ABSTRACT

Title of Dissertation: ERROR OBSERVATION IN SCHIZOPHRENIA

Monica Constance Mann-Wrobel, Doctor of Philosophy, 2009

Dissertation directed by: Jack J. Blanchard, Ph.D.
Professor, Department of Psychology

Despite the pervasive and impairing nature of social difficulties in schizophrenia, the causes of these problems are not fully understood. It has been suggested that problems with cognitive functioning contribute to the social deficits of schizophrenia. However, little is known about the neural mechanisms that underlie cognitive processes directly linked to social dysfunction in schizophrenia. Recent studies of the mirror neuron system have focused on the error-related negativity (ERN), a negatively-deflected event-related brain potential that is elicited following the commission of an erroneous response. This study examined ERN activity in schizophrenia patients and psychiatrically healthy controls during performance and observation of a confederate performing a computerized flanker task. The lateralized readiness potential (LRP) allowed for a direct comparison of brain activation reflecting response readiness verses error signaling. Correlations between ERN activity during flanker observation, social cognition (i.e., theory of mind), and community social functioning were explored. Finally, correlations between verbal memory, executive functioning, and social functioning were examined and social cognition was explored as a mediator between neurocognition and social functioning. Results indicated that controls produced a robust ERN during execution of the flanker task, whereas ERN activity among patients was comparatively attenuated in amplitude.

During observation, there were no significant group differences and no identifiable observation ERN; however, there was greater negative activity following error than correct trials in this condition for all participants. LRP activity did not parallel that of the ERN, supporting the differentiation of motor activity and error-related processing during observation. The only significant correlation to emerge between ERN activity and social cognition and social functioning was between occupational status and execution ERN activity among controls only. Unexpectedly, neurocognition and social functioning were negatively correlated in the patient group. Expectedly, these variables were positively correlated among controls. Therefore, regression analyses were conducted separately by group; however, neither neurocognition nor social cognition predicted a significant proportion of the variance in social functioning. Despite limitations, this research is discussed as a starting point for integrating the study of psychophysiological activity with social behavior and functioning, particularly in a clinical population with pronounced social deficits.

ERROR OBSERVATION IN SCHIZOPHRENIA

by

Monica Constance Mann-Wrobel

Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, College Park in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
2009

Advisory Committee

Dr. Jack Blanchard, Chair
Dr. Sarah Morris
Dr. Carl Lejuez
Dr. Barry Smith
Dr. Michael Dougherty
Dr. Norman Epstein, Dean's Representative

ACKNOWLEDGEMENTS

First, I would like to thank my graduate advisor Dr. Jack Blanchard for his academic guidance throughout my six years of graduate school. He set high standards for his students on the SRTP Institutional NRSA grant and pushed me to write a grant, which led to the development of this project and the receipt an Individual NRSA award from NIMH to fund this research. I would also like to extend my gratitude to Dr. Sarah Morris for her role in the development of this study and in my training. She was instrumental in assisting me with idea development, working through study logistics, teaching me the intricacies of ERP research, and fostering my independence and confidence with her time, patience, and respect. I would also like to thank my dissertation committee who pushed me to refine my conceptualization of this study, and in doing so, taught me the importance of attention to detail, rigorous methodological design, and good statistics. Further, there are some individuals in my personal life to which I owe infinite gratitude and whose contributions to this my life, and thus this work, must be acknowledged. My parents instilled in me the values of hard work and education, not only through their words but also through their actions. Their love, support, patience, high expectations, and fundamental belief in me provided a strong foundation to which I frequently returned during difficult times. Finally, my husband, Mike. It is impossible to adequately capture here how grateful I am to my husband for all that he is and all that he gives to me. He is my rock and stability in an unpredictable, unforgiving world, and my best friend. He reminds me of what is truly important in life, helps me to find my courage when it seems lost, and challenges me intellectually. This work is dedicated to him, since he so fundamentally, gently and invaluably saw it, and me, through.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: INTRODUCTION

Social and Cognitive Functioning in Schizophrenia

Social Impairment in Schizophrenia

Social impairment among individuals with schizophrenia is a well-documented feature of the disorder (for reviews see Mueser & Bellack, 1998; Mueser & Tarrier, 1998). The term "social functioning" is typically used as a broad, multi-dimensional construct and has been operationalized in a variety of ways. Terms such as "community functioning," "social competence," and "social functioning" are often used interchangeably; however, all terms imply overall performance across everyday domains (e.g., independent living, employment, or interpersonal relationships; Green, 1996).

Some examples of social deficits observed in schizophrenia patients include difficulty initiating or sustaining conversations and an inability to achieve goals or have needs met in situations requiring social interactions (Morrison & Bellack, 1987). Schizophrenia patients have poorer social adjustment (e.g., Mueser, Bellack, Morrison, & Wixted, 1990), less effective social skills (e.g., Liberman, 1982; Mueser, Bellack, Douglas, & Morrison, 1991), poorer social functioning in the community (e.g., Halford & Hayes, 1995), and reduced overall social competence (Bellack, Morrison, Wixted, & Mueser, 1990) compared to psychiatrically healthy groups. Impairments in social functioning can lead to broader disturbances in functioning, including difficulty finding and maintaining employment, poor parenting, and impoverished social affiliation in everyday life that can contribute to poor quality of life for many persons with the disorder (Scott & Lehman, 1998).

Social functioning impairment is a critical feature of schizophrenia, as indicated by several lines of evidence. First, impaired social functioning has long been recognized as a characteristic feature of schizophrenia by such early theorists as Kraepelin (1919/1971) and Bleuler (1911/1950). Second, modern diagnostic systems have emphasized the importance of social impairment in the diagnosis of the illness. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychological Association, 1994) includes impairment in social functioning as a criterion for the diagnosis of schizophrenia, highlighting the fundamental nature of this deficit (Penn, Corrigan, Bentall, Racenstein, & Newman, 1997; Pinkham, Penn, Perkins, & Lieberman, 2003). Third, social dysfunction is a potent predictor of long-term outcome. Social impairment has been discovered in children and adolescents who later go on to develop schizophrenia (Dworkin, et al., 1993; Hans, Marcus, Henson, Auerbach, & Mirsky, 1992; Walker, 1994). Such deficits contribute to poor premorbid social competence and social adjustment, which are strong predictors of both social and nonsocial outcomes in schizophrenia patients (Mueser, et al., 1990; Tien & Eaton, 1992; Johnstone, MacMillan, Frith, Benn, & Crow, 1990). Social functioning and competence are prognostic indictors of treatment outcome and have been shown to be inversely related to relapse (Johnstone, et al., 1990, Perlick, Statny, Mattis, & Teresi, 1992; Mueser & Tarrier, 1998). For example, poor social adjustment at the onset of the disorder has emerged as a strong predictor of more adverse long-term outcomes (Häfner, Löffler, Maurer, Hambrecht, & an der Heiden, 1999). Fourth, research indicates that although neuroleptic medication is effective for reducing symptom severity and forestalling relapses, even under optimal conditions these medications have limited effects on social

adjustment. As a result, improving the social functioning of patients with schizophrenia has become a major priority of psychosocial treatment programs, such as social skills training, family intervention, and vocational rehabilitation (Mueser & Tarrier, 1998).

Problems in social functioning are heightened during acute phases of the illness but typically persist after acute symptoms subside (Bellack, Morrison, Mueser, Wade, & Sayers, 1990), suggesting that these deficits represent a persistent and chronic source of disability for those with schizophrenia. Social functioning may also be affected by the symptoms of schizophrenia (Morrison & Bellack, 1987). Although positive symptoms (e.g., hallucinations and delusions) may adversely affect social functioning, social deficits are more commonly associated with negative symptoms (i.e. lack of sense of pleasure, loss of motivation, decreased physical activity, flat affect; Bellack et al., 1990; Dworkin et al., 1990). Less frequent social contact has been found to be associated with greater negative affect, social anhedonia, and social anxiety in schizophrenia (Blanchard, Mueser, & Bellack, 1998; Pallanti, Quercioli, & Hollander, 2004).

Thus, poor social functioning is a debilitating, yet characteristic, feature of schizophrenia that can lead to lowered quality of life in a variety of domains. Social functioning impairment in schizophrenia is pervasive and difficult to quantify. A thorough understanding of the factors that contribute to ineffective social functioning may contribute to increased specificity when defining the concept, when forming research questions, and when integrating findings. Recently, there has been increased attention in the literature on the relationship between cognitive and social functioning. This research suggests that neurocognitive functioning significantly impacts social and occupational functioning cross-sectionally and longitudinally (e.g., Koren, Seidman,

Goldsmith, & Harvey, 2006). Recognition of social cues, interpretation of social stimuli, and successful execution of social behaviors and skills (Kerns, Berenbaum, Barch, Banich, & Stolar 1999; Green, 1996; Green, Kern, Braff, & Mintz, 2000; Pinkham, et al., 2003) requires the seamless integration of multiple cognitive processes.

Cognitive Impairment in Schizophrenia

Until recently, the predominant view of neuropsychological functioning in schizophrenia was that observed cognitive impairment was merely secondary to the florid clinical symptoms of the disorder (Reichenberg & Harvey, 2007). However, it has become increasingly apparent that schizophrenia is variably accompanied by neuropsychological impairment that negatively impacts functioning (Seidman, 1983). Neuropsychological abnormalities have been observed in the majority of schizophrenia patients (Goldberg et al., 1990; Palmer et al., 1997). Currently, evidence is accumulating to suggest that impaired neuropsychological functioning is a core feature of schizophrenia rather than an artifact of psychotic symptoms, medication side effects, or part of the illness course (Elvevag & Goldberg, 2000; Kremen et al., 2000). First, neuropsychological abnormalities are apparent many years before the expression of psychotic symptoms (Aylward, Walker, & Bettes, 1984; Jones, Rodgers, Murray, & Marmot, 1994; Reichenberg et al., 2002). Second, among many patients, cognitive symptoms have been observed to be considerably developed at the time of the first psychiatric contact (Bilder et al., 2000; Saykin et al., 1994). Third, cognitive deficits are persistent and evident at similar levels of severity even when symptoms have remitted (Addington & Addington, 1993; Harvey et al., 1990; Silverstein, Osborn, & Palumbo, 1998). Fourth, similar, yet milder, abnormal neuropsychological performance has been

observed in the non-ill relatives of individuals with schizophrenia (Cannon et al., 1994, 2000; Farone et al., 1996; Keefe et al., 1994) and in those with schizophrenia-spectrum disorders (Bergman et al., 1998; Mitropoulou et al., 2002). Fifth, neurocognitive deficits do not substantially respond to treatment with atypical or typical antipsychotic medications, despite the effectiveness of these medications for psychotic symptoms (Blyler & Gold, 2000). Finally, abnormal neuropsychological functioning has been found to predict a variety of aspects of poor functional outcome including community functioning and social skill learning in schizophrenia (Green, 1996; Green et al., 2000).

There is great heterogeneity in schizophrenia not only in terms of illness course and outcome, but also in terms of cognitive functioning in schizophrenia (Kremen et al., 1994). In fact, it has been proposed that the well-documented clinical heterogeneity in schizophrenia is better characterized by variation in neuropsychological functioning than by the level of classical, psychotic symptoms (Elvevag & Goldberg, 2000). Some have argued that individuals with schizophrenia are generally impaired on a broad range of cognitive tasks, reflecting a core "generalized cognitive deficit" (Dickinson & Harvey, 2009; Dickinson, Ragland, Gold, & Gur, 2008; Dickinson, Iannone, Wilk, & Gold, 2004; Lee & Park, 2005); however, others have suggested that some cognitive impairments are more severe, such as episodic memory and executive functioning, despite the "backdrop" appearance of a generalized deficit (Reichenberg & Harvey, 2007). While the debate continues regarding generalized versus specific cognitive deficits in schizophrenia, the present study incorporated two specific cognitive factors that are consistently found to be impaired in schizophrenia and related to functional outcome: verbal memory and

executive functioning. These were examined in order better characterize the aforementioned relationship between cognitive and social functioning.

Verbal memory

Factor analytic studies on separable domains of cognitive functioning within schizophrenia have supported verbal memory as a distinct domain of cognitive functioning in this population (Nuechterlein et al., 2004). Four meta-analytic investigations have consistently reported severe impairments in immediate and delayed verbal memory in schizophrenia (Reichenberg & Harvey, 2007). Verbal memory has been suggested to be an endophenotypic marker of schizophrenia, as it is a highly heritable trait among families with a relative with schizophrenia and deficits in verbal memory are apparent in ill and non-ill relatives (Golimbet et al., 2006). In particular, long-term verbal memory demonstrated the highest heritability compared to short-term memory and verbal fluency, is likely to be independent of the influence of symptoms in patients, and is correlated with schizotypal traits (Golimbet et al., 2006). Further support for the edophenotypic properties of verbal memory comes from a meta-analysis which reported that the largest differences between controls and relatives of individuals with schizophrenia on nine neuropsychological measures was in verbal memory recall and executive functioning (Sitskoorn, Aleman, Ebisch, Appels, & Kahn, 2004). Another study examined cognitive functioning with a battery of tasks among schizophrenia patients, first degree relatives, and controls that were assessed at baseline and at a 13 month follow-up. The most severe deficit among patients and relatives was in secondary verbal memory. This deficit appeared to be relatively independent of age of onset, illness duration, and neuroleptic dosage. Dysfunction fluctuated with negative symptoms, but

persisted in remitted patients, thus providing additional support for the sensitivity and specificity required for a construct to be conjectured as an endophenotype (Wittorf, Klingberg, & Wiedemann, 2004). Deficits in verbal memory, particularly in delayed recall, are evident early in the disorder in first episode patients (Holthausen et al., 2003), in adolescents with schizophrenia-spectrum disorders (Landrø & Ueland, 2008), and deficits appear to be stable throughout the course of the illness (Rodriguez-Sanchez et al., 2008).

Declarative memory (including delayed verbal memory) relies on adequate encoding, storage or retention, and retrieval (Reichenberg & Harvey, 2007). These processes have been empirically disentangled in a number of studies and it appears that deficits in schizophrenia result from problems in the initial acquisition of material and are not the result of impaired storage or retrieval (Cirillo & Seidman, 2003). This is evident by the observation that the average impairment for recognition memory in schizophrenia patients compared to controls is substantially smaller than that of immediate or delayed free recall (Aleman et al., 1999). Additionally, rates of "forgetting" have been observed to be higher in schizophrenia, but after encoding is controlled for in the analyses, rates of forgetting are comparable between patients and controls (Gold et al., 2000). Also, processing speed has been reported to be a strong predictor of verbal memory in schizophrenia (Brebion, David, Bressan, & Pilowsky, 2006). Similarly, slowed consolidation has been suggested to play an important role in working memory deficits that are commonly observed in schizophrenia (Fuller, Luck, McMahon, & Gold, 2005).

Executive functioning

The term "executive functions" has historical roots in attempts to delineate "higher order" cognitive functions of the prefrontal cortex and has been used synonymously with the term "frontal lobe functions" (Reichenberg & Harvey, 2007). However, this is somewhat paradoxical in that studies of executive processes have at times failed to demonstrate selective impairments, or even a consistent result, in patients with frontal lobe injuries (Andres, 2003; Reitan & Wolfson, 1994). It is likely that some executive processes may be sustained by a distributed network involving multiple brain regions, rather than being solely restricted to prefrontal cortex functioning (Allain, Etcharry-Bouyx, & Le Gall, 2001; Carpenter, Just, & Reichle, 2000).

Executive functions refer to a set of processes permitting the adaptive balance of maintenance and shifting of cognitive and behavioral responses to environmental demands, permitting the control of action and long-term goal-directed behavior (Palmer & Heaton, 2000; Shallice & Burgess, 1998). These functions require consideration of current and future circumstances, generation and evaluation of response alternatives, choice and implementation of a specific course of action, and monitoring/re-evaluation in response to feedback (Reichenberg & Harvey, 2007). Abilities that have been proposed to underlie such activities are searching long-term knowledge stores, abstraction and planning, decision-making skills, initiation, self-monitoring, mental flexibility, and the inhibition of immediate responses in the pursuit of longer term goals (Palmer & Heaton, 2000).

A great deal of research has focused on executive functioning impairment in schizophrenia. This is likely due to similarities in the clinical presentation of

schizophrenia and patients with frontal lobe lesions, such as reduced spontaneity, avolition, mental rigidity, and poor social judgment (Benson & Miller, 1997; David, 1992). Additionally, the "neurodevelopmental hypothesis" of schizophrenia postulates that the disorder arises from early, fetal brain abnormalities of genetic or environmental origin that remain largely "static" until they interact with normal brain maturational processes that occur in the frontal lobes, thus linking etiology with executive functioning capacity (Murray & Lewis, 1987; Weinberger, 1987).

The Wisconsin Card Sorting Test (WCST; Milner, 1963; Nelson, 1976) is the single most widely used measure of executive functioning in the schizophrenia literature (Reichenberg & Harvey, 2007). In this task, subjects must discover, follow and switch rules for sorting cards into categories. This measure is generally interpreted as assessing abstraction/problem-solving skills and the ability to shift strategies efficiently (Lezak, Howieson, & Loring, 2004). Evidence from ten meta-analytic studies indicates that schizophrenia patient's executive functioning, as indexed by the WCST is severely impaired compared to controls (see Reichenberg & Harvey, 2007). Six meta-analytic studies of WCST performance among non-ill relatives of individuals with schizophrenia have found mild impairments among relatives on abstraction/problem-solving skills and ability to shift sets efficiently. The ability to alternate between sets appears to be the most impaired executive function in schizophrenia relatives compared with controls (see Reichenberg & Harvey, 2007). Epidemiological studies conducted on children and adolescents before they went on to develop schizophrenia and subsequent disease sequelae that can affect cognitive functioning (i.e., medication, symptoms), indicated that these individuals and their siblings were impaired on measures of concept formation,

processing speed, and executive functions such as switching, fluency, and complex motor coordination, all required processes for adequate WCST performance (Niendam et al., 2003; Cannon et al., 2006). In addition, individuals with schizophrenia-spectrum disorders have been shown to demonstrate deficits in measures of executive functioning, including performance on the WCST, fluency tasks, and dual-task processing (Diforio, Walker, & Kestler, 2000; Harvey, Reichenberg, Romero, Granholm, & Siever, 2006).

The scores most frequently analyzed from this test are perseverative errors (i.e., repeated attempts to select the same response set despite feedback that this choice is incorrect) and number of categories completed. The WCST has particular relevance for the current study in that it has been suggested that perseverative errors on this task could reflect a deficit in error-monitoring, or the on-line ability to use trial-by-trial feedback to guide behavior (Prentice, Gold, & Buchanan, 2008). Prentice and colleagues (2008) conceptualized the earliest trials of the WCST within the framework of temporal difference error (TDE) reinforcement learning models (Montague, Hyman, & Cohen,, 2004; Shultz, 2002), in which changes in dopaminergic activity reflect outcomes that are better or worse than expected, which in turn modulates behavior in accordance with feedback to maximize outcomes (Shultz, 2002; Holroyd & Coles, 2002). This is a theory that is particularly relevant to the psychophysiological indicator of error processing, error-related negativity (ERN), utilized in the current study. Prentice and colleagues (2008) found that, as early as Card 2, schizophrenia patients were significantly less able than controls to use negative feedback to rapidly direct behavior towards a rewarded response (controls were 66% likely to sort correctly vs. 40% of patients). These findings indicate that patient's difficulty with the WCST may partly stem from a failure to use

negative feedback appropriately, rather than a failure to abandon previously rewarded behavior, since these errors occurred prior to any positive feedback regarding performance (Prentice et al., 2008). In this way, the WCST may prove to have particular relevance for how individuals with schizophrenia monitor and respond to error signals in the environment.

Executive functioning has been observed to impact other cognitive processes such as attention and memory (Howieson & Lezak, 1995). In light of these observations, as well as the consistently observed impairment in executive functioning in schizophrenia, some have argued that executive functioning underlies all other cognitive impairment in the disorder (Shallice, Burgess, & Frith, 1991; Nuechterlein & Dawson, 1984). Alternatively, the considerable experimental evidence for multiple independent executive processes could help explain heterogeneity in cognitive performance (Miyake et al., 2000). However, this would not take into account the finding that many patients have more severe memory than executive functioning impairment (Hill, Ragland, Gur, & Gur, 2001; Kremen, Seidman, Farone, Toomey, & Tsuang, 2004). Models in schizophrenia currently do not specify which executive functions are fundamentally impaired and which contribute to memory or other cognitive processes (Reichenberg & Harvey, 2007). It will be important for future studies to address this limitation. The present study will seek to further examine verbal memory and executive functioning as specific cognitive factors relevant for social functioning in schizophrenia.

Relationship between Neurocognitive and Social Functioning in Schizophrenia

Neurocognitive functioning is one of the many factors that influences overall social effectiveness (Cohen, Forbes, Mann, & Blanchard, 2006). Complex cognitive

processes are required for the interpretation of stimuli during social interactions and for the execution of appropriate social behavior. It has been suggested that social functioning involves the use of "more basic," "rate limiting" cognitive processes such as attention, verbal memory, and executive functioning (Green, 1996; Green et al., 2000). There is considerable evidence to suggest that cognitive deficits are related to poor social functioning in schizophrenia patients (Green 1996; Green et al., 2000); however, the specific cognitive factors that underlie social impairment have yet to be precisely delimited and understood (Cohen et al., 2006).

There have been several investigations examining the relevance of neuropsychological functioning for social functioning. These studies indicate that verbal memory is related to social functioning impairment in schizophrenia. Addington and Addington (1999) reported that verbal memory, verbal ability, conceptual flexibility, and vigilance were associated with performance on a social problem solving task. At a 2 ½ year follow-up assessment, verbal memory and verbal ability remained associated with social problem-solving (Addington & Addington, 2000). Neurocognitive deficits were discussed by these authors as potentially responsible for poor recognition of and understanding of the subtleties of interpersonal interactions (Addington & Addington, 1998; Corrigan, Wallace, & Green, 1992).

Green (1996) conducted a meta-analytic review of the available literature examining the relationship between neurocognition and social functioning in schizophrenia. This meta-analysis was conducted in order to describe specific relationships between various neurocognitive processes (e.g., attention, working memory) and aspects of social functioning (e.g., community functioning, role-play performance) in

schizophrenia. Vigilance was related to social problem solving and skill acquisition, and card sorting (an executive functioning measure) predicted community functioning but not social problem solving (i.e., laboratory measure of subject's ability to recognize specific features of a social interaction, identify a social problem, generate solutions, and role-play the interaction to demonstrate to solution to the problem). Green concluded that verbal memory and vigilance were necessary for adequate functional outcome. This study reported that even with variability in methods between studies, limited statistical power, and variability in measures, secondary verbal memory (SVM) was described as a robust predictor of outcome; all of the seven studies including this measure showed an association with outcome, regardless of the functional outcome measure (i.e., community functional, social problem-solving, social skill acquisition). In addition, card sorting was found to be related to community outcome, in particular (Green, 1996), a finding which was replicated in 2000 with the inclusion of more studies.

In a later review which sought to update and verify the results of the 1996 paper, Green and colleagues (2000) reported that SVM was correlated with community social functioning, social problem solving, and psychosocial skill acquisition and executive functioning and was related to community social functioning in schizophrenia. Thus, both meta-analyses found that, among a variety of neuropsychological domains, delayed, or secondary, verbal memory and executive functioning were related to community social functioning in schizophrenia patients (Green, 1996; Green et al., 2000). In the 2000 meta-analysis, 37 studies were included that contained well-defined neurocognitive and functional outcome measures utilized in a schizophrenia sample. Of those, 22 studies reported using a measure of card-sorting (most often the WCST) and 18 reported using a

measure of SVM. Thus, these measures are widely-utilized and commonly accepted indicators of neurocognitive functioning that have received extensive attention in the schizophrenia literature. Although Green and colleague's review (2000) was limited in scope due to a reliance on replication studies and the exclusion of null or "paradoxical" findings, the results suggest that meaningful relationships can be observed between specific aspects of cognitive functioning and broad-based measures of social behavior, if these measures are clearly and consistently defined (Cohen et al., 2006).

Although certain aspects of neurocognition appear to be associated with social functioning in schizophrenia, these relationships have generally been found to be modest in size (Penn et al., 1997; Penn, Corrigan, & Racenstein, 1998). Other reports have not found significant relationships between neurocognitive factors and social functioning or, when relationships were observed, they were indirect through specific skills, such as social problem solving (Addington, McCleary, & Munroe-Blum, 1998; Corrigan & Toomey, 1995; Penn et al., 1995). There are several factors that may contribute to these inconsistencies. One such factor is that the broad nature of the term "social functioning" has led to considerable methodological variability among studies that have sought to examine its relationship with cognitive functioning (Cohen et al., 2006; Neinow, Docherty, Cohen, & Dinzeo, 2006). Additionally, there may be a third variable that influences the relationship between neurocognition and social functioning – a type of cognition that is functionally distinct from traditionally-conceptualized aspects of neurocognition (e.g., working memory, attention, abstract reasoning, etc.).

Investigators have begun to examine such unique aspects of cognition that may underlie social impairments in schizophrenia (Yager & Ehmann, 2006). These types of

cognitive processes have been identified as components of "social cognition." Some researchers have proposed that social cognition mediates the relationship between neurocognition and social functioning (Brekke, Day, Lee, & Green, 2005), while others propose that social cognition contributes uniquely to the variance in social functioning (Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Blair & Cipolotti, 2000). The study of social cognition in schizophrenia has the potential to contribute not only to our understanding of the neuropsychological origin of problems in social functioning in schizophrenia, but also to enhance the delivery of psychosocial interventions that target social skills and behaviors.

Social Cognition

The term "social cognition" refers to aspects of cognition that are not typically assessed by neurocognitive tasks but that potentially have an independent link to social behavior and social function (Pinkham et al., 2003). Social cognition is thought to represent a "specialized domain of cognition developed to solve social and adaptive problems" (Penn et al., 1997; p.116). Mental operations that comprise social cognition include the ability to perceive the intentions and emotional states of others and the processes that subserve behavior occurring in response to others, in particular those higher-order cognitive processes underlying the extremely diverse and flexible social behaviors that are observable within members of a species (Adolphs, 1999).

Social cognition differs from nonsocial cognition in a few specific ways. First, the classes of stimuli processed by social cognition are different from those processed by non-social forms of cognition. Stimuli used in studies of nonsocial cognition have been characterized by "numbers, words, or objects," (Corrigan & Toomey, 1995, p. 396)

which tend toward being affectively neutral and static. Social stimuli are typically personally relevant and changeable over time (Fiske & Taylor, 1991; Forgas, 1995). In addition, there are unobservable attributes of social stimuli that are vitally important (e.g., observation of interpersonal behavior provides information regarding the others' personality characteristics) for appropriate social processing, attributes that are less important for the processing of nonsocial-cognitive stimuli (Fiske & Taylor, 1991). Second, the relationship of the perceiver to nonsocial-cognitive stimuli tends to be unidirectional – the perceiver acts on the stimulus, not vice versa, whereas the relationship between the perceiver and social-cognitive stimuli tends to be interactive (Penn et al., 1997). This process has been described as "mutual cognition" (Fiske & Taylor, 1991). Furthermore, social-cognitive stimuli can change as a function of being observed, which can influence the stimulus' effect on the observer. In essence, the interpretation of social-cognitive stimuli is a subjective process that results from a combination of various neurocognitive functions and attributions regarding the particular social stimulus within its environmental context that is based upon stable personality factors, the observer's transient emotional state, or similar past experience. Third, performance is evaluated differently in studies of social and nonsocial cognition. Work on nonsocial cognition largely involves comparisons of performance on a task between a patient group and a control group whereas research in social cognition includes the examination of biases within groups in addition to deficits. Biases refer to a characteristic response style that does not necessarily indicate poor task performance (e.g., negative information processing bias commonly observed in depression; Penn et al., 1997).

Social cognition is firmly linked to social behavior and has been proposed to include at least three processing domains: theory of mind, social perception, and attributional style (Pinkham et al., 2003). Theory of mind (ToM) refers to the ability to represent the mental states of others and/or to make inferences about another's intentions. Social perception can be broken down into two general areas: facial affect recognition and social cue perception. In either case, social perception refers to the processing of some stimulus that is specifically social in nature. Attributional style refers to how one explains positive and negative social outcomes. In schizophrenia this has focused on investigating the role of attributions in hallucinations and delusions (Pinkham et al., 2003). Additional components of social cognition have been proposed by Burns (2004) to include eye gaze detection and interpretation, emotional processing, self-reference, working memory, social decision-making, conflict monitoring, and affiliative behavior. Burns (2004) also proposed that social cognition occurs in three stages: social perception (processing of sensory information), central social cognition (process of applying meaning to sensory input), and social behavior (behaviors that are initiated specifically in response to the sensory input and subsequent processing). The concept of social cognition is useful for conceptualizing the social impairment so commonly observed in schizophrenia. Further examination of social cognition in schizophrenia may lead to improved understanding of previously observed inconsistencies in the literature regarding the relationship between neurocognition and social functioning.

Social cognition deficits in schizophrenia

An accumulation of research on social cognition in schizophrenia has documented that individuals with schizophrenia show impairment in all three sub-areas of social

cognition (for reviews see Corcoran, 2001; Penn et al., 1997; Bentall, 1990). Since Frith's 1992 proposal that positive features of schizophrenia (i.e., delusions of reference and persecution) arise from problems in ToM and that negative features of the illness (i.e., blunted affect and asocial behavior) reflect these ToM deficits, problems in ToM among schizophrenia patients have been well documented in the literature (for review see Harrington, Siegert, & McClure, 2005; Corcoran, 2001). These findings indicate that patients are less able to accurately infer the feelings and intentions of another person based on clues in the environment than both nonpsychiatric controls (Langdon, Coltheart, & Ward, 2006; Corcoran & Frith, 2003; Corcoran, 2003; Randall, Corcoran, Day, & Bentall, 2003; Langdon et al., 1997; Harrington et al., 2005) and psychiatric controls (Corcoran & Frith, 1996; Corcoran, Cayhill, & Frith, 1997; Pickup & Frith, 2001; Safarti, Hardy-Bayle, Nadel, Chevalier, & Widlocher, 1997). Results conflict regarding whether individuals with schizophrenia are more impaired than individuals with autism or Asperger's disorder (Murphy, 2006; Pilowsky, Yirmiya, Arbell, & Mozes, 2000). Theory of mind deficits also have a unique relationship to functional outcome (Penn et al., 1997), are related to both positive and negative symptom features (Pinkham et al., 2003; Corcoran, Mercer, & Frith, 1995; Frith & Corcoran, 1996), become exacerbated during acute episodes of psychosis (Drury, Robinson, & Birchwood 1998), and are also found to be present during symptom remission (Inoue et al., 2006).

There is considerable evidence for abnormal facial affect recognition in schizophrenia compared to nonclinical control groups (Addington & Addington, 1998; Shaw, et al., 1999; Streit, Wölwer, & Gaebel, 1997; Kerr & Neale, 1993; for review see Edwards, Jackson, & Pattison, 2002). These deficits are greater in schizophrenia

compared to other non-psychotic, psychiatric disorders, such as major depressive disorder; however, findings are inconsistent when schizophrenia is compared to disorders that include psychotic features, such as bipolar disorder (Pinkham et al., 2003). In schizophrenia, greater impairment is evident for the perception of negative emotional facial displays compared to positive facial displays, with perhaps the greatest impairment for the perception of fear (Edwards, Pattison, Jackson, & Wales, 2001; Evangeli & Broks, 2000). Furthermore, longitudinal studies document a stable deficit in emotion perception (Addington & Addington, 1998; Gaebel & Wolwer, 1992), although there is some evidence that individuals whose symptoms are in remission may perform better on tasks that measure affect perception than individuals who are in an acute phase of the disorder (Cutting, 1981; Gessler, Cutting, Frith, & Weinman, 1989). In terms of symptoms, there is some evidence that individuals with paranoid schizophrenia are better at facial affect perception than individuals with nonparanoid subtypes of the disorder (Davis & Gibson, 2000; Kline, Smith, & Ellis, 1992; Lewis & Garver, 1995). Finally, there are mixed results regarding whether deficits in facial affect perception are part of a generalized performance deficit or whether they are specific for decoding only facial emotions (Kerr & Neale, 1993; Bellack, Blanchard, & Mueser, 1996; Heimberg, Gur, Erwin, Shatasel, & Gur, 1992; Pinkham et al., 2003), a topic that is still being debated within the social cognition literature. A notable study by Hooker and Park (2002) examined whether facial affect recognition was part of a generalized deficit in face recognition or a specific problem of affect recognition by determining whether facial recognition, facial affect recognition, or vocal affect recognition was more strongly related to outcome as measured by social functioning. Of these variables, only affect recognition (both visual

and auditory) was related to social functioning, indicating that although schizophrenia patients have general face processing deficits, affect recognition deficits in particular are related to problems in social behavior (Hooker & Park, 2002).

Unlike stimuli for facial affect recognition, social perception tasks use more dynamic stimuli that require multiple sensory modalities (e.g., video tapes of social scenarios). Individuals with schizophrenia show consistent impairment on these tasks compared to controls (Archer, Hay, & Young, 1994; Bell, Bryson, & Lysaker, 1997; Corrigan & Addis, 1995; Corrigan, Davies-Farmer, & Stolley, 1990) and impairment appears to be worse in situations involving abstract compared to concrete social cues (Leonard & Corrigan, 2001). Specifically, when individuals with schizophrenia were presented with videotapes of persons interacting socially, they demonstrated greater difficulty discerning the goals and intentions of target people than discerning what the person was wearing or saying. This finding is consistent with what would be expected based on the observed deficits in ToM or problems taking another person's perspective (Pinkham et al., 2003).

Attributional style has also been considered to be a component of social cognition. Research in this area has mostly focused on how positive symptoms impact social cognition and social behavior. Evidence suggests that individuals experiencing hallucinations are biased towards making external attributions for their perceptions and attributing internal perceptual events to an external source (Pinkham, et al., 2003). Individuals with persecutory delusions have been shown to demonstrate a reasoning bias, such that they tend to gather less evidence regarding an ambiguous event and more easily jump to conclusions than controls, which may facilitate an early acceptance of an

incorrect hypothesis. There is a strong tendency for delusional individuals to externalize blame for negative events (Garety & Freeman, 1999; Pinkham et al., 2003). Thus far, only one study has examined the relationship between attributional style and negative symptoms in schizophrenia and this study did not find a significant relationship between these two variables; however, the authors reported a significant correlation between depression in schizophrenia and negative attributional style (Addington, Addington, & Robinson, 1999).

Self-regulation has been proposed as a subcategory of social behavior by an NIMH workgroup on social neuroscience research (Cacioppo et al., 2007). Important components of self-regulation identified by this group include decision making (e.g., Bush, Luu, & Posner, 2002), performance monitoring (e.g., MacDonald, Cohen, Stenger, & Carter, 2000), action monitoring (Gehring & Knight, 2000), detection or processing of response conflict (Gehring & Fencsik, 2001), error detection and processing (Carter et al., 1998); and error outcome and predictability (Paulus, Hozack, Frank, Brown, & Schuckit, 2003). Although error monitoring has not traditionally been discussed as a component of social cognition, the present study seeks to investigate this process as one type of cognitive activity that occurs during social interactions. This component of cognitive processing may be relevant for identifying problems that patients experience when they interact with others, an idea that will be discussed below. In one intriguing study supporting this notion, persons with schizophrenia who had good self-monitoring skills (i.e., awareness of the impact of their behavior on other people) had better social skills than persons with schizophrenia with poor self-monitoring skills (Penn et al., 1999). This difference could not be accounted for by group differences in verbal IQ or education.

