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PERSONALITY DIMENSIONS AND COGNITIVE FUNCTIONING OF RELATIVES OF PERSONS DIAGNOSED WITH SCHIZOPHRENIA AND BIPOLAR I DISORDER: A COMPARATIVE AND PREDICTIVE STUDY

By

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Dedication

This dissertation is dedicated to my parents, James and Noel Paavola, whose unconditional love and support provided the foundation for this entire endeavor, and to my grandparents, Eric and Evelyn Reinbold, who have taught me the value of lifelong learning and humility. Finally, I dedicate this dissertation in memory of my brother Scott. During his life he inspired me to strive for my goals no matter how difficult they may seem. Eleven years following his death, Scott's memory continues to influence who I am and what I do each and every day.

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CHAPTER I

Introduction

Arguably, two of the most devastating mental illnesses facing psychiatric patients today are schizophrenia and bipolar I disorder. To be diagnosed with either illness can be distressing to both patients and their family members. Lifetime prevalence rates for both disorders are similar, around 1% (Kessler et al., 2005; Merikangas et al., 2007). Further devastating is that both of these disorders have been shown to aggregate in families and it is commonly accepted that there is some genetic risk associated with each disorder (Ivleva, Thaker, & Tamminga, 2008; Owen, Craddock, Jablensky, 2007). Given this genetic risk family studies have been important in attempting to better understand the etiology of both disorders.

The etiology of both schizophrenia and bipolar disorder is largely unknown. There are substantial bodies of literature investigating the etiology of both disorders, albeit separately, and without significant progress toward a greater understanding of what causes both of these illnesses. Some suggest the lack of significant progress in understanding the etiology of both schizophrenia and bipolar disorder is due in part to the nature of our current diagnostic system (Ivleva, Thaker, Tamminga, 2008; Owen et al., 2007). In recent volumes of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM; American Psychological Association, 1994, 2000), these often chronic mental illnesses are classified separately under the psychotic and mood disorder sections, respectively. However, both illnesses have been identified to share some common features, which have increasingly interested researchers. For one, although bipolar I disorder is primarily considered a mood disorder, during active phases of the illness (either manic or depressive episodes), individuals

may also experience symptoms of psychosis, not unlike the delusions and hallucinations prominent in schizophrenia (Keshavan, Diwadkar, & Rosenberg, 2005). This raises the possibility that there is not a clean biological distinction between schizophrenia and bipolar disorder.

Another striking similarity between the two psychiatric disorders is the large volume of research accumulated over the past few decades that has focused upon the family members of patients with schizophrenia and bipolar disorder. There is a long history of studying the family members of these individuals, especially using concordance studies towards determining the genetic bases of these disorders. Similarly, some of the current classifications of personality disorders (e.g. schizotypal) as described in DSM-III-R (1987) and DSM-IV-TR (2000) grew out of family studies of psychotic patients (Kendler, 1985), wherein family members of psychotic patients were found to exhibit symptoms of these major Axis I disorders, but in an attenuated form. These family studies helped to develop additional classification systems of sub-clinical forms of the illnesses, such as schizotypal personality disorder.

Schizophrenia family studies are numerous. Bipolar family studies are numerous. However, there are fewer studies that investigate similarities and differences among the family members of each patient group. Conventionally, the disorders have not been studied together. However, in the last decade, research has begun to explore the overlap in these disorders, especially following the adoption in psychiatry of the endophenotypic method of research (Gottesman & Gould, 2003; Ivleva et al., 2008). An endophenotype is considered either a symptom or "vulnerability marker" (e.g. psychosis or neurocognitive abilities) intermediary between a genotype and the expressed phenotype (e.g. schizophrenia).

According to Gottesman and Gould (2003), an endophenotype may be neurophysiological, neuroanatomical, cognitive or psychological. To investigate all of these forms and related findings would be beyond the scope of this study and interested parties are referred to Carpenter and colleagues' (2009) discussion of the proposed meta-structure for the psychoses section of the DSM-V. Here the authors provide a review of findings in these endophenotypic areas as related to psychosis research.

In that regard, one theory that has been put forth by some experts in the field is that schizophrenia and bipolar disorder may not be distinct diagnostic entities, but rather exist on a proposed "affective-psychotic spectrum" with schizophrenia lying at one end of this spectrum, non-psychotic affective disorders lying at the opposite end of the spectrum, and schizoaffective and psychotic bipolar disorders falling somewhere in the middle (Craddock, O'Donovan, & Owen, 2006; Lichtenstein et al., 2009; Valles et al., 2000). The present study will not address this ongoing debate directly. However, it may help to shape further research related to the proposed reformulation of how we understand and categorize bipolar disorder and schizophrenia. Given this potential shift in the way that we conceptualize the major psychiatric illnesses, and the fact that it is being influenced by findings from large family studies (Van Snellenberg & de Candia, 2009), it seems appropriate to devote more research to identifying similarities and differences among family members of schizophrenia patients as compared to family members of bipolar patients.

The purpose of the present study is to explore patterns of personality traits and cognition among family members of individuals diagnosed with either disorder. It will also be important to determine the extent to which both of these groups differ from persons without a family history of psychosis or severe mood disorder. Of primary interest will be to

compare the family members of schizophrenia patients with the family members of bipolar I disorder patients, in order to examine shared and unique patterns of personality and cognitive functioning. Studies have shown some clustering of specific personality traits in both family groups (Savitz & Ramesar, 2006; Silberschmidt & Sponheim, 2007; Tsuang, Stone, Tarbox, & Faraone, 2002). Similarly, researchers have identified some cognitive deficits in areas such as attention and working memory in schizophrenia and bipolar patients, as well as their family members (Diwadkar, Montrose, Dworakowski, Sweeney & Keshavan, 2006). However, both personality and neurocognitive findings have been mixed. In the area of personality research into family members of schizophrenic and bipolar disordered individuals, the somewhat inconsistent findings may in large part be due to a lack of consistent methodology, namely in choice of personality measure.

Schizophrenia and bipolar relatives have been compared in each area of functioning, separately. However, to this author's knowledge, few studies have focused upon both personality traits and neurocognition while comparing schizophrenia and bipolar disorder family members. Results of this study, therefore, may be useful in guiding future research that might combine both areas of psychological functioning. Findings from the schizophrenia family studies and findings from the bipolar disorder family studies will be reviewed in the context of both personality traits and neurocognition. The existing data that combines these two types of functioning will also be reviewed for each of the disorders, and finally, the reader will be familiarized with current findings regarding the overlapping aspects of personality and cognition as observed in both schizophrenia and bipolar patients and their family members.

Schizophrenia and Bipolar I Disorder, Briefly Defined

Schizophrenia and bipolar I disorder are currently seen as separate and distinct disorders from a diagnostic standpoint. Both disorders have a typical onset in young adulthood, which is slightly earlier in males (Murray et al., 2004). Also common to both of these mental illnesses is the difficulty a clinician or researcher can experience in arriving at either diagnosis, as both disorders are somewhat heterogeneous in nature. There are certain clinical features that must mark either disorder, yet within each disorder there is wide variation between individuals, in onset, course and presentation.

Schizophrenia is a mental illness marked by a combination of positive and negative symptoms persisting for a significant portion of time and leading to some form of impairment in a person's occupation, relationships, and/or self-care. Andreasen and Carpenter (1993) differentiate between those symptoms that are in excess of normal mental function (positive) compared to those symptoms that reflect a loss of a function that should normally be there (negative). Positive symptoms are viewed as the active or more florid symptoms of psychosis and include delusions, hallucinations, bizarre behavior, and thought disorder. Negative symptoms or the "underproductive" symptoms include affective blunting, poverty of speech and thought (alogia), anhedonia, impairments in attention, and low motivation or avolition (Andreasen & Carpenter, 1993; Andreasen & Olsen, 1982; Kay, 1990).

