, D. L. (2006). The functional significance of social cognition in schizophrenia: a review. *Schizophrenia Bulletin*, *32 Suppl 1*, S44-63. doi:10.1093/schbul/sbl029

Damasio, A. R., Everitt, B. J., & Bishop, D. (1996). The Somatic Marker Hypothesis and the Possible Functions of the Prefrontal Cortex [and Discussion]. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *351*(1346), 1413 -1420. doi:10.1098/rstb.1996.0125

Damasio, A. R., Tranel, D., & Damasio, H. (1990). Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. *Behavioural brain research*, *41*(2), 81-94.

Damasio, A. R., Tranel, D., & Damasio, H. C. (1991). Somatic markers and the guidance of behavior: Theory and preliminary testing. In *Frontal lobe function and dysfunction.*, Frontal lobe function and dysfunction. (pp. 217-229). New York, NY, US: Oxford University Press.

Davis, M. H. (1983). Measuring individual differences in empathy: Evidence for a multidimensional approach. *Journal of personality and social psychology*, *44*(1), 113-126.

Decety, J., & Jackson, P. L. (2004). The Functional Architecture of Human Empathy. *Behavioral And Cognitive Neuroscience Reviews*, *3*(2), 71-100.

Delis, D., Kaplain, E., & Kramer, J. (2001). *The Delis-Kaplan executive function scale*. San Antonio: The Psychological Corporation.

Dunn, B. D., Dalgleish, T., & Lawrence, A. D. (2006). The somatic marker hypothesis: a critical evaluation. *Neuroscience and biobehavioral reviews*, *30*(2), 239-271.

Eisenberg, N., & Miller, P. A. (1987). The relation of empathy to prosocial and related behaviors. *Psychological bulletin*, *101*(1), 91-119.

Ekman, P. (1992). An argument for basic emotions. *Cognition & Emotion. Vol 6(3-4)*, 169-200.

Eslinger, P. J., & Damasio, A. R. (1985). Severe disturbance of higher cognition after bilateral frontal lobe ablation: patient EVR. *Neurology*, *35*(12), 1731-1741.

Eslinger, P. J., Flaherty-Craig, C. V., & Benton, A. L. (2004). Developmental outcomes after early prefrontal cortex damage. *Brain and Cognition*, *55*(1), 84-103. doi:10.1016/S0278-2626(03)00281-1

Eslinger, P. J. (1998). Neurological and neuropsychological bases of empathy. *European neurology*, *39*(4), 193-199.

Fernandez-Duque, D., & Black, S. E. (2005). Impaired recognition of negative facial emotions in patients with frontotemporal dementia. *Neuropsychologia*, *43*(11), 1673-1687. doi:10.1016/j.neuropsychologia.2005.01.005

Fiszdon, J. M., & Johannesen, J. K. (2010). Functional significance of preserved affect recognition in schizophrenia. *Psychiatry Research*, *176*(2-3), 120-125. doi:10.1016/j.psychres.2009.08.006

George, M. S., Ketter, T. A., Gill, D. S., Haxby, J. V., Ungerleider, L. G., Herscovitch, P., & Post, R. M. (1993). Brain regions involved in recognizing facial emotion or identity: an oxygen-15 PET study. *The Journal of neuropsychiatry and clinical neurosciences*, *5*(4), 384-394.

Geraci, A., Surian, L., Ferraro, M., & Cantagallo, A. (2010). Theory of Mind in patients with ventromedial or dorsolateral prefrontal lesions following traumatic brain injury. *Brain Injury: [BI*, *24*(7-8), 978-987. doi:10.3109/02699052.2010.487477

Goodkind, M., Sollberger, M., Gyurak, A., Rosen, H., Rankin, K., Miller, B., & Levenson, R. (n.d.). Tracking Emotional Valence: The Role of the Orbitofrontal Cortex. *Human brain mapping, under review*.

Grattan, L. M., Bloomer, R. H., Archambault, F. X., & Eslinger, P. J. (1994). Cognitive flexibility and empathy after frontal lobe lesion. *Neuropsychiatry, Neuropsychology, & Behavioral Neurology*, *7*(4), 251-259.