Thus, a relationship between self-monitoring and social skills has been proposed and will be explored further in the current study using a psychophysiological measure of brain activity that is associated with self-monitoring.

Based on the research described above, it is apparent that schizophrenia patients show deficits in multiple aspects of social cognition, including ToM, facial affect recognition, social cue perception, and attributional style. Other factors that impact performance on social cognition tasks include the nature of the social stimulus, symptom type, and disease course (Pinkham et al., 2003); therefore, increased attention should be given to these factors in social cognition studies. In addition, there is little research available that has focused specifically on brain abnormalities associated with social cognition problems in schizophrenia. Investigations in this area have the potential to significantly increase understanding of social cognition abnormalities within psychopathology.

Relationship between social cognition, neurocognition, and social functioning

This review suggests that social cognition represents a different level of analysis for understanding socially-relevant cognitive processes than that afforded by the exclusive study of nonsocial cognition. Studies of clinical groups (including those with cortical damage, prosopagnosia, and autism/Asperger's syndrome) support the relative independence of social cognition from other aspects of cognition (Anderson et al., 1999; Blair & Cipolotti, 2000; Fine, Lumsden, & Blair, 2001). However, other more recent studies support the view that social cognition mediates the relationship between neurocognition and functional outcome in schizophrenia, suggesting that social cognition reflects elements of both domains (Brekke et al., 2005; Pinkham et al., 2003). Thus,

findings are inconsistent regarding the unique nature of social cognition. Based on the definitional properties of social cognition, some degree of overlap between social and nonsocial cognition is likely, while social cognition simultaneously offers additional, unique information regarding social processing not previously encompassed by nonsocial forms of cognition.

Brekke and colleagues (2005) tested a multi-level, biosocial, causal model of the impact of neurocognition, social cognition, social competence, and social support on functional outcome in schizophrenia. They found support for their model which demonstrated that the significant effect of neurocognition on outcome was entirely indirect through other variables in the model. Social cognition was strongly associated with neurocognition, which supports the view that these cognitive processes are not entirely discrete; neurocognition likely underlies some aspects of social cognition. Social cognition had additional direct effects on outcome, mediated the impact of neurocognition on outcome, and had effects on outcome that were partially mediated by social competence and social support.

The significance of social cognition to outcome is further highlighted by another finding that poor social cognition was related to social impairment (e.g., functional outcome) in schizophrenia even after controlling for performance on neurocognitive tasks (Penn, Combs, & Mohamed, 2001). Also, a recent investigation revealed that affect recognition (a social cognition variable) moderated the relationship between span of apprehension (one of two significant predictors of social competence) and social competence (Neinow et al., 2006). In other words, individuals with different levels of affect recognition ability were found to differ in the extent to which they were able to

benefit from span of apprehension ability. A stronger relationship was found between span of apprehension performance and social competence for patients with an above-average ability to recognize affect than for those with average or below-average ability (Neinow et al., 2006). These studies are consistent with other studies of schizophrenia demonstrating that social cognition is related to nonsocial cognitive functioning (Bryson, Bell, & Lysaker, 1997; Kee, Kern, & Green, 1998), social functioning across multiple domains (e.g., role-play performance; Bellack et al., 1992), social functioning in an inpatient setting (Penn, Spaulding, Reed, & Sullivan, 1996), and social functioning in the community (Hooker & Park, 2002; Poole, Tobias, & Vinogradov, 2000). In sum, although the influence of social cognition is not entirely independent from the influences of neurocognition, it does contribute independent variance to functional outcomes in schizophrenia beyond that of nonsocial cognition alone (Pinkham et al., 2003).

Social cognition appears to significantly influence the relationship between neurocognitive and social functioning among schizophrenia patients, providing a useful point of investigation for studies that seek to link brain processes with social functioning. The concept of social cognition implies that multiple brain systems work together to create complex processing of social stimuli. However, more information is needed on where these systems are located, how they're activated during social interactions, and how they may be impaired among individuals with behavioral-level social functioning difficulties. Studies that have examined brain activity occurring on-line during social cognitive tasks are extremely useful for characterizing brain activity related to social and intermediary cognitive processes. There has been a recent increase in research that bridges the scientific investigation of psychophysiological and socially-relevant behavior.

Further, it is imperative that this work be made applicable to clinical populations characterized by neurological, neuropsychological, and social functioning impairment, such as schizophrenia.

Social Neuroscience: Integration of Biological and Behavioral Approaches

There has been a recent movement towards the integration of social and neuroscience methods for improving the conceptualization of initiation, etiology, and maintenance of complex social behaviors. Cacioppo and colleagues (2000) argue that social factors affect and interact with biological outcomes through a variety of routes: chronic or repeated environmental stressors affect the brain, social factors impact affective processes and mental health, social factors affect beliefs and attitudes about oneself or one's life, coping strategies impact health outcomes, social factors affect biology via the influence of the social environment on health habits and health behaviors, and individual personality differences affect both brain functioning (e.g., release of and habituation of the brain to neurotransmitter levels related to patterns of emotional responding) and social functioning. The authors propose a multilevel integrative analysis of psychological variables as being essential for understanding complex human behavior (Cacioppo, Berntson, Sheridan, & McClintock, 2000). In addition, Insel and Fernald (2004) describe the influence of behavior on specific aspects of brain structure and function through the timing of evolutionary and developmental factors. On an evolutionary time scale, selective forces of the ecological niche of the animal are reflected in body shape, sensory and motor systems, and behavior. On a developmental time scale, behaviors act together with the environment to establish structural changes in

the brain that influence the organism throughout life. There is also evidence that social behavior causes changes in the brain of an adult animal (Insel & Fernald, 2004).

This integrative approach is applicable to the study of social cognition in schizophrenia. As described above, the empirical investigation of social cognition grew out of a movement that examined a set of cognitive factors believed to underlie complex behaviors involved in social interactions. Thus, the study of social cognition represents an attempt to understand social behavior on a more molecular and socially-relevant level than that derived from behavioral observations, self-reports of social functioning, or non-social neurocognitive processes. Further, because social cognition mediates the relationship between neurocognition and social functioning while also significantly contributing unique variance to social outcomes, social cognition might serve to represent an appropriate starting point for attempting to identify brain regions associated with functions believed to be uniquely social. Social cognition represents a concept with increased ecological validity for the study of complex aspects of social functioning, when compared to basic forms of neurocognition (e.g., attention, working memory, etc.). This construct is also more specific and quantifiable than traditional measures of social functioning in the community.

Examining social cognition involves the functioning of multiple neurocognitive and emotional brain systems. Studies that seek to investigate the neurobiological underpinnings of behavioral-level social cognition must examine brain processes on a systems level, rather than focusing on region-specific activity. The dysconnectivity hypothesis of schizophrenia (for review see Burns, 2004; Mithen, 1996) describes complex abnormalities found in the disorder in terms of disrupted connectivity between

multiple brain structures. This theoretical model has implications for the psychophysiological investigation of social cognition and the brain abnormalities that may be associated with such behavioral deficits.

Neural Mechanisms of Social Cognition Processes

The dysconnectivity hypothesis

An accumulation of research on cognitive models of schizophrenia converges to indicate that cognitive deficiencies exhibited by patients with schizophrenia can be linked to a breakdown in the functional integration of the prefrontal cortex with the temporal and parietal cortices (Fletcher et al., 1998; Frith, Kapur, Friston, Liddle, & Frackowiak, 1995). This has led to the development of the *dysconnectivity hypothesis* of schizophrenia. The dysconnectivity hypothesis refers to a disruption of interconnecting fibers that link spatially distributed regions in the brain (Burns, 2004). In other words, this idea refers to poorly organized or misplaced connections in the brain rather than a lack of connections. This is not a novel concept in the schizophrenia literature and has also been variously entertained for more than 100 years by well-known figures such as Camillo Golgi (1906) and Carl Wenicke (1906).

Mithen (1996) argues that humans became the creative and imaginative species that they are because of a gradual breakdown in the modularization of cognitive processes that are found among other primate species (e.g., a brain that is organized around a number of module-like processes, one for "social intelligence," one for "technical intelligence," etc.). Thus, the complexity of the human brain is evolutionarily beneficial. However, this elaborate system leaves the brain vulnerable to disruptions in connectivity that may manifest as problems in the complex social functions the brain

itself made possible (Bering, 2002). The importance of "cognitive fluidity" for the development of theory of mind (ToM) has been noted (Burns, 2004). Some of the observable deficits produced by disruptions in neural connectivity include characteristics commonly observed in schizophrenia patients and deficits that are particularly relevant to the current investigation: attributional errors (Frith, 1994), problems in self-monitoring (Frith, 1994), and deficits in ToM (Bering, 2002).

Many other theorists have emphasized problems in brain structural connectivity as it relates to social cognition impairment in schizophrenia (Adolphs, 2001; Adolphs, 2003; Gilbert et al., 2001; Grady & Keightly, 2002). It is generally believed that the sequence of events leading from the perception of a stimulus to the elicitation of a social behavior is complex and involves multiple interacting structures. The processes of social cognition have "fuzzy boundaries" and overlap with neuroanatomy involved in motivation, emotion, and communication processes. Models have been proposed that describe how the structures involved in all aspects of social cognition operate together to produce smooth processing and guide behavior. Specifically, according to Adolphs (2001), the neuroanatomical structures involved in social cognition include sensory and association neocortex for social perceptual processing (e.g., superior temporal sulcus and fusiform gyrus in the case of vision), a network consisting of amygdala, prefrontal cortex, cingulate cortex, and right somatosensory-related cortices for mediating between perception and various cognition processing components; and hypothalamus, brainstem nuclei, basal ganglia, and motor cortices in order to effect social behavior. At least three general possibilities exist for *how* these structures interact with other brain regions to produce complex social processing. First, structures may directly modulate cognition by

virtue of their extensive connectivity with the neo-cortex. Second, they may modulate emotional state, which in turn may indirectly modulate cognition. Third, they may directly modulate perceptual processing via feedback, which may be a major component of social functioning such as the recognition of facial expression. This process likely has particular relevance for the study of error observation (Adolphs, 2003). Additionally, it has been noted that schizophrenia patients show altered activation of several regions in the social cognition network – including the amygdala, the dorsal cingulate, the ventrolateral prefrontal cortex, and most dramatically in the dorsolateral prefrontal cortex (Grady & Keightley, 2002).

The concept of disrupted connectivity is not novel to the study of schizophrenia, but is one that seems too often neglected (Emery, 2000). Many investigators seem to feverishly search for one or two structures that are believed to underlie one or more features of social cognition. Whether or not the illness of schizophrenia evolved from the complex brain circuitry that humans enjoy today is debatable (Burns, 2004), but what seems clear is that normal, adaptive social cognition involves the integration of multiple brain systems and that abnormal, impaired social cognition likely results from a breakdown in the integration of various forms of information. It is also likely that structural abnormalities found in schizophrenia (e.g., hippocampal and prefrontal gray matter volume reductions) also contribute to this dysfunction in connectivity.

The recent discovery of the mirror neuron system could contribute to our understanding of the systems-level interactions of multiple brain regions that occur during processes such as social cognition. Mirror neuron activity reflects the normal functioning, rather than disconnectivity, of a variety of brain regions that work together

while observing and interpreting another person's actions. Research on the mirror neuron system has particular relevance for understanding neural activity that may underlie theory of mind reasoning or the recognition of other's errors.

The mirror neuron system

Mirror neurons are thought to provide the neural mechanism for primates to recognize a large variety of actions performed by other individuals. This class of neurons discharges both when an individual performs a particular action and when that same action is observed in another individual. Mirror neurons were originally discovered in area F5 of the monkey premotor cortex. This area was active when the monkey responded to the presentation of an object and when the monkey saw object-directed action (Di Pellegrino, Fadiga, Fogassi, Gallese, & Rozzolatti, 1992; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti, Fadiga, Fogassi, & Gallese, 1996). In order to be triggered by visual stimuli, mirror neurons require an interaction between a physical effector (i.e., hand or mouth) and an object. The sight of an object alone, of an agent mimicking an action, or of an individual making intransitive (non-object-directed) gestures are all ineffective for activating comparable neuronal activity (Rizzolatti & Craighero, 2004).

Mirror neurons also show a large degree of generalization. For example, the same mirror neurons that respond to a human hand grasping an object also respond when the hand is that of a monkey (e.g., Rizzolatti & Craighero, 2004). Additionally, the mirror neuron activity is the same regardless of whether the action is performed near or far from the observer. Mirror neuron activation is also produced independent of reward. Thus far, research indicates that a significant relationship exists between visual mirror neurons and

motor systems. Virtually all mirror neurons show congruence between the visual actions they respond to and the motor responses that they code (Rizzolatti & Craighero, 2004).

Convincing evidence is accruing to indicate that mirror neurons also exist in humans (Rizaolatti, Fogassi, & Gallese, 2001). Decety and colleagues (2002) used positron emission tomography (PET) to demonstrate that the motor cortex was activated both when people were asked to imagine grasping an object and when they actually did so. These regions in humans included Brodmann area 6 in the inferior part of the frontal gyrus of both cortical hemispheres, the anterior cingulate region, and the ventral parietal lobe (Decety, Chaminade, Grezes, & Meltzoff, 2002). This study was one of the first to support the existence of identifiable mirror neuron systems specialized for non-physical, imaginal, emotional, and/or cognitive processes (i.e., purely mental processes). Other studies have used electroencephalography (EEG) to demonstrate that when individuals observe an action performed by another individual, their motor cortex becomes active, even in the absence of overt motor activity (Gastaut & Bert, 1954; Cochin, Barthelemy, Lejeune, Roux, & Martineau, 1998; Cochin, Barthelemy, Roux, & Martineau, 1999). Functional brain imaging studies have shown that the observation of actions made by others activates, in humans, a complex network formed by the occipital, temporal, and parietal visual areas and two cortical regions whose function is predominantly motor – the rostral part of the inferior parietal lobule and the lower part of the precentral gyrus plus the posterior part of the inferior frontal gyrus (e.g., Buccino et al., 2001; Decety et al., 2002; Grafton, Arbib, Fadiga, & Rizzolatti, 1996). In summary, mirror neurons are active during observation and orchestration of goal-directed action patterns, and perhaps underlie the capacity to engage in ToM reasoning (Schulkin, 2000), a process that

inherently relies on the observation of others. Furthermore, the activation of mirror neurons appears to involve brain circuitry that overlaps with circuitry integral to social cognition (e.g., temporo-parietal cortical regions, somatosensory, and motor cortex)

Recent compelling theories have linked mirror neuron activity with the ability of humans to empathize with others, detect their mental states, infer their intentions, and predict their actions (Grèzes & Decety, 2001; Frith & Frith, 1999; Gallese & Goldman, 1998). Thus, it is possible that many of the impairments in interpersonal behavior and cognition observed in schizophrenia may be understood as failures of the mirror neuron system. Moreover, it has been suggested that the mirror neuron system transforms visual information into knowledge (Rizzolatti et al., 2001), an essential property of the processing of social cognition described by Burns (2004).

Because almost all behavior occurs in a social context, understanding these types of processes might provide a valuable link between neurobiological abnormalities and social functioning impairment observed in schizophrenia. The mirror neuron system appears to involve fundamental aspects of processing that are involved in social cognition, such as discerning and identifying the mental states of others, which then facilitates the selection of an appropriate complimentary or reciprocal action. Some investigators have discussed the similarities between the concept of ToM and the activities of mirror neurons. It has been suggested that attributing mental states to oneself is at the core of inferring the mental states of others by replicating or mimicking the mental life of other individuals (e.g., Davies & Stone, 1995). This ability to "read minds" or infer mental states of others may have evolved from the mirror neuron system in primates (Gallese & Goldman, 1998). In sum, because almost all behavior occurs in a

social context, understanding these types of processes (i.e., neurological correlates of social cognition) might provide a valuable link between neurophysiological abnormalities and social functioning impairment in schizophrenia.

Social Neuroscience Summary

Most studies that have examined brain regions involved in social cognition tasks have used hemodynamic techniques (i.e., functional magnetic resolution imaging or PET). Although these methods are technologically advanced and offer researchers exciting avenues for viewing the brain and its activation, imaging methods are not without limitations. Therefore, although the findings from neuroimaging studies are highly informative regarding localization of brain activity correlated with certain neuropsychological processes, it is likely that this methodology, if used in isolation, cannot fully inform the scientific understanding of psychophysiological processes that correlate with and possibly underlie social-cognitive processing.

Measuring brain activity with electrophysiological methods, specifically with EEG and measures derived from EEG, has several advantages over neuroimaging. First, it is a less invasive procedure than methods such as PET, which exposes subjects to radiation and limits testing to only a small number of conditions per individual. Second, event-related brain potentials (ERPs), derived from EEG, have temporal resolution of 1 millisecond or better. Neuroimaging benefits from high spatial resolution allowing brain structures to be observed with a precision of a millimeter. However, these procedures suffer from poor temporal resolution; hemodynamic measures are limited by the sluggish nature of the hemodynamic response to a resolution of several seconds. The ERP provides a different sort of information about the activity of the brain; it is most

informative regarding the timing and pattern of electrical activity and can be quite precise in this regard. Third, EEG methods are much less expensive than the hemodynamic techniques. Finally, EEG studies are much easier to carry out and less time-consuming than studies that utilize fMRI or PET, techniques that require several experts to be present for each use of the equipment.

There is a component of the ERP that is particularly relevant to the study of social cognition in schizophrenia – error-related negativity (ERN). The ERN is a negatively deflected waveform that is produced most prominently when an individual executes an error on a task. The amplitude of this waveform has been found to be reduced in schizophrenia patients, which may reflect a deficit in the error-monitoring among these individuals (Alain, McNeely, He, Christenson, & West, 2002; Kopp & Rist, 1999; Mathalon et al., 2002; Morris, Yee, & Nuechterlein, 2006). This waveform is useful in the study of the interpretation of others' actions, a concept reminiscent of theory of mind. It remains to be demonstrated whether reductions in the amplitude of this waveform are related to a behavioral-level deficit, such as the social functioning problems found among schizophrenia patients. Do patients produce an ERN when they observe other individuals commit errors on a task? If so, is the amplitude of the ERN in patients reduced relative to healthy controls or reduced relative to the ERN that follows the patient's own errors? These are questions the current study will attempt to answer. The next section will more thoroughly describe the ERN and relevant background literature.

Electrophysiological Measurement of Error Monitoring

Error-Related Negativity (ERN)

The ERN is a negatively-deflected component of the ERP that was first identified as occurring approximately 60-100 ms after the execution of incorrect, but not correct, motor responses (Falkenstein, Hohnsbein, & Hoormann, 1991; Gehring, Gross, Coles, Meyer, & Donchin, 1993). Initial attempts to understand the functional significance of the ERN led researchers to suggest that the occurrence of the ERN was best explained as reflecting the activity of an error detection system. This error-detection theory of the ERN was based on findings that the onset of the ERN was contemporaneous with the error response, the amplitude was larger when task context (e.g., instructions and reward contingencies) favored accurate rather than fast responding, and the ERN was related to error correction and compensatory activity such as post-error slowing (e.g., Coles, Scheffers, & Holroyd, 1998; Gehring, Coles, Meyer, & Donchin, 1995). The ERN is sensitive to the degree of error (Bernstein, Scheffers & Coles, 1995) and is also elicited regardless of whether the response is made with the hands, as in most ERN studies, feet (Holroyd, Dien, & Coles, 1998) or eyes (Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001).

In some task conditions, a negative deflection of the ERP resembling the ERN has also been observed following correct responses (Falkenstein, Hoormann, Christ, & Hohnsbein, 2000; Luu, Flaish, & Tucker, 2000). Additionally, studies using fMRI have detected activity during correct responses executed under conditions of high response competition (Carter et al., 1998; Kiehl, Liddle, & Hopfinger, 2000). These findings led to the development of the conflict monitoring theory of the ERN which states that the ERN

arises not specifically from the detection of errors but from the simultaneous activation of more than one response (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Carter et al., 1998). Whether the ERN reflects error detection, as supported by ERP data, or conflict monitoring, as supported by mostly fMRI studies, remains a matter of some debate. Yeung and colleagues (2004) proposed an integrative theory suggesting that the two theories of error detection and conflict monitoring are not mutually exclusive. They present data suggesting that the ERN is not an explicit signal that an error has occurred, but rather reflects the continuous evaluation of response conflict that may be used to detect errors reliably.

Efforts to localize the neural generators of the ERN using electroencephalography (EEG; Dehaene, Posner, & Tucker 1994; Holroyd et al., 1998) and magnetoencephalography (MEG; Miltner et al., 1997) have converged on the anterior cingulate cortex (ACC) as the most likely source. The ACC has long been considered part of a neural network involved in the executive control of cognition (e.g., Posner & Dahaene, 1994), with more recent research indicating a role for the ACC in reward-based selection of action (Matsumoto, Suzuki, & Tanaki, 2003; Holroyd & Coles, 2002). The involvement of the ACC is especially notable for the study of schizophrenia given the evidence that the ACC may be compromised in schizophrenia patients (e.g., Benes, Majocha, Bird, & Marotta, 1987; Benes et al., 1991; Gabriel et al., 1997).

An intriguing framework for interpreting the ERN relates this component to activity of phasic dopamine (DA) projections in the ACC (Holroyd & Coles, 2002). These authors outlined a theory stating that the mesencephalic dopamine system conveys reinforcement learning signals to the basal ganglia and frontal cortex, where these signals

are then used to facilitate the development of adaptive motor responses. Specifically, it was argued that when an error was committed in a reaction-time task, the mesencephalic dopamine system conveyed a negative reinforcement signal to the frontal cortex, where it generated the ERN by disinhibiting the apical dendrites of motor neurons in the ACC. These error signals were then used to train the ACC, ensuring that control over the motor system was released to a motor controller that was best suited for the task at hand. Disruptions of this activity in schizophrenia rendered the ACC unable to detect changes in the success or failure of ongoing events. This interpretation is consistent with longstanding theories supporting the involvement of DA in schizophrenia (e.g., Davis, Kahn, Ko & Davidson, 1991) and reports of abnormal DA transmission in the ACC of schizophrenia patients (Benes, 2000; Suhara et al., 2002).

ERN amplitude in schizophrenia and other psychological disorders

Schizophrenia patients exhibit diminished ERN amplitude in a variety of experimental tasks (Kopp & Rist, 1999; Alain et al., 2002; Mathalon et al., 2002; Bates, Kiehl, Laurens, & Liddle, 2002; Morris et al., 2006). Reduced ERN amplitude in schizophrenia does not appear to reflect generalized diminishment of response-related brain activity because schizophrenia patients also consistently exhibit enhanced ERN-like activity compared to non-ill subjects on trials in which a correct response is executed. This pattern has been reported in three of the four studies that analyzed ERPs on correct trials (Alain et al., 2002; Mathalon et al., 2002; Morris et al., 2006). Given the quickly-evolving theories and empirical developments related to the interpretation of the ERN, it is difficult to define with certainty the impaired processes that these abnormalities observed in schizophrenia could reflect. According to theories regarding the generation of

response-related negativity, this pattern of findings may be due to poor representation of the correct response due to misperception of the imperative stimulus, forgetting or inappropriate application of task rules, uncertainty about or inattention to response accuracy, poor representation of the executed response, and/or diminished emotional responding to errors (Falkenstein et al., 2000; Coles, Scheffers, & Holroyd, 2001).

Since schizophrenia is a heterogeneous disorder (Craddock, O'Donovan, & Owen, 2007; Buchanan & Carpenter, 1994; Houlihan, 1977) and since patients in the current sample were not excluded based on the presence of secondary, comorbid psychiatric conditions, the potential impact of comorbid symptoms on ERN activity is important to consider. There is evidence to suggest that ERN activity is affected by forms of psychopathology other than schizophrenia. Rather than being reduced, ERN amplitude appears to be enlarged in anxiety (Gehring, Himle, & Nisenson, 2000). This enlargement has been found specifically in obsessive-compulsive disorder (Hajcak & Simons, 2002), among individuals high in worry (Hajcak, McDonald, & Simons, 2003), or those with high "trait" anxiety (Moser, Hajcak, & Simons, 2005), but not in specific phobia (Hajcak & Simons, 2002; Hajcak et al., 2003) or during state-induced fear (Moser et al., 2005). Evidence on the ERN in depression is mixed with a recent study reporting that depressed subjects demonstrated a significant increase in the amplitude of the ERN (Chiu & Deldin, 2007), while other studies report that ERN amplitude is reduced in depression (Ruchsow et al., 2004; Ruchsow et al., 2006). ERN studies indicate that high negative affect and high negative emotionality are related to increased amplitude of the ERN (Hajcak, McDonald, & Simons, 2004; Luu, Collins, & Tucker, 2000). Both anxiety and depression can be characterized as disorders high in negative affect (Clark & Watson, 1991).

Impulsivity, a characteristic feature of borderline personality disorder, has been found to be related to reduced self-monitoring of behavior and research indicates that ERN amplitude is reduced among those with borderline personality disorder compared with control subjects (de Bruijn et al., 2006; Ruchsow et al., 2006). Consistent with these findings is a study that found that individuals scoring highly on a measure of behavioral inhibition displayed increased ERN amplitudes, while those scoring highly on behavioral activation displayed decreased ERN amplitudes (Boksem, Tops, Wester, Meijman, & Lorist, 2006). No study has directly examined the relationship between the ERN and substance abuse/dependence, but investigations reporting an association between reduced ERN and high impulsivity have implications for substance use disorders (Potts, George, Martin, & Barratt, 2006).

Based on this literature review it is apparent that ERN abnormalities vary as a function of clinical diagnosis. For the purposes of this study, individuals with schizophrenia as well as individuals with elevations in impulsivity and behavioral activation could be expected to demonstrate reduced ERN amplitudes. However, schizophrenia patients do not tend to show abnormalities on behavioral activation when compared with controls (Scholten, van Honk, Aleman, & Kahn, 2006). It is presently unclear exactly how depression and anxiety, conditions related to the enhancement of ERN amplitude, could impact ERN data in schizophrenia patients.

ERN generation in a social context

Although the mirror neuron system has been recognized in humans and theorized to include complex-higher order social and emotional processes, there are few strong empirical links between social and emotional processes and the activity of the basic

motor system. The next step in linking mirror neurons to social and more complex cognitive processes is to examine activity in areas such as the ACC, an area where motor control and higher cognitive functions are thought to interface, and determine whether similar activity is present during the execution of an action and its observation. In the case of the ACC, the ERN is a useful tool for carrying out such a test (Bates, Patel, & Liddle, 2005).

To date, there are three investigations that have examined the ERN during observation of other's actions in normal participants (Miltner, Brauer, Hecht, Trippe, & Coles 2004; van Schie, Mars, Coles, & Bekkering, 2004; Bates et al., 2005). These studies of healthy participants provide evidence that the systems underlying the generation of the ERN are also active when participants observe an error being committed by another person. Miltner and colleagues (2004) demonstrated that when participants were required to count or press a button when they observed an error committed by a virtual subject, they generated an ERP waveform that showed many of the characteristics of the ERN. The virtual subject in this study was a computer simulation of a confederate performing a choice reaction-time task (Bernstein et al., 1995). Participants were instructed that they were observing the stimuli and responses of another subject in another room perform the same task they just completed. These investigators were the first to attempt to bridge the literature on mirror neurons and error monitoring by suggesting that the correspondence between brain activity in the observed individual and in the observer can be extended to include the commission of errors. However, it has been argued that since this study utilized simulated rather than real task

performance during the observation condition, the extent of parallel activation of the motor system is questionable.

In a study by van Schie and colleagues (2004), participants completed a two-choice speeded reaction time task, the Eriksen flanker task (Eriksen & Eriksen, 1974), and then observed an experimenter perform the same task. The ERN was recorded as a measure of ACC activity and the lateralized readiness potential (LRP) was used as a measure of relative activation of the observers' motor cortices. The LRP is a negative ERP component that provides a measure of lateralized motor activity in preparation to make a response. This component has been shown to begin around 1000 ms prior to planned hand movements and is observed broadly over the scalp, but is most prominent centrally (Mathalon et al., 2002). Van Schie and colleague's (2004) results confirmed the hypothesis that the ERN was observed during observation of incorrect but not correct responses, and that the LRP was enhanced following correct responses, but diminished following incorrect responses. Not only did these result indicate the presence of neural activity reflecting both error processing and action monitoring during the observation of another's actions, but activity from the ERN was differentiated from that of the LRP indicating the presence of simultaneous activity of separate but distinct neural systems. Thus, a possible pathway for observational learning which incorporates multiple mirror systems is proposed.

Bates and colleagues (2005) attempted to replicate the findings of van Schie and colleagues (2004) while addressing some limitations of the study. This study used a different computerized cognitive task – a Go/NoGo task involving the presentation of letters. During error observation, an ERN-like potential with spatial distribution similar to

the ERN following error execution was observed. This study also tested the hypothesis that the ERN potential was distinct from the stimulus-locked N2 component; this hypothesis was supported. Bates and colleagues (2005) noted the utility of the observation ERN paradigm to studies of psychiatric conditions, including schizophrenia, in which monitoring of other's behavior is likely compromised. However, to date, there have been no published studies of the ERN in a social context in schizophrenia and it is unknown whether ERN abnormalities observed in prior studies of schizophrenia will persist when a patient observes someone else making errors.

Assessing social processes in schizophrenia using psychophysiological methods has several advantages. Due to symptoms such as thought disorder or poverty of speech, some patients have difficulty expressing their social experiences via traditional psychological methods, such as overt behavior or self-report measures. Because of the nature of the cognitive processes that underlie the interpretation of and response to complex social events, these processes cannot be completely described or fully understood through self-report or simple behavioral observation. This novel use of psychophysiological methods provides a window of understanding into a process that is largely unavailable to self-report.

CHAPTER 2: RATIONALE

This study investigated social cognitive functioning in schizophrenia through the use of traditional neuropsychological modalities as well as with psychophysiological methodology and a novel observation paradigm. Poor social functioning is a well-documented feature of schizophrenia; however, the causes of these problems have not been fully described. A type of cognition, "social cognition," has been observed to be uniquely related to social difficulties among individuals with schizophrenia while also partially mediating the relationship between neurocognition and social functioning. However, little is known about the underlying neural mechanisms of social dysfunction in schizophrenia. Work in this area has begun to elucidate patterns of brain activity that are related to simply observing another's intentions or actions (i.e., the mirror neuron system). Investigation of the mirror neuron system has recently been expanded to human research on the error-related negativity, or ERN. The ERN is a negatively-deflected component of the event-related brain potential (ERP) that is elicited when an individual makes an erroneous response. Recent studies have demonstrated that healthy participants generate an ERN not only when they make an error, but also when they observe another individual make an error. These findings have implications for elucidating a neurophysiological mechanism involved in the ability to predict and evaluate the behaviors of others, an ability that is crucial for observational learning and effective social performance.

Several studies have reported that the amplitude of the ERN associated with error commission is attenuated in schizophrenia patients compared to normal controls but it remains unknown whether schizophrenia patients generate an ERN during when

observing another person. The present study examined the ERN during error observation in schizophrenia with an innovative paradigm for quantifying activity related to the interpretation of social stimuli. This research has broad implications not only for clarifying the nature of social functioning impairment in this population, but also for enhancing treatment by examining a specific aspect of social behavior (e.g., error monitoring) that could be targeted as part of psychosocial interventions.

The aims and hypotheses of this project were based on an accumulation of evidence demonstrating reduced ERN amplitude among individuals with schizophrenia when errors were committed. In addition, the literature on the nature and prevalence of social impairments in individuals with schizophrenia implies that this population may have deficits in processing information related to other people's actions. Specifically, there were four aims and hypotheses of the research:

1) To extend prior findings of abnormalities in response-related ERPs among schizophrenia patients by testing the hypothesis that ERN deficits will be present when patients observe another person make errors on a task. It was hypothesized that compared to normal controls, schizophrenia patients would exhibit an attenuated ERN during the execution of the flanker task and when observating a confederate perform the task.

2) To determine whether observation ERN activity is distinct from primary motor cortex activity as measured by the lateralized readiness potential (LRP). It was hypothesized that brain activity associated with error detection (ERN) will be independent of activity that reflects motor preparation (LRP) in the observation

condition in both schizophrenia patients and controls. In this way, the validity of the observation task for specifically measuring error monitoring, rather than general action observation, can be elucidated.

3) To examine the relationships between ERN activity during execution and observation with social cognition and social functioning in both groups. In addition, the relationship between execution and observation ERN activity and clinical symptoms in the schizophrenia group will examined. It is hypothesized that reduced ERN amplitude during the observation condition will be related to poor social cognition (i.e., theory of mind) and worse community social functioning. The association between the ERN and positive and negative symptoms of schizophrenia will also be explored, although there are no specific hypotheses regarding this relationship since evidence supports the association of ERN activity with both positive and negative symptoms (Frith, 1987; Frith & Done, 1989).

4) To examine the relationship between neurocognitive functioning and community social functioning and to explore whether social cognition mediates the relationship between neurocognition and social functioning. It is hypothesized that verbal memory and executive functioning will be positively correlated with community social functioning among individuals with schizophrenia given prior empirically support for this relationship (Green, 1996, Green et al., 2000). It is also hypothesized that social cognition, as measured by theory-of-mind, will contribute a significant portion of variance to social functioning above and beyond that of neurocognition among all participants (Brekke et al., 2005)

CHAPTER 3: METHODOLOGY

Participants

Two groups of subjects (schizophrenia patients and non-psychiatric comparison subjects) participated in the study. Twenty clinically stable schizophrenia outpatients were recruited from the Mental Health Clinic and Partial Hospitalization Program at the Baltimore VA Medical Center (BVAMC) and outpatient clinics at the University of Maryland Medical System (UMMS) using existing procedures for identifying, screening, and enrolling study participants. These recruitment procedures are routinely employed for research studies that are part of the Mental Illness Research, Education, and Clinical Center (MIRECC) and are described in more detail below. All patients were required to have a primary DSM-IV diagnosis of schizophrenia or schizoaffective disorder as determined by Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1994) administered by doctoral-level MIRECC clinical research staff. Eighteen psychiatrically healthy comparison subjects were recruited via advertising fliers posted within the BVAMC and University of Maryland Medical Center. All of the comparison subjects completed the study. However, one control participant did not make any errors during execution of the Flanker task. Since ERP activity during execution of errors is a crucial dependent variable in this study, this subject was excluded from data analysis. Efforts were taken to match the groups with respect to age, education, sex, parental education and ethnicity.

Non-psychiatric subjects were excluded if they reported a personal history of schizophrenia, schizoaffective disorder, major depressive disorder, or bipolar disorder, or an anxiety disorder of sufficient severity to require hospitalization or to prevent subject

from working more than 25% time on average during the last year. The presence of these disorders was assessed via the Structured Clinical Interview for DSM-IV (SCID), which was administered by doctoral-level MIRECC clinical research staff. In addition, volunteers were excluded if there was a reasonably definitive family history of schizophrenia or schizoaffective disorder per subject's report of hospitalizations, symptoms, and/or treatment by mental health professionals. To achieve matching on demographic characteristics, some individuals who responded to the advertisement were not enrolled in the study if they were not well matched to participants in the patient group.

Participants in both groups were excluded if they had a history of neurological disorder (e.g., stroke, seizures, brain tumor; multiple sclerosis, dementia, head injury), documented mental retardation, physical limitations that would prevent performance of experimental tasks, or alcohol or substance dependence per SCID within the last 6 months. Potential control participants were screened over the phone in order to rule out the presence of any exclusion criteria prior to scheduling study appointments. All participants were between 18 and 50 years old.