The hallmark feature of bipolar I disorder is affective dysregulation. Individuals with bipolar disorder (of all types) usually experience recurrent and fluctuating cycles of major depression and mania/hypomania, with intermittent periods of recovery. A person does not need to experience episodes of depression in order to be diagnosed with bipolar I disorder, and many individuals do not become clinically depressed throughout the course of their

illness (Merikangas et al., 2007). Furthermore, individuals may or may not experience symptoms of psychosis during manic and depressed episodes. However, Craddock and colleagues (2006) suggest that cases of bipolar disorder with a mix of mood and psychotic features are common. In describing symptoms of psychosis experienced by patients during acute episodes of mania, Murray and colleagues (2004) assert that these patients are often indistinguishable from patients with schizophrenia.

Historical Contributions to the Classification of Schizophrenia and Bipolar Disorder

Dementia praecox versus manic-depressive illness. German psychiatrist Emil Kraepelin's (1919/1971) diagnostic classification of mental disorders remains the foundation of our understanding of schizophrenia and bipolar disorder today. The early family studies of psychosis followed Emil Kraepelin's well-known, psychiatric classification system of what had previously been considered a unitary concept of psychosis. Formerly regarded as separate disorders, Kraepelin unified hebephrenia, catatonia and paranoia under the general heading of "dementia praecox," which he regarded as all chronic and progressively degenerative diseases. He was insistent in his belief that dementia praecox was a "brain disease" and that some toxin in the brain caused it to "autointoxicate" itself and create the progressive symptoms that he had observed in his patients (Noll, 2000).

Kraepelin is also credited with being the first to distinguish what he called "dementia praecox" from affective psychosis, which he referred to as "manic-depressive illness" (Greene, 2007; Zubin & Spring, 1977). Current proponents of the "affective-psychotic spectrum" theory suggest we are coming full circle in regard to how we conceptualize bipolar disorder and schizophrenia, as they favor a rejection of what has commonly been referred to as the "Kraepelinian Dichotomy" (Craddock & Owen, 2005; Greene, 2007). Kraepelin's

system was also considered distinct in that he was the first to propose that these mental disorders were manifestations of underlying biological illnesses. Kraepelin believed dementia praecox was a progressive disease resulting in permanent functional impairment. In contrast, he saw manic-depression as an intermittent illness with a much better prognosis. Kraepelin's major focus in distinguishing the two disorders from one another was based upon this idea of disease progression and prognosis.

Kraepelin (1921/1987) also introduced a dimensional view of manic-depressive illness, or "insanity" as he called it. He identified "fundamental states" as premorbid characteristics of patients with mood disorders. He stated, "There are certain temperaments which may be regarded as rudiments of manic-depressive insanity. They may throughout the whole of life exist as peculiar forms of psychic personality without further development; but they may also become the point of departure for a morbid process which develops under peculiar conditions and runs its course in isolated attacks" (1921/1987, p. 118). Kraepelin's approach to manic-depressive illness has been described as temperament-centered (Akiskal et al., 1998; Savitz & Ramesar, 2006). Kraepelin's (1921/1987) "fundamental states" were broken into the categories of depressive, hyperthymic or manic, irritable and cyclothymic and remain fairly well reflected in the most recent version of the DSM-IV-TR (APA, 2000).

Bleuler's four sub-types. In contrast, Eugene Bleuler (1911/1950) disagreed with Kraepelin's focus on the negative prognosis of dementia praecox as the defining characteristic of the disorder and instead renamed it "schizophrenia." The origin of the label schizophrenia came from the Greek words for "to split" and "mind." For Bleuler, this new term stressed what he believed was the fundamental nature of the psychotic disorders. That is, the splitting or dissociation of psychic functions. Bleuler argued that there are psychic

splits in areas of functioning that characterize normal trains of thought, normal functions of affect, and normal functions of behavior. Bleuler divided the clinical picture of schizophrenia into four fundamental symptoms, which included loosening of associations, autism, ambivalence, and loss of affective responsiveness. He believed the fundamental symptoms were caused directly by the disease process itself and were present to some degree during the entire course of the illness. Bleuler also identified secondary or accessory symptoms such as delusions, hallucinations, transient catatonic episodes, and behavioral disturbances. These secondary symptoms were observed to come and go throughout the course of the illness and were found in other mental disorders as well, e.g. bipolar disorder. The current clinical representation of schizophrenia in the DSM-IV is highly reminiscent of Bleuler's fundamental four subtypes. The paranoid and catatonic subtypes of schizophrenia are still used today. The hebephrenic type was renamed "disorganized" and the current "undifferentiated" type is the replacement for "simple schizophrenia." Bleuler is credited with recognizing the heterogeneity that existed within the schizophrenias (Noll, 2000).

Schizotaxia and schizotypy. Another important contribution to our current understanding of psychotic disorders was the work of Paul Meehl (1962, 1989). Meehl (1962) was the first to use the term "schizotaxia" to demonstrate that schizophrenia was "a neurologic disorder of genetic origin" (Meehl, 1989, p. 935). Schizotaxia was the conjecture he used to succinctly describe a "neural integrative defect" that he believed was genetically transmitted and served to predispose groups of individuals to develop schizophrenia or the milder schizotypy. Meehl asserted that schizotaxia is the only thing that is inherited in schizophrenia. However, according to Meehl, schizotaxia does not necessarily lead to the development of schizophrenia. He believed that there were certain environmental factors

interacting with “polygenic potentiators” that could push a schizotaxic person in the direction of psychopathology. According to Meehl’s (1989) theory, some of these potentiators included anxiety, aggression, energy level, and dominance.

Meehl used the term “schizotypy” to refer to the unusual personality organization that may result from the interaction between schizotaxia and certain social learning experiences in one’s environment. He identified four “core behavior traits” of these individuals. First, a schizotypal person was seen to experience cognitive slippage or very mild forms of thought disorder. Second, schizotypal individuals were described as interpersonally aversive, which included feelings of distrust, an expectation of rejection, and a conviction that they were unlovable. Third, their experiences were marked by anhedonia in that their capacity to experience pleasure was less than that of the general population. Finally, schizotypal individuals were described as ambivalent.

According to Meehl, the “schizotype” may develop schizophrenia, but this is not always the case. Meehl hypothesized that one of the most causal influences that could “potentiate” the decompensation from schizotype to schizophrenic was the “schizophrenogenic mother,” a term Meehl borrowed from the psychoanalysts. However, in his theory Meehl (1989) stated that only 10% of schizotypes will actually decompensate to develop schizophrenia. The remaining schizotypes will range in functioning from generally normal functioning to less extreme versions of the schizophrenia spectrum disorders (schizoid, paranoid and schizotypal personality disorders). In DSM-IV nomenclature, these disorders fall under the general category “cluster A personalities” (APA, 1994, 2000).

Features of the “schizophrenia spectrum” may include poor social skills, social isolation, aloofness, cold demeanor, eccentric behavior, eccentric speech, nervousness,

irritability, anhedonia, avolition, and poor affective control (Berenbaum, Taylor & Cloninger, 1994; Kendler, 1985). These behavioral deviances may or may not reach a threshold to diagnose a personality disorder. Meehl's theory was influential in developing subsequent diathesis-stress models of schizophrenia (Fowles, 1992; Zubin & Spring, 1977), as well as providing a theoretical framework for the family studies of schizophrenia and personality (Berenbaum et al., 1994).

Temperament, Personality Disorders, and Personality Traits

Temperament, character and personality are terms that are often used interchangeably, but have been distinguished by personality theorists to define different constructs (Cloninger, 1987, Akiskal et al., 2006). Consistent with theorists such as Cloninger and Akiskal, temperament and character are thought to be two components of personality. Succinctly, Goldsmith and colleagues (1987) identify temperament as an aspect of an individual that remains stable over time and is heritable. It is a predisposition towards certain patterns of reactivity, mood, and sensitivity. Character is not as well-defined and is more often not easily distinguished from temperament and personality (Evans et al., 2005). Cloninger (1999) has described character as self-conscious goals and emotions developing in a stepwise manner that are influenced by both temperament and experience. By the third edition of his seminal text, Kraepelin (1913) began to trace the origins of his two major syndromes and identified two premorbid temperaments. The "cyclothymic disposition" included four variants and was seen by Kraepelin to be inclined toward manic-depressive insanity. The "autistic temperament" was disposed toward dementia praecox.