Harlow, J. M. (1868). Recovery from the passage of an iron bar through the head. *Publication of Massachusetts Medical Society*, *2*.

Harmer, C. J., Thilo, K. V., Rothwell, J. C., & Goodwin, G. M. (2001). Transcranial magnetic stimulation of medial-frontal cortex impairs the processing of angry facial expressions. *Nature Neuroscience*, *4*(1), 17-18. doi:10.1038/82854

Harmer, C. J., Perrett, D. I., Cowen, P. J., & Goodwin, G. M. (2001). Administration of the beta-adrenoceptor blocker propranolol impairs the processing of facial expressions of sadness. *Psychopharmacology*, *154*(4), 383-389.

Harms, M. B., Martin, A., & Wallace, G. L. (2010). Facial emotion recognition in autism spectrum disorders: a review of behavioral and neuroimaging studies. *Neuropsychology Review*, *20*(3), 290-322. doi:10.1007/s11065-010-9138-6

Heberlein, A. S., Padon, A. A., Gillihan, S. J., Farah, M. J., & Fellows, L. K. (2008). Ventromedial frontal lobe plays a critical role in facial emotion recognition. *Journal of cognitive neuroscience*, *20*(4), 721-733.

Henry, J. D., Phillips, L. H., Crawford, J. R., Ietswaart, M., & Summers, F. (2006). Theory of mind following traumatic brain injury: The role of emotion recognition and executive dysfunction. *Neuropsychologia*, *44*(10), 1623-1628.

Hess, U., & Blairy, S. (2001). Facial mimicry and emotional contagion to dynamic emotional facial expressions and their influence on decoding accuracy. *International Journal of Psychophysiology. Vol 40(2)*, *40*, 129-141.

Hoffman, M. L. (2000). *Empathy and moral development: Implications for caring and justice.* New York, NY, US: Cambridge University Press. (.

Hoffman, M. L. (1990). Empathy and justice motivation. *Motivation and Emotion.Special Issue: Empathy*, *14*(2), 151-172.

Hooker, C., & Park, S. (2002). Emotion processing and its relationship to social functioning in schizophrenia patients. *Psychiatry Research*, *112*(1), 41-50.

Hooker, C. I., Verosky, S. C., Germine, L. T., Knight, R. T., & D'Esposito, M. (2010). Neural activity during social signal perception correlates with self-reported empathy. *Brain Research*, *1308*, 100-113. doi:10.1016/j.brainres.2009.10.006

Hornak, J., Bramham, J., Rolls, E. T., Morris, R. G., O'Doherty, J., Bullock, P. R., & Polkey, C. E. (2003). Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. *Brain : a journal of neurology*, *126*(Pt 7), 1691-1712.

Hornak, J., O'Doherty, J., Bramham, J., Rolls, E. T., Morris, R. G., Bullock, P. R., & Polkey, C. E. (2004). Reward-related reversal learning after surgical excisions in orbito-frontal or dorsolateral prefrontal cortex in humans. *Journal of cognitive neuroscience*, *16*(3), 463-478.

Hornak, J., Rolls, E. T., & Wade, D. (1996). Face and voice expression identification in patients with emotional and behavioural changes following ventral frontal lobe damage. *Neuropsychologia*, *34*(4), 247-261.

Ickes, W. (1993). Empathic accuracy. *Journal of Personality.Special Issue: Viewpoints on personality: Consensus, self-other agreement, and accuracy in personality judgment*, *61*(4), 587-610.

Ickes, W., Stinson, L., Bissonnette, V., & Garcia, S. (1990). Naturalistic social cognition: Empathic accuracy in mixed-sex dyads. *Journal of personality and social psychology*, *59*(4), 730-742.

Ickes, W. J. (. (1997). *Empathic accuracy.* New York, NY, US: Guilford Press. (.

Krämer, U. M., Mohammadi, B., Doñamayor, N., Samii, A., & Münte, T. F. (2010). Emotional and cognitive aspects of empathy and their relation to social cognition--an fMRI-study. *Brain Research*, *1311*, 110-120. doi:10.1016/j.brainres.2009.11.043

Kringelbach, M. L., & Rolls, E. T. (2003). Neural correlates of rapid reversal learning in a simple model of human social interaction. *NeuroImage*, *20*(2), 1371-1383.