Regarding the recruitment of patients, research staff discussed this study with clinicians in relevant VA and UMMS outpatient programs in Baltimore. Potential patient subjects were identified by their primary clinicians who were aware of study entry criteria. These clinicians were then asked to identify clinically stable patients with primary diagnoses of schizophrenia or schizoaffective disorder who were likely to be interested in participation. In addition, participants with primary diagnoses of schizophrenia or schizoaffective disorder were identified by screening of medical records

and clinical appointment calendars at VA and University clinics. Members of the research staff obtained approval from each potential patient participant's clinician prior to approaching the potential participant regarding the study. Once approval from the clinician was obtained, a member of the research staff then individually approached subjects who met study criteria in order to explain the study and noted that the patient's clinician was aware that the research staff would be approaching them to discuss the study.

An Evaluation to Sign Consent (ESC) form was used to ensure patients' understanding of the study. A member of the MIRECC research staff met with potential participants as many times as needed to discuss the research study with them. Participants were required to give adequate responses on the ESC form to ensure that they understood the risks of the study and how they would respond if they experienced any distress or wished to withdraw from the study. Any person who was not able to give adequate responses on the ESC was not asked to sign a consent form or to participate in the study. All study-related procedures were approved by the Institutional Review Boards at the University of Maryland School of Medicine and the University of Maryland, College Park, and the Baltimore VAMC Research Committee.

Measures

Flanker Task

To examine group differences in ERN and LRP amplitude during social observation, EEG and behavioral data was recorded while participants performed a flanker task (execution condition) and while they observed a study confederate perform

the same task (observation condition). The stimuli and timing of the flanker task were similar to those used by Kopp and Rist (1999) and Morris and colleagues (2006).

The flanker task was selected because responding to a set of stimuli with the corresponding hand is relatively automatic and does not require participants to learn and remember a set of complex response rules. This task has been well-tolerated by schizophrenia patients in several ERN studies (Kopp & Rist, 1999; Kopp, Mattler, & Rist, 1994; Jones, Hemsley, & Gray, 1991; Morris et al., 2006) and the accuracy of schizophrenia patients' performance on this task is similar to that of non-patients (Kopp et al., 1994; Morris et al., 2006). The use of this simple task is believed to facilitate the interpretation of the ERP data by minimizing the likelihood that any differences observed in ERP activity are not due to group differences in strategy, working memory function, error frequency or perceived task difficulty. Finally, the flanker task is an optimal choice since it elicits the types of errors that elicit a robust ERN (i.e., speeded response errors due to “slips” rather than “mistakes” due to faulty information or memory).

In the sound-attenuated, dimly lit testing room, participants sat approximately 1 meter from a computer monitor on which the flanker stimuli and feedback were displayed. During the flanker task, participants are shown an array of shapes and asked to respond by pressing a button with the hand corresponding to the direction of a target arrow. Each trial on the flanker task began with the onset of two pairs of flanker stimuli which were equilateral triangles or squares arranged in a vertical array. The flanker stimuli were displayed for 100 ms before the middle triangle, the target, appeared and the entire array was displayed for 50 ms. There was an equal number of facilitation (flanking triangles oriented in the same direction as the target), interference (flanking triangles

oriented in the opposite direction as the target), and neutral (squares used instead of triangles) trials. The three different types of trials were presented in random order. Participants were instructed to respond by pressing a button on a standard computer keyboard with the hand that corresponded to the direction in which the target was pointing. Participants were asked to respond by pressing either the "A" key on a standard keyboard to indicate that the target triangle pointed to the left, or the "L" key to indicate that the target triangle pointed to the right. Before beginning testing, subjects were informed that they could win a financial bonus depending on their task performance. To increase motivation and encourage fast responding likely to generate errors, participants were told that they would receive a 2 cent bonus for each correct response, a 2 cent penalty for each incorrect response and a 5 cent penalty for responses that were too slow. The monetary value of these rewards and punishments have been used in similar studies with patients and control subjects and appear to be an adequate incentive for participants to perform as quickly and as accurately as possible (Morris et al., 2006). All participants were given a preset response time of 500 ms to input a response before being told that their response was "too slow." However, we expected that there would be substantial variability in each individual's response time (i.e., controls subject's response time would likely be much faster than patients), potentially introducing a confound resulting from patients having a greater proportion of trials excluded from processing due to slow responses or, conversely, controls not making enough errors on the task to perform data analyses on these trials. To address this potential problem, the number of committed errors was monitored during the first 3 blocks and if fewer than 6 errors were observed, then a response time cut-off of 350 ms was used for the 5 remaining blocks of trials.

Feedback indicating whether the response was correct, incorrect or too slow and indicating the monetary reward or penalty was displayed on the monitor for 1,000 ms following each trial (2,000 ms after the offset of the target and flankers). Then, after 1,000 ms the next trial began with the presentation of the next set of flanker stimuli. All participants performed 24 practice trials before beginning 8 blocks of 54 trials each for a total of 432 trials.

In the observation condition, which always followed the execution condition, the participants were instructed to observe the confederate performing the flanker task and to count the number of errors made by the confederate. It was expected that asking participants to count errors would increase the observer's engagement in the observational task (i.e., van Schie et al., 2004). The Day 2 assessor also served as the confederate during the observation condition. The confederate performed the flanker task in the same way as the participant during the execution trail (i.e., by pressing the "A" or "L" keys); however, the confederate exaggerated the response by raising her finger before pressing the response key in order to draw attention to the response choice. The response keys were within the participants' field of vision during fixation on the monitor. Once the keyboard and confederate responses were verbally confirmed to be observable by the subject, participants were instructed to maintain fixation on the computer screen and to identify response accuracy without making eye movements or directing their gaze elsewhere. During this condition, participants viewed the same set of stimuli on the same computer as in the execution condition. In order to maximize similarity between the execution and observation conditions, the financial contingencies were the same in the two conditions: if the confederate subject made an error, the observer lost 2 cents, if the

confederate made a correct response, the observer gained 2 cents, and if the confederate was too slow, the observer lost 5 cents. The confederate maintained a 15% overall error rate, as this has proven to elicit a robust ERN in studies of error execution (Gehring et al., 1993), but the number of errors made in each block was varied so that the counts would not be predictable. The confederate was signaled to commit an error on a trial by wearing an earphone that produced a 40 ms tone initiated 100 ms prior to the presentation of the flanker array. A total of 5 blocks of 54 trials each, for a total of 270 trials were completed in this condition.

Social Cognition

One important aspect of social cognition that has been shown to be relevant for understanding the actions and intentions of others and is likely related to specific brain processes (e.g., mirror neurons) is theory of mind (ToM). Nonverbal ToM measures are commonly utilized within schizophrenia populations since there is data to suggest that patients may have difficulty processing the complex details of more traditional, verbal ToM tasks (Russell, Reynaud, Herba, Morris, & Corcoran, 2006; Safarti et al., 1997; Langdon and Coltheart, 1999; Harrington et al., 2005). Theory of mind in the current study was assessed using a picture sequencing task developed by Langdon and colleagues (1997) and based on the work of Baron-Cohen, and colleagues (1986) who created the original version of this task. The original task was revised and intended to demonstrate selective ToM deficits not explained by poor IQ/executive functioning among those at risk for psychosis and with schizophrenia (Langdon et al., 2006). Further, this task incorporates picture sequences that require simpler levels of inferences than is required by false belief sequences. False belief stories are believed to be the "gold standard"

measure for ToM (Brüne, 2005) and require an individual to grasp that others can hold false beliefs that are different from one's own (correct) knowledge. This picture-sequencing task includes comparison sequences such as Mechanical, Capture, and Social (described in detail below) in order to parse out various levels of social cognitive functions that are required for accurate ToM. Since those early revisions, this task has been used in several studies of ToM in schizophrenia patients (Langdon, Coltheart, Ward, & Catts, 2002; Langdon, Davies, & Coltheart, 2002; Harrington et al., 2005; Langdon, Coltheart, & Ward, 2006) with these studies consistently finding that individuals with schizophrenia were more impaired on this measure of ToM compared with control participants. This task has also been used among non-clinical adults who reported schizotypal traits and found to indicate poor ToM functioning compared to non-schizotypal adults (Langdon & Coltheart, 1999). Therefore, it seems that this task is a useful measure of ToM among schizophrenia patients in that it is a nonverbal measure, provides comparison picture sequences to the "gold standard" false belief sequences (i.e., Capture, Social, described below), was adapted to assess aspects of cognition that are purely social rather than solely reliant on proper executive functioning or high IQ, and has consistently shown that schizophrenia patients, as well individuals on the schizophrenia-spectrum demonstrate ToM deficits on this task, suggesting a selective deficit among this particular population.

The picture sequencing task developed by Langdon and colleagues (1997) allows for the assessment of four story domains of action interpretation: mechanical, social-script, capture and false belief. False belief stories depict a character that is unaware of an event that occurred in a story and acts on this misinformation. The participant must then

infer that this character acted on the basis of their own false belief about the situation for a correct response (Frith & Corcoran, 1996; Baron-Cohen et al., 1986). The false belief stories are the primary ToM measure. The other domains of this task are included to control for and isolate the collection of processes that are involved in determining false beliefs. Social script stories control for the ability to construct sequences of social actions independent of inferences regarding beliefs or intentions. Mechanical stories assess physical cause-and-effect reasoning. Capture stories requires the inhibition of a highly salient, misleading cue in order to attend to other, less salient story details that determine the correct order, a skill that is required for good false belief performance (Langdon et al., 2006).

Following procedures outlined by Langdon and colleagues (1997), participants were read instructions and given two practice trials before they begin the task. Then, 16 experimental stories were presented in pseudo-random order (each of the four story domains contains four stories). Each story involves four cards. Cards are placed face down in front of participants in a pre-determined, incorrect sequence. Participants are then asked to turn the cards over and arrange them in a logical sequence of events. No time limit was placed on each story trial, but the time taken to complete each trial was recorded. The order of the cards was also recorded and scored by the examiner. Each sequence scored two points if the first card was positioned correctly, two points if the last card was positioned correctly, and one point each for the second and third cards being positioned correctly. Summary scores were created for each story domain as well as across domains to provide a ToM Total Score.

Neurocognition

There are several methodological limitations with regard to the assessment of social cognition: 1) research on social cognition in schizophrenia is relatively preliminary, 2) the operationalization of social cognition is currently quite broad, and 3) measures of social cognitive functioning are not well standardized and psychometric properties have not been systematically examined (Penn et al., 1997; Bora, Eryavuz, Kayahan, Sungu, & Veznedaroglu, 2006). Given these limitations and because social cognition tasks commonly require the integration of "more basic" neurocognitive abilities, the inclusion of well-validated neurocognitive measures commonly utilized in studies of schizophrenia contributes to greater understanding of estimates of social cognition ability derived from this research. Further, the relationship of cognitive, social cognitive, and social functioning to psychophysiological components of error monitoring is of particular interest given the focus of this research. Therefore, the addition of these measures and subsequent analyses aided the conceptualization of the social cognition processes being examined in this study.

Verbal memory

The Logical Memory I subtest of the Wechsler Memory Scales-III (WMS-III; Wechsler, 1945) assesses Immediate Verbal Memory and the Logical Memory II subtest assesses Secondary Verbal Memory. The WMS-Revised (Wechsler, 1987) has been demonstrated to have high internal consistency (Moore & Baker, 1997). Additionally, factor analytic studies have reported that a three factor model frequently emerges with verbal memory as a distinct factor in the normal population (Jurden, Franzen, Callahan, & Ledbetter, 1996) and clearly-defined clinical samples (e.g., intractable epilepsy; Moore & Baker, 1997), despite some debate (Loring, 1989; Elwood, 1991). The verbal memory

subtests of the WMS have been examined in a variety of neuropsychological populations and can be useful for identifying such conditions as mild brain injury in adults (Guilmette & Rasile, 1995), neurological impairment in children (Beardsworth & Bishop, 1994), right temporal lobectomy in epileptic patients (Naugle et al., 1993), and amphetamine dependence (McKetin & Mattick, 1998); mild dementia (Brooker, 1997). As described above, verbal memory has been suggested to be a correlate and predictor of the specific type of functional outcome that is being examined in this study (i.e., community social functioning; Green et al., 2000). In addition, the verbal memory subtests of the WMS have been used extensively in schizophrenia samples (Gold et al., 1992) and the validity of these specific subtests for use in a schizophrenia sample has been supported (Gold et al., 1992). The utilization of neurocognitive measures commonly used with this sample is of importance as this will allow direct comparison with prior work. (Gold & Harvey, 1993; Green & Nuechterlein, 2004).

During the Logical Memory I test, participants are read a story only once by the neuropsychological assessor during their Day 1 appointment and asked to recall as much as they can remember about the story. The assessor records the subject's responses based on a template from the WMS in which catch phrases of the story main ideas are indicated. The subject scores 1 point for each phrase that they recite with no prompting. The procedure is repeated with a second story; however, this story is also read a second time and participants are asked to recall all that they can remember following both the first and second readings. Points are added up for each story to create a summary recall score for that story. Then these are summed to create an overall recall score for the Immediate Verbal Memory subtest. Then after a 20-30 minute delay, the Logical

Memory II test is given in which the participant is asked to remember all that they can about both stories with no prompting from the assessor. The same scoring procedure was repeated for this subtest, creating a summary score for Secondary Verbal Memory. The Recognition subtest was also administered, but scores were not reported in this study. This subtest requires participants to answer 30, forced-choice, yes-no questions about whether specific information main ideas was or was not contained in the stories that were read to them.

Executive functioning

The Metacognitive version (Koren et al., 2006) of the Wisconsin Card Sorting Test (WCST; Berg, 1948) was selected as a measure of executive functioning. The WCST has been described by its authors as measuring a range of executive functions including, "strategic planning, organized searching, utilizing environmental feedback to shift cognitive sets, directing behavior towards achieving a goal, and modulating impulsive responding" (Heaton, Chelune, Talley, Kay, & Curiss, 1993, p.1). The WCST has been described as a well-validated measure of executive functioning (Lezak, 1995; Kolb & Wishaw, 1990). Impairment on the WCST has been shown to be particularly sensitive to frontal lobe lesions, the brain region associated with executive functions (Milner, 1963). Recent investigations with fMRI indicate that the prefrontal cortex is selectively activated during WCST performance (Rezai, Andreasen, Alliger, & Cohen, 1993; Weinberger, Berman, & Chase, 1988). However, these findings have not always been replicated (Anderson, Damasio, Jones, & Tranel, 1991; Cantor-Graae, Warkentin, Franzen, & Risberg, 1993) and some have criticized evidence for WCST validity by arguing that it does not specifically correlate with frontal lobe functioning impairment

(Ozonoff, 1995). The WCST demonstrates strong test-retest reliability in clinical and non-clinical populations, despite the claim that individuals benefit from prior exposure to task (Tate, Perdices, & Maggiotto, 1998; Ingram, Greve, Fishel, & Soukup, 1999). The cross-cultural validity of the WCST has been documented in several studies (Rey, Feldman, Rivas-Vazquez, Levin, & Benton, 1999). Finally, in addition to being uniquely related to community social functioning (Green et al., 2000), there is research to suggest that the complex reasoning and memory processes that the WCST captures are among the more salient and persistent cognitive deficits in schizophrenia (Goldberg et al., 1987).

The concept of metacognition grew out of a movement in the literature which sought to address the "real world" or functional impact of cognitive deficits in schizophrenia. This research indicates that neurocognitive deficits are a key determinant or predictor of social, occupational, and independent living functioning, in contrast to positive symptoms of schizophrenia which apparently have little impact (Green, Kern, Robertson, Sergi, & Kee, 2000). However, many leading researchers in this field have observed that the study of neuropsychological functioning in schizophrenia may not in fact be measuring the "right stuff" in terms of generalization of cognitive skills across domains or into action often not being assessed, the lack of identification of mediating or moderating variables between cognition and functioning, and the commonly observed modest correlations between these two domains (Koren et al., 2006). Koren and colleagues (2006) propose that focusing on social cognition (Corrigan & Penn, 2001) and learning potential (Green et al., 2000) as mediators between cognition and functioning is limited in that they do not take into account intrinsic control over one's own performance. Therefore, two important aspects of metacognition are proposed –

monitoring (the subjective evaluation of one's own performance) and control (the manner in which one's behavior is direct by this evaluation; Koren et al., 2006). As such, this task was selected since it provides standard and reliable measurement outputs for card sorting (i.e., total errors, categories completed, etc.) as well novel variables that reflect metacognitive processes (i.e., global monitoring, monitoring resolution, control sensitivity) that are suggested to mediate the relationship between cognition and functioning, as has been proposed with social cognition. Assessing alternative mediators of cognition and functioning, such as metacognition, allows for the comparison of various constructs that are proposed to link these two domains (i.e., social cognition, observation ERN).

The Metacognitive version of the WCST was administered on the computer. Four key "cards" which vary in shape, color, and number were displayed throughout the task. Participants were then presented one at a time with cards displayed on the monitor that varied with respect to these variables and were asked to match this target card with one of the four key cards. No instructions were provided on how to match the cards, but participants were told whether each choice was "right" or "wrong." Before participants received feedback on their choice, they were asked to indicate how confident they were that their selection was correct, using a 0-100 scale with "0" indicating no confidence, "50" indicating somewhat confident, and "100" indicating very confident. Then participants were asked to indicate whether or not they wanted to include this choice in a final score. For the purposes of this study, no final score was provided but participants were still asked to make this choice. Because of these additional metacognitive tasks, this version of the WCST presents the first 64 cards out of the full set of 128 and all

participants receive the same 64 cards. For most participants this task took between 20-30 minutes to complete. Perseverative errors, or the number of errors committed after receiving feedback that a particular response set is incorrect, is traditionally reported as the main output variable for this task and is considered the be the more reliable indicator than other WCST variables (Tan, Zou, Qu, & Guo, 2002). However, this version of the WCST only provided output on total errors. Total errors are reported in subsequent analyses since evidence suggests that perseverative errors are highly correlated with total errors and other WCST variables (Bowden et al., 1998).

Social Functioning

Social functioning in the community was measured using the Social Functioning Scale (SFS; Birchwood et al., 1990), a questionnaire designed to specifically measure areas of functioning relevant to the activities of individuals with schizophrenia. The SFS was originally developed to address some limitations related to the application of commonly utilized social functioning measures to a schizophrenia population. Individuals with schizophrenia were often not functioning in the roles being assessed by traditional social functioning measures (e.g., current work, marital, parental roles). Most of these measures required a normative judgment made by raters, such as rating behavior in terms of the severity of the problem. This makes judgments about a schizophrenia group problematic in that these individuals are largely unemployed, single, or don't live interpedently. Therefore, problems could be magnified, strengths ignored, with no available checks on the judgments of individual raters. As a result of these issues, the SFS was developed to be a comprehensive measure of social functioning meant to permit comparisons between subscales and raters and to increase sensitivity to the level of

impairment in schizophrenia as well as assess clinically-relevant domains of social functioning (e.g., "fundamental" characteristics of functioning: social engagement, independence, daily activities; Birchwood et al., 1990).

In addition to being clinically applicable to individuals with schizophrenia, the SFS was chosen for use in the current study because it has been shown to be a reliable, valid, and sensitive measure of social functioning (Birchwood et al., 1990). Scores on the SFS have been found to be related to treatment outcome (Yildiz, Veznedaroglu, Eryavuz, & Kayahan, 2004), symptom improvement (Ryu, et al., 2006) and the onset of schizophrenic illness (Grant, Addington, Addington, & Konnert, 2001). Additionally, use of the scale has been validated cross-culturally (Vázquez Mórejon & G-Bóveda, 2000). Although it is a self-report measure of social functioning, the questionnaire has strong psychometric properties and has been shown to be related to clinician and family ratings of functioning (Birchwood et al., 1990).

The questionnaire assesses seven major areas of social functioning: Social Engagement/Withdrawal (i.e., amount of time spent with others), Interpersonal Communication (i.e., number of friends, ability to hold logical conversation), Prosocial Activities (i.e., leisure activities involving others), Recreation (i.e., leisure activities involving self), Independence-Competence (i.e., ability to maintain personal hygiene, independence, etc.), Independence-Performance (i.e., how often personal hygiene, independent behaviors are performed), and Employment/Occupation (i.e., current employment status, how long since last employment, etc.). This measure was administered in an interview format by the same research staff who administered the SCID to study participants. Various functions within these domains were rated as

occurring on a 0-3 scale with higher scores indicating better functioning. Scores were summed to create raw summaries for the functional domains described above as well as a total raw score. Scaled scores were calculated for each domain, then these scaled values were averaged to create a variable referred to as the SFS average scaled score.

Psychiatric Symptoms

For the purposes of examining the relationships between symptoms, social functioning and ERP data, ratings of patients' current symptoms were obtained using the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1981). The BPRS and SANS are commonly used, well-established measures that assess the positive and negative symptoms of schizophrenia.

Brief Psychiatric Rating Scale

The Brief Psychiatric Rating Scale is an instrument designed for rapid and reliable assessment of clinical symptoms across a broad range of psychiatric patients (e.g., patients with schizophrenia, depression, dementia). However, this scale was originally developed to be used in inpatient settings. It initially attained widespread use in schizophrenia populations, and as such, is intended for use with patients with moderate to severe forms of psychopathology, rather than outpatients with mild symptoms (Faustman & Overall, 1999). The BPRS is clinician-rated, meant to be completed in about 20 to 30 minutes, and provides evaluation of 18 symptom constructs spanning much of the range of psychiatric manifestation. Adequate reliability levels for the BPRS have been reported in several studies. Inter-rater reliability of the BPRS is high (r = .85, except for the Tension item r = .56) when used by trained and experienced raters (Overall & Gorham,

1962; Hedlund & Vieweg, 1980). Many studies have investigated the correlations between BPRS subscales and other indicators of psychopathology among schizophrenia patients and in general these studies report strong correlations between measures (Faustman & Overall, 2004). For instance, BPRS depressive symptoms was found to be highly correlated with the Hamilton Rating Scale for Depression (r = .80, Hamilton, 1960; Newcomer, Faustman, Yeh, & Csernansky, 1990). Improvements in BPRS scores have been found to be related to positive response to antipsychotic medication (Beitinger, Lin, Kissling, & Leucht, 2008; Leucht, Shamsi, Busch, Kissling, & Kane 2008) and empirically-supported psychosocial interventions (Rosenberg, Mueser, Jankowski, Salyers, & Acker, 2004) in individuals with schizophrenia. Evidence for the cross-cultural validity of the BPRS comes from many international studies examining BPRS factors or the relationships between BPRS scores and moderators of psychotic symptoms, such as smoking or expressed emotion (Ruggeri et al., 2005; Chan, Ungvari, Shek, & Leung, 2003; Uzun, Cansever, Basoğlu, & Ozşahin, 2003; Marom, Munitz, Jones, Weizman, & Hermesh 2002).

The present study used the 18-item version of the BPRS (Overall & Klett, 1972) to measure a variety of the positive symptoms of schizophrenia as well as mood symptoms. Symptoms are scored on a range from 1-7 with 1 indicating that a symptom is "not present" and 7 indicating that a symptom is "very severe." As has been recommended by others (Hedlund & Vieweg, 1980), these scores were converted to a 0-6 scale in order to utilize a common sense anchor of "0" for "not present and in order to be consistent with SANS scoring criteria. Numerous factor analytic studies conducted on this version of the scale support the emergence of four factors that are often labeled as

Thinking Disturbance, Withdrawal/Retardation, Hostile/Suspiciousness, and Anxious Depression (Overall & Klett, 1972; Overall & Beller, 1984; Malla, Norman, Williamson, Cortese, & Diaz, 1993; Mueser, Curran, & McHugo, 1997). These factors are obtained by summing the severity ratings for the three symptom items which load most highly on these factor dimensions. A total pathology scores is obtained by summing the ratings on all BPRS items. Some ratings on this scale are based upon observation of the patient made by the assessor during the interview. These items include Emotional Withdrawal, Tension, Mannerisms and Posturing, Motor Retardation, and Uncooperativeness. All other ratings are obtained by patient self-report of their symptoms during the week preceding the appointment. Examples of these items include Somatic Concern, Anxiety, Depressed Mood, Grandiosity, Hallucinatory Behavior, and Unusual Thought Content.

Scale for the Assessment of Negative Symptoms

The SANS was developed by Andreasen (1989; 1994) to assess the negative symptoms of schizophrenia that had been overlooked by scientists and diagnosticians. The term "negative symptoms" was originally used to describe the loss of brain functioning and was subsequently applied to neurological and psychiatric disorders to describe a reduction in behavior or functioning (Hughlings-Jackson, 1931). The SANS has been reported to demonstrate strong inter-rater reliability and good internal consistency (Andreasen, 1982; Walker, Harvey, & Perlman, 1988). Discriminant validity of this measure has been demonstrated in investigations that have repeatedly supported the distinction between positive and negative symptoms of schizophrenia, which are thought to reflect distinct etiological and neurobiological processes (Andreasen & Olsen, 1982; Johnstone, Owens, Frith, & Crow, 1985; Walker, et al., 1988; Kay, 1990;

McGlashan & Fenton, 1992). Negative symptoms as measured by the SANS have been found to correlate with poor premorbid adjustment (Mueser, Bellack, Morrison, & Wixted, 1990), lower overall functioning (Pogue-Geile, 1989), impairment in independent living (Revheim et al., 2006), impaired cognitive functioning, and brain injury/atrophy as compared to schizophrenia patients with primarily positive symptoms (Andreasen & Olsen, 1982; Flaum & Andreasen, 1995). In addition, negative symptoms as measured by the SANS have been found to be a better predictor than cognitive impairment of psychosocial functioning (e.g., relationships, recreational and occupational activities; Milev, Ho, Arndt, & Andreasen, 2005). Cross-cultural validity of the SANS has been provided by studies showing consistently high reliability in a variety of cultural settings (Andreasen, 1989).

The SANS is a 22-item measure designed to assess four negative symptom domains: Affective Flattening, Alogia (i.e., poverty of speech and thought), Avolition (i.e., low motivation, apathy), and Anhedonia/Asociality. All individual items of the Affective Flattening and Alogia domains are rated by observations from the interviewing during the assessment. Avolition and Anhedonia/Asociality are self-reported by the patient for the two-week time period preceding the appointment. All symptom ratings were made on a 0-5 scale with "0" representing "not at all present" and "5" indicating that the symptom is "severe." Following the individual items with each negative domain, the interviewer provides a global rating of that symptom. Although these global ratings were developed to be ideal for use as summary indicators of each negative symptom (Andreasen, 1994), it has been noted that individual item scores are more reliable than the global ratings (Andreasen, 1989). Since the global ratings could introduce more

variability in symptom ratings, a summary score was calculated for each negative symptom domain and used in subsequent analyses, rather than global ratings.

Procedure

MIRECC staff with at least a master's degree in psychology or related field administered the informed consent procedures for schizophrenia patients. Assessors were thoroughly trained in consenting procedures by a research administrator from the MIRECC. After providing consent, the first study appointment was scheduled to occur at least 24 hours following the consent appointment to allow the patients ample time to fully consider their participation.

During the first study appointment, referred to as the Day 1 appointment, patients completed the SCID, the SFS, the ToM task, and tests of immediate and secondary verbal memory, in that order. The SCID and SFS were administered by one doctoral-level clinician and the SCID was video-taped for supervision purposes. The ToM and cognitive tasks were administered by a master-level MIRECC staff member who was well-trained in the administration of these instruments. Clinicians administering the SCID attended bi-monthly supervision meetings in which video-tapes were regularly viewed by other assessors as well as senior psychologists with expertise in the administration of structured diagnostic clinical interviews. These meetings are meant to provide checks on individual ratings and diagnoses and to increase the diagnostic rigor of MIRECC research studies. Medication information was obtained during the pre-consent screening process and confirmed with the participants during this appointment. Control participants completed consent procedures and the same Day 1 measures at one appointment. The Day 1

appointment lasted between 2-3 hours and all participants were paid $10 for their completion of this assessment.

Day 2 testing sessions took place in the MIRECC Clinical Psychophysiology lab, located in the BVAMC. During this appointment, patients were administered the BPRS and SANS prior to EEG recording by a masters-level clinical psychology graduate student who was trained in the administration of these measures. The BPRS and SANS were video-taped for supervision purposes. The assessor attended bi-monthly supervision meetings in which video-tapes were viewed by senior psychologists and ratings were discussed and confirmed. Next, a computerized version of the Metacognitive version of the WCST was administered to all participants. If subjects did not have sufficient experience using a computer, the experimenter assisted participants with the completion of this task (i.e., moving and clicking the mouse). Finally, EEG recordings were obtained for all participants using a Neuroscan Synamps amplifier and Quickcap electrode cap with 32 sintered silver-silver/chloride electrodes. To identify electrical artifact in the EEG arising from eye movements, electrooculogram (EOG) was recorded using four additional electrodes placed above and below the left eye and at the outer edge of both eyes. Reference electrodes were placed on the earlobes and the nose. All tasks and measures of the Day 2 assessment were administered by the same masters-level clinical psychology graduate student. The entire testing session including both conditions lasted between 2 ½ - 3 hours and subjects had short rest breaks between blocks of trials and between conditions. At the end of the session, participants were debriefed about the nature of the study, given the opportunity to ask questions, and paid for their

participation. All participants were paid $40 plus the maximum bonus of $10 at the conclusion of their participation, regardless of number of errors or correct responses.

Data Processing

ERN

EEG data was sorted into response-locked epochs beginning 1 second before and extending 1 second beyond the response. These epochs were created for each trial in both execution and observation conditions. Artifact arising from vertical and horizontal eye movement in the EEG was minimized using an automated eye movement subtraction algorithm (Gratton et al., 1983). Epochs contaminated by subject movement were excluded. A 0-phase shift 1-14 Hz 24 dB band-pass filter was applied to select the optimal voltage range. A 200 ms pre-response baseline was subtracted from the selected epochs and four averages were computed for each subject: correct and incorrect responses for both the execution and observation conditions. For each participant, the ERN was scored using methods similar to van Schie and colleagues (2004). In the execution condition, the latency of the ERN was identified by locating the largest negativity in the 150 ms after the response. Once that latency was identified, the average amplitude of a 50 ms window centered on that latency was scored for both the error and correct response averages. This allows for quantification and comparison of the response-related ERP even when there may not be an identifiable negative deflection (i.e., after correct responses). In the observation condition, the latency of the ERN was identified by locating the largest negativity in the period from 0-250 ms after the response. This window was identified by examining the results of previous observation ERN studies (van Schie et al., 2004; Bates et al., 2005) and by visual inspection of group averaged

waveforms from the current data. The average amplitude was scored in a 50 ms window centered on that latency for the error and correct response averages. Consistent with previous studies of the ERN, negativity was maximal at FCz during the execution condition and among control participants; thus, data from that site were used in all subsequent ERN analyses. Data from the FCz electrode was also used for analyses of the observation condition, since there is evidence to suggest a similar localization of activity (van Schie et al., 2004) and since we are hypothesizing that the source of the observation ERN is the same as the execution ERN.

LRP

Response-locked epochs were identified beginning at 600 ms prior to the response and ending 500 ms after the response for both execution and observation conditions. Artifact arising from vertical and horizontal eye movement in the EEG was minimized using an automated eye movement subtraction algorithm (Gratton et al., 1983). Epochs contaminated by subject movement were excluded. A 0-phase shift 4 Hz 24 dB low pass filter was applied. A -550 – -450 ms pre-response baseline was subtracted from the selected epochs and four averages were computed for each subject: correct and incorrect responses for both the execution and observation conditions. As noted in van Schie and colleagues (2004), the LRP was maximal over the hemisphere contralateral to the executed response, regardless of the accuracy of the response. In both the execution and observation conditions, the LRP was derived for correct and incorrect responses separately by creating an ERP waveform from the data recorded from an electrode contralateral to the response hand (specifically, electrode sites C3 or C4, depending upon which hand executes the response) then subtracting the waveform computed from the

corresponding recording site ipsilateral to the response hand. In the execution condition, epochs and waveforms were locked to the participant's own response and in the observation condition, the participant's (observer's) epochs and waveforms were locked to the confederate's response.

CHAPTER 4: RESULTS

The present study sought to investigate brain activity following self- and confederate-generated errors in schizophrenia patients and non-psychiatric control subjects during execution and observation of a simple, computerized, forced-choice task. Measures of social functioning, social cognition, neurocognition, and symptoms were included in order to contribute to the conceptualization of the functional significance of the ERN as well as to characterize the theoretical underpinnings of error-related negativity that is hypothesized to occur during observation. First, statistical considerations for interpretation of these data are described. Second, demographic characteristics of the entire sample are described. Chi squared analyses and t-tests were used to determine whether the schizophrenia group differed from the control group on any demographic variables such as sex, race, age, and education. Clinical characteristics (i.e., medication status, diagnostic subtype) of the schizophrenia group are also discussed. Third, behavioral data from the flanker task (i.e., accuracy, response time) are presented and group differences on these variables are examined. Fourth, in order to examine the first aim of this study, ERN activity is reported. Specifically, differences between activity during correct and incorrect trials, execution and observation conditions, and patient and control groups are presented. Fifth, LRP activity is described and, as with the ERN, the effects of accuracy, condition, and group are reported. Sixth, correlations between ERN activity and measures of social cognition, social functioning, and symptoms are examined. Next, correlations between neurocognition, social cognition, social functioning are reported. In order to better characterize our measure of social cognition and to replicate prior work, a regression analysis is used to describe the whether social cognition

mediates the relationship between neurocognition and social functioning. Finally, exploratory analyses are presented in order to assist with interpretation of unexpected results with respect to psychophysiological activity during observation and correlations between neurocognitive and social functioning in schizophrenia patients.

Statistical Considerations

For all analyses, an alpha level of .05 was adopted and the Greenhouse-Geisser statistic was used to adjust for repeated measures analyses. *A priori* power calculations were conducted in order to determine the sample size required to detect significant effects, assuming an alpha level of .05, a medium effect size (d = .5), and power estimated at .80. The sample size was estimated at N = 102. Unfortunately, it was not possible to collect data on a sample this large given that ERP research is time and resource-demanding and exclusion criteria for patients and controls were stringent. In most studies utilizing resource-demand methodologies (e.g., fMRI, ERP), sample size is inevitably limited. Reduced sample sizes have become an accepted standard in these areas of research, with the acknowledgment that additional methodological and statistical considerations are required (Luck, 2005). A total sample size of approximately 40 or less is common in most ERN studies (Morris et al., 2006; Curran, DeBuse, & Leynes, 2007; Heldmann, Russeler, & Munte, 2005; Bates et al., 2005). Based on these considerations, a sample size of 40 (schizophrenia = 20, controls = 20) was selected as adequate for the detection of ERP effects.

In the present study, data were collected for 20 schizophrenia patients and for 18 controls. One control subject did not commit any errors on the flanker task during the execution condition. Therefore, this subject's data were removed from subsequent

analyses since the commission of errors is a primary variable of interest and necessary for comparison with activity related to errors during observation. The final sample size was 20 for schizophrenia patients and 17 for controls. Power was recalculated *post-hoc* to estimate the ability of this study to detect significant effects. With an alpha level of .05 and the given sample size, the power required to detect medium effect sizes (d = .5) is estimated at .44. This substantial reduction in power must be considered when interpreting these results.

Due to uneven group sizes (schizophrenia = 20, controls = 17), accuracy and condition effects are considered non-orthogonal independent variables. Type III Sum of Squares was used in order to address issues of non-orthogonality. This statistic tests each effect (e.g., condition) while holding the other effect (e.g., accuracy) constant at its mean. In addition, Levene's test for error variance was computed to test the assumption of homogeneity of variances between the two groups. This statistic was, however, nonsignificant in all tests, indicating that this basic assumption was not violated. Partial eta-squared effect size estimates are reported for all significant and nonsignificant main effects and interactions.