There are numerous theories of personality that have been put forth in sociological, psychological and psychiatric literature (e.g. the Five Factor Model, Millon's circumplex

configurations, Cloninger's three dimensional model, Cloninger and Svrakic's seven factor model, the DSM diagnostic system, psychoanalytic theories). It would be beyond the scope of this paper to review any of these in great detail. Furthermore, there is a large body of empirical instruments that are used to measure and quantify personality. Some of these include Costa and McCrae's (1992) Revised Neuroticism, Extraversion, and Openness Personality Inventory (NEO-PI-R, Clark's (1993) Schedule for Nonadaptive and Adaptive Personality (SNAP), and Stangl & Zimmerman's (1997) Structured Interview for DSM-IV Personality, 4th Edition (SIDP-IV). Some personality theorists propose dimensional models with supporting empirical measures (Costa and McCrae, 1992), whereas others propose more categorical systems (DSM-IV-TR; APA, 2000). Another distinguishing feature among personality theories is the extent to which that model reflects "normal" personality functioning as compared to pathological personality.

One important dimensional theory is that of Cloninger, Svrakic, and Przybeck (1993). Cloninger and his colleagues have made some significant contributions to the field with their genetic and family studies of both temperament and personality. Cloninger's original model of personality was based on three dimensions of temperament including Harm Avoidance, Novelty Seeking, and Reward Dependence as measured by the self-report inventory he developed which was called the Tri-Dimensional Personality Questionnaire (Cloninger, 1986). He later added a fourth dimension of Persistence. Per the model, temperament was biologically influenced and inherited. It consisted of these heritable biases in memory processing that involved perceptual processing and encoding of both visuospatial and affective information. Likening his system to theories of conditioning and non-associative learning, he believed these processes were organized around specific brain systems that were

responsible for autonomic responses involved in the activation, maintenance and inhibition of behavior. He had intended that these four dimensions would provide differential diagnosis of personality disordered populations, but he has since argued that they did not provide enough information related to variance in the traits to distinguish clinical from non-clinical populations. Cloninger, Svrakic, and Przybeck (1993) revised the model to add self-directedness, cooperativeness, and self-transcendence. Cloninger and his group believed these reflected larger dimensions of character, which took into account more abstract processing of sensory data.

The dominant categorical model of personality is that of the DSM-IV (APA, 1994). The DSM-IV diagnostic system of personality disorders has often been criticized for its lack of dimensionality and the seemingly indistinct boundaries between normal and abnormal personality traits (Widiger, 2003). Opponents suggest that personality exists on a continuum from adaptive to maladaptive without a definitive line separating function and dysfunction. DSM-IV assesses traits dichotomously (i.e. as present or absent). In contrast to DSM-IV, dimensional systems may lack clinical specificity even though they account for a wider range of personality functioning (Clark, 1993). One advantage of using the DSM-IV system in empirical research is that it is probably the most well-known system. Furthermore, DSM-IV does not need to be used in a purely categorical fashion. DSM-IV employs a trait-dimensional model in its classification of Axis II disorders (Clark & Kruger, 2008). Traits are more stable than personality disorders, themselves, per se, and can exist on a continuum or dimension. Traits can also be conceptualized as a fundamental unit of description and when grouped together can more specifically describe a given individual (Reichborn-Kjennerud, 2008). The current DSM-IV-TR (APA, 2000) classification of personality

includes ten categories of disorders. These 10 categories are then divided into three clusters (A, B, and C), which allows for genetic comparison of the diagnoses contained within each cluster. Cluster A, described as the "odd and eccentric" cluster, consists of the schizoid, paranoid and schizotypal personalities (APA, 2000). Cluster B, is described as the "dramatic, emotional and erratic" cluster, and is comprised by the antisocial, narcissistic, borderline and histrionic personalities. Cluster C, described as the "anxious and fearful" cluster, includes the avoidant, obsessive-compulsive, and dependent personalities. The interested reader is referred to the DSM-IV-TR for more detailed descriptions of each of the 10 personality disorders and specific traits comprising these.

Personality Traits of Relatives of Schizophrenia Patients

Both Kraepelin (1919/1971) and Bleuler (1911/1950) observed that some close relatives of patients with schizophrenia presented with odd or eccentric personalities that were clinically similar to schizophrenia, albeit without demonstrating overt psychosis. One of the first important studies of personality functioning in schizophrenia families was the Copenhagen Adoption Study (Kety, Rosenthal, Wender, Schulsinger, & Jacobsen, 1975; as cited in Kendler et al., 1993). In an attempt to determine the incidence of schizophrenia in the biological and adoptive relatives of schizophrenia patients, Kety and colleagues first reviewed hospital records and then later conducted personal interviews with these relatives. They found a statistically significant higher rate of what they considered to be "borderline or uncertain schizophrenia" (based on a newly devised diagnostic set) in the biological relatives of schizophrenia as compared to control subjects. Based upon the results of this study, the schizotypal personality disorder, which first appeared in DSM-III (APA, 1980), was identified.

A large body of research has been collected comparing the personality traits of relatives of schizophrenics. Some studies have shown that all three cluster A personality disorders are at increased risk in the relatives of schizophrenia probands (Kendler et al., 1993; Maier, Lichtermann, Minges, & Heun, 1994; Parnas et al., 1993; Thaker, Adami, Moran, Lahti, & Cassady, 1993). However, it is most common to find studies where only schizotypal personality disorder is prevalent in the family members of schizophrenia patients (Kendler & Gardner, 1997; Torgersen, Onstad, Skre, 1993). In his review of personality disorder findings, Reichborn-Kjennerud (2008) asserts that these results suggest that schizotypal personality disorder is the personality disorder with the closest familial relationship to schizophrenia.

It is fairly well accepted that there is a greater incidence of schizotypal traits in family members of schizophrenia patients when compared to controls without a family history of schizophrenia (Appels, Sitskoorn, Vollema, & Kahn, 2004; Kendler, Thacker, Walsh, 1996). However, there is a lack of consistency among findings related to elevated traits (Cortes et al., 2009), which can make comparison of studies and generalizability of findings quite difficult. A Turkish study by Bora and Veznedaroglu (2007) compared the relatives of schizophrenia patients to healthy controls based on Cloninger's biopsychosocial model of personality. Prior research comparing schizophrenia patients to community controls has consistently shown higher scores on the temperament variable of Harm Avoidance (HA) for the patient group (Guillem, Bicu, Semkovska, & Debruille, 2002) when applying Cloninger's model. Bora and Veznedaroglu (2007) attempted to extend these findings to family members as they believe that personality features may represent vulnerability indicators of schizophrenia. In the 2007 study, not all relatives of schizophrenia patients showed

significantly higher scores on harm avoidance. Rather, only the relative group that also had significant scores on ratings of schizotypy showed higher harm avoidance when compared with controls. Additionally, this group showed significantly higher Self Transcendence scores when compared to controls. The non-schizotypal relative group differed from controls, but in the temperament and character dimensions of self-directedness and cooperativeness, which were both higher than in the control group.

In a study that focused upon traits as opposed to personality disorders, Berenbaum, Taylor and Cloninger (1994) interviewed relatives of schizophrenia patients, relatives of affective disordered patients, and relatives of non-psychiatric surgical patients. These subjects also completed the Multi-dimensional Personality Questionnaire (MPQ), a self-report measure which provides mean scores on 11 "normal primary personality traits." Relatives of schizophrenics only differed from the other groups on the trait of Social Closeness, leading the study group to conclude that this aspect of the MPQ may not just reflect personality traits, but other aspects of social behavior similar to symptoms of schizophrenia, such as anhedonia, or extreme social anxiety and may therefore reflect Meehl's (1989) milder form of schizophrenia. With regard to the relatives of the affective disordered patients included in Berenbaum and colleagues' (1994) study, although there were some elevations on the scale of well-being and negative emotionality, the sample of these individuals was quite small and as a result further analyses could not be conducted nor could significant conclusions be drawn.