Kringelbach, M. L., & Rolls, E. T. (2004). The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. *Progress in neurobiology*, *72*(5), 341-372.

Lamm, C., Batson, C. D., & Decety, J. (2007). The Neural Substrate of Human Empathy: Effects of Perspective-taking and Cognitive Appraisal. *Journal of cognitive neuroscience*, *19*(1), 42-58.

Levenson, R. W., & Ruef, A. M. (1992). Empathy: a physiological substrate. *Journal of personality and social psychology*, *63*(2), 234-246.

Levenson, R. W. (. (2003). *Blood, Sweat, and Fears: The Autonomic Architecture of Emotion*. Annals of the New York of Sciences: Vol. 1000. New York, NY, US: New York University Press.

Lough, S., Kipps, C. M., Treise, C., Watson, P., Blair, J. R., & Hodges, J. R. (2006). Social reasoning, emotion and empathy in frontotemporal dementia. *Neuropsychologia*, *44*(6), 950-958.

Mah, L., Arnold, M. C., & Grafman, J. (2004). Impairment of social perception associated with lesions of the prefrontal cortex. *The American Journal of Psychiatry*, *161*(7), 1247-1255.

Mah, L. W. Y., Arnold, M. C., & Grafman, J. (2005). Deficits in Social Knowledge Following Damage to Ventromedial Prefrontal Cortex. *Journal of Neuropsychiatry & Clinical Neurosciences*, *17*(1), 66-74.

Malatesta, C. Z., Izard, C. E., Culver, C., & Nicolich, M. (1987). Emotion communication skills in young, middle-aged, and older women. *Psychology and Aging*, *2*(2), 193-203.

Mathersul, D., Palmer, D. M., Gur, R. C., Gur, R. E., Cooper, N., Gordon, E., & Williams, L. M. (2009). Explicit identification and implicit recognition of facial emotions: II. Core domains and relationships with general cognition. *Journal of Clinical and Experimental Neuropsychology*, *31*(3), 278-291. doi:10.1080/13803390802043619

McDonald, S., Flanagan, S., Rollins, J., & Kinch, J. (2003). TASIT: A new clinical tool for assessing social perception after traumatic brain injury. *The Journal of head trauma rehabilitation*, *18*(3), 219-238.

Mead, G. H. (1934). *Mind, Self, and Society from the Standpoint of a Social Behaviorist*. University of Chicago Press: Chicago.

Mendez, M. F., Lauterbach, E. C., & Sampson, S. M. (2008). An evidence-based review of the psychopathology of frontotemporal dementia: a report of the ANPA Committee on Research. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *20*(2), 130-149. doi:10.1176/appi.neuropsych.20.2.130

Meunier, M., Bachevalier, J., & Mishkin, M. (1997). Effects of orbital frontal and anterior cingulate lesions on object and spatial memory in rhesus monkeys. *Neuropsychologia.Special Issue: Cortical and subcortical circuits for perception and memory*, *35*(7), 999-1015.

Milders, M., Ietswaart, M., Crawford, J. R., & Currie, D. (2008). Social behavior following traumatic brain injury and its association with emotion recognition, understanding of intentions, and cognitive flexibility. *Journal of the International Neuropsychological Society: JINS*, *14*(2), 318-326. doi:10.1017/S1355617708080351

Miller, B. L. (. (., & Cummings, J. L. (. (. (2007). *The human frontal lobes: Functions and disorders (2nd ed.)*. New York, NY, US: Guilford Press.

Mueser, K. T., Doonan, R., Penn, D. L., Blanchard, J. J., Bellack, A. S., Nishith, P., & DeLeon, J. (1996). Emotion recognition and social competence in chronic schizophrenia. *Journal of Abnormal Psychology*, *105*(2), 271-275.

Narumoto, J., Yamada, H., Iidaka, T., Sadato, N., Fukui, K., Itoh, H., & Yonekura, Y. (2000). Brain regions involved in verbal or non-verbal aspects of facial emotion recognition. *Neuroreport*, *11*(11), 2571-2576.