Demographics and Clinical Characteristics

Analyses of demographic variables were conducted in order to demonstrate that any observed group differences could not be better accounted for by possible confounding factors such as sex, race, age, or education (see Table 1). Although these data clearly demonstrated that more men than women (68% men, 32% women) and more African Americans than Caucasians (73% African Americans, 27% Caucasians) participated in this study, chi squared analyses indicated that the groups did not differ

with respect to sex, (X^2= 0.31, p > .05), and race, (X^2= 3.19, p > .05). Independent samples t-tests indicated that the groups also did not significantly differ on age (t [1, 35] = .52, p > .05) or parent's highest education (t [1, 31] = 1.30, p > .05). However, controls reported having completed more years of education than patients, (t [1, 35] = 2.52, p < .05).

In order to characterize the schizophrenia group, descriptive statistics for illness severity, medication, and symptoms were calculated (see Table 2). The mean age of first psychiatric treatment was 21.64 years, with a range from 5-33 years. The mean age of first psychiatric hospitalization was 22.62 years, with a range from 16-33 years. The mean age of initial diagnosis of schizophrenia was 21.88 years, with a range from 5-31 years of age. These results are consistent with prior work which establishes period of highest risk for onset of schizophrenia among men, the predominant gender in this study, in the early to mid-20's (American Psychiatric Association, 1994). The average number of psychiatric hospitalizations was 5.43 with a standard deviation of 8.10. Forty percent of the patient sample reported 1-5 hospitalizations, whereas two individuals reported 30 hospitalizations, indicating a substantial range in these data. The average number of suicide attempts was less than one (m = 0.89, sd = 2.78). Fifty-five percent of patients reported no suicide attempts; one person reported 15 attempts. Seven patients were classified as paranoid subtype, 2 as disorganized subtype, and 8 as undifferentiated subtype. No patients were classified as deficit subtype (i.e., primary negative symptoms).

Examination of medication status was conducted separately for antipsychotics and mood/anxiety medications. Each patient was assigned one antipsychotic medication classification according to the number and type of medication they were taking: 1) one

first generation antipsychotic (FGA), 2) one second generation antipsychotic (SGA), 3) a combination of an FGA and an SGA, or 4) more than one SGA. As shown in Table 1, 15% of the sample was taking one FGA, 50% was taking one SGA, 30% was taking an FGA and an SGA, and 5% was taking more than one SGA. Taken together, these data indicate that 45% were taking an FGA and 85% were on an SGA, alone or in combination. Next, patients were classified in terms of mood/anxiety medications. These classifications were: 1) one antidepressant, 2) one antianxiety, 3) one mood stabilizer (e.g., lithium, depakote), and 4) more than one mood/anxiety medication. Forty percent of the sample was taking one antidepressant in combination with antipsychotic medication. No patients were taking an antianxiety medication in the absence of other mood medications and 5% of the sample was on a mood stabilizer in combination with antipsychotic medication. Thirty percent of the sample reported being on more than one mood/anxiety medication. Overall, 75% of the current sample was being treated with one or more anxiety/mood medications in addition to antipsychotics (see Table 2).

During the Day 1 clinical interview, fourteen patients were diagnosed with Schizophrenia and six were diagnosed with Schizoaffective Disorder according to DSM-IV criteria. The presence of comorbid mood symptoms (i.e., depression and mania) was assessed according to DSM-IV criteria. One control participant met criteria for a Past Major Depressive Episode and was assigned a lifetime diagnosis of Past Major Depressive Disorder, but did not meet criteria for any current symptoms of depression and was not currently taking antidepressant medication. There were seven patients who met DSM-IV criteria for a Past Major Depressive Episode. Of these seven, three received a primary diagnosis of Schizoaffective Disorder and four were diagnosed with

Schizophrenia. Anxiety and personality disorder symptoms were not assessed during the Day 1 interview; therefore, a chart review of participants in the patient group was conducted in order to determine the current or lifetime prevalence of these symptoms. Chart review was approved by the Institutional Review Boards prior to the initiation of this study. Two patients were diagnosed with Post-Traumatic Stress Disorder, two were diagnosed with Personality Disorder Not Otherwise Specified, one was diagnosed with Obsessive-Compulsive Disorder, and one was diagnosed with Borderline Personality Disorder. Current symptoms assessed among patients with the BPRS were in the moderate to severe range (least severe: Hostility/Suspiciousness = 4.45; most severe: Anxious/Depression = 6.75). Negative symptoms assessed with the SANS ranged from questionable to mild (least severe: Alogia = 1.50; most severe: Affective Flattening = 2.05; see Table 2). These low scores for negative symptoms are consistent with a lack of deficit subtype patients in this sample.

Flanker Behavioral Data

In order to describe behavior during ERP data collection, group differences in accuracy during execution, response time during execution, and accuracy of error recognition in the observation condition were examined. Mixed-model ANOVAs were used to examine these group differences as well as paired-sample t-tests when relevant.

Accuracy was calculated as the percentage of correct trials out of total trials, excluding "too slow" trials in which no accuracy feedback was provided. A mixed-model ANOVA was conducted to examine accuracy during the execution condition on the three types of flanker trials (i.e., facilitation, interference, neutral). The group x flanker type interaction (F [2, 70] = 4.27, $p < .05$; $\eta^2_p = .12$) and the main effects for group (F [1, 35]

= 8.75, $p < .01$; $\eta^2_p = .20$) and flanker type were significant (F [2, 70] = 83.10, $p < .01$; $\eta^2_p = .70$). In order to examine the effect of flanker type, repeated-measures ANOVAs were conducted and indicated a significant effect for flanker type for both patients (F [2, 38] = 44.94, $p < .01$; $\eta^2_p = .70$) and controls (F [2, 32] = 58.95, $p < .01$; $\eta^2_p = .79$). In order to follow up on the significant effect of group and the group x flanker type interaction, repeated-measures ANOVAs were conducted with all combinations of flanker type separately for controls and patients. These results suggested that controls were more accurate on facilitation compared to interference (F [1, 16] = 62.74, $p < .01$; $\eta^2_p = .80$) and neutral trials (F [1, 16] = 12.28, $p < .01$; $\eta^2_p = .43$), and neutral compared to interference trials (F [1, 16] = 58.89, $p < .01$; $\eta^2_p = .79$). Patient's accuracy on the three trial types was comparable to that of controls; patients were more accurate during facilitation compared to interference (F [1, 19] = 45.63, $p < .01$; $\eta^2_p = .71$) and neutral trials (F [1, 19] = 9.62, $p < .01$; $\eta^2_p = .34$), and on neutral trails compared to interference trials (F [1, 19] = 48.26, $p < .01$; $\eta^2_p = .72$). Independent samples t-tests were used to examine group differences between the three Flanker types. As expected, patients were significantly less accurate than controls on all three types: facilitation (t [1, 35] = 2.00, $p < .05$), interference (t [1, 35] = 2.90, $p < .01$), and neutral (t [1, 35] = 2.20, $p < .05$; see Figure 1).

Similarly, a mixed model ANOVA was conducted to examine accuracy and group differences in response time (RT). There was a significant main effect of flanker type (F [2, 70] = 140.59, $p < .01$; $\eta^2_p = .80$); however, the group x flanker type interaction (F [2, 70] = 1.45, $p = .24$) and the main effects for group (F [1, 35] = 1.15, $p = .29$) were nonsignificant. In order to follow up on the significant effect of flanker type, repeated-

measures ANOVAs were conducted with all combinations of flanker type separately among both controls and patients. These results indicated a shorter response time on facilitation compared to interference (F [1, 36] = 223.43, $p < .01$; $\eta^2_p = .86$) and neutral trials (F [1, 36] = 85.94, $p < .01$; $\eta^2_p = .71$), and neutral compared to interference trials (F [1, 36] = 69.77, $p < .01$; $\eta^2_p = .66$; see Figure 1). If participants made fewer than 6 errors during the first three blocks of trials, they were assigned a shorter RT cut-off (350 ms) for the remaining trials in order to increase the likelihood of committing errors. Twelve controls and 3 patients were assigned this shorter RT cut-off for trials following the third block. Therefore, it is apparent that controls responded faster than patients as evidenced by the analyses above and by the observation that more controls than patients completed trials with the shorter RT cut-off.

Since the range of possible response times was restricted by the nature of the flanker task, an analysis of responses identified as "too slow" was conducted in order to better describe response variability. A mixed-model ANOVA was conducted to explore group and flanker type effects for the percentage of trials identified as "too slow." The main effect of flanker type was significant (F [2, 70] = 29.57, $p < .01$; $\eta^2_p = .46$) and the group x flanker type interaction (F [2, 70] = 0.84, $p = .38$; $\eta^2_p = .02$) and the main effect of group (F [1, 35] = .58, $p = .45$; $\eta^2_p = .02$) were nonsignificant. Follow-up repeated measures ANOVAs were used to explore the effect of flanker type among all participants. There were more trials identified as "too slow" during interference compared to facilitation (F [1, 36] = 29.39, $p < .01$; $\eta^2_p = .45$) and neutral trials (F [1, 36] = 33.35, $p < .01$; $\eta^2_p = .48$) and during neutral trials compared to facilitation trials (F [1, 36] = 5.15, $p < .05$; $\eta^2_p = .13$).

Participants were asked to count the number of errors occurring in the observation condition as a check on attention and to increase motivation and task relevance. Accuracy in the observation condition was computed as the percentage of correctly identified errors using the following formula for each block of trials: Accuracy = 1 – (absolute value of [number of errors reported – actual number of errors]/actual number of errors). Then the values for each block were averaged to provide one composite score for observation accuracy. This statistic reflects the accuracy of subject's monitoring regardless of whether they over- or under-reported errors. As shown in Figure 1, a univariate ANOVA indicated that patients were significantly worse at counting errors during observation compared to controls (F [1, 34] = 7.74, $p < .01$).

Error-Related Negativity

Following the steps of EEG data processing outlined in the previous section, individuals' averaged waveforms were combined to produce group averaged waveforms for the purposes of visual comparison of ERN activity between groups. These waveforms will be described in subsequent sections. Next, a group (schizophrenia vs. controls) x condition (execution vs. observation) x accuracy (correct vs. incorrect) omnibus, mixed model ANOVA was computed for ERN amplitude as measured at the FCz electrode. The group x condition x accuracy interaction was significant (F [1, 35] = 4.70 $p < .05$; η^2_p = .12) as well as the accuracy x group interaction (F [1, 35] = 7.95, $p < .01$; η^2_p = .19), condition x group interaction (F [1, 35] = 4.71, $p < .05$; η^2_p = .12), and accuracy x condition interaction (F [1, 35] = 31.70, $p < .01$; η^2_p = .48). The main effects of accuracy (F [1, 35] = 49.58, $p < .01$; η^2_p = .59) and condition (F [1, 35] = 7.02, $p < .05$; η^2_p = .17) were also significant. The main effect of group approached significance (F [1, 35] = 3.73,

$p = .06$; $\eta^2_p = .10$). Significant interactions and main effects were explored with follow-up repeated-measures ANOVAs and independent samples t tests when appropriate.

Execution Condition

Group averaged waveforms for ERN activity during execution and observation conditions are presented in Figure 2. Controls demonstrated a large increase in activity that peaked at approximately 30 ms following error responses compared to correct responses during the execution condition. Patients also demonstrated increased activity during error compared to correct trials peaking at approximately 50 ms following the response; however, this difference is substantially smaller than that observed among controls. Topographical maps indicated that the negativity during error trials is concentrated in the frontal and central regions of the scalp and this activity is greater among controls than patients. This distribution of activity is consistent with prior work on the ERN and source localization studies which suggests that this activity originates in the ACC, located in fronto-central areas of the cortex and supports the analysis of activity at the FCz electrode site where activity is maximal.

A group x accuracy mixed-model ANOVA was conducted with ERN data from the execution condition in order to break down the significant omnibus interaction effects. In the execution condition, the group x accuracy interaction was significant (F [1, 35] = 7.19, $p < .05$; $\eta^2_p = .17$), as well as main effects of accuracy (F [1, 35] = 46.30, $p < .01$; $\eta^2_p = .57$) and group (F [1, 35] = 5.07, $p < .05$; $\eta^2_p = .13$). Repeated measures ANOVAs conducted separately by group in order to examine accuracy effects demonstrated the presence of a larger ERN following error responses compared to correct responses for controls (F [1, 16] = 33.64, $p < .01$; $\eta^2_p = .68$) and patients (F [1, 19] =

11.56, $p < .01$; $\eta^2_p = .38$). Independent samples t-tests of group differences on ERN amplitude indicated a significant difference between patients and controls on ERN activity following errors (t [1, 35] = -2.81, $p < .01$) but not correct responses (t [1, 35] = 0.37, $p = .71$). Group means are shown in Figure 4.

Observation Condition

Group averaged waveforms for the observation condition are shown in Figure 2. Contrary to expectations, activity among controls in this condition appears to be more positive on error compared to correct trials with topographical mapping indicating widely distributed positive activity where increased negative activity would be expected. Thus, there does not appear to be clear ERN activity in this condition among controls. Patient data during observation more closely approximates ERN-like activity (peak negativity occurs around 225 ms); however, there does not appear to be substantial differentiation between activity during correct and error trials, suggesting that these processes are likely indistinct. Among patients, topographical mapping indicates a small amount of negative activity in fronto-central regions.

A group (patients, controls) x accuracy (correct, error) mixed model ANOVA was computed for ERN amplitude during the observation condition. There was a significant main effect of accuracy (F [1] = 8.97, $p < .01$; $\eta^2_p = .20$); however, the group x accuracy interaction (F [1, 35] = 1.72, $p = .20$; $\eta^2_p = .05$) and the main effect of group were nonsignificant (F [1, 35] = .04, $p = .84$; $\eta^2_p = .00$). A repeated measures ANOVA was conducted for accuracy in the observation condition for all participants. These analyses demonstrated that there was greater negative activity following errors than correct trials

during observation in all participants (F [1, 36] = 8.24, $p < .01$; $\eta^2_p = .19$). These effects are demonstrated by the area report means in Figure 4.

Lateralized Readiness Potential

Group averaged waveforms were computed from individually averaged waveforms for LRP activity. A 2 (group) x 2 (condition) x 2 (accuracy) omnibus, mixed model ANOVA was computed for LRP amplitude. This test was used to determine whether patterns of LRP activity on correct and incorrect trials differed between the groups in the two conditions. If patterns of group differences in LRP activity are different than those observed for the ERN, this would indicate that brain activity associated with the execution or observation of errors is qualitatively different from activity associated with anticipation of movements and allows an assessment of the specificity of the ERN abnormality. The analysis of this component is useful for more specifically quantifying observation activity and for beginning to understand processes involved in error observation.

Figure 3 displays the group averaged waveforms for LRP activity during execution and observation conditions. As expected, the LRP was robust and easily identifiable, occurring between -100 to -25 ms prior to the response, reflecting action preparation. Activity was comparable for error and correct trials and for patients and controls during execution. Lateralized readiness potential activity during observation was somewhat more difficult to interpret. Controls demonstrated a small negativity at the time of the response (0 ms) on error trials but not on correct trials. Lateralized readiness potential activity in patients was highly variable and inconsistent and it does not appear that patients produced an identifiable LRP in this condition.

The main effect of condition was significant (F [1, 35] = 53.29, $p < .01$; $\eta^2_p = .60$) with greater negative activity evident during execution than observation. The group x condition x accuracy interaction for LRP activity was nonsignificant, (F [1, 35] = 2.92, $p = .10$; $\eta^2_p = .08$). Main effects for group (F [1, 35] = 1.57, $p = .22$; $\eta^2_p = .04$) and accuracy (F [1, 35] = 2.98, $p = .09$; $\eta^2_p = .08$) were also nonsignificant.

Correlations of ERN Activity with Social Cognition, Social Functioning, and Symptoms

In order to examine the relationship between error-related activity in execution and observation conditions with social functioning and social cognition, correlations between these variables were calculated. Since scores on the Social Functioning Scale (SFS) are continuous, correlational analyses were used to explore the associations between the seven SFS subscale scores and a summary score for this measure and ERN amplitude. A strong correlation between poor social functioning and decreased ERN amplitude in patients could provide evidence that deficits in ERN generation are related to impaired social functioning which might help identify one of the mechanisms responsible for pervasive problems in social functioning in schizophrenia.

In addition, correlations between execution and observation ERN amplitude and psychiatric symptoms in schizophrenia patients were calculated in order to better characterize psychiatric symptoms that may relate to psychophysiological activity. It was difficult to predict whether psychophysiological measures would correlate with any specificity with positive or negative symptoms since there are theoretical bases for expecting relationships with either or both types of symptoms. It has been suggested, for example, that failure to appreciate other people's motivations and intentions (i.e., failures in ToM) may lead to paranoid delusions and delusions of reference (e.g., Frith, 1987;

Frith & Done, 1989). Alternatively, it is reasonable to hypothesize that individuals who have difficulty interpreting other people's actions will not succeed at or enjoy interpersonal interactions and will exhibit negative symptoms such as social withdrawal and anhedonia. These predictions are not mutually exclusive, so correlational analyses among these variables are exploratory.

There were no significant correlations of ERN activity with social functioning or social cognition among schizophrenia patients, but there were some significant correlations with symptoms. Ratings on the Thinking Disturbance (TD) subscale of the BPRS were correlated with ERN amplitude in the execution condition ($r = .50$, $p < .05$) such that more severe TD was associated with smaller (i.e., less negative) ERN amplitude during error execution. The correlation between the SANS Avolition rating and ERN amplitude in the execution condition was significant ($r = .48$, $p < .05$) such that more severe avolition symptoms were associated with reduced ERN amplitude following execution of errors (see Table 3).

Among control participants, Occupation/Employment status, as measured by the SFS was negatively correlated with ERN execution activity ($r = -.52$, $p < .05$). This indicated that, as expected, greater competence in occupation and employment status was correlated with larger ERN amplitudes during execution of the flanker task. Greater Interpersonal Communication, as measured by the SFS, was unexpectedly associated with reduced ERN amplitude in the observation condition ($r = .55$, $p < .05$), suggesting that better scores on Interpersonal Communication were related to more positive (i.e., smaller) ERNs during the observation condition. There were no significant correlations with social cognition among controls (see Table 4).

In order to increase the range of possible scores on the social functioning and social cognition measures, the patient and control groups were combined and correlations with ERN activity were computed. Among all participants, functioning in Occupation/Employment on the SFS was negatively correlated with ERN amplitude during execution (r = -.56, p < .01), indicating that better functioning was associated with larger ERN amplitude. In addition, ToM Total Score (r = -.44, p < .01) and ToM False Beliefs (r = -.40, p < .05) were significantly correlated with ERN activity during execution. These correlations suggest that better theory of mind reasoning abilities were related to greater ERN amplitude following error execution (see Table 5).

Neurocognition, Social Cognition, and Social Functioning

Group means on neurocognitive, social cognitive, and social functioning variables were compared (see Table 6). It was expected that schizophrenia patients would demonstrate poorer functioning on these measures compared with controls. Next, correlations between verbal memory, executive functioning, and community social functioning were explored in an attempt to replicate the findings from Green and colleagues (1996, 2000). Correlations between cognitive and social functioning were also conducted among controls. A regression analysis was conducted to examine whether social cognition mediates the relationship between neurocognition and social functioning. This analysis was intended to replicate previous findings on the mediational nature of social cognition between these constructs (Brekke et al., 2005).

Group Differences

Group differences were examined in order to replicate the collection of findings in the literature indicating that patients have deficits in cognitive, social cognitive and social

functioning abilities compared to controls. In addition, describing group differences will aid in the interpretation of the subsequent correlational and mediational analyses. Independent samples t-tests demonstrated that patients performed more poorly than controls on all neurocognitive and social cognitive measures: ToM Total Score (t [1, 35] = 4.29, $p < .01$), ToM False Beliefs (t [1, 35] = 4.47, $p < .01$), immediate verbal memory (t [1, 35] = 3.47, $p < .01$), secondary verbal memory (t [1, 35] = 2.67, $p < .05$), and WCST total errors (t [1, 35] = -3.12, $p < .01$). There were significant group differences for some of the SFS subscales: SFS Recreation (t [1, 35] = 3.91, $p < .01$), SFS Independence Competence (t [1, 35] = 2.01, $p < .05$), SFS Occupation/Employment (t [1, 35] = 3.16, $p < .01$), SFS Scaled Summary Score (t [1, 35] = 3.38, $p < .01$) with patients demonstrating poorer social functioning than controls.

Correlations

Correlations between neurocognitive measures and community social functioning among schizophrenia patients were generally in the unexpected direction. Immediate verbal memory was negatively correlated with the SFS Scaled Summary Score (r = -.54, $p < .05$), suggesting that poor verbal memory was related to better overall social functioning among patients. In addition, negative correlations were observed between Immediate Verbal Memory (IVM) and Social Engagement/Withdrawal (r = -.45, $p <$ .05), IVM and Recreation (r = -.54, $p < .05$), Secondary Verbal Memory (SVM) and Independence Performance (r = -.47, $p < .05$), and SVM and Independence Competence (r = -.47, $p < .05$). A positive correlation was observed between WCST Total Errors and Interpersonal Communication (r = .45, $p < .05$), indicating that increased errors on the WCST are related to better interpersonal communication (see Table 7). These results are

surprising and inconsistent with hypotheses as well as with a large of body of research supporting the relationship between poor neurocognition and poor social functioning among schizophrenia patients. In order to more closely examine these unexpected correlations, a scatterplot illustrating the correlation between the SFS Scaled Summary Score and IVM is displayed in Figure 6. This figure illustrates that there is an outlier who received the highest on IVM and the lowest score on the SFS. With the removal of this outlier, the correlation was still negative, though nonsignificant (r = -.37, p = .12). In addition, the removal of this same outlier influenced the relationship between IVM and SFS Social Engagement/Withdrawal (r = -.32, p = .19) and SVM and SFS Independence Competence (r = -.26, p = .27); however, even with the removal of this outlier, correlations remained negative.

Given the unexpected correlations between neurocognitive variables (i.e., immediate verbal memory, secondary verbal memory, WCST total errors) and social functioning (i.e., scaled scores on the SFS) among patients, these correlations were calculated among control participants. Examining correlations among controls could assist with determining whether the choice of measures in this study was problematic or if correlations among patients are spurious. In contrast to the patient sample, these correlations appeared to be in the expected direction and indicated that better cognitive functioning is related to better social functioning. As shown in Table 8, Immediate Verbal Memory was positively correlated with SFS Independence/Performance (r = .72, p < .01), SFS Recreation (r = .64, p < .01), SFS Independence Competence (r = .49, p < .05), SFS Occupation/Employment (r = .58, p < .05), and SFS Scaled Summary Score (r = .70, p < .01). Secondary Verbal Memory correlated with SFS Independence

Performance (r = .50, p < .05), SFS Occupation/Employment (r = .62, p < .01), and SFS Scaled Summary Score (r = .54, p < .05). Finally, WCST Total Error was negatively correlated with SFS Occupation/Employment (r = -.64, p < .01). As with patients, a scatterplot illustrating the correlation between the SFS Scaled Summary Score and IVM among controls is presented in Figure 7. However, contrary to findings in patients, this plot demonstrates the positive correlation between these variables. These analyses provide support for the existence of meaningful, reliable positive correlations between neurocognitive and social functioning among the measures selected in this study.

Mediation

Although a regression analysis examining the mediation of social cognition between neurocognition and social functioning was discussed as one of the main hypotheses of the study, this analysis was not conducted on these data due to the nonsignificant correlations between the variables to be entered into the model: neurocognition, social cognition, and social functioning. Secondary Verbal Memory (SVM) and WCST Total Errors were combined to create a neurocognitive composite score that would have served as the first step in the model. SVM and executive functioning were chosen as the variables for this model because these have been demonstrated to be most strongly correlated with community social functioning (Green, 1996, 2000; Reichenberg & Harvey, 2007). The correlations between this composite score and the SFS Summary Scaled Score and the composite score and ToM Total Score (e.g., the "mediator") were examined as required preliminary steps before conducting a test of mediation (Baron & Kenny, 1986). These correlations were nonsignificant among patients (composite and SFS, r = -.14, p = .26; composite and ToM, r = -.21, p = .38) and

controls (composite and SFS, $r = .28$, $p = .26$; composite and ToM, $r = .01$, $p = .97$). In addition, the low sample size would make the interpretation of a regression analysis extremely difficult. This regression analysis was intended to replicate the work and Brekke and colleagues (2005); however, in the Brekke study, the regression was conducted on data from 139 participants at baseline and on 100 of those same participants at a 12-month follow up. For the present study, it was concluded that the low sample size and lack of correlations among the variables in the model would render this analysis uninterpretable and thus, was not conducted.

Exploratory Analyses

One surprising result of this study was that there were no differences between patients and controls on brain activity during error trials in the observation condition. Since the observation condition always occurred after the execution condition, participants could have become fatigued by that time in the experiment. Such fatigue could have increased reliance on trial-by-trial feedback rather than focusing attention on the confederate's response as instructed. The possibility that participants could have increased their attention to the feedback during the observation condition is explored by examining the feedback ERN. In addition, the metacognitive variables provided by this version of the WCST are examined and correlations between metacognition and social cognition and social functioning are explored. Metacognition has been conceptualized as uniquely contributing to the variance in social functioning, just as social cognition/ToM has been described (Koren et al., 2006). In this way, metacognition is characterized as a parallel process to the concept of social cognition. These variables could add to our understanding of such mediation processes given the limitations of the social cognition

measure utilized in this study (i.e., assessment of only one domain of social cognition, limited reliability/validity). Correlations between the metacognitive variables, the ToM task, and the SFS will be described.

Feedback-Related Negativity

The feedback ERN (fERN) refers to an increase in negative activity that occurs up to 250 ms following negative, but not positive, feedback about task performance (Holroyd & Coles, 2002; Luu et al., 2003; Nieuwenhuis, Yeung, Holroyd, Schurger, & Cohen, 2004). Although not a primary study aim, the fERN was examined since feedback was provided following each response on the flanker task. Participants may have simply attended to feedback during the observation condition, rather than the confederate's response, in order to provide accurate error counts. Previous studies of the observation ERN did not include feedback as part of their experimental task (van Schie et al., 2004; Bates et al., 2005). Therefore, examining feedback-negativity is informative for characterizing task demands that could have influenced psychophysiological activity during observation.

The procedures for data processing and identification of the error-related feedback negativity were comparable to the ERN procedures described above for the response-locked ERN (i.e., epoching, filtering, baseline-correction, and averaging). Group averaged waveforms were created from individual averages (see Figure 5). As shown in this figure, among controls in the execution condition, there was a long increase in activity beginning approximately 50 ms preceding error feedback and continuing until 100 ms after the onset of feedback. This activity in controls appeared to be maximal at 25 ms after the feedback. Activity during correct trials and among schizophrenia patients

during execution appeared relatively flat. It is of particular interest for the present study that controls demonstrated a noticeable increase in activity for error trials, peaking at 80 ms following feedback, in the observation condition. Schizophrenia patients had a small increase in activity during error trials at approximately 160 ms following the feedback during observation. In addition, as shown in the topographical maps in Figure 5, activity among controls during observation error trials was maximally distributed in frontal and central regions. This is in contrast to mapping of fERN activity among patients and even among controls in the execution condition in which activity is parietally-distributed. Maximal activity at fronto-central regions of the scalp supports the notion that this ERP truly reflects fERN activity, given that many prior studies indicate that ERN activity is generated from the anterior cingulate cortex (e.g., Holroyd & Coles, 2002). This further supports the notion that controls, in particular, may have increased their attention to feedback during the observation condition as a strategy for correctly identifying errors. It should be noted that all activity following feedback during observation is quite small in amplitude. However, it does appear that, descriptively, the feedback negativity is more apparent among control participants than patients and that this activity is specifically heightened among controls during the observation condition, suggesting that perhaps controls adopted a strategy of attending to the feedback rather than the response during this task.

These data were analyzed by identifying the maximal negativity following the feedback during the execution (0-150 ms search window) and observation (0-250 ms search window) conditions. Then the average amplitude in a 50 ms window surrounding this peak was calculated as an area report. These procedures were similar to the ERN area

report procedures described above. Next, these values were analyzed with an omnibus, mixed model 2 (group) x 2 (accuracy) x 2 (condition) ANOVA to test main effects and interactions. The main effects of condition (F [1, 35] = 7.28, $p < .05$ $\eta^2_p = .17$) and accuracy (F [1, 35] = 19.58, $p < .01$; $\eta^2_p = .36$) were significant. The group x condition x accuracy interaction (F [1, 35] = 2.164, $p = .15$; $\eta^2_p = .06$) and the main effect of group were nonsignificant (F [1, 35] = 1.04, $p = .32$; $\eta^2_p = .03$). No significant two-way interactions emerged. Examination of the means indicated that the feedback ERN was larger during the execution than the observation condition and larger following error than correct trials across all participants.

Wisconsin Card Sorting Task - Metacognitive Variables

The WCST Metacognitive Version provides standard WCST scores as well as variables that reflect the metacognitive processes of monitoring and control. The following analyses focused on the meta-cognitive variables from this task as they have been suggested to reflect intermediate cognitive processes between neurocognition and social functioning, much like social cognition (Koren et al., 2006). The magnitude of correlations between the WCST meta-cognitive variables and social cognition and social functioning measures were examined in order to determine whether these variables add to the conceptualization of mediational processes (e.g., social cognition). The meta-cognitive variables fall into two categories: Free Response and Monitoring/Control. These categories contain the following variables: 1) Free Response: Total Volunteered Sorts (total number of responses that were volunteered by the participant to be included in a "final score"), Total Correct Volunteered Sorts, Accuracy Score (Total Correct Volunteered Sorts divided by Total Volunteered Sorts), Free Choice Improvement

(Accuracy Score minus Quantity Score), 2) Monitoring/Control: Global Monitoring (Total Correct minus Total Volunteered Sorts), Monitoring Resolution (the extent to which confidence judgments distinguished between correct and incorrect responses, computed as the confidence in correctness of a given response multiplied by the actual correctness of the response), and Control Sensitivity (the degree to which the control process was dependent on monitoring computed as the confidence in correctness of a given response multiplied by the actual decision to volunteer a given response).

Correlations were computed between these WCST and metacognitive variables and summary scores of social cognition (ToM Total Score) and social functioning (SFS Scaled Summary Score) in all participants and are shown in Table 9. There were many significant correlations between WCST metacognitive variables and social cognition and social functioning scores. ToM Total Score was significantly correlated with Total Correct Volunteered Sorts ($r = .54$, $p < .01$), Accuracy Score ($r = .54$, $p < .01$), and Global Monitoring ($r = -.44$, $p < .01$). These results are generally in the expected direction and suggest that greater ToM scores was correlated with more correct volunteered sorts and a greater proportion of correct volunteered responses. One unexpected correlation was the negative correlation with Global Monitoring, which suggests that greater ToM scores were associated with poorer global monitoring (i.e., getting a smaller number correct given the number of volunteered sorts). A few significant correlations between these WCST variables and the SFS emerged. The SFS Scaled Summary Score was significantly correlated with Total Correct Volunteered Sorts ($r = .32$, $p < .05$), and Control Sensitivity ($r = .47$, $p < .05$). These correlations suggest that better social functioning as measured by the SFS is correlated with more correct

volunteered sorts and greater control sensitivity (i.e., greater dependence of control on monitoring among those with good social functioning).

CHAPTER 5: DISCUSSION

The purpose of this study was to investigate the social and functional significance of an ERP component related to error detection and conflict monitoring, the error-related negativity (ERN). In particular, this study examined "mirror neuron" qualities of this component through an observation paradigm in which participants were asked to observe a confederate perform errors while their EEG was recorded. This research was specifically focused on ERN activity in individuals with schizophrenia, as prior work indicates that ERN amplitude during flanker task performance is reduced and social impairment is profound in this group. Additionally, schizophrenia patients have been shown to have deficits in theory of mind (ToM), a component of social cognition that involves taking another person's perspective and has been suggested to mediate the relationship between neurocognition and social functioning. Could psychophysiological activity during an observation paradigm reflect social cognitive processes involved in perspective-taking? In addition, could this relationship be identified in schizophrenia and related to behavioral-level social functioning deficits? The four specific aims of this research were to: 1) replicate prior studies demonstrating reduced ERN amplitude in individuals with schizophrenia and utilize an observation paradigm to examine the presence of observation ERN activity among schizophrenia patients and controls, 2) determine whether the pattern of activity occurring during error observation is functionally distinct from an ERP reflecting motor processes and preparation for responding, the LRP, 3) examine correlations between ERN activity, social cognition, social functioning, and psychiatric symptoms, 4) replicate the relationship between specific neurocognitive measures (i.e., immediate and secondary verbal memory, card

sorting) and community social functioning as well as determine whether social cognition mediates the relationship between neurocognition and social functioning. Results, theoretical issues, study limitations, remaining questions, and future directions related to these aims will be discussed below.

Demographics, Clinical Characteristics, and Behavioral Data

The present study is characterized by an older, male, and African-American sample. While the groups were effectively matched with respect to demographic characteristics, it will be useful for future studies to investigate the observation ERN and its relationship to social functioning among a more diverse participant sample.

All of the schizophrenia patients who were enrolled in this study were on antipsychotic medication and 75% were also taking mood/anxiety medication. Almost all were on medication and may continue to remain on antipsychotics for much of their lives. Medication use in schizophrenia is an empirically-supported practice and treatment of acute psychosis with medication is an ethical responsibility for clinicians (Janicak, 2006). However, medications can significantly impact cognitive functioning with some studies noting improved cognitive functioning following administration of neuroleptic medication (Spohn & Strauss, 1989), and others indicating that anticholinergic medication produced drug-induced memory impairments that can be indistinguishable from memory deficits thought to be a fundamental aspect of schizophrenia (e.g., Blanchard & Neale, 1992). Thus, medication could artificially alter true group differences in cognitive functioning. A common approach for addressing medication effects has been to "standardize" the measurement of medication status by converting drug dose to chlorpromazine unit equivalents. There are some problems with this strategy – various

medications are not necessarily equated on all dimensions (i.e., impact on various neurotransmitter systems; Spohn, 1973) and the degree of pathology likely determined the dose level. Some investigators have sought to address these problems by covarying the effects of the drug statistically. This has been widely regarded as a misuse of the analysis of covariance (e.g., Lord, 1967, 1969). One alternative to using chlorpromazine equivalents or statistical covariation is to examine cognition functioning in a medication-free sample. However, there are also many methodological problems inherent in the use of this type of sample (e.g., low generalizability, symptoms of the illness may impede ability to tolerate testing). It has been suggested that simply reporting patient's medication type and dosage level is sufficient for the advancement of scientific understanding of the disease process in schizophrenia (Spohn, 1973, Blanchard & Neale, 1992). This was the approach the current study took for addressing the difficult issue of medication on cognitive performance. It is not surprising that all of the schizophrenia patients in this study were stabilized on antipsychotic medication. It is more surprising, however, that 75% of the patient sample was taking a medication for either mood or anxiety symptoms. Future studies will need to address the impact that mood/anxiety medications have on psychophysiological and cognitive factors beyond the effects of antipsychotic medication in schizophrenia patients.

The behavioral data from the flanker task indicated that patients and controls had comparable levels of accuracy across flanker trial types. Lower accuracy and slower response times (i.e., more participant responses recorded as "too slow") during interference trials and greater accuracy and better response time (i.e., fewer responses recorded as "too slow") during facilitation trials was observed. These behavioral results

are consistent with previous research indicating that interference trials increased the level of response competition in ERN studies (Coles, Gratton, Bashore, Eriksen, & Donchin, 1985; Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999). Group comparisons on flanker trial type indicated that schizophrenia patients were significantly less accurate than controls on all flanker types. Yet, there were no significant group differences with respect to response time. This is not surprising given the restriction in range that was imposed by nature of the flanker task. Accuracy of error counts during observation were analyzed and as expected, schizophrenia patients performed significantly worse than controls.