Features of the avoidant personality disorder have also been linked to schizophrenia. In a study of first-episode psychotic patients, Keshavan, Duggal, Veeragandham and colleagues (2005) found higher levels of cluster C personality disorder characteristics in

schizophrenia patients as compared to healthy controls. The authors employed a semi-structured interview called the Personality Disorder Evaluation that allowed them to obtain dimensional scores for each of the DSM-III-R (APA, 1987) personality types. In the schizophrenia patients, both the schizotypal and avoidant personalities were the most frequent and the avoidant personality dimensional scores correlated with all three of the cluster A personalities when considering the schizophrenia patient group. This led the researchers to conclude that there may be an association between avoidant personality features and schizophrenia that goes beyond the potential for overlapping constructs. Keshavan, Duggal and their group (2005) suggested that this may be representative of Meehl's (1962) core symptom of "social aversiveness" in his definition of schizotypy. Similarly, Kendler and colleagues (1995) found that the avoidant-related symptoms in schizotypy were the only factor to differentiate between schizophrenia relatives and psychotic affective illness in the Roscommon Family Study.

In a more recent study, Fogelson and colleagues (2007) examined the rates of avoidant personality disorder among three groups. Their sample included 362 first degree relatives of schizophrenia probands, 201 relatives of ADHD probands, and 245 relatives of community controls. The presence of avoidant personality disorder was determined via the Structured Clinical Interview for DSM-III-R: Personality Disorders (SCID-II) by Spitzer and colleagues in 1990 (as cited in Fogelson et al., 2007) and diagnostic consensus meeting. Specific avoidant personality characteristics that were most prevalent in the family members of the schizophrenia patients were "avoids social or occupational activities" and "exaggerates the potential difficulties." The frequency of avoidant personality disorder was found to be significantly higher in the schizophrenia relatives as compared to both of the other groups.

This was also the case when the authors controlled for schizotypal and paranoid personality disorders, which allowed them to conclude that avoidant personality disorder may be a separate schizophrenia-spectrum disorder and not just a sub-clinical form of the cluster A personalities. Finally, Fogelson and his group conjectured that their findings may reflect the prominence of social dysfunction in not just schizophrenia patients, but their unaffected relatives as well, which they suggest may represent a vulnerability to schizophrenia.

Some studies have looked at specific family relationships when investigating the personality traits of relatives of schizophrenia patients. One particularly important area of research involves studying the children of schizophrenia patients. The incidence of schizophrenia in the general population is approximately 1% (Kessler et al., 2005). In contrast, adolescent children of schizophrenia patients are 15 to 30 times more likely to develop the illness than the general population (Gottesman and Shields, 1982). Therefore, when the average age of onset for schizophrenia is taken into account, the biological offspring of patients during a critical period represent a high-risk group. Further research with adolescent and young adult children of schizophrenia patients, as well as the development of interventions suited to their needs, may be the most prognostically appropriate approach. These types of studies have revealed interesting findings related to personality functioning and neurocognitive function.

Diwadkar and colleagues (2006) recruited a sample of high risk for schizophrenia (HR-S) adolescents and compared them to a control group of adolescents without any family history of psychosis on measures of schizotypy, a measure of prefrontal function (the Wisconsin Card Sorting task), and a measure of spatial working memory called the oculomotor delayed response (ODR) task. Following clinical assessment, the HR-S group

was divided into two groups reflecting whether or not they were exhibiting schizotypal spectrum psychopathology. The HR-S group that was negative for symptoms of schizotypy (HR-NSSP) was not significantly different from the control group when composite schizotypy scores were compared. Findings from the neurocognitive tasks revealed no differences in performance on working memory tasks between controls and the HR-NSSP group. Ratings of schizotypy were highly correlated (r=.49) with the number of errors on the Wisconsin Card Sorting task (a measure of executive functioning). Working memory results from the ODR task did not show significant differences between the three groups, although healthy controls tended to be more accurate than either of the high risk groups. Performance on the ODR task has been shown to improve with age. Notably, when the three groups were analyzed for age-related improvements, the older participants in both high-risk groups performed worse than their younger counterparts. This was not the case for the healthy controls, where older participants showed improved task performance. The authors concluded that the findings may suggest an association between schizotypy and developmental deficits in working memory.

Personality Traits of Relatives of Bipolar Disordered Patients

Many of the bipolar family studies that have been related to personality traits and/or personality functioning have come out of research into the affective temperaments (Kraepelin, 1921/1987) and the "bipolar spectrum" (Akiskal, 1984; Akiskal et al., 1998). This is a theoretical area that has been heavily championed and investigated by the American psychiatrist, Hagop Akiskal. Akiskal (1984) believes the hyperthymic and cyclothymic temperaments represent milder expressions of, and are related to, bipolar disorder. Similar to theories of schizophrenia, these subclinical states or affective temperaments are expected to

be prevalent in families of bipolar disordered patients. That is, when they do not progress into a diagnosable axis I mood disorder. The interested reader is referred to Savitz and Ramesar's (2006) review of the relationship between bipolar affective disorder and personality. The authors summarize current research surrounding each of Kraepelin's (1921/1987) four fundamental states (depressive/dysthymic, manic/hyperthymic, irritable, and cyclothymic). Different forms of affective illness have been shown to be related to each of these temperaments (Akiskal et al., 2006). However, findings overlap to some extent and there exists no direct relationships between any particular affective illness and temperament. For example, the cyclothymic temperament has been found to be related to bipolar II disorder, but bipolar II disorder has also been linked to the hyperthymic temperament (Hantouche et al., 1998). The cyclothymic temperament reflects rapid and unpredictable mood swings between the depressive and hyperthymic poles of the bipolar spectrum and has been shown to be associated to some extent with DSM-III (1980) diagnoses of borderline personality disorder (Akiskal, Chen, Davis et al., 1985).

In a study comparing the personality traits of first-degree relatives of bipolar individuals with community controls, Maier, Minges, Lichtermann and Heun (1995) found that only obsessive-compulsive personality disorder was significantly more prevalent among bipolar relatives when compared with relatives of controls. All other personality disorder comparisons were not significant. There was a trend toward greater prevalence of any personality disorder in bipolar relatives (12.6%) as compared to relatives of controls (9.4%). However, this difference did not reach statistical significance. Maier and colleagues used a structured interview to determine lifetime prevalence of a personality disorder diagnosis and also included a self-report measure, the Munich Personality Test (MPT) by von Zerssen in

1988 (as cited by Maier et al., 1995) to assess six personality factors. The personality factors measured by the MPT included extraversion, neuroticism, frustration tolerance, rigidity, isolation tendencies, and esoteric tendencies. Of the six factors, only rigidity differentiated between the bipolar and control relatives. A major limitation of this study was in the make-up of the bipolar group as it included all forms of bipolar illness.

There have been a number of recent studies that have consistently used the same measure of temperament to explore the manifestations of personality related traits in the family members of bipolar-disordered individuals (e.g. Evans et al., 2005; Kesebir et al., 2005; Mendlowicz, Jean-Louis, Kelsoe, & Akiskal, 2005). The measure used in all three of the aforementioned studies is the Temperament Evaluation of Memphis, Pisa, Paris and San-Diego-Autoquestionnaire (TEMPS-A). The TEMPS-A was designed by Akiskal and colleagues in 1998 to assess the four basic affective temperaments of the "bipolar spectrum" and is a self-report questionnaire containing 110 items.

In a comparison of bipolar disorder patients, their unaffected relatives and community controls, Mendlowicz and colleagues (2005) found elevated cyclothymic and anxiety-related traits in the patient and relative groups when compared to controls. The patient group was also significantly more elevated on both scales when compared to the relative group. Similar findings marked the study by Evans and her colleagues (2005) wherein they compared bipolar relatives and controls. A drawback to both of these studies was the combination of bipolar II and bipolar I in the same groups. Evans and colleagues (2005) pointed out that these two groups may represent clinically different groups and this cannot be ruled out based on the findings. Kesebir and colleagues (2005) improved on this limitation by including only bipolar I disordered patients (n=100) and their relatives (n=219) in their sample. They also

utilized a control group (n=319) that was matched on age and gender with both probands and relatives. Using the Turkish version of the TEMPS-A, the authors computed dominant temperament type based on the z scores of the affective temperaments produced by the scale. Kesebir and colleagues (2005) reported a graded distribution of dominant temperament with hyperthymic temperament being significantly more common in the patient group as compared to the relative group as compared to the control group. Results of all of these studies suggest that the relatives of bipolar patients are distinguishable from members of the population without a family history of bipolar disorder and therefore may share common personality traits.