Perner, & Lang. (1999). Development of theory of mind and executive control. *Trends in Cognitive Sciences*, *3*(9), 337-344.

Preston, S. D., & de Waal, F. B. M. (2002). Empathy: Its ultimate and proximate bases. *Behavioral and Brain Sciences*, *25*(1), 1-20.

Rankin, K. P., Gorno-Tempini, M. L., Allison, S. C., Stanley, C. M., Glenn, S., Weiner, M. W., & Miller, B. L. (2006). Structural anatomy of empathy in neurodegenerative disease. *Brain : a journal of neurology*, *129*(Pt 11), 2945-2956.

Rankin, K. P., Kramer, J. H., & Miller, B. L. (2005). Patterns of cognitive and emotional empathy in frontotemporal lobar degeneration. *Cognitive and behavioral neurology : official journal of the Society for Behavioral and Cognitive Neurology*, *18*(1), 28-36.

Ridout, N., O'Carroll, R. E., Dritschel, B., Christmas, D., Eljamel, M., & Matthews, K. (2007). Emotion recognition from dynamic emotional displays following anterior cingulotomy and anterior capsulotomy for chronic depression. *Neuropsychologia*, *45*(8), 1735-1743.

Richter, D & Kunzmann, U (2010). Age differences in three facets of empathy: Performance based evidence. *Psychology and Aging.*

Rolls, E. T. (2004). The functions of the orbitofrontal cortex. *Brain and cognition*, *55*(1), 11-29.

Rolls, E. T., Hornak, J., Wade, D., & McGrath, J. (1994). Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. *Journal of neurology, neurosurgery, and psychiatry*, *57*(12), 1518-1524.

Saver, J. L., & Damasio, A. R. (1991). Preserved access and processing of social knowledge in a patient with acquired sociopathy due to ventromedial frontal damage. *Neuropsychologia*, *29*(12), 1241-1249.

Shamay-Tsoory, S. G., Aharon-Peretz, J., & Perry, D. (2009). Two systems for empathy: a double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. *Brain : a journal of neurology*, *132*(Pt 3), 617-627.

Shamay-Tsoory, S. G., Tomer, R., Berger, B. D., & Aharon-Peretz, J. (2003). Characterization of empathy deficits following prefrontal brain damage: the role of the right ventromedial prefrontal cortex. *Journal of cognitive neuroscience*, *15*(3), 324-337.

Shamay-Tsoory, S. G., Tomer, R., Goldsher, D., Berger, B. D., & Aharon-Peretz, J. (2004). Impairment in cognitive and affective empathy in patients with brain lesions: anatomical and cognitive correlates. *Journal of clinical and experimental neuropsychology*, *26*(8), 1113-1127.

Shamay-Tsoory, S. G., Shur, S., Harari, H., & Levkovitz, Y. (2007). Neurocognitive basis of impaired empathy in schizophrenia. *Neuropsychology*, *21*(4), 431-438. doi:10.1037/0894-4105.21.4.431

Shamay-Tsoory, S. G., & Aharon-Peretz, J. (2007). Dissociable prefrontal networks for cognitive and affective theory of mind: A lesion study. *Neuropsychologia*, *45*(13), 3054-3067.

Shaw, P., Bramham, J., Lawrence, E. J., Morris, R., Baron-Cohen, S., & David, A. S. (2005). Differential effects of lesions of the amygdala and prefrontal cortex on recognizing facial expressions of complex emotions. *Journal of cognitive neuroscience*, *17*(9), 1410-1419.

Shur, S., Shamay-Tsoory, S. G., & Levkovitz, Y. (2008). Integration of emotional and cognitive aspects of theory of mind in schizophrenia and its relation to prefrontal neurocognitive performance. *Cognitive Neuropsychiatry. Vol 13(6)*, *13*, 472-490.

Spinella, M. (2005). Prefrontal substrates of empathy: Psychometric evidence in a community sample. *Biological psychology*, *70*(3), 175-181.