Error-Related Negativity

Execution

Visual inspection as well as statistical analyses indicated the presence of a robust ERN in control participants during execution of the Flanker task. As hypothesized, an ERN was apparent for schizophrenia patients, but was reduced in amplitude compared to control subjects. The magnitude of this group difference is further illustrated by the difference in the effect sizes for accuracy between the groups, with controls demonstrating a medium effect size (controls $\eta^2_p = .68$) and patients demonstrating a small effect size ($\eta^2_p = .38$). These findings are consistent with a large body of research revealing a reduction in ERN amplitude in schizophrenia patients compared to controls on a variety of experimental tasks (Alain et al., 2002; Mathalon et al., 2002; Bates, et al., 2002) and on the flanker task in particular (Kopp & Rist, 1999; Morris et al., 2006).

The predominant theoretical explanations of the ERN would suggest that, based on the current data, schizophrenia patients could have a deficit in either detecting errors

(Coles et al., 1998; Falkenstein et al., 1991, 2000; Nieuwenhuis et al., 2001; Scheffers et al., 1996), monitoring response conflict (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Carter et al., 1998), or using feedback to guide future responses and reducing undesirable outcomes, also known as the reward prediction theory (Holroyd & Coles, 2002). Recently, a new theory has expanded on the reward prediction theory and articulates that a larger ERN would be observed following a more sizable discrepancy between expected and actual outcome, regardless of valence of feedback (Oliveira, McDonald, & Goodman, 2007). More specifically, this theory suggests that the amplitude of the ERN is fundamentally connected with expectancy. In their study, Oliveira and colleagues (2007) reported an enhanced ERN following unexpected positive and negative feedback, but little to no ERN activity following expected positive and negative feedback. They proposed that the ACC acts as part of a generalized performance monitoring system activated by violations in expectancy (Oliveira, et al., 2007). Therefore, previous findings of increased ERN amplitude following solely negative rather than positive feedback (Holroyd & Coles, 2002; Yeung et al., 2004) could simply reflect a bias among non-psychiatric participants to expect rewards regardless of whether rewards or penalties are more or less likely for a given task. It is likely that individuals with schizophrenia have more negative learning histories and more punishing social environments than controls which could lead patients to have lower expectancies for positive feedback, resulting in reductions in ERN amplitude. Alternatively, and more relevant to the flanker task, it could be that committing more errors (patients committed more errors across all flanker stimulus types) reduced the salience or novelty of an

incorrect response, which could have increased the expectancy, and therefore likelihood of future errors.

Coles and colleagues (2001) proposed that the representation of the appropriate response depends critically on the perception of stimulus information and of correct stimulus-response mapping. Perhaps individuals with schizophrenia misperceived the stimulus, forgot response mapping rules, or applied them incorrectly as evidenced by the reduction in ERN amplitude among schizophrenia patients compared to controls. Although working memory was not directly assessed in the current study, it is unlikely that the presence of working memory deficits in patients was driving the reduction in ERN amplitude. The flanker task is a very simple task that elicits nearly automatic responding and does not require complex rules to be held in short or long-term memory. Furthermore, impairment in memory or difficulty maintaining a working representation of the correct response has been found to be unrelated to ERN activity. In other words, elicitation of an ERN has been shown to be dependent on knowing the correct response, but failing to execute the correct response (Dehaene, Posner, & Tucker, 1994), known as a "slip" rather than a "mistake" or an inaccurate intention resulting from faulty knowledge (Reason, 1990, as cited in Dehaene et al., 1994). Other factors contributing to response "slippage," such as problems in perception, motor coordination, or working memory, were not examined in the present study, but warrant consideration in future research.

Observation

The observation condition was the primary experimental manipulation in this study and was intended to replicate prior work demonstrating an observation ERN among

non-ill participants (van Schie et al., 2004; Bates et al., 2005; Miltner et al., 2005) as well as to explore the existence of this component among schizophrenia patients. ERN findings in this condition are mixed. Based on visual inspection of group averaged waveforms, no clear ERN component was apparent. In fact, it seemed that an event-related potential that approximated an ERN was more evident among patients than controls. This was also indicated by topographical scalp mapping showing negativity at fronto-central regions of the cortex. In addition to visual inspection, data were quantified by identifying individual peak minimums in the post-error data and scoring the amplitude within a 50 ms window surrounding this peak in both error and correct trials. These values were used for statistical analyses. Consistent with a lack of an apparent ERN, no significant differences between patients and controls on ERN activity during observation were observed. However, a significant effect of accuracy emerged, with more negativity following error than correct responses among all participants. This finding is promising and although the effect size is small ($\eta^2_p = .19$), it does not appear that this manipulation failed to elicit error-related brain activity across the board. Differentiation between activity during error and correct trials provides tentative support for the validity of this paradigm. However, given the lack of a robust ERN in controls and no significant group differences in activity, additional considerations of these data are warranted.

Several methodological constraints may have affected ERN activity during observation and contributed to null group differences. The flanker task used in this study was long (1 – 1.5 hours) and repetitive, which could have induced boredom and fatigue in some participants, particularly among control subjects. Mental fatigue has been suggested to be specifically related to deficits in action monitoring (Boksem, Meijman, & Lorist,

2006) and motivation and attention have been found to be essential for observing a robust ERN (Gehring et al., 1993; Gehring & Knight, 2000; Tucker et al., 1999; Dikman & Allen, 2000; Luu et al., 2000). Mental fatigue could be viewed as an effort-reward imbalance; when perceived effort becomes greater than the reward, motivation will dissipate (Tops et al., 2004). Perhaps controls in this study were particularly vulnerable to this effort-reward imbalance; they may have perceived the small financial rewards (i.e., + 2 cents per correct trial) to be too little when compared with required mental effort. In addition, the flanker task used in the present study was lengthy in order to provide sufficient opportunities for each participant to commit enough errors so that meaningful individual averages could be calculated. It is likely that some of these errors were produced as a result of mental fatigue or reduced motivation. By the time participants began the observation condition, increased fatigue could have lead to a reduction in ERN amplitude in this condition among controls, thereby contributing to null group differences. However, it should be noted that the length of the flanker task during execution was comparable to that in prior studies reporting robust ERNs (Kopp & Rist, 1999; Kopp, et al., 1994; Jones, et al., 1991; Morris et al., 2006). Additionally, it is possible that practice or habituation effects during execution could have reduced ERN amplitude in the observation condition. The decision not to counterbalance the execution and observation conditions was made following consultation with Dr. van Schie (personal communication, 3/23/2007) who expressed that the chance of finding an ERN during the observation condition would be higher after subjects had extensive familiarity with the task by doing it themselves. All prior ERN studies required subjects to execute a task before observing a confederate perform the task. Utilizing procedures that were as similar

as possible to prior error observation studies was believed to be of particular importance for enhancing comparisons with prior work, especially since this was the first study to examine observation activity among a clinical population. However, this raises the question, is direct experience with a specific task necessary for observation or "mirror" activity to occur? This would be a worthwhile avenue for future research and could easily be examined by varying the order of execution and observation conditions.

Another factor that could have reduced overall observation ERN activity and contributed to null group differences has to do with the passive nature of the flanker task. It is noteworthy that empathic reactions typically emerge in a dyadic social interaction in which the emotions of one member of the dyad directly influence the other member (Shulte-Ruther, Markowitsch, Shah, Fink, & Piefke, 2008). Empathy has been defined as a process by which *emotional* inference are made about another's mental state (Schulte-Ruther, Markowitsch, Fink, & Piefke, 2007). Empathy and theory of mind have both been described as involving perspective-taking abilities and have been shown to activate overlapping regions of the brain (Hooker, Verosky, Germine, Knight, & D'Esposito, 2008); thus they can be viewed as very similar processes. Perhaps the use of the flanker task in the observation condition was not interactive enough for participants to feel "invested" in the responses, rewards, and punishments of the confederate. It could be argued that this task was more passive than other tasks that have been used in psychophysiological and neuroanatomical studies of mirror neuron properties related to social cognition processes (Shulte-Ruther et al., 2008; Knutson, McClellan, & Grafman, 2008). Such studies have utilized emotional attribution tasks that involve interpreting facial expressions or hand gestures that are likely more salient and interactive than the

flanker task. Perhaps control participants were more sensitive to this effect since these mental and emotional capacities are believed to be more preserved in controls. On the other hand, previous studies which found an identifiable observation ERN among non-psychiatric participants have relied on the flanker task during observation (van Schie et al., 2004; Miltner et al., 2005).

It is well-established that schizophrenia is characterized by a heterogeneous symptom presentation and comorbid psychiatric conditions, including depression, anxiety, or Axis II disorders (Craddock et al., 2007; Buchanan & Carpenter, 1994; Houlihan, 1977). Seventy-five percent of schizophrenia patients included in this sample were on medication for mood/anxiety symptoms. It could be that comorbid psychiatric symptoms influenced psychophysiological activity, which could have impacted ERN activity during observation among patients. Anxiety, and perhaps depression, has been demonstrated to be related to increased ERN amplitude compared with controls (Gehring et al., 2000; Moser et al., 2005; Chiu & Deldin, 2007). Perhaps the presence of anxiety and depression symptoms in the current patient sample served to enhance observation ERN activity which could have contributed to the null group differences in this condition. This study did not explicitly rule out comorbid anxiety and depression symptoms. Based on visual inspection of the group averaged waveforms in the observation condition, it appeared that patient's activity more closely approximated an observation ERN than controls. Six patients in this study had a diagnosis of Schizoaffective Disorder and four patients with a diagnosis of Schizophrenia reported having a history of a Major Depressive Episode. Three patients had a diagnosable anxiety disorder according to chart review. However, it is unlikely that the null group differences in the observation

condition are the result of the influence of anxiety and depression among the patient group. If comorbid anxiety/depression symptoms were magnifying the ERN in the patient group, this would be expected to be observed more dramatically during execution of the flanker task than during observation. ERN amplitude was substantially reduced among patients compared to controls during execution. Furthermore, the correlation between observation ERN activity and the Anxious Depression subscale of the BPRS in patients was nonsignificant (r = -.04). Thus, despite the presence of anxiety and depression in the patient sample, it is unlikely that these symptoms contributed directly to a lack of group differences in the observation ERN. However, it will be useful for future investigations to more closely examine the presence of current anxiety and depression symptoms by ruling out subjects with comorbid disorders from the schizophrenia group and including a psychiatric control group.

There were some notable differences between the present study and previous observation ERN research that make direct comparisons tenuous. Such differences could have served to attenuate ERN amplitude during observation for both patients and controls in the present study, which could have contributed to a lack of an identifiable ERN component in this condition. The most apparent difference and the one that has the most relevance for ERN amplitude is that of age differences. Participants in prior observation ERN studies ranged in age from 19-34 years (van Schie et al., 2004), 18-27 years (Bates et al. 2005), or had an average age of 23 years (Milter et al., 2005). In contrast, control participants in the present study ranged in age from 22-55 years with 52.9% of this group between 50-55 years of age. The schizophrenia group ranged in age from 23-55 years with 50% of the sample between 48-55 years of age. ERN amplitude, as well as the

amplitude of other ERP components (e.g., P300; Yamaguchi & Knight, 1991), has been shown to be reduced in older individuals (Mathewson, Dywan, & Segalowitz, 2005). Having an older sample could have served to further reduce ERN amplitude during observation, a condition in which the ERN is already attenuated compared to execution tasks among healthy subjects (e.g., van Schie et al., 2004).

Another difference between this study and prior research on the observation ERN is that prior studies did not provide feedback following each trial. Van Schie et al. (2004) provided feedback regarding average response time and number of errors following each block rather than each trial. Participants in Bates et al. (2005) received negative feedback only if responses were too slow. In this case, errors were defined as responses which occurred after a pre-determined response time cut-off (450 ms). Miltner and colleagues (2005) did not provide feedback to participants regarding performance following trials or blocks. It is possible that subjects in the current study could have simply relied on feedback during the observation condition rather than attending the confederate's response. Therefore, the feedback ERN was examined. These analyses indicated that the feedback ERN was larger during execution than observation and that it was larger following error than correct trials. However, there were no significant interactions or group effects. Thus, it is possible that providing feedback following each trial increased reliance on the feedback rather than the confederate's response during observation for both patients and controls. This could have contributed to a reduction in the amplitude of the response-locked ERN for both participant groups.

Lateralized Readiness Potential

The lateralized readiness potential (LRP) was examined in order to compare activity related to error processing, originating in the ACC, with activity reflecting response preparation, originating in the motor cortex. Our hypothesis was simply that LRP activity would show a differential pattern of activation compared to the ERN, specifically in the observation condition. For the LRP, there was a significant effect of condition with a medium effect size, indicating that LRP activity was substantially greater during execution compared with observation. This is consistent with a prior study which reported an overall reduction in LRP amplitude during observation (van Schie et al., 2004). Notably, LRP activity in the current study was comparable between patients and controls and between error and correct trials during execution. This contrasts with previous work which has shown that the LRP was reduced in amplitude on error compared to correct trials in normal participants (Mathalon et al., 2002; van Schie et al. 2004). It has been suggested that a reduction in the LRP during error trials reflects greater response hand equivocation during error commission. This is in contrast to correct responses in which participants experience less uncertainty, or less response conflict, about their response choice (Mathalon et al., 2002). The lack of accuracy effects in the current data seem to reflect similar modes of response preparation for both correct and error trials, indicating that participants experienced comparable levels of equivocation regarding both types of response choices. These findings are unexpected given that prior studies reporting accuracy effects of the LRP utilized the flanker task (van Schie et al., 2004). However, Mathalon and colleagues (2002), using a picture-word verification task, demonstrated that among individuals with schizophrenia there was no significant

differentiation between LRP activity on correct and error trials. Our data in the schizophrenia group are consistent with these findings, suggesting that patients demonstrated comparable levels of response ambiguity for both error and correct responses.

In the observation condition, there were no significant group or accuracy effects of LRP activity. Visual inspection of the group averaged waveforms suggests the presence of some differentiation between error and correct responses among controls compared to patients; however, the activity is very small in amplitude (less than 2 microvolts). These findings are in contrast to a prior report demonstrating significant differentiation between error and correct activity during observation, with a larger LRP following correct responses and a diminished LRP following errors (van Schie et al., 2004). They are also inconsistent with the only mirror neuron study in schizophrenia to date examining motor cortex activation during observation using transcranial magnetic stimulation (TMS). This study reported reduced motor facilitation during action observation in schizophrenia patient compared to controls, despite preserved cortical excitability (Enticott et al., 2008). These authors conceptualized the mirror neuron system as coding for the intention of behavior, much like the LRP has been theorized to reflect response readiness. Diminished effects of LRP activity in the observation could be due to increased attention to feedback in this condition, as discussed above. If participants were not attending to the confederate's response (i.e., motor movements), then it would be expected that activity originating from brain areas devoted to processing response preparation would be reduced. This lack of group differences could reflect problems with the observation task noted above (i.e., administration of individual trial feedback, mental

fatigue, low motivation) and/or low power due to a small sample size. It could be the case that with the inclusion of additional participants and modifications to the observation task, that evidence for mirrored activity in the motor cortex regions as measured by the LRP could be observed.

Social Cognition

A measure of theory of mind (ToM) was included as a measure of social cognition since there is a theoretical link between the interpretation of other's mental states and brain activity generated by the observation of other's behavior. Theory of mind was examined through correlations between ToM and ERN activity and group differences on ToM. Lastly, regression analyses examining the mediation of ToM between neurocognition and social functioning were conducted and will be described with neurocognitive findings.

First, correlations between ToM and execution and observation ERN activity were examined separately by group and no significant correlations emerged from these analyses. However, when the groups were combined in order to increase the sample size as well the range, both ToM Total Score and ToM False Beliefs were negatively correlated with ERN activity in the execution condition (better ToM was correlated with a larger ERN). This effect seemed to be largely driven by control subjects who demonstrated correlations with medium effect sizes, yet these correlations for control subjects alone did not reach significance due to the reduced sample size. Contrary to this study's hypothesis that ToM would be related to observation ERN activity, these results indicated that better ToM skills were related to a larger ERN during execution only. However, this is not entirely surprising given the lack of a clear observation ERN.

The present study is the first time that the relationship between social cognition and the ERN has been systematically examined; therefore, the significant correlations between ToM and ERN activity during execution warrant further consideration. However, the small sample size of the present study should be taken into account when considering any significant correlations among the behavioral measures (i.e., neurocognition, social cognition, social functioning). A reduction in sample size and reduction in power (i.e., ability to detect Type II errors) in the data can significantly impact correlational analyses by minimizing the presence of meaningful relationships or leading to spurious correlations that would not otherwise be observed with the addition of more subjects. Therefore, correlations should be interpreted with caution and considered as preliminary evidence for such relationships warranting further testing with a larger sample size.

The relationship between error execution and ToM is not necessarily obvious and it could be easy to assume that these correlations simply reflect generally intact cognitive abilities among controls. Alternatively, it could be the case that the processing, identifying, and responding to self-made errors on a simple task such as the flanker, reflects some of the same problems-solving and perception abilities that are measured by the ToM task. Perhaps what is most relevant for having a strong ToM is being able to react and respond to one's own errors effectively.

Research differentiating ToM from embodied simulation as divergent processes for conceptualizing other's actions, intentions, and emotions has relevance for interpreting the absence of a correlation between ToM and observation ERN activity. ToM has been defined as the process of holding a "theory" about another person's mental

contents as individuated and separate from the observer (Dennett, 1987). Some have argued that this position implies that ToM reflects a uniquely human cognitive capacity that comes online only after earlier language, motor, and perceptual abilities are established (Baron-Cohen, Leslie, & Frith, 1985). Further, ToM has been suggested to be distinct from other forms of social cognition that rely on immediate perceptual judgments and are seen early in development (i.e., facial emotion recognition, social perception; Kerr, 2008). This view of ToM is contrasted with the concept of Embodied Simulation (ES), which hypothesizes that humans perceive another's state of mind by simulating his/her actions, emotions, and goals in the "mirror neuron system" of the brain (Kerr, 2008). Embodied Simulation holds that knowledge of the mental states of others is "direct," "automatic," and the result of perceptual, rather than cognitive acts that come "on-line" in early infancy and are also seen in other primates (Barret & Henzi, 2005; Csibra, 2007). Kerr (2008) proposes that perhaps ToM and ES are two parallel processes that underlie distinct components of intersubjectivity. It could be the case that the proposed relationship in the present study between ToM and error observation activity does not fully capture the cognitive complexity inherent in ToM processing. If ToM is conceptualized as a deliberate, effortful series of complex human-specific cognitive processes, then the links with mirror neuron theories seem less compelling. Yet, the temporo-parietal junction, an area which has been identified as specifically activated during ToM functions, has also been shown to be activated during tasks requiring automatic, perceptual processing (i.e., attention orienting; Mitchell, 2008). The activation of a common brain region for these two seemingly divergent processes suggests that both cognitive and perceptual processes are involved in the inference of other's mental states

and that perhaps humans utilize these two systems fluidly and flexibly (Kerr, 2008). More work is needed before ToM, as well as other aspects of social cognition, and mirror neuron activity can be specifically and more meaningfully related. This study represents a starting point for beginning to integrate these concepts into psychophysiological research on clinical populations characterized by deficits in the social and cognitive processes under investigation.

There were significant group differences on both ToM Total Score and ToM False Beliefs, with the schizophrenia group performing more poorly on these measures than controls. These findings are consistent with a large body of research which suggests that individuals with schizophrenia have trait deficits in ToM compared with controls (for reviews see Bora, Yucel, & Pantelis, 2009; Brüne, 2005; Harrington et al., 2005). Although some factors can influence ToM impairment in schizophrenia (i.e., symptoms, intellectual functioning), nearly all published studies report ToM impairment in schizophrenia and meta-analyses report large effect sizes (Bora et al., 2009; Brune, 2005; Harrington et al., 2005).

Social Functioning

Social functioning was measured by the Social Functioning Scale (SFS; Birchwood et al., 1990), a self-report measure that was developed for use specifically with a schizophrenia population to overcome some of the limitations of applying standard social functioning measures to this population (i.e., relevance of functioning categories, floor effects). First, differences between schizophrenia patients and controls on the SFS were examined. Results indicated that individuals with schizophrenia reported poorer overall social functioning, recreation, independence/competence, and

occupation/employment functioning than controls. These group differences are consistent with a large body of evidence that documents marked, broad social impairment in schizophrenia compared with non-ill individuals (Mueser & Bellack, 1998; Mueser & Tarrier, 1998; Morrison & Bellack, 1987; Mueser et al., 1990; Halford & Hayes, 1995; Bellack et al., 1990). This finding is also consistent with research reporting that schizophrenia patients have difficulty finding and maintaining employment (Chabungbam, Avasthi, & Sharan, 2007; Twamley, Narvaez, Becker, Bartels, & Jeste, 2008), living independently in the community (Silverstein et al., 2006; DeLuca, Moser, & Bond, 2008), and initiating and engaging in pleasurable activities (Horan et al., 2006; Gard, Kring, Gard, Horan, & Green, 2007).

Correlations between ERN activity and social functioning were conducted in order to investigate the relevance of the ERN for social functioning in the community. These correlations indicated that Occupation/Employment status was negatively correlated with execution ERN activity in both patients and controls. The direction of this relationship suggested that better occupational functioning was associated with a larger ERN during execution. An unexpected correlation emerged among control participants; interpersonal communication was positively correlated with observation ERN activity, indicating that better interpersonal communication was associated with a smaller ERN during observation. Since there was no evidence for a well-defined observation ERN among controls, significant correlations with activity in this condition should be interpreted with caution. However, the correlation between occupation/employment and the ERN during execution is promising given that the execution condition produced expected ERN activity in patients and controls. Although these correlations are

interesting in that there appears to be something specific about occupational functioning that seems related to the ERN, as previously stated, these correlations should be interpreted cautiously as they are limited by low power and a small sample size. The relationship between the ERN and specific aspects of social functioning, such as occupational functioning, in normal participants should be explored further in future studies to establish the validity of such a relationship.

Neurocognition

Neurocognitive tasks that assessed immediate verbal memory (IVM), secondary verbal memory (SVM), and executive functioning were included in this study to enhance the conceptualization of the social cognition task as well as to replicate previously observed relationships between these specific neurocognitive functions and community social functioning (Green, 1996; Green et al., 2000; Brekke et al., 2005). Group differences between patients and controls on these neurocognitive measures indicated that patients performed significantly worse than controls on all neurocognitive measures. These results are consistent with an accumulation of research supporting the specific impairment of verbal memory and executive functioning in schizophrenia patients compared with controls (Reichenberg & Harvey, 2007; Nuechterlein et al., 2004; Lee & Park, 2005; Niendam et al., 2003; Cannon et al., 2006).

Correlations were explored between neurocognitive variables and community social functioning, as measured by the SFS, in order to replicate the relationship between these specific measures described by Green and colleagues (1996; 2000). Analyses were conducted separately, first for the schizophrenia group and then for controls. Correlations in schizophrenia patients were in the opposite direction as expected – the better the

neurocognitive functioning, the worse the social functioning. Specifically, IVM was negatively correlated with overall social functioning, Social Engagement/Withdrawal, and Recreation. SVM was negatively correlated with Independence Performance and Independence Competence. A positive, and equally unexpected, correlation was observed between WCST total errors and Interpersonal Communication. These results are contrary to a large body of research showing that cognitive and social functioning are positively correlated among both schizophrenia patients and non-ill comparison subjects (Goldberg et al., 1990; Palmer et al., 1997; Elvavag & Goldberg, 2000; Kremen et al., 2000).

Correlations between these variables were examined in control subjects in order to examine whether these results were representative of the entire sample under investigation or whether they were specific to the schizophrenia group. Correlations in control subjects were in the expected direction – better neurocognitive scores were related to better social functioning. Specifically, IVM was positively correlated with overall social functioning, Independence Performance, Recreation, Independence Competence, and Occupation/Employment. SVM was positively correlated with SFS total, Independence Performance, and Occupation/Employment. WCST total error was negatively correlated with Occupation/Employment. The direction of these correlations is consistent with prior research discussed above.

The unexpected correlations in schizophrenia patients are intriguing, given that they are inconsistent with previous research (Green, 1996, 2000; Cohen et al., 2006). Clinical heterogeneity in the schizophrenia sample could have exerted some influence over these unexpected correlations. Schizophrenia is a heterogeneous disorder in terms of etiology (Cardno & Farmer, 1995), symptom presentation (Craddock et al., 2007;

Buchanan & Carpenter, 1994; Houlihan, 1977), and neuropsychological functioning (Gambini, Campana, Garghentini, & Scarone, 2003; Kremen et al., 2004). Neuropsychological functioning, in particular, in schizophrenia can range from near-normal to globally impaired, dementia-like performance (Seidman, 1983; Heinrichs & Zakzanis, 1998). Even with the small sample in the current study, heterogeneity is apparent in terms of clinical subtype and medication status. Thirty-five percent of the current sample was classified as "paranoid" subtype and 40% were identified as "undifferentiated." Additionally, medication data reveal that 75% of the patients in this sample were being treated with one or more mood/anxiety medication, indicating the presence of substantial comorbidity. Unfortunately, it is difficult to control for clinical variability and comorbidity in schizophrenia research, especially if the study is to retain external validity and meaningful generalizability. Clinical heterogeneity has a significant impact on even the largest studies and could lead to extensive variability between studies, ultimately hampering replication (Craddock et al., 2007). The discussion of heterogeneity is relevant for characterizing the unexpected correlations between neurocognition and social functioning within schizophrenia. However, given the limited scope of the present study these issues cannot be fully addressed within the scope of this research. Increased awareness and attempts to respond to the problem of heterogeneity in the larger scientific community will benefit future research in this area.

It has been suggested that during stable phases of schizophrenia, cognitive deficits may be more profound and ultimately more readily observable as acute psychotic symptoms remit (Bora et al., 2009). Schizophrenia participants in the current sample were required to be considered "clinically stable" by their mental health providers in

order to be included. It could be that patients in the current sample were functioning well in the community and more likely to be in remitted phases of the illness with fewer psychotic symptoms, thus enhancing ability to detect cognitive deficits. Alternatively, because patients in this sample are older, they could be more susceptible to disease sequelae (e.g., medication side effects, repeated hospitalizations) than younger individuals with schizophrenia, which could increase measurable cognitive deficits. Patients who have been ill for longer but who are also identified as "clinical stable" and functioning reasonably well in the community, have likely developed compensatory strategies to cope with cognitive dysfunction, thus increasing social effectiveness but remaining quite impaired on standard neuropsychological tests.

Alternatively, it could be the case that the neurocognitive tasks under investigation in the present study were actually more broad-based than specific indicators of cognitive functioning. It has been suggested that the Wisconsin Card Sorting Task captures variance from a variety of sources, including cognitive functions such as abstracting and rule-learning (Kéri, Kelemen, Benedek, & Janka, 2001; Perrine, 1993), working memory (Glahn et al., 2000; Gold et al., 1997), attention (Amos et al., 2000), and behavioral modulation (Koren et al., 1998; Li, 2004). As a result, the WCST may not reflect one unitary construct of cognitive functioning, but instead capture multiple, parallel cognitive processes (Koren et al., 1998). Some have argued that the WCST is more of a measure of general intellectual functioning rather that a measure of a meaningful subcategory of cognitive functioning (Greve, Stickle, Love, Bianchini, & Stanford, 2005). Therefore, the WCST may be tapping other cognitive processes other than what is typically considered to be "executive functioning," contributing to increased

variability in performance between patients and controls on this measure. Along these same lines, of the measure of verbal memory included in the present study could also be capturing other cognitive functions that contribute effective verbal memory. It could be the case that IVM reflects both short-term and long-term memory, rather than exclusively short-term memory functions. Furthermore, verbal memory and executive functioning may overlap in the cognitive processes that they recruit. For instance, it could be that executive functioning captures many of the same functions as verbal memory, in particular secondary, or delayed, verbal memory. If these measures are tapping multiple cognitive constructs, or overlapping in the cognitive processes that are presumed to be unique, then additional variability could have been introduced into the current data and contributed to unexpected correlations among patients.

Likewise, limitations of the social functioning measure, the Social Functioning Scale (SFS), could have contributed to unexpected correlations in schizophrenia patients. The SFS is a self-report inventory of community social functioning and while self-report measures have are low cost, require little staff time, and little staff training, there are also some disadvantages to the use of this assessment modality. There is some controversy regarding the validity of self-report methods for assessing social functioning in severely mentally ill (SMI) subjects, particularly those with psychosis (Atkinson, Zibin, & Chuang, 1997; Arfken, 1997; Rohland & Langbehn, 1997). It has been argued that SMI individuals may not be accurate reporters of their behaviors that are specific and historical, that cognitive impairment may make it difficult to understand abstract questions and make objective self-appraisals or judgments, and that emotional and symptom impairments may distort self-reports (Bellack et al., 2007; Morgando, Smith,

Lecrubier, & Widlöcher, 1991). Perhaps in the current study, schizophrenia participants over-estimated their social functioning, reporting it to be better than is actually the case. The integration of multiple data sources from multiple informants is generally considered to be a good practice for increasing internal validity. However, self-report is often required to collect information regarding subjective, internal experiences that even close others would not have access to (Awad, Voruganti, & Heslegrave, 1997). Methods for assessing social functioning other than self-report have been well-validated in the literature (i.e., social role-plays, experience-sampling method) and provide more naturalistic observations of social behavior and social competence than self-report (Bellack et al., 1990; Myin-Germeys, Nicolson, & Delespaul, 2001; Gard et al., 2007). Future studies would benefit from assessing social functioning via self-report as well as through an additional modality such as role-plays, informant reports, or experience-sampling methods. Further, the meta-analyses from Green and colleagues (1996, 2000), which these analyses attempted to replicate, stated that the measures of community functioning included in their meta-analyses were the most varied category of functional outcome included. Only two studies included in the 2000 meta-analysis utilized the SFS and there was a wide range of community functioning measures within other studies (i.e., Social Adjustment Scale; Quality of Life Scale, Global Adjustment Scale, etc.). Measurements of community functioning were based on self-report as well as from hospital charts and caregiver reports. Thus, future studies seeking to truly replicate these findings should examine community functioning from a variety of informant sources. Finally, these correlations were observed among a very small number of subjects. Future

studies should re-examine these relationships with more varied assessment approaches, as well as with larger sample sizes.

The metacognitive variables provided by this version of the WCST were explored since, similarly to social cognition, metacognition is hypothesized to represent a collection of intermediary cognitive processes (i.e., monitoring and control) between basic neurocognitive functioning and complex social behaviors (Koren et al., 2006). Scores on the ToM measure were significantly correlated with total volunteered sorts, accuracy, and global monitoring. Additionally, SFS total score was correlated with total volunteered sorts and control. Thus, it seems that social cognition may reflect monitoring processes whereas community social functioning may more likely involve control processes. These metacognition variables appear to be relevant to both social cognition and social functioning, particularly within schizophrenia. The may be useful for more specifically delineating the cognitive processes that link cognitive with social functioning, which could contribute to greater understanding of these deficits in schizophrenia. The similarities and differences between metacognition and social cognition and the relevance for functioning should be explored in future investigations.

Summary and Conclusions

In summary, some of the findings from the present study were consistent with prior research and study hypotheses, whereas some findings were surprising and unexpected. This study was quite novel in that it was the first investigation of observation ERN activity in schizophrenia and the first to examine the relationship between ERN activity and social cognition and social functioning. During execution, the robust ERN among controls and attenuated ERN among patients supports prior work and the

effectiveness of the flanker task to elicit ERN activity. During observation, no distinguishable ERN was observed among controls and there were no significant group differences. However, accuracy effects in the observation condition provided some preliminary support for the use of this paradigm and suggest that it did not completely fail to produce evidence for the "mirror" processing of other's errors. Some modifications to the observation task (e.g., refraining from providing trial-by-trial feedback, increasing motivation, task relevance and reducing boredom) and increased sample size may enhance the validity of this observation paradigm. Significant correlations between execution ERN activity and ToM and occupational/employment functioning in all participants suggested that error-related processing may be particularly relevant for specific types of functioning and this observation warrants further attention in future studies. Neurocognition was differentially correlated with social functioning between the two groups, with unexpected correlations emerging in the patient group. This could be due to a variety of influences such as heterogeneity, over-compensation for cognitive impairment, or the utility of socially-effective coping strategies given the older, more clinically stabilized sample. Neither neurocognition nor social cognition significantly contributed to the variance in social functioning in either patients or controls. In order to address the limitations of the current study, it will be most useful for future research to focus on refining the design of the observation paradigm, increasing sample size, increasing sample variability (e.g., race, sex, age), more carefully measuring and controlling for comorbidity among patients, and using a wider variety of empirically-validated social cognition and social functioning measures. Importantly, this study sought to logically integrate theories and research in mirror neurons, psychophysiology, and

cognitive and social functioning in schizophrenia in order to examine a proposed relationship between a biological marker and complex functioning in the "real world." Examining brain activity with evoked-potentials allows for superior temporal resolution and good quantification of brain activity associated with social functions, thus adding to a collection of fMRI research which has elucidated the specific brain regions involved in social processing. Although not entirely expected, the findings of this research are promising and provide clear directions for the expansion of future work in this area.