Combined Studies of Familial Personality

In a recent study, Silberschmidt and Sponheim (2008) compared the personality characteristics of first-degree relatives of people with schizophrenia, first-degree relatives of people with bipolar I disorder, and nonpsychiatric control participants using a new measure. Although Silberschmidt and Sponheim's study primarily looked at genetic polymorphisms, what were of particular relevance for the current study are the findings related to personality. Silberschmidt and Sponheim selected a measure of personality that they described as better able to characterize a full range of personality pathology than measures used in previous studies. They employed Livesley and Jackson's (2008) Dimensional Assessment for Personality Pathology – Basic Questionnaire (DAPP-BQ). Silberschmidt and Sponheim (2008) described the DAPP-BQ as a self-report measure containing 290 items that comprise 18 scales. Significant differences were found when schizophrenia relatives were compared to controls, as well as when they were compared to the relatives of bipolar I disordered patients. Compared to controls, the schizophrenia family group scored lower on stimulus

seeking and higher on restrictive expression and social avoidance. The schizophrenia family group was found to have lower scores on narcissism, rejection of the ideas of others, stimulus-seeking, passive-aggressive oppositionality, and self-harm. Converting these descriptors into terminology found in the DSM-IV (1994), the authors pointed out that these findings may be quite consistent with the personality traits of avoidant personality disorder, even though it is not generally believed to be part of the schizophrenia spectrum of personality disorders. These findings may lend more support to Fogelson and colleagues' (2007) assertion that avoidant personality disorder should be included in the schizophrenia spectrum as a disorder separate and distinct from the other cluster A personalities.

Relatives of bipolar patients in the Silberschmidt and Sponheim (2008) study showed scale elevations that were unshared with the schizophrenia group. These included affective lability, cognitive dysregulation, identity problems, insecure attachment, and self-harm. The authors conjectured that these elevations were consistent with a precursor for a bipolar temperament, which they identified as "hyperthymic temperament" and is consistent with previous findings within the bipolar family studies that specifically looked at the family members of patients with bipolar I disorder (Kesebir et al., 2005). Results of this study support the idea that the three groups (SCH relatives, BP relatives, and nonpsychiatric controls) can be distinguished from one another on measures of personality, especially when these measures contain specific scales. It may also support the theory that those who carry a genetic risk for the major psychiatric illnesses may also show subclinical manifestations of these illnesses.

Cognitive Deficits in Schizophrenia and Bipolar Disorder Patients

There is a large body of literature establishing that patients with schizophrenia show cognitive deficits when compared with the normal population and other psychiatric groups (e.g. Bora, Yücel & Pantelis, 2010; Krabbendam, Arts, van Os, & Aleman, 2005; Saykin et al., 1991). Keefe and Fenton (2007) assert that patients with schizophrenia perform 1.5 to 2.0 standard deviations below healthy controls on a variety of cognitive tasks. Several key areas of cognitive functioning have been implicated as impaired in schizophrenia patients including verbal memory, working memory, motor speed, attention, executive function and verbal fluency (Keefe et al., 2004). Numerous studies have supported the notion that cognitive deficits represent core features of schizophrenia (Green et al., 2004) and these deficits have been found to exist both during active phases of the illness, as well as before the onset of psychotic symptoms. It has also been determined that deficits in cognitive performance are not only the result of clinical symptoms or the side effects of pharmacological treatment (Harvey & Keefe, 2001), but may represent an underlying component of the illness.

Recently, the National Institute of Mental Health (NIMH) began an initiative called the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) that was charged with designing a test battery to be used in the standardized evaluation of cognitive changes in schizophrenia for use in both clinical trials and other research studies (Green et al., 2004; Nuechterlein et al., 2004). The MATRICS group defines a cognitive deficit as disturbance in an underlying cognitive process, which may or may not be observed in clinical observation and standard clinical instruments, but can be detected by appropriately designed cognitive performance tasks (Green et al., 2004). A

subcommittee of this group examined factor analytic studies of cognitive performance in schizophrenia in order to identify the most important domains of functioning to be assessed with such a battery. They identified six separable factors which included working memory, attention/vigilance, verbal learning and memory, visual learning and memory, reasoning and problem solving (executive functioning), and speed of processing. Greater understanding of the patterns of these deficits may lead to improvements in treatment including, but not limited to, early interventions with high-risk relatives and/or patients in the prodromal phase of the illness (Harvey & Keefe, 2001).

A current trend in schizophrenia treatment that could be extended to relatives of patients with schizophrenia, as well as other psychiatric groups who may show similar cognitive deficits is cognitive remediation therapy (CRT). Using a computerized program, CRT provides exercises targeted at training specific cognitive functions known to be impaired in schizophrenia, especially attention and executive functioning. This is proving to be a promising mode of treatment with a recent study showing significant improvement nine months following a three month long treatment (Poletti et al., 2010). Schizophrenia participants were assessed at baseline, three months and nine months using the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al., 2004), the Continuous Performance Test (Rosvold, Mirksy, Sarason, Bransome & Beck, 1956), and the Wisconsin Card Sort (Heaton, 1981).

To be able to extend CRT to bipolar I patients could be promising as well. However, less is known about the cognitive deficits manifested in patients with this illness. Kraepelin (1921/1987) originally proposed that manic-depression could be differentiated from dementia praecox due to the lack of cognitive deficits, yet recent studies have suggested this may not

be the case (Krabbendam et al., 2005). Unfortunately, due in part to both the heterogeneous nature of the illness and the heterogeneity of the studies that have examined cognitive deficits in bipolar disorder, the pattern of cognitive functioning in bipolar disorder patients remains less clear and less researched than the same in schizophrenia. In general, patients with bipolar illness have been shown to exhibit similar impairments in cognitive functioning when compared to schizophrenia patients (Murray et al., 2004). Daban and colleagues (2006) found these impairments were especially in the domains of attention, memory, and executive function. However, bipolar patients differed from schizophrenia patients in that these impairments were less severe. Daban and his group also found that bipolar patients differed from schizophrenia patients in that they showed higher general intelligence scores. Krabbendam and colleagues (2005) conducted a meta-analysis that reviewed 31 studies comparing patients with schizophrenia to patients with bipolar disorder on neuropsychological tasks. Combined effect sizes were calculated for 11 cognitive domains based on results of the 31 studies included in the meta-analysis. The authors found that deficits in schizophrenia were more severe than in bipolar disorder on nine out of eleven cognitive domains. One argument for this difference is that cognitive deficits in bipolar disorder may be more state-dependent than what is observed in schizophrenia (Keefe & Fenton, 2007).

Cognitive Constructs, Defined

The three areas of cognitive functioning that have shown impairment in both groups and are of particular interest in the current study are attention, working memory, and executive functioning. Deficits in these domains of cognitive functioning are considered by some to be the most important for daily functioning (Trivedi et al., 2008). Thus, focusing

upon them may be of particular importance. Attention, working memory and executive functioning share some overlap within and across measures and studies, but will be defined historically, as well as in the context of findings from the identification of the six cognitive factors completed as part of the MATRICS initiative (Nuechterlein et al., 2004). The three cognitive constructs of primary concern for the purposes of this study will be briefly described herein.

Attention. Mirsky, Anthony, Duncan, Ahearn and Kellam (1991) derived four components of attention via a factor analytic study. They identified the first factor of attention as "focus/execute," which refers to an individual's capacity to focus on and scan stimuli, and additionally execute responses in a quick manner. Reitan's (1958) Trail Making Test and the Digit Symbol-Coding subtest of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III; Wechsler, 1997) each measure this first factor. "Sustained attention" was identified as the second factor by Mirksy and his group. It involves the capacity to maintain focused attention and is most often measured with continuous performance tests. In their review of cognitive factors in schizophrenia, the MATRICS group (see Nuechterlein et al., 2004) noted that the most commonly used measure of sustained attention in schizophrenia research was various forms of the Continuous Performance Test (CPT; Rosvold et al., 1956). The MATRICS group noted that studies in normal subjects have seen an overlap in attention and working memory, but that a measure that emphasizes sustained attention or vigilance such as what can be gleaned from the CPT is a separate factor from working memory in schizophrenia. In contrast to "focus/execute," there is greater demand for prolonged vigilance than for scanning of stimuli. The third attentional component was labeled "shift" and involves the capacity to shift one's attention from one stimulus to another. It involves

flexibility and can be measured by the Wisconsin Card Sorting test (Heaton, 1981), which is a common measure used in schizophrenia research. Finally, the fourth attentional factor is "encoding." Encoding is the capacity to serially incorporate, manipulate, store and recall information. Two subtests from the WAIS-III (Wechsler, 1997) commonly are used to measure this factor including Arithmetic and Digit Span.