Sprengelmeyer, R., Rausch, M., Eysel, U. T., & Przuntek, H. (1998). Neural structures associated with recognition of facial expressions of basic emotions. *Proceedings.Biological sciences / The Royal Society*, *265*(1409), 1927-1931.

Stuss, D. T., Bisschop, S. M., Alexander, M. P., Levine, B., Katz, D., & Izukawa, D. (2001). The Trail Making Test: a study in focal lesion patients. *Psychological Assessment*, *13*(2), 230-239.

Troyer, A. K., Moscovitch, M., Winocur, G., Leach, L., & Freedman, M. (1998). Clustering and switching on verbal fluency tests in Alzheimer's and Parkinson's disease. *Journal of the International Neuropsychological Society: JINS*, *4*(2), 137-143.

Vuilleumier, P., Armony, J. L., Driver, J., & Dolan, R. J. (2001). Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron*, *30*(3), 829-841.

Zaki, J., Weber, J., Bolger, N., & Ochsner, K. (2009). The neural bases of empathic accuracy. *PNAS Proceedings of the National Academy of Sciences of the United States of America. Vol 106(27)*, 11382-11387.

Table 1
Participant demographic data

	Normal control (n =12)	*OFC (n = 6)*	*DLPFC (n = 6)*	*Test statistics*
Males	7	3	4	$\chi^2(2, N = 24) = .34$, *ns*
Age (*SD*)	53.4 (13.8)	48.3 (16.8)	59.5 (9.1)	F (2,21) = 1.00, $p > .05$
Education (*SD*)	16.4 (1.8)	14.5 (2.5)	15.7 (3.8)	F(2,21) = 1.09, $p > .05$
Lesion size in cc (*SD*)	n/a	118.2 (140.9)	104.58 (55.9)	F(1,11) = .05, $p > .05$
Months since injury	n/a	220.1 (89.8)	34.7 (15.5)	F(1,11) = .16, $p > .05$

Table 2
Group means and SD for self-reported cognitive empathy variables.

	NC	*OFC*	*DLPFC*	*F*	*p* value	η^2
IRI-Comp	$.41_a$	$-.42_b$	$-.40_b$	4.18	.03	.30
IRI-PT	3.67	3.36	3.40	1.11	.35	.10
IRI-FS	3.58_a	2.57_b	2.52_b	4.72	.02	.32

In all analyses, age was included as a covariate. Groups with different subscripts differed from each other at $p < .05$ or below. The IRI-Comp score is a z-score, but the IRI-PT and IRI-FS are both absolute empathy levels.

Table 3
Group means and SD for empathic accuracy variables.

	NC	*OFC*	*DLPFC*	*F*	*p* value	η^2
Eyes Test						
Total	.77	.73	.64	2.70	.09	.21
Male	$.81_a$	.72	$.65_b$	3.93	.04	.28
Female	.73	.75	.62	1.30	.29	.12
Positive	.78	.78	.64	1.52	.24	.13
Negative	.77	.67	.67	1.69	.21	.14
Morphing Test						
Total	240.9_a	217.5	194.6_b	5.25	.02	.34
Negative	48.7_a	45.4_a	35.0_b	13.83	< .001	.58
Anger	46.4	44.9	35.5	2.94	.07	.23
Disgust	52.5_a	47.2_a	33.8_b	8.66	.002	.46
Fear	47.7	44.4	38.3	3.23	.06	.24
Sad	48.2_a	44.1_a	33.5_b	9.55	.001	.49
Happy	46.1	36.3	54.2	2.61	.10	.21
Empathic Accuracy Films						
Total	5.8	5.7	5.3	1.07	.36	.10
Positive	1.9	1.6	1.7	1.07	.36	.10
Negative	2.0	2.0	2.0	--	--	--
Self-conscious	1.8	2.0	1.6	1.63	.22	.14
Emotion tracking task						
Total	$.13_a$	$.38_a$	$-.63_b$	4.21	.03	.30
Male	.03	.39	-.44	1.87	.18	.16
Female	$.21_a$	$.34_a$	$-.75_b$	6.11	.01	.38
Young	.01	$.46_a$	$-.48_b$	2.28	.13	.19
Middle	$.19_a$	$.24_a$	$-.62_b$	4.29	.03	.30
Old	.14	.38	-.66	3.35	.06	.25
Cross correlations						
Total	.56	.72	.40	2.99	.07	.33
Male	.52	.72	.47	1.25	.31	.11
Female	$.60_a$	$.72_a$	$.32_b$	4.88	.02	.33
Deviation Score						
Total	.60	.56	.88	3.10	.07	.24
Male	.61	.55	.81	1.66	.22	.14
Female	$.58_a$	$.57_a$	$.91_b$	3.85	.04	.28