Table 1

Demographic Characteristics

	Schizophrenia (N = 20)		Controls (N = 17)		p value
	M	*SD*	*M*	*SD*	
Sex					
Male	13		12		
Female	7		5		1.00
Age	45.8	7.2	47.2	8.9	.61
Years of education	12.2	2.2	14.2	2.7	.02*
Highest parental education	11.4	4.2	13.0	2.9	.20
Race					
African American	17		10		
Caucasian	3		7		.14

* $p < .05$

Table 2

Clinical Characteristics of the Schizophrenia Group (N = 20)

	M	*SD*
Illness course and severity		
Age at first psychiatric treatment	21.64	6.20
Age at first hospitalization	22.62	4.85
Age when first diagnosed with SZ	21.88	6.27
Number of hospitalizations	5.43	8.10
Number of suicide attempts	0.89	2.78
BPRS factor scores		
Thinking Disturbance	5.20	2.76
Withdrawal/Retardation	6.70	3.67
Hostility/Suspiciousness	4.45	2.11
Anxious/Depression	6.75	4.03
Total Score	36.20	9.08
SANS		
Affective Flattening	2.05	1.43
Alogia	1.50	1.10
Avolition	1.95	1.40
Asociality/Anhedonia	1.80	1.24
Total Score	33.90	16.14

Table 2, continued

Clinical Characteristics of the Schizophrenia Group (N = 20)

	Number (Percentage)
Diagnostic subtype	
Paranoid	7 (35%)
Disorganized	2 (10%)
Deficit	0 (0%)
Undifferentiated	8 (40%)
Medication status	
Antipsychotics	
FGA	3 (15%)
SGA	10 (50%)
FGA + SGA	6 (30%)
> 1 SGA	1 (5%)
Mood/anxiety	
Antidepressant	8 (40%)
Antianxiety	0 (0%)
Mood stabilizer	1 (5%)
> 1 mood/anxiety medication	6 (30%)

FGA = First Generation Antipsychotic

SGA = Second Generation Antipsychotic

Table 3

Correlations of Execution and Observation ERN Amplitude with Social Functioning, Theory of Mind, and Psychiatric Symptoms in Schizophrenia Patients (N = 20)

	Execution ERN	Observation ERN
SFS Social Engagement/Withdrawal	.37	.03
SFS Interpersonal Communication	.25	.06
SFS Independence Performance	-.17	.13
SFS Recreation	.21	.06
SFS Prosocial	.29	.05
SFS Independence Competence	-.01	.08
SFS Occupation/Employment	-.39	.24
SFS Scaled Summary Score	.23	.15
Theory of Mind Total	-.10	-.14
Theory of Mind False Belief	-.07	.17
BPRS Thinking Disturbance	.50*	.20
BPRS Withdrawal/Retardation	-.05	-.28
BPRS Hostility/Suspiciousness	-.03	.13
BPRS Anxious Depression	.11	-.04
BPRS Summary Score	.34	-.02
SANS Affective Flattening	-.29	-.33
SANS Alogia	.15	-.02

Table 3, continued

Correlations of Execution and Observation ERN Amplitude with Social Functioning, Theory of Mind, and Psychiatric Symptoms in Schizophrenia Patients (N = 20)

	Execution ERN	Observation ERN
SANS Avolition	.48*	-.34
SANS Asociality/Anhedonia	.22	-.02
SANS Summary Score	.13	-.32

* $p < .05$

Table 4

Correlations of Execution and Observation ERN Amplitude with Social Functioning and Theory of Mind in Healthy Controls (N = 17)

	Execution ERN	Observation ERN
SFS Social Engagement/Withdrawal	-.44	-.12
SFS Interpersonal Communication	-.09	.55*
SFS Independence Performance	.14	.11
SFS Recreation	-.08	.14
SFS Prosocial	.13	.36
SFS Independence Competence	.16	.16
SFS Occupation/Employment	-.52*	.16
SFS Scaled Summary Score	-.15	.30
Theory of Mind Total	-.45	-.17
Theory of Mind False Belief	-.37	-.29

* $p < .05$

Table 5

Correlations of Execution and Observation ERN Amplitude with Social Functioning and Theory of Mind in All Participants (N = 37)

	Execution ERN	Observation ERN
SFS Social Engagement/Withdrawal	-.15	-.07
SFS Interpersonal Communication	.01	.22
SFS Independence Performance	-.04	.11
SFS Recreation	-.18	.01
SFS Prosocial	.04	.15
SFS Independence Competence	-.08	.07
SFS Occupation/Employment	-.56**	.12
SFS Scaled Summary Score	-.20	.14
Theory of Mind Total	-.44**	-.19
Theory of Mind False Belief	-.40*	-.07

* $p < .05$

** $p < .01$

Table 6

Means and Standard Deviations on Neurocognition, Social Cognition, and Social Functioning Measures

	M	*SD*
Patients		
Immediate Verbal Memory	28.30	10.22
Secondary Verbal Memory	15.55	9.17
WCST Total Errors	33.70	11.45
ToM Total	59.75	12.17
ToM False Belief	9.40	5.69
SFS Social Engagement/Withdrawal	115.60	12.95
SFS Interpersonal Communication	124.80	20.75
SFS Independence Performance	111.03	6.67
SFS Recreation	109.43	15.42
SFS Prosocial	112.05	14.58
SFS Independence Competence	112.65	8.69
SFS Occupation/Employment	100.25	12.15
SFS Scaled Summary Score	112.26	7.03
Controls		
Immediate Verbal Memory	41.76	13.37
Secondary Verbal Memory	24.41	11.04
WCST Total Errors	21.71	12.01

Table 6, continued

Means and Standard Deviations on Neurocognition, Social Cognition, and Social Functioning Measures

	M	*SD*
ToM Total	75.76	10.25
ToM False Belief	16.88	4.23
SFS Social Engagement/Withdrawal	123.29	12.41
SFS Interpersonal Communication	131.77	16.58
SFS Independence Performance	112.50	8.67
SFS Recreation	128.77	14.45
SFS Prosocial	122.00	15.94
SFS Independence Competence	118.29	8.26
SFS Occupation/Employment	112.94	12.21
SFS Scaled Summary Score	121.37	9.36

Table 7

Correlations between Neurocognition and Social Functioning in Schizophrenia Patients (N = 20)

	Immediate Verbal Memory	Secondary Verbal Memory	WCST Total Errors
SFS Social Engagement/Withdrawal	-.45*	-.44	-.24
SFS Interpersonal Communication	-.29	-.05	.45*
SFS Independence Performance	-.41	-.47*	.19
SFS Recreation	-.54*	-.34	-.05
SFS Prosocial	-.29	-.05	-.07
SFS Independence Competence	-.38	-.47*	.22
SFS Occupation/Employment	.33	.21	-.03
SFS Scaled Summary Score	-.54*	-.36	.15

* $p < .05$

Table 8

Correlations between Neurocognition and Social Functioning in Controls (N = 17)

	Immediate Verbal Memory	Secondary Verbal Memory	WCST Total Errors
SFS Social Engagement/Withdrawal	.38	.26	-.47
SFS Interpersonal Communication	.48	.40	-.01
SFS Independence Performance	.72**	.50*	-.20
SFS Recreation	.64**	.37	-.21
SFS Prosocial	.42	.30	-.22
SFS Independence Competence	.49*	.44	-.16
SFS Occupation/Employment	.58*	.62**	-.64**
SFS Scaled Summary Score	.70**	.54*	-.36

* $p < .05$

Table 9

Correlations between Meta-Cognitive WCST Variables, Social Cognition, and Social Functioning (N = 37)

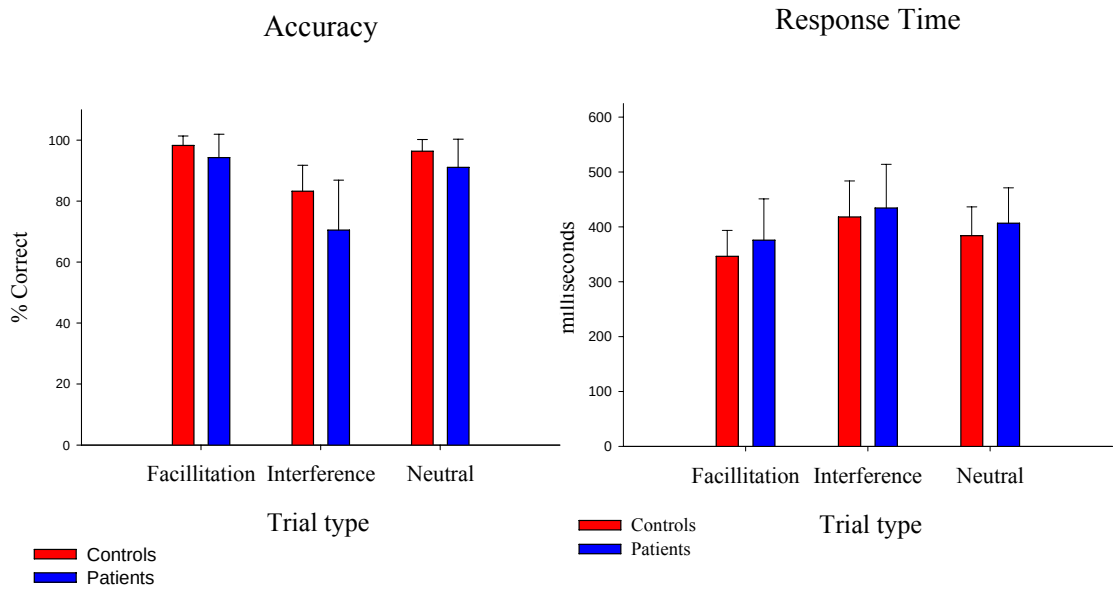
	ToM Total	SFS Scaled Summary
Total Volunteered Sorts	.16	.19
Total Correct Volunteered Sorts	.54**	.32*
Accuracy Score	.54**	.30
Free Choice Improvement	-.09	-.12
Global Monitoring	.44**	-.18
Monitoring Resolution	-.12	.22
Control Sensitivity	.13	.47*

* $p < .05$

** $p < .01$

Figure 1

Flanker Behavioral Data



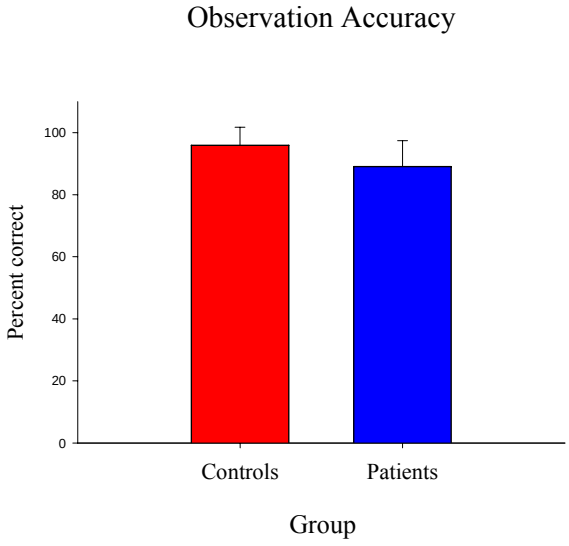


Figure 2

Response-Locked Group ERN Averages with Topographical Mapping of Peak Negativity during Incorrect Trials

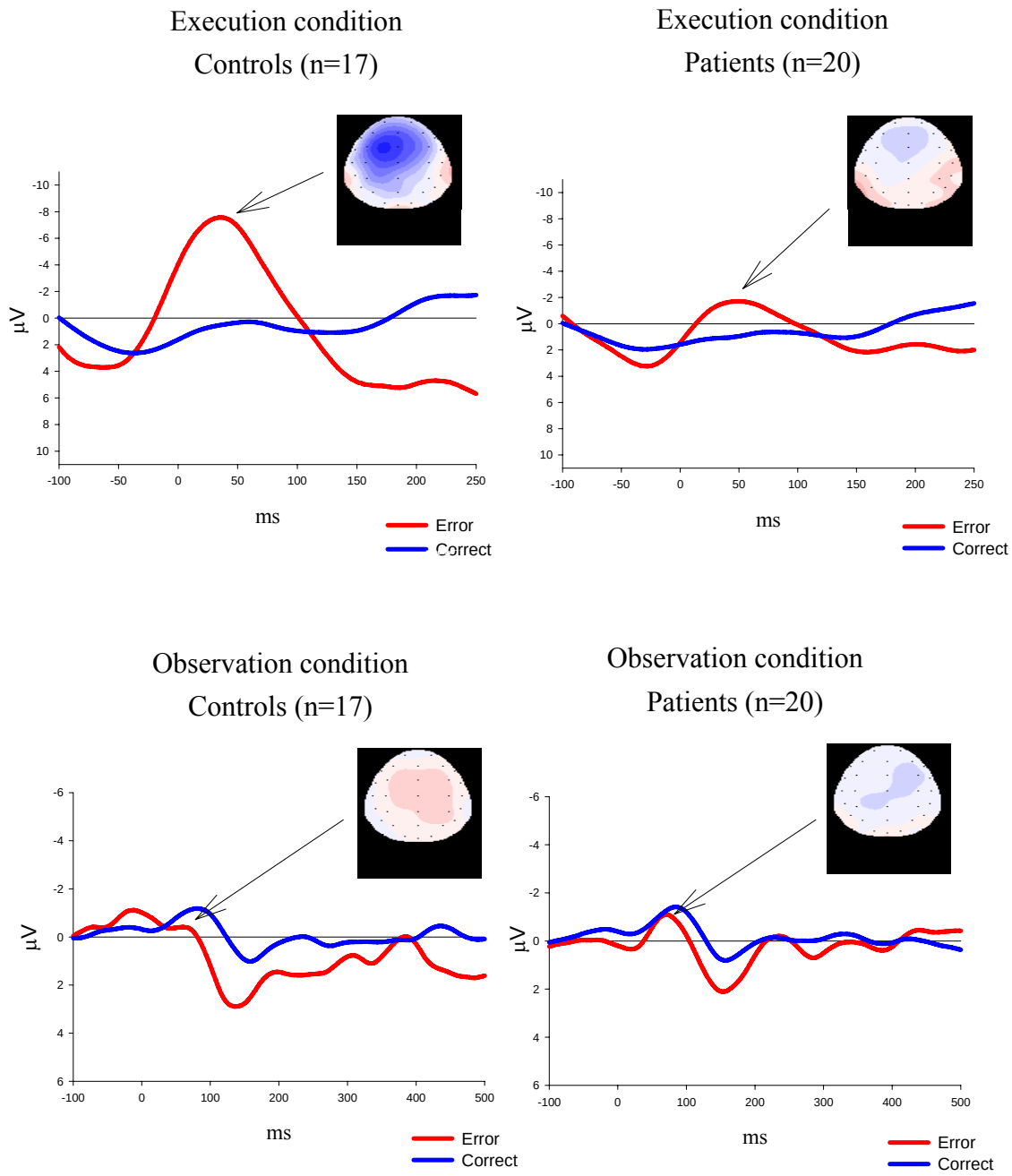


Figure 3

Response-Locked Group LRP Averages

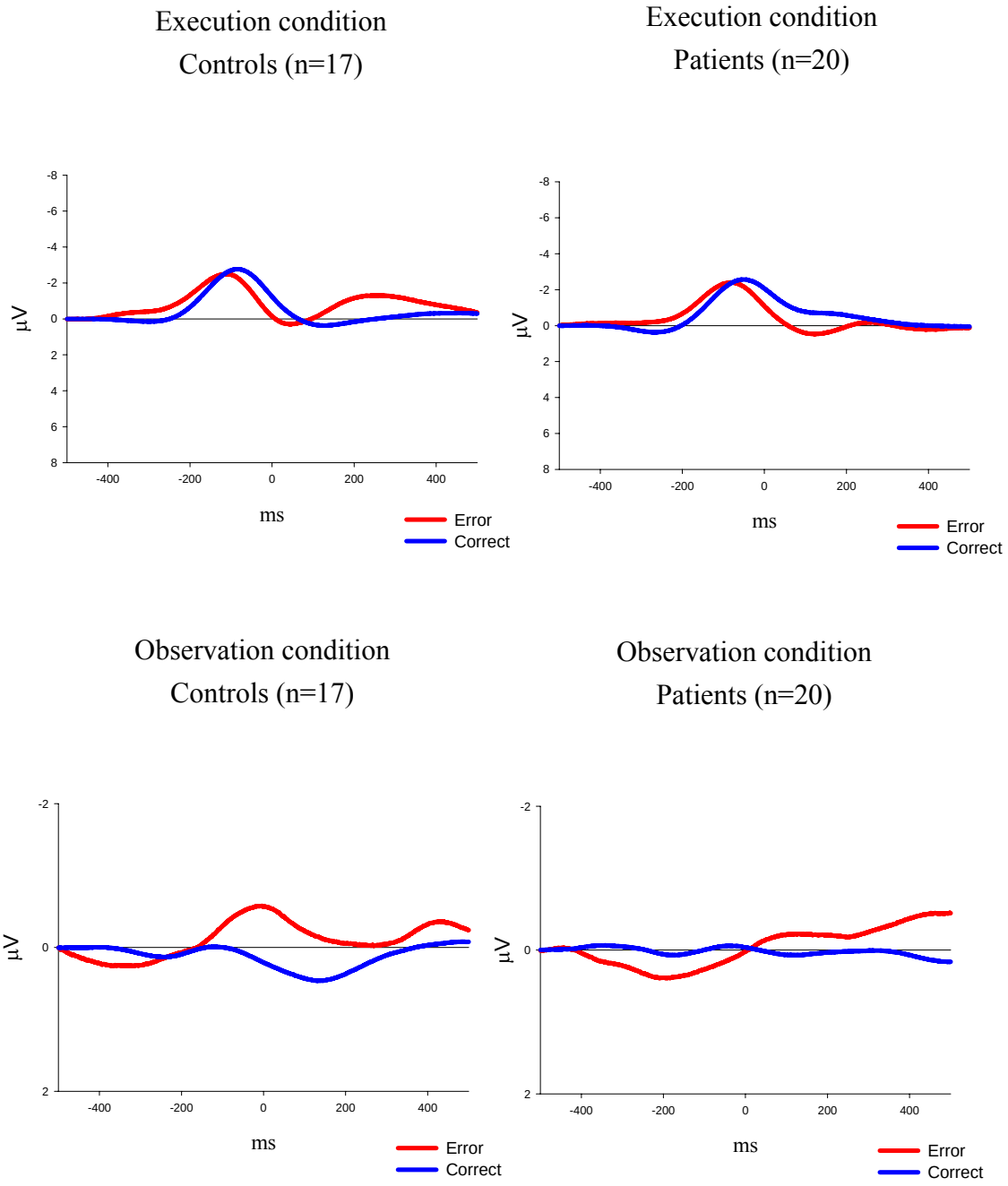


Figure 4

Average Amplitude of the ERN and the LRP during Execution and Observation

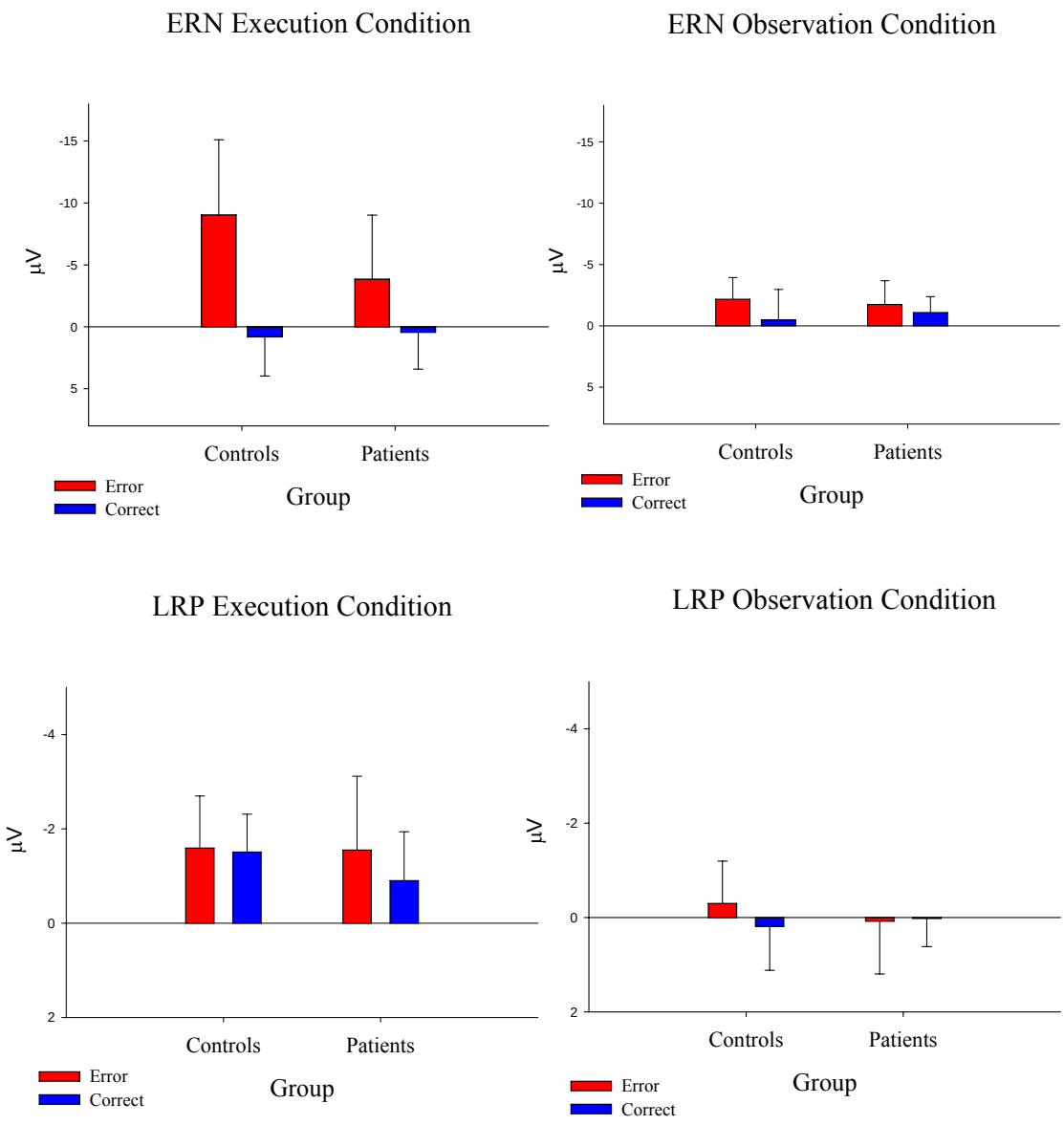


Figure 5

Feedback-Locked Group Averages

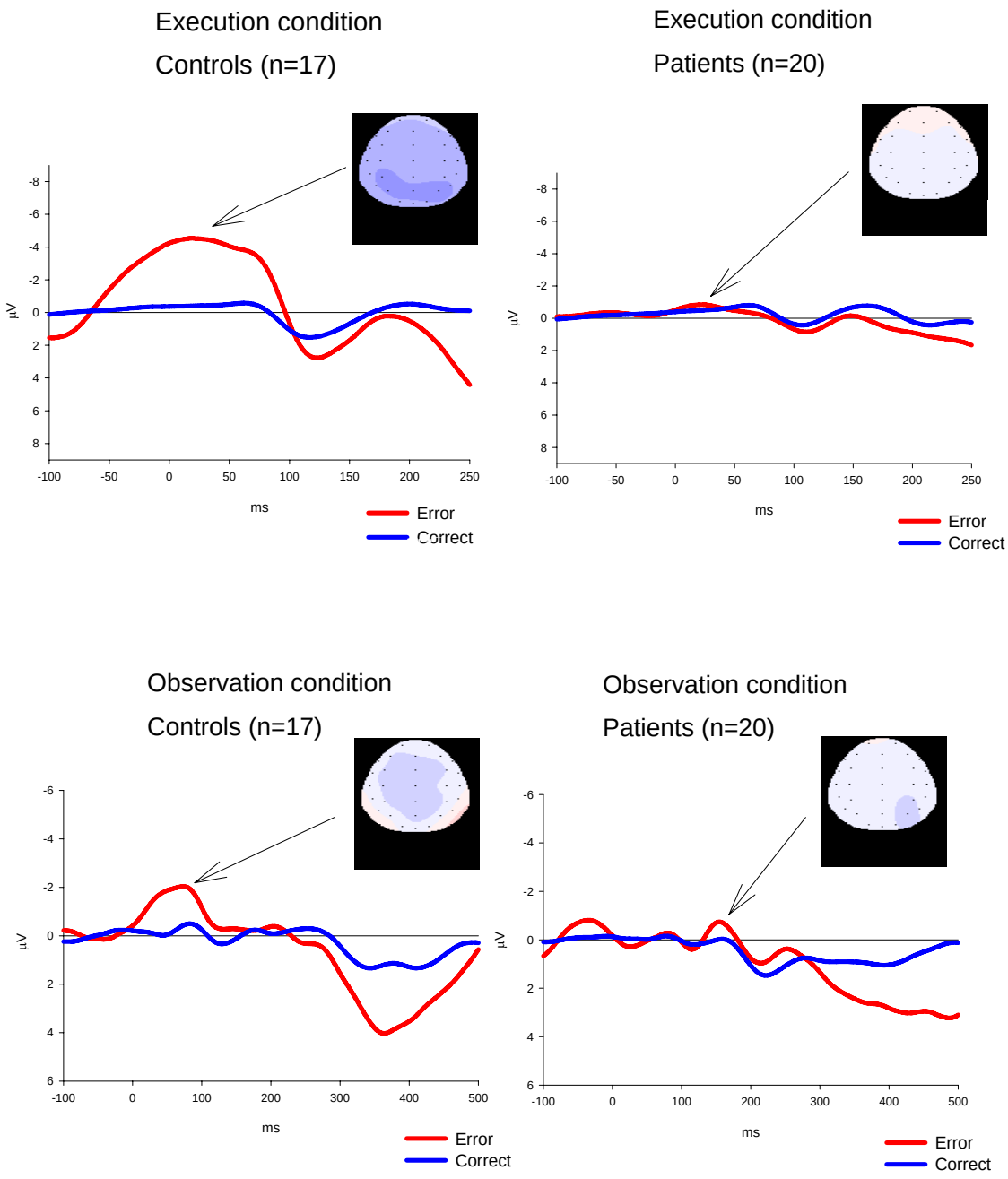


Figure 6

Scatterplot of Correlations between Intermediate Verbal Memory and Social Functioning in Schizophrenia Patients (N = 20)

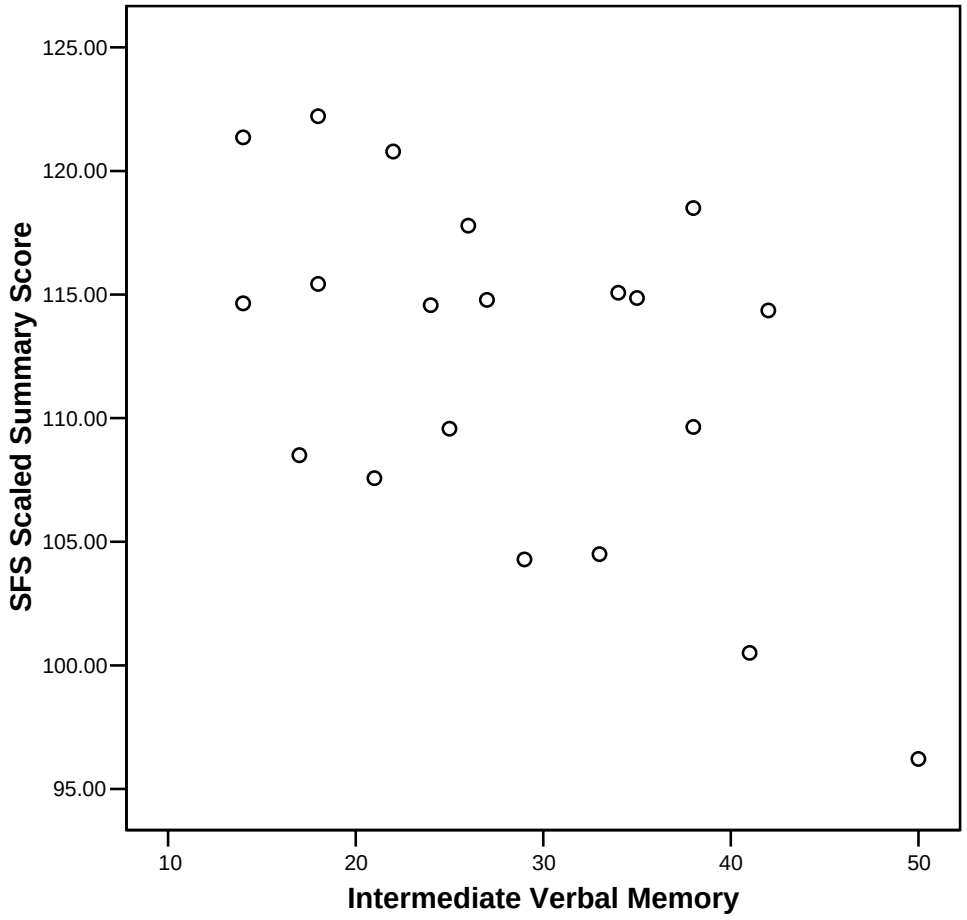
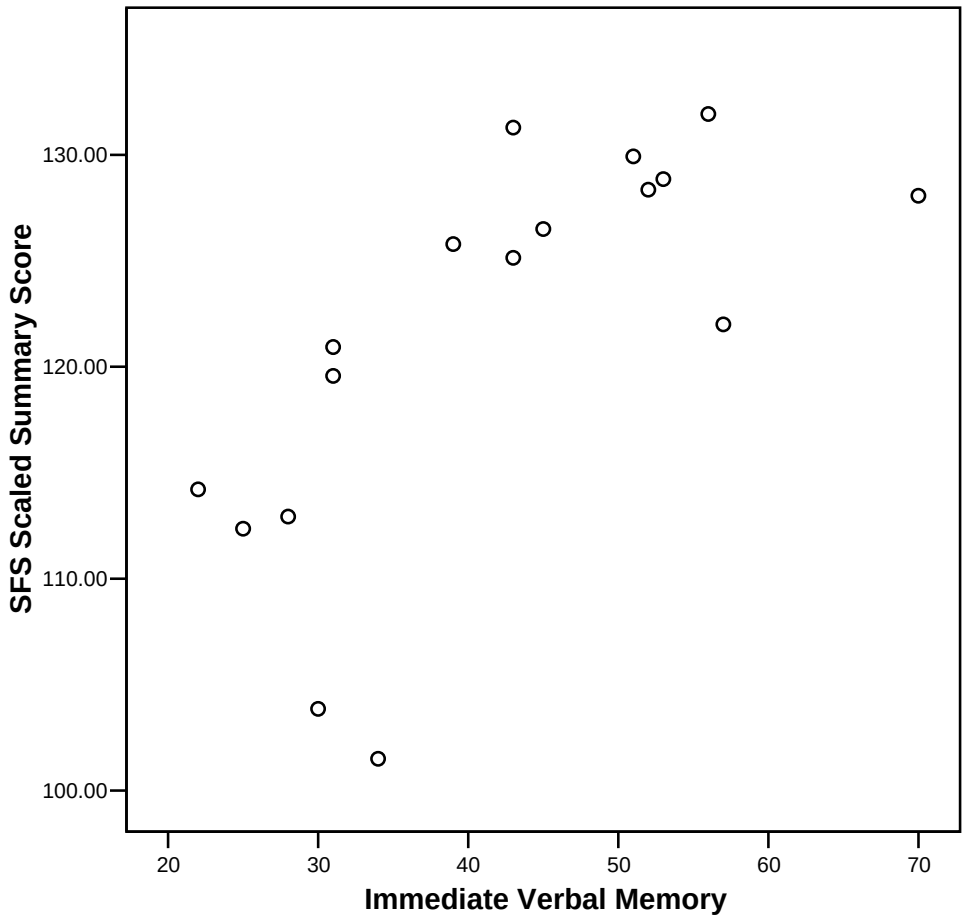


Figure 7

Scatterplot of Correlations between Intermediate Verbal Memory and Social Functioning in Control Participants (N = 17)



REFERENCES

Addington, J., & Addington, D. (1993). Premorbid functioning, cognitive functioning, symptoms and outcome in schizophrenia. *Journal of Psychiatry and Neuroscience, 18*, 18-23.

Addington, J., & Addington, D. (1998). Facial affect recognition and information processing in schizophrenia and bipolar disorder. *Schizophrenia Research, 32(3),* 171-181.

Addington, J., & Addington, D. (1999). Neurocognitive and social functioning in schizophrenia. *Schizophrenia Bulletin, 25(1),* 173-182.

Addington, J., & Addington, D. (2000). Neurocognitive and social functioning in schizophrenia: A 2.5 year follow-up study. *Schizophrenia Research, 44(1),* 47-56.

Addington, J., & Addington, D. (2005). Patterns of premorbid functioning in first episode psychosis: Relationship to 2-year outcome. *Acta Psychiatrica Scandinavica, 112(1),* 40-46.

Addington, D., Addington, J., & Robinson, G. (1999). Attributional style and depression in schizophrenia. *Canadian Journal of Psychiatry, 44(7)*, 697-700.

Addington, J., McCleary, L., Munroe-Blum, H. (1998). Relationship between cognitive and social dysfunction in schizophrenia. *Schizophrenia Research, 34(1-2)*, 59-66.

Addington, J., van Mastrigt, S., & Addington, D. (2003). Patterns of premorbid functioning in first-episode psychosis: Initial presentation. *Schizophrenia* Research, 62(1-2), 23-30.

Adolphs, R. (1999). Social cognition and the human brain. *Trends in Cognitive Science, 3,* 469-479.

Adolphs, R. (2001). The neurobiology of social cognition. *Current Opinion in Neurobiology, 11*, 231-239.

Adolphs, R. (2003). Cognitive neuroscience of human social behaviour. *Nature, 4*, 165-178.

Alain, P., Etcharry-Bouyx, F., & Le Gall, D. (2001). A case study of selective impairment of the central executive component of working memory after a focal frontal lobe damage. *Brain and Cognition, 45,* 21–43.

Alain, C., McNeely, H. E., He, Y., Christensen, B. K., & West, R. (2002). Neurophysiological evidence of error-monitoring deficits in patients with schizophrenia. *Cerebral Cortex, 12,* 840-846.

Aleman, A., Hijman, R., de Haan, E. H., & Kahn, R. S. (1999). Memory impairment in schizophrenia: A meta-analysis. *American Journal of Psychiatry, 156,* 1358–1366.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Amos, A. (2000). A computational model of information processing in the frontal cortex and basal ganglia. *Journal of Cognitive Neuroscience, 12(3),* 505-519.

Anderson, S. W., Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1999). Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nature Neuroscience, 2*, 1032-1037.

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.

Andreasen, N. C. (1982). Negative symptoms in schizophrenia: Definition and reliability. *Archives of General Psychiatry, 39(7),* 784-788.

Andreasen, N. C. (1989). Scale for the Assessment of Negative Symptoms (SANS). *British Journal of Psychiatry, 155(Suppl 7),* 53-58.

Andreason, N. C. (1994). *Scale for the Assessment of Negative Symptoms (SANS)*. Iowa City: Department of Psychiatry, University of Iowa College of Medicine.

Andreasen, N. C., & Olsen, S. A. (1982). Negative v positive schizophrenia: Definition and validation. Archives of General Psychiatry, 39(7), 789-794.

Andres, P. (2003). Frontal cortex as the central executive of working memory: Time to revise our view. *Cortex, 39,* 871–895.

Archer, J., Hay, D. C., & Young, A. W. (1994). Movement, face processing, and schizophrenia: Evidence of a differential deficit in expression analysis. *British Journal of Clinical Psychology, 33*, 517-528.

Arfken, C. L. (1997). Self-reported life satisfaction. *American Journal of Psychiatry, 154(10),* 1478.

Atkinson, M., Zibin, S., & Chuang, H. (1997). Characterizing quality of life among patients with chronic mental illness: A critical examination of the self-report methodology. *American Journal of Psychiatry, 154(1),* 99-105.

Awad, A. G., Voruganti, L. N., & Heslegrave, R. J. (1997). Measuring quality of life in patients with schizophrenia. *Pharmacoeconomics, 11(1),* 32-47.

Aylward, E., Walker, E., & Bettes, B. (1984). Intelligence in schizophrenia: Meta-analysis of the research. *Schizophrenia Bulletin, 10*, 430-459.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic and statistical considerations. *Journal of Personality and Social Psychology, 51*, 1173-1182.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1986). Mechanical, behavioural and Intentional understanding of picture stories in autistic children. *British Journal of Developmental Psychology, 4(2)*, 113-125.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have a 'theory of mind'? *Cognition, 21(1),* 37-46.

Barrett, L., & Henzi, P. (2005). The social nature of primate cognition. *Proceedings of the Royal Society of London, 272,* 1865–1875.

Bates, A. T., Kiehl, K. A., Laurens, K. R., & Liddle, P. F. (2002). Error-related negativity and correct response negativity in schizophrenia. *Clinical Neurophysiology, 113,* 1454-1463.

Bates, A. T., Patel, T. P., & Liddle, P. F. (2005). External behavior monitoring mirrors internal behavior monitoring. *Journal of Psychophysiology, 19(4),* 281-288.

Beardsworth, E., & Bishop, D. (1994) Assessment of long-term verbal memory in children. *Memory, 2(2),* 129-148.

Beitinger, R., Lin, J., Kissling, W., & Leucht, S. (2008). Comparative remission rates of schizophrenic patients using various remission criteria. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 32(7),* 1643-1651.

Bell, M., Bryson, G., & Lysaker, P. (1997). Positive and negative affect recognition in schizophrenia: A comparison with substance abuse and normal control subjects. *Psychiatry Research, 73*, 73-82.

Bellack, A. S., Blanchard, J. J., & Mueser, K. T. (1996). Cue availability and affect perception in schizophrenia. *Schizophrenia Bulletin, 22*, 535-544.