Working memory. Working memory was first described by Baddeley (1992) as a "brain system that provides temporary storage and manipulation of the information necessary for such complex cognitive tasks as language comprehension, learning, and reasoning" and "requires the simultaneous storage and processing of information" (p. 556). According to the MATRICS group, the most common measures in the schizophrenia research that loaded on this factor were subtests from the WAIS-III (Wechsler, 1997) that included Arithmetic, Digit Span, and Letter-Number Sequencing, as well as the *N*-back working memory task (Cohen et al, 1997). Each of these tasks involves short-term storage and mental manipulation of information.

Executive functioning. Executive functioning comprises several higher order processes. Lezak (1995) describes executive functions as containing four components, which include volition, planning, purposive action, and effective performance. Together these components measure one's ability to determine wants and needs, generate alternatives, formulate and accomplish goals, inhibit impulses, and monitor performance. According to Lezak, abstract thinking and mental flexibility also fall under executive functioning. Nuechterlein and colleagues (2004) chose to label this factor that emerged in the MATRICS research as "reasoning and problem solving", as opposed to executive functioning, so as not to confuse it with the central executive component of working memory. According to

Nuechterlein and colleagues (2004) the cognitive measures that loaded highly on this factor were the Wisconsin Card Sorting test (Heaton, 1981), the Matrix Reasoning and Block design subtests of the WAIS-III (Wechsler, 1997), and the Tower of Hanoi or Tower of London procedures.

Cognitive Deficits in Schizophrenia Relatives

Cognitive deficits are found in the biological relatives of schizophrenia patients as compared to normal volunteers (Faraone et al, 2000; Keefe, et al., 2004,). Egan and colleagues (2001) compared a specific group of schizophrenia relatives (i.e. siblings) to healthy controls on a variety of cognitive tasks. This group used the Wisconsin Card Sort test (computing number of perseverative errors) as a measure of working memory/executive function and found that siblings performed significantly worse ($p=.01$) than control subjects. Sibling group performance compared to healthy controls on the WCST remained significantly worse when the researchers excluded sibling participants diagnosed with schizophrenia spectrum disorders from the sibling group. A Chinese study by Ma and colleagues (2007) yielded similar findings when a group of schizophrenia parents and a group of schizophrenia siblings were compared to healthy controls. Both the parent and sibling group showed significantly worse performance on a test of executive function (WSCT) when compared to controls. The parent group, but not the sibling group, showed worse performance based on the total score on the Tower of Hanoi, a measure of executive function comparable to the Tower of London. Attention was also compared in these three groups based on performance on the Arithmetic, Digit Span and Digit Symbol subtests of the Chinese version of the WAIS-III. The parent group performed significantly worse when compared to controls on all three attention tasks. The sibling group showed worse

performance as compared to controls on Digit Symbol and Digit Span only. There were no significant differences between parents and siblings on any measure of attention or executive function.

Similar to personality related schizophrenia studies, the high risk for schizophrenia adolescent group has been an important group to investigate in order to identify cognitive deficits in family members. Non-affected first-degree relatives of patients have shown cognitive abnormalities that are characteristic of schizophrenia. However, these deficits have been shown to a lesser degree than in patient groups. Faraone and colleagues (2000) found deficits in executive function tasks when comparing nonpsychotic relatives of schizophrenic patients to healthy controls. In the Faraone study, tests of executive function included the Wisconsin Card Sorting Test, delayed recall conditions of the Wechsler Memory Scales Logical Memory stories (WMS-R), the immediate and delayed recall scores on the WMS-R Visual Reproductions and a dichotic (digits) listening task. The most significant group differences occurred on both sets of memory tasks. Significant conclusions were not drawn by the authors, but they suggested that future research might investigate the possibility of defects in working memory, sustained attention or encoding that underlie the impairments exhibited by the relative group.

In an exploratory study designed to examine the relationship between basic symptoms and cognitive abilities in first-degree relatives of schizophrenics, 24 first-degree relatives were matched with controls based on gender and age (Bove, 2008). As described by the author, basic symptoms are a recent line of research with high-risk groups that aims to capture “subclinical self-experienced disturbances that are phenomenologically clearly distinct from attenuated or frank psychotic symptoms” (Bove, 2008, p. 323). The belief is

that they may serve as predictors of first-episode psychotic breaks and are thought to appear well before the onset of schizophrenia. A battery of cognitive tests was administered including the Continuous Performance Test (CPT), the *N*-back Working Memory task, the Negative Priming Test (NPT) and the Span of Apprehension (SPAN). These tests were selected as they provide measures of the neurocognitive domains that were of greatest interest to the author. Based on his review of the literature, Bove (2008) focused upon the cognitive processes that are the most impaired among relatives of patients with schizophrenia, namely attention, working memory and executive functioning (Snitz, MacDonald, & Carter, 2006). Hypotheses from Bove's (2008) study were partially supported. The relative group was only slightly impaired on cognitive performance when compared with controls and in general this was only on conditions of each measure that required higher order thinking. Bove pointed out that on all measures the first condition was the easiest for participants. In general, there were no group differences observed between relatives and controls on the first condition of any measure. With regard to specific findings on the CPT, the relative group showed a trend toward less capacity to discriminate target from non-target stimuli (the discriminability index) over all the trials in all three CPT conditions. However, the finding was only significant for the CPT-14 condition. On the *N*-back, a measure of working memory, the relative group was only significantly different from the control group on the condition that required more cognitive resources to maintain and manipulate information. In other words, this was a task that required higher executive function processes. The SPAN involves serial scanning processes and is a measure related to the focus/execute component of attention (Mirsky et al., 1991). Reaction time (RT) on the SPAN was significantly different when comparing the relative and control groups. The

relative group showed longer RTs. Results of the Bove (2008) study suggest that the relative group showed the greatest impairment in cognitive processes on the SPAN when compared to controls.

Cognitive Deficits in Bipolar Disorder Relatives

Cognitive deficits in bipolar families have been found, but with less consistency across studies when compared to schizophrenia family research. Glahn and colleagues (2010) compared bipolar patients, unaffected bipolar relatives, and healthy controls on twenty neurocognitive tasks. They found that although the bipolar relative group did not exhibit impaired performance on many of the tasks, some deficits did emerge when compared with healthy controls. These deficits were observed on a digit symbol coding task, an object delayed response task, letter-number span, and immediate and delayed facial memory. Pertinent to the present study, the digit symbol coding task is a measure of both attention and processing speed. The object delayed response task is a measure of working memory.

Bora, Yücel, and Pantelis (2009) completed a meta-analysis that attempted to review data for 18 cognitive variables within the bipolar and bipolar family studies. First, they looked at 45 studies that compared the cognitive performances of euthymic bipolar disorder patients with healthy controls. Next, they looked at 17 studies that compared the cognitive performances of first-degree relatives of bipolar disorder patients with healthy controls. In 17 of the 18 meta-analyses conducted for each cognitive test, bipolar disorder patients performed significantly worse than control subjects. Tests that showed medium to large effect sizes included those of executive function, verbal memory, sustained attention and psychomotor speed. With regard to the Wisconsin Card Sorting Test (WSCT), which is a

test of executive function, there was a fair amount of heterogeneity between studies. The authors attributed this heterogeneity to lower sample sizes in two of the forty-five studies. In 6 of 18 cognitive measures, relatives of bipolar disorder patients perform significantly worse ($p < 0.05$) than controls. These tests included Stroop, Trailing Making Test B, WCST (perseverative errors), CPT omission, Wechsler Memory Scale Immediate Recall subtest and Wechsler Memory Scale Verbal Learning subtest. However, the effect sizes for these findings were small. Bora and colleagues (2009) concluded that executive function, in particular set shifting and response inhibition, and not working memory or verbal fluency, may be related to genetic risk for bipolar disorder. They also noted that this was the first study to examine sustained attention in bipolar disorder family members. The impairments in sustained attention were found in both patients and their family members suggesting that failure to detect targets may be a possible trait marker for bipolar disorder. In contrast, a similar meta-analysis of schizophrenia patients and the family members showed impairments in sustained attention, but primarily in the areas of false alarming and target sensitivity (Sitskoorn, Aleman, Ebisch, Appels, & Kahn, 2004). This comparison suggested to Bora and colleagues (2009) that deficits in sustained attention may differ when bipolar families are compared to schizophrenia families.