In all analyses, age was included as a covariate. Groups with different subscripts differed from each other at $p < .05$ or below. For the Eyes Test, score represents the mean correct; for morphing test, score represents a composite of total correct and sensitivity; emotion tracking task score is a composite of the cross correlation and deviation score (reverse scored). Cross correlation and deviation scores are also individually reported.

Table 4

Correlations between self-reported cognitive empathy and neuropsychological variables.

	Working memory/attention				Inhibition				Cognitive flexibility					
	Comp	NB	DC	DS	Comp	CPT	Str	Flk	Comp	Let	Cat	ED	SD	SS
IRI-Comp	.10	.22	.04	.40	.22	.38	-.08	.24	.14	.17	.31	-.40	.13	.10
IRI-PT	.28	-.24	-.15	.47†	.31	.42	-.10	.47†	.04	.21	-.09	-.29	.02	.21
IRI-FS	-.12	.56†	.22	.13	.01	-.14	-.02	-.11	.16	.04	.54†	-.30	.17	-.06

Partial correlations, holding age constant. Abbreviations for neuropsychological variables are as follows: Comp = composite for that domain; NB = N-back; DC = Dot Counting; DS = Digit Symbol; CPT = Continuous performance task; Str = Stroop task; Flk = Flanker task; Let = Letter Fluency; Cat = Category Fluency; ED = Design fluency, empty dots; SD = Design fluency, switch Dots; SS = Set Shift. Abbreviations for cognitive empathy variables are as follows: IRI-Comp = composite of perspective-taking and fantasy scales of the Interpersonal Reactivity Index (IRI); IRI-PT = perspective-taking scale of the IRI; IRI-FS = fantasy scale of the IRI. † = $p > .05$ and $< .10$; * = $p < .05$, ** = $p < .001$.

Table 5

Correlations between empathic accuracy performance on static tasks and neuropsychological variables.

	Working memory/attention				Inhibition				Cognitive flexibility					
	Comp	NB	DC	DS	Comp	CPT	Str	Flk	Comp	Let	Cat	ED	SD	SS
Eyes Test														
Total	.49†	-.09	.58*	.57*	.57†	.49†	.56†	.29	.76**	.35	.70*	.67*	.60*	.13
Male	.37	-.07	.36	.52†	.42	.31	.46†	.19	.71*	.31	.64*	.58*	.57†	.18
Female	.50†	-.09	.67*	.52†	.61*	.55†	.54†	.32	.68*	.32	.63*	.64*	.52†	.08
Negative	.59*	.09	.74*	.65*	.68*	.68*	.44	.50†	.74*	.24	.86**	.48†	.71*	.06
Positive	.24	.07	.33	.27	.30	.26	.37	.05	.41	.24	.15	.77*	.27	-.03
Morphs														
Total	.61*	.08	.42	.82**	.71*	.56†	.65*	.47†	.88**	.53†	.57†	.72*	.65*	.38
Negative	.55†	.08	.40	.70*	.64*	.33	.87**	.28	.92**	.63*	.58*	.62*	.53†	.60*
Angry	.35	.27	-.01	.50†	.32	.02	.69*	-.02	.66*	.52†	.13	.63*	.37	.54†
Disgust	.73*	.52†	.52†	.50†	.70*	.47	.75*	.43	.68*	.48†	.36	.77**	.31	.33
Fear	.28	-.28	.28	.61*	.49†	.32	.52†	.31	.72*	.51†	.76**	-.01	.41	.52†
Sad	.28	-.18	.35	.47†	.40	.16	.67*	.08	.70*	.41	.44	.52†	.51†	.41
Happy	.20	.01	.09	.33	.20	.51†	-.38	.43	.01	-.16	.03	.28	.31	-.40