Bellack, A. S., Green, M. F., Cook, J. A., Fenton, W., Harvey, P. D., Heaton, R. K., Laughren, T., Leon, A. C., Mayo, D. J., Patrick, D. L., Patterson, T. L., Rose, A., Stover, E., & Wykes, T. (2007). Assessment of community functioning in people with schizophrenia and other severe mental illnesses: A white paper based on an NIMH-sponsored workshop. *Schizophrenia Bulletin, 33(3),* 805-822.

Bellack, A. S., Morrison, R., Mueser, K. T., Wade, J. H., & Sayers, S. L. (1990). Role play for assessing social competence of psychiatric patients. *Psychological Assessment: A Journal of Consulting and Clinical Psychology, 2(3),* 248-255.

Bellack, A. S., Morrison, R. L., Wixted, J. T., Mueser, K. T. (1990). An analysis of social competence in schizophrenia. *British Journal of Psychiatry, 156*, 809-818.

Bellack, A. S., Mueser, K. T., Wade, J., Sayers, S., et al. (1992). The ability of schizophrenics to perceive and cope with negative affect. *British Journal of Psychiatry, 160*, 473-480.

Benes, F. M. (2000). Emerging principles of altered neural circuitry in schizophrenia. *Brain Research Reviews, 31,* 251-269.

Benes, F. M., Majocha, R., Bird, E. D., & Marotta, C. A. (1987). Increased vertical axon numbers in cingulated cortex of schizophrenics. *Archives of General Psychiatry, 44,* 1017-1021.

Benes, F. M., McSparren, J., Bird, E. D, & SanGiovanni, J. P., et al. (1991). Deficits in small interneurons in prefrontal and cingulate cortices of schizophrenic and schizoaffective patients. *Archives of General Psychiatry, 48(11),* 996-1001.

Benson, D. F., & Miller, B. L. (1997). Frontal lobes: Clinical and anatomic aspects. In T. E. Feinberg & M. J. Farah (Eds.), *Behavioral neurology and neuropsychology* (pp. 401–408). New York: McGraw-Hill.

Bentall, R. P. (1990). The illusion of reality: A review and integration of psychological research on hallucinations. *Psychological Bulletin, 107*, 82-95.

Berg, E. A. (1948). A simple, objective technique for measuring flexibility in thinking. *Journal of General Psychology,* 1948, *39, 15-22.*

Bergman, A. J., Harvey, P. D., Roitman, S. L., Mohs, R. C., Marder, D., Silverman, J. M., et al. (1998). Verbal learning and memory in schizotypal personality disorder. *Schizophrenia Bulletin, 24,* 635–641.

Bering, J. M. (2002). The existential theory of mind. *Review of General Psychology, 6(1),* 3-24.

Bernstein, P. S., Scheffers, M. K., & Coles, M. G. H. (1995). "Where did I go wrong?" A psychophysiological analysis of error detections. *Journal of Experimental Psychology: Human Perception and Performance, 21(6),* 1312-1322.

Bilder, R. M., Goldman, R. S., Robinson, D., Reiter, G., Bell, L., Bates, J. A., et al. (2000). Neuropsychology of first-episode schizophrenia: Initial characterization and clinical correlates. *American Journal of Psychiatry, 157,* 549-559.

Birchwood, M., Smith, J., Cochrane, R., Wetton, S., et al. (1990). The Social Functioning Scale: The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *British Journal of Psychiatry, 157,* 853-859.

Blair, R. J. R., & Cipolotti, L. (2000). Impaired social response reversal: A case of "acquired sociopathy." *Brain, 123*, 1122-1141.

Blanchard, J. J., Horan, W. P., & Collins, L. M. (2005). Examining the latent structure of negative symptoms: Is there a distinct subtype of negative symptom schizophrenia? *Schizophrenia Research, 77(2-3)*, 151-165.

Blanchard, J. J., Mueser, K. T., & Bellack, A. S. (1998). Anhedonia, positive and negative affect, and social functioning in schizophrenia. *Schizophrenia Bulletin, 24(3)*, 413-424.

Blanchard, J. J., & Neale, J. M. (1992). Medication effects: Conceptual and methodological issues in schizophrenia research. *Clinical Psychology Review, 12(3),* 345-361.

Bleuler, E. (1950). *Dementia praecox or the group of schizophrenias* (J. Zinkin, Trans.). New York: International Universities Press. (Original work published 1911).

Blyler, C. R., & Gold, J. M. (2000). Cognitive effects of typical antipsychotic treatment: Another look. In T. Sharma & P. D. Harvey (Eds.), *Cognition in schizophrenia: Impairments, importance and treatment strategies* (pp. 241–265). New York: Oxford University Press.

Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology, 72(2),* 123-132.

Boksem, M. A., Tops, M., Wester, A. E., Meijman, T. F, & Lorist, M. M. (2006). Error-related ERP components and individual differences in punishment and reward sensitivity. *Brain Research, 1101(1),* 92-101.

Bora, E., Eryavuz, A., Kayahan, B., Sungu, G., & Veznedaroglu, B. (2006). Social functioning, theory of mind and neurocognition in outpatients with schizophrenia; mental state decoding may be a better predictor of social functioning than mental state reasoning. *Psychiatry Research, 145(2-3),* 95-103.

Bora, E., Yucel, M., & Pantelis, C. (2009). Theory of mind impairment in schizophrenia: meta-analysis. Schizophrenia Research, 109(1-3), 1-9.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological Review, 108(3),* 624-652.

Botvinick, M., Nystrom, L. E., Fissell, K., Carter, C. S., & Cohen, J. D. (1999). Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature, 402 (6758),* 179-81.

Bowden, S. C., Fowler, K. S., Bell, R. C., Whelan, G., Clifford, C. C., Ritter, A. J., & Long, C. M. (1998). The reliability and internal validity of the Wisconsin Card Sorting Test. *Neuropsychological Rehabilitation, 8(3),* 243-254.

Brébion, G., David, A, S., Bressan, R. A., & Pilowsky, L. S. (2006) Processing Speed: A Strong Predictor of Verbal Memory Performance in Schizophrenia. *Journal of Clinical and Experimental Neuropsychology, 28(3),* 370-382.

Brekke, J., Day, D. D., Lee, K. S., & Green, M. F. (2005). Biosocial pathways to functional outcome in schizophrenia. *Schizophrenia Research, 80*, 213-225.

Brooker, A. E. (1997). Performance on the Wechsler Memory Scale-Revised for patients with mild traumatic brain injury and mild dementia. *Perceptual and Motor Skills, 84(1),* 131-138.

Brüne, M. (2005) 'Theory of Mind' in Schizophrenia: A Review of the Literature. *Schizophrenia Bulletin, 31(1),* 21-42.

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.

Buccino, G., Binkofski, F., Fink, G. R., Fadiga, L., Fogassi, L., et al. (2001). Action observation activates premotor and parietal areas in a somatotopic manner: An fMRI study. *European Journal of Neuroscience, 13*, 400-404.

Buchanan, R. W., & Carpenter, W. T. (1994). Domains of psychopathology: An approach to the reduction of heterogeneity in schizophrenia. *Journal of Nervous and Mental Disease, 182(4),* 193-204.

Burns, J. K. (2004). An evolutionary theory of schizophrenia: Cortical connectivity, metarepresentation, and the social brain. *Behavioral and Brain Sciences, 27*, 831-885.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences, 4,* 215-222.

Cacioppo, J.T., Amaral, D., Blanchard, J.J., Cameron, J.L., Carter, C.S., Crews, D., Fiske, S., Heatherton, T., Johnson, M.K., et al. (2007). Social Neuroscience: Progress and Promise. *Perspectives on Psychological Science, 2(2),* 99-123.

Cacioppo, J. T., Berntson, G. G., Sheridan, J. F., & McClintock, M. K. (2000). Multilevel integrative analyses of human behavior: Social neuroscience and the complementing nature of social and biological approaches. *Psychological Bulletin, 126(6),* 829-843.

Cannon, T. D., Huttunen, M. O., Lonnqvist, J., Tuulio-Henriksson, A., Pirkola, T., Glahn, D., et al., (2000). The inheritance of neuropsychological dysfunction in twins discordant for schizophrenia. *American Journal of Human Genetics, 67,* 369-382.

Cannon, M., Moffitt, T. E., Caspi, A., Murray, R. M., Harrington, N., & Poulton, R. (2006). Neuropsychological performance at the age of 13 years and adult schizophreniform disorder: A prospective birth cohort study. *British Journal of Psychiatry, 189,* 463–464.

Cannon, T. D., Zorrilla, L. E., Shtasel, D., Gur, R. E., Gur, R. C., Marco, E. J., et al. (1994). Neuropsychological functioning in siblings discordant for schizophrenia and healthy volunteers. *Archives of General Psychiatry, 51,* 651-661.

Cantor-Graae, E., Warkentin, S., Franzén, G., & Risberg, J. (1993). Frontal lobe challenge: A comparison of activation procedures during rCBF measurements in normal subjects. Neuropsychiatry, Neuropsychology, & Behavioral Neurology, 6(2), 83-92.

Cardno, A. G., & Farmer, A. E. (1995). The case for or against heterogeneity in the etiology of schizophrenia: The genetic evidence. *Schizophrenia Research, 17(2),* 153-159.

Carpenter, P. A., Just, M. A., & Reichle, E. D. (2000). Working memory and executive function: Evidence from neuroimaging. *Current Opinion in Neurobiology, 10,* 195–199.

Carter, C. S. Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science, 280*, 747-749.

Chabungbam, G., Avasthi, A., & Sharan, P. (2007). Sociodemographic and clinical factors associated with relapse in schizophrenia. *Psychiatry and Clinical Neurosciences, 61(6),* 587-593.

Chan, G. W. L., Ungvari, G. S., Shek, D. T. L., & Leung, J. P. (2003). Impact of Deinstitutionalisation on the Quality of Life of Chinese Patients with

Schizophrenia: A Longitudinal Pilot Study. *Hong Kong Journal of Psychiatry, 13(4),* 2-5.

Chiu, P. H., & Deldin, P. J. (2007). Neural evidence for enhanced error detection in major depressive disorder. *American Journal of Psychiatry, 164(4),* 608-616.

Cirillo, M. A., & Seidman, L. J. (2003). Verbal declarative memory dysfunction in schizophrenia: From clinical assessment to genetics and brain mechanisms. *Neuropsychology Review, 13,* 43–77.

Clark, L. A., & Watson, D. (1991). Theoretical and empirical issues in differentiating depression from anxiety. In Becker, Joseph; Kleinman, Arthur (Eds.) *Psychosocial aspects of depression* (pp. 39-65). Hillsdale, NJ, England: Lawrence Erlbaum Associates, Inc.

Cochin, S., Barthelemy, C., Lejeune, B., Roux, S., & Martineau, J. (1998). Perception of motion and qEEG activity in human adults. *Electroencephalography in Clinical Neurophysiology, 107*, 287-295.

Cochin, S., Barthelemy, C., Roux, S., & Martineau, J. (1999). Observation and execution of movement: Similarities demonstrated by quantified electroencephalography. *European Journal of Neuroscience, 11*, 1839-1842.

Cohen, A. S., Forbes, C. F., Mann, M. C., & Blanchard, J. J. (2006). Specific cognitive deficits and differential domains of social functioning impairment in schizophrenia. *Schizophrenia Research, 81,* 227-238.

Coles, M. G. H., Gratton, G., Bashore, T. R., Eriksen, C. W., & Donchin, E. (1985). A psychophysiological investigation of the continuous flow model of human information processing. *Journal of Experimental Psychology: Human Perception and Performance, 11(5),* 529-553.

Coles, M. G. H., Scheffers, M. K., & Holroyd, C. (1998). Berger's dream? The error-related negativity and modern cognitive psychophysiology. In H. Witted, U. Zweiner, B. Schack, & A. Döring (Eds.), *Quantitative and Topological EEG and MEG analysis* (pp. 96-102). Jena-Erlangen, Germany: Druckhaus Mayer Verlag.

Coles, M. G. H., Scheffers, M. K., & Holroyd, C. (2001). Why is there an ERN/Ne on correct trials? Response representations, stimulus-related components, and the theory of error-processing? *Biological Psychology, 56(3),* 173-189.

Corcoran, R. (2001). Theory of mind and schizophrenia. In P. W. Corrigan & D. L. Penn (Eds.), *Social Cognition and Schizophrenia* (pp. 149-164). Washington, DC: American Psychological Association.

Corcoran, R. (2003). Inductive reasoning and the understanding of intention in

schizophrenia. *Cognitive Neuropsychiatry, 8(3)*, 223-235.

Corcoran, R., Cayhill, C., & Frith, C. D. (1997). The appreciation of visual jokes in people with schizophrenia: A study of mentalizing ability. *Schizophrenia Research, 24(3)*, 319-327.

Corcoran, R., & Frith, C. D. (1996). Conversational conduct and the symptoms of schizophrenia. *Cognitive Neuropsychiatry, 1(4)*, 305-318.

Corcoran, R., & Frith, C. D. (2003). Autobiographical memory and theory of mind: Evidence of a relationship in schizophrenia. *Psychological Medicine, 33(5)*, 897-905.

Corcoran, R., Mercer, G., & Frith, C. D. (1995). Schizophrenia, symptomatology and social inference: Investigating "theory of mind" in people with schizophrenia. *Schizophrenia Research, 17*, 5-13.

Corrigan, P. W., & Addis, I. B. (1995). The effect of cognitive complexity on a social sequencing task in schizophrenia. *Schizophrenia Research, 16*, 137-144.

Corrigan, P. W., Davies-Farmer, R. M., & Stolley, M. R. (1990). Social cue recognition in schizophrenia under variable levels of arousal. *Cognitive Therapy Research, 14*, 353-361.

Corrigan, P. W., & Penn, D. L. (2001). *Social Cognition and Schizophrenia.* Washington, DC: American Psychological Association Press.

Corrigan, P. W., & Toomey, R. (1995). Interpersonal problem solving and information processing deficits in schizophrenia. *Schizophrenia Bulletin, 21*, 395-403.

Corrigan P. W., Wallace, C. J., Green, M. F. (1992). Deficits in social schemata in schizophrenia. *Schizophrenia Research, 8(2),* 129-135.

Craddock, N., O'Donovan, M. C., & Owen, M. J. (2007). Phenotypic and genetic complexity of psychosis: Invited commentary on...Schizophrenia: A common disease caused by multiple rare alleles. *British Journal of Psychiatry, 190(3),* 200-203.

Csibra, G. (2007). Action mirroring and action understanding: An alternative account. In P. Haggard, Y. Rosetti, & M. Kawato (Eds.), *Sensorimotor foundations of higher cognition* (Vol. XXII, pp. 427–451). Oxford: Oxford University Press.

Curran, T., DeBuse, C., & Leynes, P. A. (2007). Conflict and criterion setting in recognition memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 33(1),* 2-17.

Cutting, J. (1981). Judgment of emotional expression in schizophrenia. *British Journal of Psychiatry, 139*, 1-6.

David, A. S. (1992). Frontal lobology—psychiatry's new pseudoscience. *British Journal of Psychiatry, 161,* 244–248.

Davis, P. J., & Gibson, M. G. (2000). Recognition of posed and genuine facial expressions of emotion in paranoid and nonparanoid schizophrenia. *Journal of Abnormal Psychology, 109*, 445-450.

Davies, M., & Stone, T. eds. (1995). *Mental Simulation*. Blackwell.

Davis, K. L., Kahn, R. S., Ko, G., & Davidson, M. (1991). Dopamine in schizophrenia: A review and reconceptualization. *American Journal of Psychiatry, 148(11),* 1474-1486.

de Bruijn, E. R. A., Grootens, K. P., Verkes, R. J., Buchholz, V., Hummelen, J. W., & Hulstijn, W. (2006). Neural correlates of impulsive responding in borderline personality disorder: ERP evidence for reduced action monitoring. *Journal of Psychiatric Research, 40(5),* 428-437.

Decety, J., Chaminade, T., Grezes, J., & Meltzoff, A. N. (2002). A PET exploration of the neural mechanisms involved in reciprocal imitation. *Neuroimage, 15*, 265-272.

Dehaene, S., Posner, M. I., & Tucker, D. M. (1994). Localization of a neural system for error detection and compensation. *Psychological Science, 5,* 303-305.

DeLuca, N. L., Moser, L. L., & Bond, G. R. (2008). Assertive community treatment. In Mueser, K. T., & Jeste, D. V. (Eds.) *Clinical handbook of schizophrenia* (pp. 329-338). New York, NY, US: Guilford Press.

Dennett, D. C. (1987). *The intentional stance.* Cambridge, MA, US: The MIT Press.

Dickinson, D., & Harvey, P. D. (2009). Systemic hypotheses for generalized cognitive deficits in schizophrenia: A new take on an old problem. *Schizophrenia Bulletin, 35(2),* 403-414.

Dickinson D., Iannone V. N., Wilk C. M., & Gold J. M. (2004). General and specific cognitive deficits in schizophrenia. *Biological Psychiatry; 55 (8),* 826-33.

Dickinson, D., Ragland, D. J., Gold, J. M., Gur, R. C. (2008). General and specific cognitive deficits in schizophrenia: Goliath defeats David? *Biological Psychiatry, 64(9),* 823-827.

Diforio D., Walker E. F., & Kestler L. P. (2000). Executive functions in adolescents with

schizotypal personality disorder. *Schizophrenia Research 42 (2),* 125-34.

Dikman, Z. V., & Allen, J. J. B. (2000). Error monitoring during reward and avoidance learning in high- and low-socialized individuals. *Psychophysiology, 37(1),* 43-54.

Di Pellegrino, G., Fadiga, L., Fogassi, L., Gallese, V., & Rizzolatti, G. (1992). Understanding motor events: A neurophysiological study. *Experimental Brain Research, 91*, 176-180.

Drury, V. M., Robinson, E. J., & Birchwood, M. (1998). "Theory of mind" skills during an acute episode of psychosis and following recovery. *Psychological Medicine, 28*, 1101-1112.

Dworkin, R., Clark, S. C., Lipsitz, J. D., Amador, X. F., Kaufmann, C. A., Opler, L. A., White, S. R., & Gorman, J. M. (1993). Affective deficits and pain insensitivity in schizophrenia. *Motivation and Emotion, 17*, 245-276.

Dworkin, R. H., Green, S. R., Small, N. E., Warner, M. L., et al. (1990). Positive and negative disorder. *American Journal of Psychiatry, 147(9),* 1234-1236.

Edwards, J., Jackson, H. J., & Pattison, P. E. (2002). Emotion recognition via facial expression and affective prosody in schizophrenia: A methodological review. *Clinical Psychology Review, 22*, 789-832.

Edwards, J., Pattison, P. E., Jackson, H. J., & Wales, R. J. (2001). Facial affect and affective prosody recognition in first-episode schizophrenia. *Schizophrenia Research, 48(2-3)*, 235-253.

Elvevag, B., & Goldberg, T. E. (2000). Cognitive impairment in schizophrenia is the core of the disorder. *Critical Reviews in Neurobiology, 14,* 1-21.

Elwood, R. W. (1991). Factor structure of the Wechsler Memory Scale--Revised (WMS--R) in a clinical sample: A methodological reappraisal. *Clinical Neuropsychologist, 5(4),* 329-337.

Emery, N. J. (2000). The eyes have it: The neuroethology, function, and evolution of social gaze. *Neuroscience and Biobehavioral Reviews, 24*, 581-604.

Enticott, P. G., Hoy, K. E., Herring, S. E., Johnston, P. J., Daskalakis, Z. J., & Fitzgerald, P. B. (2008). Reduced motor facilitation during action observation in schizophrenia: A mirror neuron deficit? *Schizophrenia Research, 102(1-3),* 116-121.

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception and Psychophysics, 16,* 143-149.

Evangeli, M., & Broks, P. (2001). Face processing in schizophrenia: Parallels with the effects of amygdala damage. *Cognitive Neuropsychiatry, 5(2)*, 81-104.

Falkenstein, M., Hohnsbein, J., & Hoormann, J. (1991). Effects of cross modal divided attention on late ERP components. II. Error processing choice reaction tasks. *Electroencephalography and Clinical Neurophysiology, 78*, 447-455.

Falkenstein, M., Hoormann, J., Christ, S., & Hohnsbein, J. (2000). ERP components on reaction errors and their functional significance: A tutorial. *Biological Psychology, 51,* 87-107.

Faraone, S. V., Seidman, L. J., Kremen, W. S., Toomey, R., Lyons, M. J., & Tsuang, M. T. (1996). Neuropsychological functioning among the elderly nonpsychotic relatives of schizophrenic patients. *Schizophrenia Research, 21,* 27-31.

Faustman W.O., Overall J.E. (1999). The brief psychiatric rating scale. In: Maruish, M. (Ed.), *The Use of Psychological Testing for Treatment, Planning and Outcome Assessment, second edition* (pp. 791– 830). Lawrence Erlbaum Associates, Hillsdale, NJ.

Fenton, W. S., & McGlashan, T. H. (1992). Testing systems for assessment of negative symptoms in schizophrenia. *Archives of General Psychiatry, 49(3),* 179-184.

Fine, C., Lumsden, J., & Blair, R. J. R. (2001). Dissociation between "theory of mind and executive functions in a patient with early left amygdala damage. *Brain, 124*, 287-298.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (1994). *Structured Clinical* Interview for DSM-IV: Patient Edition (SCID-I/P, Version 2.0). New York: Biometrics Research Department.

Fiske, S. T., & Taylor, S. (1991). *Social Cognition* (2nd ed.). New York: McGraw-Hill.

Flaum, M., & Andreasen, N. (1995). The reliability of distinguishing primary versus secondary negative symptoms. *Comprehensive Psychiatry, 36(6),* 421-427.

Fletcher, P. C., McKenna, P. J., Frith, C., Grasby, P. M., Friston, K. J., & Dolan, R. J. (1998). Brain activations in schizophrenia during a graded memory task studies with functional neuroimaging. *Archives of General Psychiatry, 55(11),* 1001-1008.

Forgas, J. P. (1995). Mood and judgment: The affect infusion model (AIM). *Psychological Bulletin, 117*, 39-66.

Frith, C. D. (1987). The positive and negative symptoms of schizophrenia reflect impairments in the perception and initiation of action. *Psychological Medicine, 17(3),* 631-648.

Frith, C. D. (1992). *The cognitive neuropsychology of schizophrenia.* Hillsdale, NJ, England.

Frith, C. D. (1994). Theory of mind. In A. S. David & J. C. Cutting (Eds.), *The Neuropsychology of Schizophrenia* (pp. 147-151). East Sussex, England: Erlbaum.

Frith, C. D., & Corcoran, R. (1996). Exploring "theory of mind" in people with schizophrenia. *Psychological Medicine, 26*, 521-530.

Frith, C. D., & Done, D. J. (1989). Experiences of alien control in schizophrenia reflect a disorder in the central monitoring of action. *Psychological Medicine, 19(2)*, 359-363.

Frith, C. D., & Frith, U. (1999). Interacting minds – a biological basis. *Science, 286(5445),* 1692-1695.

Frith, C. D., Kapur, N., Friston, K. J., Liddle, P. F., & Frackowiak, R. S. J. (1995). Regional cerebral activity associated with the incidental processing of pseudo-words. *Human Brain Mapping, 3(2),* 153-160.

Fuller, R. L., Luck, S. J., McMahon, R. P., & Gold, J. M. (2005). Working Memory Consolidation Is Abnormally Slow in Schizophrenia. *Journal of Abnormal Psychology, 114(2),* 279-290.

Gabriel, S. M., Haroutunian, V., Powchik, P., Honer, W. G., Davidson, M., Davies, P., & Davis, K. L. (1997). Increased concentrations of presynaptic proteins in the cingulate cortex of subjects with schizophrenia. *Archives of General Psychiatry, 54(6),* 559-566.

Gaebel, W., & Wolwer, W. (1992). Facial expression and emotional face recognition in schizophrenia and depression. *European Archives of Psychiatry and Clinical Neuroscience, 242*, 46-52.

Gallese, V., Fadiga, L., Fogassi, L., & Rizzolatti, G. (1996). Action recognition in the premotor cortex. *Brain, 119*, 593-609.

Gallese, V., & Goldman, A. (1998). Mirror neurons and the simulation theory of mind-reading. *Trends in Cognitive Sciences, 2(12),* 493-501.

Gambini, O., Campana, A., Garghentini, G., & Scarone, S. (2003). No evidence of a homogeneous frontal neuropsychological profile in a sample of schizophrenic

subjects. The Journal Of Neuropsychiatry And Clinical Neurosciences, 15(1), 53-7.

Gard, D. E., Kring, A. M., Gard, M. G., Horan, W. P., & Green, M. F. (2007). Anhedonia in schizophrenia: Distinctions between anticipatory and consummatory pleasure. *Schizophrenia Research, 93(1-3),* 253-260.

Garety, P. A., & Freeman, D. (1999). Cognitive approaches to delusions: A critical review of theories and evidence. *British Journal of Clinical Psychology, 38*, 113-154.

Gastaut, H. J., & Bert, J. (1954). EEG changes during cinematographic presentation; moving picture activation of the EEG. *Electroencephalography and Clinical Neurophysiology 6 (3),* 433-44;

Gehring, W. J., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1995). A brain potential manifestation of error-related processing. In G. Karmos, V. Csepe, I. Czigler, & J. E. Desmedt (Eds.), *Perspectives of event-related potentials research* (EEG Suppl. 44, pp. 261-272). North-Holland: Elsevier.

Gehring, W. J., & Fencsik, D. E. (2001). Functions of the medial frontal cortex in the processing of conflict and errors. *Journal of Neuroscience, 21*, 9430-9437.

Gehring, W. J., Gross, B., Coles, M. G., Meyer, D. E., & Donchin, E. (1993). A neural system for error-detection and compensation. *Psychological Science, 4(6),* 385-390.

Gehring, W. J., Himle, J., & Nisenson, L. G. (2000). Action-monitoring dysfunction in obsessive-compulsive disorder. *Psychological Science, 11(1),* 1-6.

Gehring, W. J., & Knight, R. T. (2000). Prefrontal-cingulate interactions in action monitoring. *Nature Neuroscience, 3*, 516.

Gessler, S., Cutting, J., Frith, C. D., & Weinman, J. (1989). Schizophrenic ability to judge
facial emotion: A controlled study. *British Journal of Clinical Psychology, 28*, 19-29.

Gilbert, P., Birchwood, M., Gilbert, J., Trower, P., Hay, J., Murray, B., Meaden, A., Olsen, K., & Miles, J. N. V. (2001). An exploration of evolved mental mechanisms for dominant and subordinate behaviour in relation to auditory hallucinations in schizophrenia and critical thoughts in depression. *Psychological Medicine, 31(6),* 1117-1127.

Glahn, D. C., Cannon, T. D., Gur, R. E., Ragland, J. D., & Gur, R. C. (2000). Working memory constrains abstraction in schizophrenia. *Biological Psychiatry, 47 (1),* 34-42.

Gold, J. M., Carpenter, C., Randolph, C., Goldberg, T. E., & Weinberger, D. R. (1997). Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. *Archives of General Psychiatry, 54(2),* 159-165.

Gold, J. M., & Harvey, P. D. (1993). Cognitive deficits in schizophrenia. *Psychiatric Clinics of North America, 16(2),* 295-312.

Gold, J. M., Randolph, C., Carpenter, C. J., Goldberg, T. E., & Weinberger, D. R. (1992). The performance of patients with schizophrenia on the Wechsler Memory Scale–Revised. *The Clinical Neuropsychologist, 6,* 367–373.

Gold, J. M., Rehkemper, G., Binks, S. W., III, Carpenter, C. J., Fleming, K., Goldberg, T. E., et al. (2000). Learning and forgetting in schizophrenia. *Journal of Abnormal Psychology, 109,* 534–538.

Goldberg, T. E., Ragland, J. D., Torrey, E. F., Gold, J. M., Bigelow, L. B., & Weinberger, D. R. (1990). Neuropsychological assessment of monozygotic twins discordant for schizophrenia. *Archives of General Psychiatry, 47,* 1066-1072.

Goldberg, T. E., Weinberger, D. R., Berman, K. F., Pliskin, N. H., et al. (1987). Further evidence for dementia of the prefrontal type in schizophrenia? A controlled study of teaching the Wisconsin Card Sorting Test. *Archives of General Psychiatry, 44(11),* 1008-1014.

Golgi, C. (1906). *Neuron doctrine: Theory and facts.* Nobel Lecture, Nobel Institute, Stockholm. December 11, 1906. www.nobel.se/

Golimbet, V. E., Alfimova, M. V., Kaleda, V. G., Lavrushina, O. M., Korovaitseva, G. I., Lezheiko, T. V., & Abramova, L. I. (2006). Verbal memory deficit in schizophrenia as a possible endophenotype of the disease. In Murray, William H. (Ed.) *Schizoaffective Disorders: New research* (pp. 165-186). Hauppauge, NY, US: Nova Science Publishers.

Górna, K., Jaracz, K., & Rybakowski, F. (2005). Social functioning in first-episode schizophrenia: 1-year follow-up study. *Archives of Psychiatry and Psychotherapy, 7(2)*, 5-19.

Grady, C. L., & Keightley, M. L. (2002). Studies in altered social cognition in neuropsychiatric disorders using functional neuroimaging. *Canadian Journal of Psychiatry, 48*, 327-336.

Grafton, S. T., Arbib, M. A., Fadiga, L., & Rizzolatti, G. (1996). Localization of grasp

representations in humans by PET: 2. Observations compared with imagination. *Experimental Brain Research, 112*, 103-111.

Grant, C., Addington, J., Addington, D., & Konnert, C. (2001). Social functioning in first- and multiepisode schizophrenia. *Canadian Journal of Psychiatry, 46(8),* 746-749.

Gratton G, Coles M.G.H, & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology, 55*, 468–484.

Green, M.F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry, 153,* 321-330.

Green, M.F., Kern, R.S., Braff, D.L., & Mintz, J. (2000). Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the "right stuff"? *Schizophrenia Bulletin 26,* 119-136.

Green, M. F., Kern, R. S., Robertson, M. J., Sergi, M. J., & Kee, K. S. (2000). Relevance of neurocognitive deficits for functional outcome in schizophrenia. In: Sharma, T., Harvey, P. D., (Eds.) *Cognition in Schizophrenia*. *Impairments, Importance, and Treatment Strategies* (pp. 178-192). New York, NY: Oxford University Press.

Green, M. F., & Nuechterlein, K. H. (2004). The MATRICS initiative: developing a consensus cognitive battery for clinical trials. *Schizophrenia Research, 72 (1),* 1-3.

Greve, K. W., Stickle, T. R., Love, J. M., Bianchini, K. J., & Stanford, M. S. (2005). Latent structure of the Wisconsin Card Sorting Test: A confirmatory factor analytic study. *Archives of Clinical Neuropsychology, 20(3),* 355-364.

Grèzes, J., & Decety, J. (2001). Functional anatomy of execution, mental simulation, observation, and verb generation of actions: a meta-analysis. *Human Brain Mapping, 12*, 1-19.

Guilmette, T. J., & Rasile, D. (1995). Sensitivity, specificity, and diagnostic accuracy of three verbal memory measures in the assessment of mild brain injury. *Neuropsychology, 9(3),* 338-344.

Häfner, J., Löffler, W., Maurer, K., Hambrecht, M., & an der Heiden, W. (1999). Depression, negative symptoms, social stagnation and social decline in the early course of schizophrenia. *Acta Psychiatrica Scandinavica, 100(2)*, 105-118.

Hajcak, G., McDonald, N., & Simons, R. F. (2003). Anxiety and error-related brain activity. *Biological Psychology, 64(1-2),* 77-90.

Hajcak, G., McDonald, N., & Simons, R. F. (2004). Error-related psychophysiology and negative affect. *Brain and Cognition, 56(2),* 189-197.

Hajcak G., & Simons R. F. (2002). Error-related brain activity in obsessive-compulsive undergraduates. *Psychiatry Research 110 (1),* 63-72.

Halford, W. K., & Hayes, R. L. (1995). Social skills in schizophrenia: Assessing the relationship between social skills, psychopathology and community functioning. *Social Psychiatry and Psychiatric Epidemiology, 30(1),* 14-19.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery & Psychiatry, 23,* 56-61.

Hans, S. L., Marcus, J., Henson, L., Auerbach, J. G., & Mirsky, A. F. (1992). Interpersonal behavior of children at risk for schizophrenia. *Psychiatry, 55*, 314-335.

Harrington, L., Siegert, R. J., & McClure, J. (2005). Theory of mind in schizophrenia: A critical review. *Cognitive Neuropsychiatry, 10(4)*, 249-286.

Harvey, P. D., Keefe, R. S., Moskowitz, J., Putnam, K. M., Mobs, R. C., & Davis, K. L. (1990). Attentional markers of vulnerability to schizophrenia: Performance of medicated and unmedicated patients and normals. *Psychiatry Research, 33*, 179-188.

Harvey, P. D., Reichenberg, A., Romero, M., Granholm, E., & Siever, L. J. (2006). Dual-task information processing in schizotypal personality disorder: Evidence of impaired processing capacity. *Neuropsychology, 20(4),* 453-460.

Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., & Curtiss, G. (1993). *Wisconsin Card Sorting Test Manual: Revised and Expanded (WCST).* Odessa, FL: Psychological Assessment Resources.

Hedlund, J. L., & Vieweg, B. W. (1980). The Brief Psychiatric Rating Scale (BPRS): A Comprehensive Review. *Journal of Operational Psychiatry, 11(1)*, 50-64.

Heimberg, C., Gur, R. E., Erwin, R. J., Shatasel, D. L., & Gur, R. C. (1992). Facial emotional discrimination, III: Behavioral findings in schizophrenia. *Psychiatry Research, 43*, 253-265.

Heinrichs, R. W., & Zakzanis, K. K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology, 12(3),* 426-445.

Heldmann, M., Rüsseler, J., & Münte, T. F. (2005). Event-related potentials in a decision-making task with delayed and immediate reward conditions. *Journal of Psychophysiology, 19(4),* 270-274.

Hill, S. K., Ragland, J. D., Gur, R. C., & Gur, R. E. (2001). Neuropsychological differences among empirically derived clinical subtypes of schizophrenia. *Neuropsychology, 15,* 492–501.

Holroyd, C. B., Dien, J., & Coles, M. G. H. (1998). Error-related scalp potentials elicited by hand and foot movements: Evidence for an output-independent error-processing system in humans. *Neuroscience Letters, 241,* 1-4.

Holroyd, C. B., & Coles, M. G. H. (2002). The neural basis of human error processing: Reinforcement learning, dopamine, and the error-related negativity. *Psychological Review, 109(4),* 679-709.

Holthausen, E. A., Wiersma, D., Sitskoorn, M. M., Hijman, R., Dingemans, P. M., Schene, A. H., et al. (2002). Schizophrenic patients without neuropsychological deficits: Subgroup, disease severity or cognitive compensation? *Psychiatry Research, 112,* 1–11.

Hooker, C., & Park, S. (2002). Emotion processing and its relationship to social functioning in schizophrenia patients. *Psychiatry Research, 112(1)*, 41-40.

Hooker, C. I., Verosky, S. C., Germine, L. T., Knight, R. T., & D'Esposito, M. (2008). Mentalizing about emotion and its relationship to empathy. Social Cognitive and Affective Neuroscience, 3(3), 204-217.

Horan, W. P., Kring, A. M., & Blanchard, J. J. (2006). Anhedonia in schizophrenia: A review of assessment strategies. *Schizophrenia Bulletin, 32(2),* 259-273.

Houlihan, J. P. (1977). Heterogeneity among schizophrenic patients: Selective review of recent findings (1970-75). *Schizophrenia Bulletin, 3(2),* 246-258.