Studying cognitive functioning in the family members of bipolar disordered individuals provides a unique opportunity to distinguish between state and trait qualities of functioning. In a small study conducted in India (Trivedi et al., 2008), 10 first-degree siblings of bipolar patients were compared with 10 age-, sex- and education-matched healthy controls without a family history of psychiatric illness on measures of attention, working memory and executive function. Tests included computerized versions of the CPT, the WCST, and the

Spatial Working Memory Test (SWMT). Significant differences between the sibling and control groups were not found on the SWMT. Significant differences were found between the two groups on two components of the CPT. Siblings showed a greater number of commission and omission errors as compared to controls. Response time on the CPT did not differ between groups. On the WCST, siblings committed significantly more ($p < 0.002$) perseverative errors than controls, which is suggestive of impaired set-shifting ability. Deficits in the planning and problem-solving abilities of bipolar siblings was also indicated given the significantly lower ($p < 0.02$) completion of categories when compared to controls. These findings are similar to those in the schizophrenia research. However, given a small sample size, the generalizability of this study is limited. It would be important to replicate this study.

The Relationship Between Personality and Cognition in Schizophrenia Relatives

A few studies look at the intersection between personality and cognitive deficits among family members of schizophrenia patients. However, these studies have primarily focused upon schizotypal personality functioning in isolation. Tsuang, Stone, Tarbox and Faraone (2002) suggest that their conceptualization of Meehl's (1962) "schizotaxia" captures related personality features and cognitive deficits that represent a liability to schizophrenia. Tsuang and colleagues define criteria for schizotaxia as a combination of the negative symptoms observed in schizotypal personality (e.g. social withdrawal and impairment, restricted affect) and cognitive deficits in attention, working memory and executive functioning. They suggest that it may not be the positive symptoms of schizotypal personality (e.g. magical symptoms, attenuated delusions), but the negative symptoms that are most related to cognitive deficits seen in both family members and patients with schizophrenia.

In a study investigating the relationship between neurocognitive deficits and symptoms of schizotypal personality disorder, Johnson and colleagues (2003) compared 50 unaffected co-twins of schizophrenia patients with 123 control twins on measures of complex attention, working memory and executive functioning. Twins in the control group lacked a history of schizophrenia spectrum disorders and Axis I psychosis in both themselves and their first-degree relatives. All participants were assessed for personality disorder symptoms using the Structured Clinical Interview for the DSM-III-R Personality Disorders (SCID-II; Spitzer & Williams, 1986). Symptoms of schizotypal personality disorder (SPD) were evaluated as not present, subthreshold, or threshold and then sums of scores from the threshold and subthreshold symptoms were computed. The authors employed a mixed model regression analyses to determine the relationship between the number of schizotypy symptoms, genetic risk for schizophrenia (i.e. whether the twin belonged to the schizophrenia family control group), and the interaction between genetic risk and SPD symptoms as related to neurocognitive functioning. Johnson and colleagues found that together the SPD symptoms and group membership predicted deficits in attention, executive functioning, verbal memory and visual memory. Results of the study suggest that schizotypal symptoms alone do not predict cognitive deficits.

Findings were similar in a study by Avila and colleagues (2006) that compared performance on the Continuous Performance Test – Identical Pairs Version (CPT-IP) between individuals with schizophrenia spectrum personality disorders (SSPD) and those without SSPD traits. Group comparisons were made based on two criteria which yielded four groups: SSPD relatives, Non-SSPD relatives, SSPD community controls and Non-SSPD community controls. Participants were first grouped according to whether or not they were

recruited from a family with schizophrenia or as a community control. Second, they were grouped into the SSPD or Non-SSPD groups based on clinician ratings after interview using the SIDP. Each group's performance on the CPT-IP was also compared to the performance of schizophrenia patients on the same measure. The authors found that the relative group exhibiting SSPD symptoms showed CPT-IP deficits comparable to schizophrenia patients. No significant differences were observed between any other groups. This study also lends support to the theory that schizophrenia spectrum disorder symptoms in the absence of a family history of psychotic illness may not predict impairment on cognitive tasks traditionally identified as indicators of risk for schizophrenia.

Fogelson and his colleagues (2010) investigated the relationship between avoidant personality traits and performance on cognitive tasks in the relatives of persons with schizophrenia. The study sample consisted of 367 relatives of persons with schizophrenia and 245 relatives of community controls. The authors used the Structured Clinical Interview for DSM-III-R: Personality Disorders (SCID-II) as a measure of personality (Spitzer et al., 1990). Based on the SCID-II, they determined whether a diagnosis of avoidant personality disorder was present or absent in all participants. Group differences were significant ($p < .001$). Thirty-four relatives of persons with schizophrenia (9.4%) were diagnosed with avoidant personality disorder as compared to five control relatives (2%). A dimensional score on the avoidant personality scale (avoidant sum) was also calculated by summing the items comprising it. The cognitive tasks in this study consisted of the SPAN, two versions of the CPT (degraded stimulus and 3-7), the TMT-B, and the WAIS vocabulary subscale. The DS-CPT is a measure of sustained, visual attention whereas the 3-7 CPT is an attention/vigilance task that additionally relies upon sustained working memory. Although the SPAN is also

generally considered a measure of attention, it requires rapid encoding and visual search to detect target letters and is more related to the focus/execute component of attention (Mirsky et al., 1991). The TMT-B is a measure of visual search and visual-spatial ability. The WAIS vocabulary subtest was included in the study as a measure of verbal ability. According to Fogelson and colleagues, these measures were selected because first-degree relatives of schizophrenia probands have exhibited impaired performance on them in past research.

Results of the main regression analyses showed that the avoidant dimensional score (avoidant sum) predicted performance on the SPAN, the 3-7 CPT, and the TMT-B (Fogelson et al, 2010). Higher avoidant dimensional scores were associated with lower scores on these cognitive measures in the schizophrenia relative group. In contrast, avoidant dimensional scores were not found to predict performance on any cognitive task in the community control group. Avoidant dimensional scores were highly correlated with both paranoid and schizotypal dimensional scores for relatives and controls. Therefore, a secondary analysis was conducted with the data from the schizophrenia relatives group using a regression model that adjusted for paranoid and schizotypal symptoms. The authors found that the avoidant dimensional score continued to predict impaired performance on the SPAN when controlling for paranoid and schizotypal symptoms. Therefore, the authors could conclude that avoidant, paranoid, and schizotypal personality disorders may not be fully independent from each other in predicting cognitive performance, but that avoidant symptoms may explain some additional variability at least with regard to the SPAN, one measure of attention. Results of Fogelson and colleagues' (2010) study lend support to previous research (Fogelson et al., 2007) that showed avoidant personality symptoms are more prominent in schizophrenia families as compared to community controls. It also expanded upon previous findings to

suggest that there is a relationship between avoidant personality traits and cognitive performance in the first-degree relatives of schizophrenia patients, but no relationship between the same traits and cognitive performance in community controls.

Studies investigating the intersection between personality and cognitive deficits in bipolar family members seem notably absent from the literature with the exception of a study combined with schizophrenia families that will be discussed herein.