Partial correlations, holding age constant. Abbreviations for neuropsychological variables are as follows: Comp = composite for that domain; NB = N-back; DC = Dot Counting; DS = Digit Symbol; CPT = Continuous performance task; Str = Stroop task; Flk = Flanker task; Let = Letter Fluency; Cat = Category Fluency; ED = Design fluency, empty dots; SD = Design fluency, switch Dots; SS = Set Shift. † = p > .05 and < .10; * = p < .05; ** = p < .001.

Table 6
Correlations between empathic accuracy performance on the emotion tracking task and neuropsychological variables.

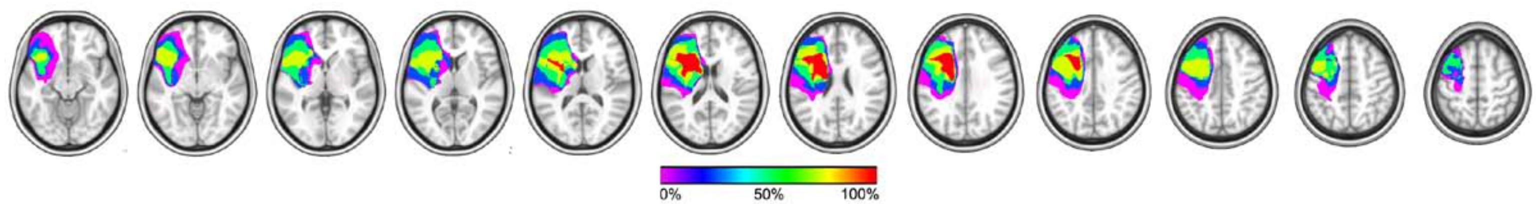
	Working memory/attention				Inhibition				Cognitive flexibility					
	Comp	NB	DC	DS	Comp	CPT	Str	Flk	Comp	Let	Cat	ED	SD	SS
Emotion tracking task														
Total	.51†	.59*	.20	.27	.33	-.04	.67*	.11	.46†	.23	.19	.24	.35	.54†
Male	.62*	.72*	.22	.33	.38	.09	.59*	.20	.46†	.19	.19	.37	.40	.42
Female	.38	.41	.17	.19	.27	-.13	.69*	.03	.43	.26	.19	.12	.27	.60*
CC Total	.69*	.60*	.34	.49†	.62*	.26	.88**	.30	.71*	.56†	.34	.56	.27	.60*
CC Male	.68*	.78**	.27	.36	.52†	.30	.63*	.29	.50†	.43	.15	.72*	.12	.30
CC Female	.51†	.27	.33	.49†	.55†	.14	.88**	.23	.72*	.55†	.43	.25	.35	.74*
Dev Total	.34	.51†	.03	.14	.10	-.22	.47†	-.03	.30	.03	.10	.03	.37	.47†
Dev Male	.38	.50†	.03	.24	.14	-.14	.40	.05	.33	.00	.17	.03	.49†	.43
Dev Female	.27	.48†	.03	.03	.07	-.28	.50†	.10	.23	.07	.02	.02	.22	.47†

Partial correlations, holding age constant. Abbreviations for neuropsychological variables are as follows: Comp = composite for that domain; NB = N-back; DC = Dot Counting; DS = Digit Symbol; CPT = Continuous performance task; Str = Stroop task; Flk = Flanker task; Let = Letter Fluency; Cat = Category Fluency; ED = Design fluency, empty dots; SD = Design fluency, switch Dots; SS = Set Shift. Abbreviations for cognitive empathy variables are as follows: CC = cross correlation measure of the emotion tracking task; Dev = deviation measures of the emotion tracking task; Total = collapsing across male and female stimuli; † = p > .05 and < .10; * = p < .05, ** = p < .001.

Figure 1

Horizontal MRI slices showing the group-averaged reconstruction of the extent of lesion overlap in each patient group. Percentage of overlap is indicated by the color code. A) DLPFC patients; B) OFC patients.

A:



B.