Howieson, D. B., & Lezak, M. D. (1995). Separating memory from other cognitive problems. In A. D. Baddeley, B. A. Wilson, & F. N. Watts (Eds.), *Handbook of memory disorders* (pp. 411–426). Chichester, United Kingdom: Wiley.

Hughlings-Jackson, J. (1931). A study of convulsions. In: Taylor, J. (Ed.) *Selected Writings. Volume 1, Selected Writings of John Hughlings Jackson* (pp. 8-36). London, Hodder and Stoughton.

Inoue, Y., Yamada, K., Hirano, M., Shinohara, M. et al. (2006). Impairment of theory of mind in patients in remission following first episode schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience, 256(5)*, 326-328.

Insel, T. R., & Fernald, R. D. (2004). How the brain processes social information: Searching for the social brain. *Annual Review of Neuroscience, 27*, 697-722.

Janicak, P. G. (2006). The CATIE study and its implications for antipsychotic drug use. *Essential Psychopharmacology, 7(1),* 53-63.

Johnstone, E. C., MacMillan, J. F., Frith, C. D., Benn, D. K., & Crow, T. J. (1990). Further investigation of the predictors of outcome following first schizophrenia episodes. *British Journal of Psychiatry, 157*, 182-189.

Johnstone, E. C., Owens, D. G., Frith, C. D., & Crow, T. J. (1987). The relative stability of positive and negative features in chronic schizophrenia. *British Journal of Psychiatry, 150,* 60-64.

Jones, S. H., Hemsley, D. R., & Gray, J. A. (1991). Contextual effects on choice reaction time and accuracy in acute and chronic schizophrenics: Impairment in selective attention or in the influence of prior learning? *British Journal of Psychiatry, 159*, 415-421.

Jones, P., Rogers, B., Murray, R., & Marmot, M. (1994). Child development risk factors for adult schizophrenia in the British 1946 birth cohort. *Lancet, 344,* 1398-1408.

Jurden, F. H., Franzen, M. D., Callahan, T., & Ledbetter, M. (1996). Factorial equivalence of the Wechsler Memory Scale: revised across standardization and clinical samples. *Applied Neuropsychology, 3(2),* 65-74.

Kay, S. R. (1990). Positive-negative symptom assessment in schizophrenia: Psychometric issues and scale comparison. *Psychiatric Quarterly, 61(3),* 163-178.

Kee, K. S., Kern, R. S., & Green, M. F. (1998). Perception of emotion and neurocognitive functioning in schizophrenia: What's the link? *Psychiatry Research, 81(1)*, 57-65.

Keefe, R. S., Silverman, J. M., Roitman, S. E., Harvey, P. D., Duncan, M. A., Alroy, D., et al. (1994). Performance of nonpsychotic relatives of schizophrenic patients on cognitive tests. *Psychiatry Research, 53*, 1-12.

Kéri, S., Kelemen, O., Benedek, G., & Janka, Z. (2001). Different trait markers for schizophrenia and bipolar disorder: A neurocognitive approach. *Psychological Medicine, 31(5),* 915-922.

Kerns, J. G., Berenbaum, H., Barch, D. M., Banich, M. T., & Stolar, N. (1999). Word production in schizophrenia and its relationship to positive symptoms. *Psychiatry Research, 87(1),* 29-37.

Kerr, C. E. (2008). Dualism redux in recent neuroscience: 'Theory of mind' and 'embodied simulation' hypotheses in light of historical debates about perception, cognition, and mind. *Review of General Psychology, 12(2),* 205-214.

Kerr, S. L., & Neale, J. M. (1993). Emotion perception in schizophrenia: Specific deficit or further evidence of generalized poor performance? *Journal of Abnormal Psychology, 102(2)*, 312-318.

Kiehl, K. A., Liddle, P. F., & Hopfinger, J. B. (2000). Error processing and the rostral anterior cingulate: An event-related fMRI study. *Psychophysiology, 37(2),* 216-223.

Kline, J., Smith, J. E., & Ellis, H. C. (1992). Paranoid and nonparanoid schizophrenic processing of facially displayed affect. *Journal of Psychiatry Research, 26*, 169-182.

Knutson, K. M., McClellan, E. M., & Grafman, J. (2008). Observing social gestures: An fMRI study. Experimental Brain Research, 188(2), 187-198.

Kolb, B., & Whishaw, Q. (1990). *Fundamentals of human neuropsychology* (3rd ed.). New York: Freeman.

Kopp, B., Mattler, U., & Rist, F. (1994). Selective attention and response competition in schizophrenic patients. *Psychiatry Research, 53,* 129-139.

Kopp, B., & Rist, B. (1999). An event-related brain potential substrate of disturbed response monitoring in paranoid schizophrenic patients. *Journal of Abnormal Psychology, 108(2),* 337-346.

Koren, D., Seidman, L. J., Goldsmith, M., & Harvey, P. D. (2006). Real-world cognitive--and metacognitive—dysfunction in schizophrenia: A new approach for measuring (and remediating) more "right stuff." *Schizophrenia Bulletin, 32(2)*, 310-326.

Koren, D., Seidman, L. J., Harrison, R. H., Lyons, M. J., Kremem, W. S., Caplan, B., Goldstein, J. M., Faraone, S. V., & Tsuang, M. T. (1998). Factor structure of the Wisconsin Card Sorting Test: Dimensions of deficit in schizophrenia. *Neuropsychology, 12(2),* 289-302.

Kraepelin, E. (1971). *Dementia praecox and paraphrenia.* Edinburgh, Scotland: Livingstone. Original work published 1919).

Kremen, W. S., Seidman, L. J., Pepple, J. R., Lyons, M. J., Tsuang, M. T., & Faraone, S. V. (1994). Neuropsychological risk indicators for schizophrenia: A review of family studies. *Schizophrenia Bulletin, 20,* 103–119.

Kremen, W. S., Seidman, L. J., Faraone, S. V., Toomey, R., & Tsuang, M. T. (2000). The paradox of normal neuropsychological function in schizophrenia. *Journal of Abnormal Psychology, 109,* 743-752.

Kremen, W. S., Seidman, L. J., Faraone, S. V., Toomey, R., & Tsuang, M. T. (2004). Heterogeneity of schizophrenia: A study of individual neuropsychological profiles. *Schizophrenia Research, 71,* 307–321.

Landrø, N. I., & Ueland, T. (2008). Verbal memory and verbal fluency in adolescents with schizophrenia spectrum disorders. *Psychiatry and Clinical Neurosciences, 62(6),* 653-661.

Langdon, R., & Coltheart, M. (1999). Mentalising, schizotypy, and schizophrenia. *Cognition, 71(1)*, 43-71.

Langdon, R., Coltheart, M., & Ward, P. B. (2006). Empathic perspective-taking is impaired in schizophrenia: Evidence from a study of emotion attribution and theory of mind. *Cognitive Neuropsychiatry, 11(2)*, 133-155.

Langdon, R., Coltheart, M., Ward, P.B., & Catts, S. V. (2002). Mentalising, executive planning and disengagement in schizophrenia. *Cognitive Neuropsychiatry, 6(2)*, 81-108.

Langdon, R., Davies, M., & Coltheart, M. (2002). Understanding minds and understanding communicated meanings in schizophrenia. *Mind & Language, 17(1-2)*, 68-104.

Langdon, R., Michie, P. T., Ward, P. B., McConaghy, N., Catts, S. V., & Coltheart, M. (1997). Defective self and/or other mentalising in schizophrenia: A cognitive neuropsychological approach. *Cognitive Neuropsychiatry, 2(3)*, 167-193.

Lee, J., & Park, S. (2005). Working memory impairments in schizophrenia: A meta-analysis. *Journal of Abnormal Psychology, 114,* 599–611.

Leonard, C., & Corrigan, P. W. (2001). Social perception in schizophrenia. In P. W. Corrigan & D. L. Penn (Eds.), *Social Cognition in Schizophrenia* (pp. 73-95). Washington, DC: American Psychological Association.

Leucht, S., Shamsi, S. A. R., Busch, R., Kissling, W., & Kane, J. M. (2008). Predicting antipsychotic drug response--Replication and extension to six weeks in an international olanzapine study. *Schizophrenia Research, 101(1-3),* 312-319.

Lewis, S. F., & Garver, D. L. (1995). Treatment and diagnostic subtype in facial affect recognition in schizophrenia. *Journal of Psychiatry Research, 29*, 5-11.

Lezak, M. D. (1995). *Neuropsychological assessment* (3rd ed.). New York: Oxford University Press.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological assessment* (4th ed.). New York: Oxford University Press.

Li, C. S. (2004). Do schizophrenia patients make more perseverative than non-perseverative errors on the Wisconsin Card Sorting Test? A meta-analytic study. *Psychiatry Research, 129(2),* 179-90.

Liberman, R. P. (1982). Assessment of social skills. *Schizophrenia Bulletin, 8(1)*, 62-84.

Lord, F. M. (1967). A paradox in the interpretation of group comparisons. *Psychological Bulletin, 68(5),* 304-5.

Lord, F. M. (1969). Statistical adjustments when comparing preexisting groups. (1969). *Psychological Bulletin, 72(5),* 336-337.

Loring, D. W. (1989). The Wechsler Memory Scale--Revised, or the Wechsler Memory Scale--Revisited? *Clinical Neuropsychologist, 3(1),* 59-69.

Luck, S. J. (2005). *An Introduction to the Event-Related Potential Technique.* Cambridge, MA: Massachusetts Institute of Technology Press.

Luu, P., Collins, P., & Tucker, D. M. (2000). Mood, personality, and self-monitoring: Negative affect and emotionality in relation to frontal lobe mechanisms of error monitoring. *Journal of Experimental Psychology, 129(1),* 43-60.

Luu, P., Flaish, T., & Tucker, D. M. (2000). Medial frontal cortex in action monitoring. *Journal of Neuroscience, 20,* 464-469.

MacDonald, A. W., Cohen, J. G., Stenger, V. A., & Carter, C. S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science, 288*, 1835-1838.

Malla, A. K., Norman, R. M. G., Williamson, P., Cortese, L., & Diaz, F. (1993). Three syndrome concept of schizophrenia: A factor analytic study. *Schizophrenia Research 10*, 143-150.

Marom, S., Munitz, H., Jones, P. B., Weizman, A., & Hermesh, H. (2002). Familial expressed emotion: Outcome and course of Israeli patients with schizophrenia. *Schizophrenia Bulletin, 28(4),* 731-743.

Mathalon, D. H., Fedor, M., Faustman, W. O., Gray, M., Askari, N., & Ford, J. M. (2002). Response-monitoring dysfunction in schizophrenia: An event-related potential study. *Journal of Abnormal Psychology, 111(1),* 22-41.

Mathewson, K. J., Dywan, J., & Segalowitz, S. J. (2005). Brain bases of error-related ERPs as influenced by age and task. *Biological Psychology, 70(2),* 88-104.

Matsumoto, K., Suzuki, W., & Tanaka, K. (2003). Neuronal correlates of goal-based motor selection in the prefrontal cortex. *Science, 301,* 229-232.

McKetin, R., & Mattick, R. P. (1998). Attention and memory in illicit amphetamine users: Comparison with non-drug-using controls. *Drug and Alcohol Dependence, 50(2),* 181-184.

Milev, P., Ho, B., Arndt, S., & Andreasen, N. C. (2005). Predictive Values of Neurocognition and Negative Symptoms on Functional Outcome in Schizophrenia: A Longitudinal First-Episode Study with 7-Year Follow-Up. *American Journal of Psychiatry, 162(3),* 495-506.

Milner, B. (1963). Effects of different brain lesions on card sorting. *Archives of Neurology, 9,* 100–110.

Miltner, W. H. R., Brauer, J., Hecht, H., Trippe, R., & Coles, M. G. H. (2004). Parallel brain activity for self-generated and observed errors. In M. Ullsperger & M. Falkenstein (Eds.), *Errors, Conflicts, and the Brain. Current Opinions on Performance Monitoring* (pp. 124-129). Leipzig: MPI of Cognitive Neuroscience.

Miltner, W. H. R., Lemke, U., Weiss, T., Holroyd, C., Scheffers, M. K., & Coles, M. G. H. (1997). The source of the magnetic equivalent of the error-related negativity. *Psychophysiology, 34(suppl.),* S65.

Mitchell, J. P. (2008). Activity in right temporoparietal junction is not selective for theory-of-mind. *Cerebral Cortex, 18 (2),* 262–271.

Mithen, S. (1996). The early prehistory of human social behaviour: Issues of archaeological inference and cognitive evolution. In W. G. Runciman, J. Maynard, and R. I. M. Dunbar (Eds.), *Evolution of Social Behaviour Patterns in Primates and Man* (pp. 145-177).

Mitropoulou, V., Harvey, P. D., Maldari, L. A., Moriarty, P. J., New, A. S., Silverman, J. M., et al. (2002). Neuropsychological performance in schizotypal personality disorder: Evidence regarding diagnostic specificity. *Biological Psychiatry, 52,* 1175–1182.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41,* 49–100.

Montague, P.R., Hyman, S.E., Cohen, J.D., 2004. Computational roles for dopamine in behavioural control. *Nature 431,* 760–767.

Moore, P. M., & Baker, G. A. (1997). Psychometric properties and factor structure of the Wechsler Memory Scale--Revised in a sample of persons with intractable epilepsy. *Journal of Clinical and Experimental Neuropsychology, 19(6),* 897-905.

Morgado, A., Smith, M., Lecrubier, Y., & Widlöcher, D. (1991). Depressed subjects unwittingly overreport poor social adjustment which they reappraise when recovered. *Journal of Nervous and Mental Disease, 179(10),* 614-619.

Morris, S. E., Yee, C. M., & Nuechterlein, K. H. (2006). An electrophysiological analysis of error-monitoring in schizophrenia. *Journal of Abnormal Psychology, 115(2),* 239-250.

Morrison, R., & Bellack, A. S. (1987). Social functioning of schizophrenic patients: Clinical and research issues. *Schizophrenia Bulletin, 13,* 715-725.

Moser, J. S., Hajcak, G., & Simons, R. F. (2005). The effects of fear on performance monitoring and attentional allocation. *Psychophysiology, 42(3),* 261-268.

Mueser, K. T., & Bellack, A. S. (1998). Social skills and social functioning. In K. T. Mueser and N. Tarrier (Eds.), *Handbook of Social Functioning in Schizophrenia* (pp. 79-96). Needham Heights, MA: Allyn & Bacon.

Mueser, K. T., Bellack, A. S., Douglas, M. S., & Morrison, R. L. (1991). Prevalence and stability of social skill deficits in schizophrenia. *Schizophrenia Research, 5(2),* 167-176.

Mueser, K. T., Bellack, A. S., Morrison, R. L., & Wixted, J. T. (1990). Social competence in schizophrenia: Premorbid adjustment, social skills, and domains of functioning. *Journal of Psychiatry Research, 24*, 51-63.

Mueser, K. T., Curran, P. J., & McHugo, G. J. (1997). Factor structure of the Brief Psychiatric Rating Scale in schizophrenia. *Psychological Assessment, 9(3),* 196-204.

Mueser, K. T., & Tarrier, N. (1998). *Handbook of Social Functioning in Schizophrenia*. Needham Heights, MA: Allyn & Bacon.

Murphy, D. (2006). Theory of mind in Asperger's syndrome, schizophrenia and personality disordered forensic patients. *Cognitive Neuropsychiatry, 11(2),* 99-111.

Murray, R. M., & Lewis, S. W. (1987). Is schizophrenia a neurodevelopmental disorder? *British Medical Journal, 295,* 681–682.

Myin-Germeys, I., Nicolson, N. A., & Delespaul, P. A. E. G. (2001). The context of delusional experiences in the daily life of patients with schizophrenia. *Psychological Medicine, 31(3),* 489-498.

Naugle, R. I., Chelune, G. J., Cheek, R., Lüders, H., & Awad, I. A. (1993). Detection of changes in material-specific memory following temporal lobectomy using the Wechsler Memory Scale-Revised. *Archives of Clinical Neuropsychology: The Official Journal Of The National Academy Of Neuropsychologists, 8(5),* 381-395.

Nelson, Hazel E. (1976). A modified card sorting test sensitive to frontal lobe defects. *Cortex, 12(4),* 313-324.

Newcomer, J. W., Faustman, W. O., Yeh, W., & Csernansky, J. G. (1990). Distinguishing depression and negative symptoms in unmedicated patients with schizophrenia. *Psychiatry Research, 31(3),* 243-250.

Niendam, T. A., Bearden, C. E., Rosso, I. M., Sanchez, L. E., Hadley, T., Nuechterlein, K. H., et al. (2003). A prospective study of childhood neurocognitive functioning in schizophrenic patients and their siblings. *American Journal of Psychiatry, 160,* 2060–2062.

Nienow, T. M., Docherty, N. M., Cohen, A. S., & Dinzeo, T. J. (2006). Attentional dysfunction, social perception, and social competence: What is the nature of the relationship? *Journal of Abnormal Psychology, 115(3)*, 408-417.

Nieuwenhuis, S., Ridderinkhof, K. R., Blom, J., Band, G., & Kok, A. (2001). Error-related brain potentials are differentially related to awareness of response errors: Evidence from an antisaccade task. *Psychophysiology, 38(5),* 752-760.

Nieuwenhuis, S., Yeung, N., Holroyd, C. B., Schurger, A., & Cohen, J. D. (2004). Sensitivity of Electrophysiological Activity from Medial Frontal Cortex to Utilitarian and Performance Feedback. *Cerebral Cortex, 14(7),* 741-747.

Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E.; Green, M. F., & Heaton, R. K. (2004). Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research, 72(1),* 29-39.

Nuechterlein, K. H., & Dawson, M. E. (1984). Information processing and attentional functioning in the developmental course of schizophrenic disorders. *Schizophrenia Bulletin, 10,* 160–203.

Oliveira, F. T. P., McDonald, J. J., & Goodman, D. (2007). Performance monitoring in the anterior cingulate is not all error related: Expectancy deviation and the representation of action-outcome associations. *Journal of Cognitive Neuroscience, 19(12),* 1994-2004.

Overall, J. E., & Beller, S. A. (1984). The Brief Psychotic Rating Scale (BPRS) in geropsychiatric research: I. Factor structure on an inpatient unit. *Journal of Gerontology, 2*, 187-193.

Overall, J. E., & Gorham, D. R. (1962). The Brief Psychiatric Rating Scale. *Psychological Reports, 10,* 799-812.

Overall, J. E., & Klett, C. J. (1972). *Applied Multivariate Analysis.* McGraw Hill, NY.

Ozonoff, S. (1995). Executive functions in autism. In Schopler, Eric; Mesibov, Gary B (Eds.) *Learning and cognition in autism* (pp. 199-219). New York, NY, US: Plenum Press.

Pallanti, S., Quercioli, L., & Hollander, E. (2004). Social anxiety in outpatients with schizophrenia: A relevant cause of disability. *American Journal of Psychiatry, 161(1)*, 53-58.

Palmer, B. W., & Heaton, R. K. (2000). Executive dysfunction in schizophrenia. In T. Sharma & P. D. Harvey (Eds.), *Cognition in schizophrenia: Impairments, importance and treatment strategies* (pp. 51–72). Oxford, United Kingdom: Oxford University Press.

Palmer, B. W., Heaton, R. K., Paulsen, J. S., Kuck, J., Braff, D., Harris, M. J., et al. (1997). Is it possible to be schizophrenic and yet neuropsychologically normal? *Neuropsychology, 11,* 437-446.

Paulus, M. P., Hozack, N., Frank, L., Brown, G. G., & Schuckit, M. A. (2003). Decision making by methamphetamine-dependent subjects is associated with error-rate-independent decrease in prefrontal and parietal activation. *Biological Psychiatry, 53*, 65-74.

Penn, D. L., Combs, D., & Mohamed, S. (2001). Social cognition and social functioning in schizophrenia. In Patrick W. Corrigan and David L. Penn (Eds.), *Social Cognition and Schizophrenia* (pp. 97-121). Washington, DC, US: American Psychological Association.

Penn, D. L., Corrigan, P. W., Bentall, R. P., Racenstein, J. M., & Newman, L. (1997). Social cognition in schizophrenia. *Psychological Bulletin, 121(1)*, 114-132.

Penn, D. L., Corrigan, P. W., Martin, J., Inhen, G., Racenstein, J. M., Nelson, D., Cassisi, J., & Hope, D. A. (1999). Social cognition and social skills in schizophrenia: The role of self-monitoring. *Journal of Nervous and Mental Disease, 187(3)*, 188-190.

Penn, D. L., Corrigan, P. W., & Racenstein, J. M. (1998). Cognitive factors and social adjustment in schizophrenia. In K. T. Mueser and N. Tarrier (Eds.), *Handbook of Social Functioning in Schizophrenia* (pp. 213-223). Needham Heights, MA: Allyn & Bacon.

Penn, D. L., Mueser, K. T., Spaulding, W., Hope, D. A., et al. (1995). Information processing and social competence in chronic schizophrenia. *Schizophrenia Bulletin, 21(2)*, 269-281.

Penn, D. L., Spaulding, W., Reed, D., & Sullivan, M. (1996). The relationship of social cognition to ward behavior in chronic schizophrenia. *Schizophrenia Research, 20(3)*, 327-335.

Perlick, D., Stastny, P., Mattis, S., & Teresi, J. (1992). Contribution of family, cognitive, and clinical dimensions to long-term outcome in schizophrenia. *Schizophrenia Research, 6*, 257-265.

Perrine, K. (1993). Differential aspects of conceptual processing in the Category Test and Wisconsin Card Sorting Test. *Journal of Clinical and Experimental Neuropsychology, 15(4),* 461-473.

Pickup, G. J., & Frith, C. D. (2001). Theory of mind impairments in schizophrenia: Symptomatology, severity, and specificity. *Psychological Medicine, 31(2)*, 207-220.

Pilowsky, T., Yurmiya, N., Arbelle, S., & Mozes, T. (2000). Theory of mind abilities in children with schizophrenia, children with autism, and normally developing children. *Schizophrenia Research, 42(2)*, 145-155.

Pinkham, A. E., Penn, D. L., Perkins, D. O., & Lieberman, J. (2003). Implications for the neural basis of social cognition for the study of schizophrenia. *American Journal of Psychiatry, 160(5)*, 815-824).

Pogue-Geile, M. F. (1989). The prognostic significance of negative symptoms in schizophrenia. British Journal of Psychiatry, 155(Suppl 7), 123-127.

Poole, J. H., Tobias, F. C., & Vinogradov, S. (2000). The functional relevance of affect recognition errors in schizophrenia. *Journal of International Neuropsychological Society, 6(6)*, 649-658.

Posner, M. I., & Dehaene, S. (1994). Attentional networks. *Trends in Neuroscience, 17(2),* 75-79.

Potts, G. F., George, M. R., Martin, L. E., & Barratt E. S. (2006). Reduced punishment sensitivity in neural systems of behavior monitoring in impulsive individuals. *Neuroscience Letters, 397(1-2),* 130-134.

Prentice, K. J., Gold, J. M., & Buchanan, R. W. (2008). The Wisconsin Card Sorting impairment in schizophrenia is evident in the first four trials. *Schizophrenia Research, 106(1),* 81-87.

Randall, F., Corcoran, R., Day, J. C., & Bentall, R. P. (2003). Attention, theory of mind, and causal attributions in people with persecutory delusions: A preliminary investigation. *Cognitive Neuropsychiatry, 8(4)*, 287-294.

Reichenberg, A., & Harvey, P. D. (2007). Neuropsychological impairments in schizophrenia: Integration of performance-based and brain imaging findings. *Psychological Bulletin, 133(5),* 833-858.

Reitan, R. M., & Wolfson, D. (1994). A selective and critical review of neuropsychological deficits and the frontal lobes. *Neuropsychology Review, 4,* 161–198.

Revheim, N., Schechter, I., Kim, D., Silipo, G., Allingham, B., Butler, P., & Javitt, D. C. (2006). Neurocognitive and symptom correlates of daily problem-solving skills in schizophrenia. *Schizophrenia Research, 83(2-3),* 237-245.

Rey, G. J., Feldman, E., Rivas-Vazquez, R., Levin, B. E., & Benton, A. (1999). Neuropsychological test development and normative data on Hispanics. *Archives of Clinical Neuropsychology, 14(7),* 593-601.

Rezai, K., Andreasen, N. C., Alliger, R., & Cohen, G. (1993). The neuropsychology of the prefrontal cortex. *Archives of Neurology, 50(6),* 636-642.

Rizzolatti, G., & Craighero, L. (2004). The mirror neuron system. *Annual Review of Neuroscience, 27*, 169-192.

Rizzolatti, G., Fadiga, L., Fogassi, L., & Gallese, V. (1996). Premotor cortex and the recognition of motor actions. *Cognitive Brain Research, 3*, 131-141.

Rizzolatti, G., Fogassi, L., & Gallese, V. (2001). Neurophysiological mechanisms underlying the understanding and imitation of action. *Nature Review of Neuroscience, 2*, 661-670.

Rodríguez-Sánchez, J. M., Pérez-Iglesias, R., González-Blanch, C., Pelayo-Terán, J. M., Mata, I., Martínez, O., Sánchez-Cubillo, I., Vázquez-Barquero, J. L., & Crespo-Facorro, B. (2008). 1-year follow-up study of cognitive function in first-episode non-affective psychosis. *Schizophrenia Research, 104(1-3),* 165-174.

Rohland, B. M, & Langbehn, D. R. (1997). 'Characterizing quality of life among patients with chronic mental illness: A critical examination of the self-report methodology': Commentary. *American Journal of Psychiatry, 154(10),* 1478-1479.

Rosenberg, S. D., Mueser, K. T., Jankowski, M. K., Salyers, M. P., Acker, K. (2004). Cognitive-Behavioral Treatment of PTSD in Severe Mental Illness: Results of a Pilot Study. *American Journal of Psychiatric Rehabilitation, 7(2),* 171-186.

Ruchsow, M., Herrnberger, B., Beschoner, P., Grön, G., Spitzer, M., & Kiefer, M. (2006). Error processing in major depressive disorder: Evidence from event-related potentials. *Journal of Psychiatric Research, 40(1),* 37-46.

Ruchsow, M., Herrnberger, B., Wiesend, C., Grön, G., Spitzer, M., & Kiefer, M. (2004). The effect of erroneous responses on response monitoring in patients with major depressive disorder: A study with event-related potentials. *Psychophysiology, 41(6),* 833-840.

Ruggeri, M., Koeter, M.,C Schene, A., Bonetto, C., Vàzquez-Barquero, J. L., Becker, T., Knapp, M., Knudsen, H. C., Tansella, M., & Thornicroft, G. (2005). Factor solution of the BPRS-expanded version in schizophrenic outpatients living in five European countries. *Schizophrenia Research, 75(1),* 107-117.

Russell, T. A., Reynaud, E., Herba, C., Morris R., & Corcoran, R. (2006). Do you see what I see? Interpretations of intentional movement in schizophrenia. *Schizophrenia Research, 81(1)*, 101-111.

Ryu, Y., Mizuno, M., Sakuma, K., Munakata, S., et al. (2006). Deinstitutionalization of long-stay patients with schizophrenia: The 2-year social and clinical outcome of a comprehensive intervention program in Japan. *Australian and New Zealand Journal of Psychiatry, 40(5),* 462-470.

Safarti, Y., Hardy-Bayle, M., Nadel, J., Chevalier, J., & Widlocher, D. (1997). Attribution of mental states to others by schizophrenic patients. *Cognitive Neuropsychiatry, 2*, 1-17.

Saykin, A. J., Shtasel, D. L., Gur, R. E., Kester, D. B., Mozley, L. H., Stafiniak, P., et al., (1994). Neuropsychological deficits in neuroleptic naïve patients with first-episode schizophrenia. *Archives of General Psychiatry, 51,* 124-131.

Scheffers, M. K., Coles, M. G. H., Bernstein, P., Gehring, W. J., & Donchin, E. (1996). Event-related brain potentials and error-related processing: An analysis of incorrect responses to go and no-go stimuli. *Psychophysiology, 33(1),* 42-53.

Scholten, M. R. M., van Honk, J., Aleman, A., & Kahn, R. S. (2006). Behavioral inhibition system (BIS), Behavioral activation system (BAS) and schizophrenia: Relationship with psychopathology and physiology. *Journal of Psychiatric Research, 40(7),* 638-645.

Schulkin, J. (2000). Theory of mind and mirroring neurons. *Trends in Cognitive Sciences, 4(7)*, 252-254.

Schulte-Rüther, M., Markowitsch, H. J., Fink, G. R., & Piefke, M. (2007). Mirror neuron and theory of mind mechanisms involved in face-to-face interactions: A functional magnetic resonance imaging approach to empathy. *Journal of Cognitive Neuroscience, 19(8),* 1354-1372.

Schulte-Rüther, M., Markowitsch, H. J., Shah, N. J., Fink, G. R., & Piefke, M. (2008). Gender differences in brain networks supporting empathy. *Neuroimage, 42(1),* 393-403.

Schultz, W., 2002. Getting formal with dopamine and reward. *Neuron 36,* 241–263.

Scott, J. E., & Lehman, A. F. (1998). Social functioning in the community. In K. T. Mueser and N. Tarrier (Eds.), *Handbook of Social Functioning in Schizophrenia* (pp. 1-19). Needham Heights, MA: Allyn & Bacon.

Seidman, L. J. (1983). Schizophrenia and brain dysfunction: An integration of recent neurodiagnostic findings. *Psychological Bulletin, 94,* 195-238.

Shallice, T., & Burgess, P. W. (1998). The domain of supervisory processes and temporal organization of behaviour. In A. C. Roberts, T. W. Robbins, & L. Weiskrantz (Eds.), *The prefrontal cortex: Executive and cognitive functions* (pp. 22–35). New York: Oxford University Press.

Shallice, T., Burgess, P. W., & Frith, C. D. (1991). Can the neuropsychological case-study approach be applied to schizophrenia? *Psychological Medicine, 21,* 661–673.

Shaw, R. J., Dong, M., Lim, K. O., Faustman, W. O., Pouget, E. R., & Alpert, M. (1999). The relationship between affect expression and affect recognition in schizophrenia. *Schizophrenia Research, 37(3)*, 245-250.

Silverstein, S. M., Hatashita-Wong, M., Wilkniss, S., Bloch, A., Smith, T., Savitz, A., McCarthy, R., Friedman, M., & Terkelsen, K. (2006). Behavioral rehabilitation of the 'treatment-refractory' schizophrenia patient: Conceptual foundations, interventions, and outcome data. *Psychological Services, 3(3),* 145-169.

Silverstein, S. M., Osborn, L. M., & Palumbo, D. R. (1998). Rey-Osterrieth Complex Figure Test performance in acute, chronic, and remitted schizophrenia patients. *Journal of Clinical Psychology, 54,* 985-994.

Sitskoorn, M. M., Aleman, A., Ebisch, S. J., Appels, M. C., & Kahn, R. S. (2004). Cognitive deficits in relatives of patients with schizophrenia: A meta-analysis. *Schizophrenia Research, 71,* 285–295.

Spohn, H. E. (1973). The case for reporting the drug status of patient subjects in experimental studies of schizophrenic psychopathology. *Journal of Abnormal Psychology, 82(1),* 102-106.

Spohn, H. E., & Strauss, M. E. (1989). Relation of neuroleptic and anticholinergic medication to cognitive functions in schizophrenia. *Journal of Abnormal Psychology, 98(4),* 367-380.

Streit, M., Wölwer, W., & Gaebel, W. (1997). Facial-affect recognition and visual scanning behaviour in the course of schizophrenia*. Schizophrenia Research, 24(3)*, 311-317.

Suhara, T., Okubo, Y., Yasuno, F., Sudo, Y., Inoue, M., Ichimiya, T., et al. (2002). Decreased dopamine D_2 receptor binding in the anterior cingulate cortex in schizophrenia. *Archives of General Psychiatry, 14,* 25-30.

Tan, Y., Zou, Y., Qu, Y., & Guo, X. (2002). Stability of commonly used measures in the Wisconsin Card Sorting Test. *Chinese Mental Health Journal, 16(12),* 831-833.

Tien, A. Y., & Eaton, W. W. (1992). Psychopathologic precursors and sociodemographic risk factors for the schizophrenia syndrome. *Archives of General Psychiatry, 49*, 37-46.

Tops, M., Lorist, M. M., Wijers, A. A., & Meijman, T. F. (2004). To stress or relax: neurochemical aspects of activity and rest. *Gedrag en Organisatie, 17,* 32-42.

Tucker, D. M., Hartry-Speiser, A., McDougal, L., Luu, P., & deGrandpre, D. (1999). Mood and spatial memory: Emotion and right hemisphere contribution to spatial cognition. *Biological Psychology, 50(2),* 103-125.

Twamley, E. W., Narvaez, J. M., Becker, D. R., Bartels, S. J., & Jeste, D. V. (2008). Supported employment for middle-aged and older people with schizophrenia. *American Journal of Psychiatric Rehabilitation, 11(1),* 76-89.

Uzun, O., Cansever, A., Basoğlu, C., & Ozşahin, A. (2003). Smoking and substance abuse in outpatients with schizophrenia: a 2-year follow-up study in Turkey. *Drug and Alcohol Dependence, 70 (2),* 187-92.

Van Schie, H. T., Mars, R. B., Coles, M. G. H., & Bekkering, H. (2004). Modulation of activity in medial frontal and motor cortices during error observation. *Nature Neuroscience, 7(5),* 549-554.

Vázquez Mórejon, A. J., & G-Bóveda, R. J. (2000). Social Functioning Scale: New contributions concerning its psychometric characteristics in a Spanish adaptation. *Psychiatry Research, 93(3),* 247-256.

Walker, E. F. (1994). Developmentally moderated expressions of the neuropathology underlying schizophrenia. *Schizophrenia Bulletin, 20*, 453-480.

Walker, E. F., Harvey, P. D., & Perlman, D. (1988). The positive/negative symptom distinction in psychoses: A replication and extension of previous findings. Journal of Nervous and Mental Disease, 176(6), 359-363.

Wechsler, D. (1945). *Wechsler Memory Scale.* San Antonio, TX, US: Psychological Corporation.

Wechsler, D. (1987). *Wechsler Memory Scale – Revised.* New York: Psychological Corporation.

Weinberger, D. R. (1987). Implications of normal brain development for the pathogenesis of schizophrenia. *Archives of General Psychiatry, 44,* 660–669.

Weinberger, D. R., Berman, K. F., & Chase, T. N. (1988) Mesocortical dopaminergic function and human cognition. *Annals of the New York Academy of Sciences, 537,* 330-338.

Wernicke, C. (1906). *Grundrisse der Psychiatrie.* Thieme.

Wittorf, A., Klingberg, S., & Wiedemann, G. (2004). Secondary verbal memory: A potential endophenotype of schizophrenia. *Psychiatric Research, 38(6),* 601-612.

Yager, J. A., & Ehmann, T. S. (2006). Untangling social function and social cognition: A review of concepts and measurement. *Psychiatry: Interpersonal and Biological Processes, 69(1)*, 47-68.

Yamaguchi, S., & Knight, R. T. (1991). Age effects on the P300 to novel somatosensory stimuli. *Electroencephalography And Clinical Neurophysiology, 78(4),* 297-301.

Yeung, N., Botvinick, M. M., & Cohen, J. D. (2004). The neural basis of error detection: Conflict monitoring and the error-related negativity. *Psychological Review, 111(4),* 931-959.

Yildiz, M., Veznedaroglu, B., Eryavuz, A., & Kayahan, B. (2004). Psychosocial skills training on social functioning and quality of life in the treatment of schizophrenia: A controlled study in Turkey. *International Journal of Psychiatry in Clinical Practice, 8(4),* 219-225