Personality Traits and Cognitive Deficits in Schizophrenia and Bipolar Families

To this author's knowledge there exists only one study that looks at both personality dimensions and neuropsychological performance of relatives with schizophrenia as compared to relatives with an affective illness within that same study (Laurent, Gilvarry, Russell, Murray, 2002) and it is quite specific. The findings are related to and contribute significantly to the foundation of the present study, but are significantly different in that they are looking at slightly different groups than that of the current study. Laurent and colleagues recruited participants from a larger scale psychosis study by asking the individuals with psychotic disorders who were involved in their study if they might contact their family members. The researchers recruited a total of 188 family member participants for this combined study. One-hundred participants were the first-degree relatives of patients with schizophrenia, whereas the other 88 participants were a mixture of relative types and made up what was called the affective psychosis family group, namely their relative was either diagnosed with schizoaffective disorder or manic-depressive psychosis. Participants completed two measures that assessed executive and attentional functioning, as well as a self-report personality assessment measure called the Eysenck Personality Questionnaire (EPQ; as cited in Laurent et al., 2002). The EPQ yields mean scores on four scales that measure three dimensions of

personality, including psychoticism (P), extraversion (E), neuroticism (N), and lie (L). Neurocognitive tests included Reitan's (1958, 1978) Trail Making Test (TMT) and the Thurstone (1938, 1949) Verbal Fluency Test (VFT). For the TMT, a time score that eliminated psychomotor speed and ability (TMT B – TMT A) was computed in order to assess frontal functions. The EPQ data was analyzed by taking gender into account. Demographically, male and female subgroups did not appear to be different at pre-analysis. In regard to personality findings, the mean score for males on the Psychoticism scale was significantly higher in the schizophrenia subgroup than in the affective psychosis subgroup. High scores on the P scale correspond to an individual who is described as solitary, hostile towards others, indifferent about people, lacking empathy, having a proclivity for odd and unusual things, and possessing feelings of guilt and sensitivity to others. The mean score for females on the Lie scale was significantly higher in the affective psychosis subgroup than in the schizophrenia subgroup. The Lie scale was designed to be a measure of dissimulation, but the authors suggest it may also be an underlying personality trait. For the neuropsychological scores, the only significant findings were in the schizophrenia group where high scores on the Extraversion scale were correlated with low scores on the TMT. Finally, logistical regression analyses were conducted to determine whether or not scores on the extraversion, neuroticism and psychoticism scales could predict neuropsychological performance and none was predicted in either the schizophrenia or affective psychotic group. Laurent and colleagues' major finding is consistent with previous research that suggests relatives of schizophrenia patients show more impairments on cognitive tasks.

In light of research reviewed throughout this paper thus far, the Laurent et al. (2002) study leaves an opening to refine their research. An important aim of Laurent and

colleagues' study was to investigate whether or not any relationships existed between personality dimensions (as measured by the EPQ) and cognitive performance (as measured by the Trail Making Test and the Verbal Fluency Test). The use of the EPQ may not have provided enough specificity to accurately capture the variety of personality traits that may contribute to group differences between schizophrenia relatives and bipolar relatives. Given that the affective group was also notably relatives of *psychotic* affective-disordered individuals, it might have been expected that there would also be a level of psychoticism in these family members that would not distinguish themselves from the family members of the schizophrenia patients. It may also have been more useful to employ a measure where groups could be analyzed without having to split these into male and female subgroups. Furthermore, use of more tests of executive function and attention may be appropriate in order to increase opportunity to achieve significant results. The Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al., 2004) or measures of attention used more frequently in previous studies (i.e. CPT) may be more appropriate in assessing these subtle differences.

Summary and Statement of the Problem

The etiology of both schizophrenia and bipolar disorder remains largely unknown. Studying both relatives of and patients diagnosed with either disorder has long been one method of research that has attempted to answer some of these questions (Akiskal, 1984; Bleuler, 1911/1950; Kraepelin, 1919/1971; Meehl, 1962). It is now commonly accepted that there is some genetic risk associated with both schizophrenia and bipolar disorder, and that the severe mental illnesses have been shown to run in families (Ivleva et al., 2008; Owen et al, 2007). Some families may have multiple members diagnosed with schizophrenia or

bipolar disorder. Other families may show "softer" signs of either disorder that may manifest in aspects of personality and/or cognitive functioning. These subtler features and deficits associated with both disorders are of particular interest in the present study. It may be advantageous for researchers to focus on these subtle signs or possible vulnerabilities to schizophrenia and bipolar disorder, especially in unaffected relatives who are not influenced by symptoms and illness states. Research focused in this regard could provide greater insight into the question of whether or not there exists an "affective-psychotic spectrum" (Craddock, et al, 2006).

First-degree relatives of patients with schizophrenia show patterns of personality functioning that seem to be unique to their group, yet subtly related to the clinical manifestations of schizophrenia. Studies have shown greater incidence of the schizophrenia-spectrum personality traits in the family members of schizophrenia patients when compared to controls (e.g. Parnas et al., 1993). Increased incidence of avoidant personality features in this group has also been observed and may represent a separate schizophrenia-spectrum disorder that is marked by social dysfunction (Fogelson et al., 2007) and related impairments in cognition (Fogelson et al., 2010). It has similarly been established, albeit less consistently, that the first-degree relatives of patients with bipolar disorder may present with a unique constellation of personality dimensions that do seem to be different from both the normal population and the personality functioning of the schizophrenia relative group. To borrow terminology from the schizophrenia-spectrum literature, Akiskal's (1984) hyperthymic and cyclothymic temperament could represent the bipolar spectrum personality traits. The cyclothymic temperament has shown some association with DSM-III (APA, 1980) diagnoses of borderline personality (Akiskal, Chen, Davis et al., 1985). Relatives of bipolar disorder

patients have also shown increased incidence in the DSM-IV-TR (APA, 2000) cluster C category with elevations for both generalized anxiety-related traits (Mendlowicz et al., 2005) and obsessive-compulsive personality traits, specifically a rigidity factor, when compared with controls (Maier et al., 1995). These bipolar family studies, in particular, reflect some inconsistent findings and would benefit from further study.

Deficits in attention, working memory and executive functioning mark the histories of schizophrenia patients and their family members, and to a somewhat lesser degree, the histories of bipolar I disorder patients and their biological relatives. There have been significantly fewer studies devoted to investigating cognitive deficits in the family members of bipolar patients. Deficits in cognitive functioning may exist on a continuum with schizophrenia patients and their relatives performing worse on these measures than the bipolar patients and their relatives. Continued research that utilizes more consistent research methodology, in other words, including the same measures across studies and groups, may help to answer this question.

If we pursue the view that cognitive deficits may represent an expression of the genetic vulnerability towards developing schizophrenia or bipolar disorder, it may be advantageous to begin to further the research by looking at the cognitive profiles of the bipolar family members. From this perspective, relatives, as well as patients, would exhibit some of these deficits albeit on a continuum of functioning. However, bipolar family members may not present with the same difficulties as have been encountered when studying bipolar patients only (Keefe & Fenton, 2004).

Furthermore, the exploration of the personality and cognitive functioning of bipolar and schizophrenia relatives may provide an important line of inquiry since these both are

areas that could be targeted prior to the onset of significant symptoms in individuals at high-risk for developing either disorder. Both personality functioning and cognitive deficits have been shown to be evident prior to the onset of the active symptoms of the schizophrenia (Diwadkar et al., 2006). Given that there is some overlap, especially when considering neuropsychological findings, a major question that remains is whether or not there might be a relationship between personality dimensions and cognitive deficits. There have been few studies that attempt to address this question. Expanding upon the 2002 study by Laurent and her colleagues, the present study will also attempt to explore the relationship between the cognitive deficits and personality traits observed in family members of both schizophrenia and bipolar patients. This study will attempt to address some of the limitations of Laurent and colleagues' study by including a group of healthy comparison participants who lack any personal or family history of major mental illness. Furthermore, this study will also attempt to combine aspects of both dimensional and categorical theories of personality by employing a measure that assesses the DSM-IV categorical model of personality, but through applying it more dimensionally. Using a measure that captures the DSM-IV model of personality may also provide findings that will have greater clinical utility than the dimensional model employed by Laurent. Specific cognitive deficits will be investigated in the context of recommendations from the MATRICS group (Nuechterlein et al., 2004) to be consistent with current trends in the literature. Specific measures will be selected that meet criteria set forth by the MATRICS group.

The purpose of the present study is to combine the two areas of familial research by looking at personality and cognitive functioning for both groups of relatives in comparison to each other and to healthy controls The prevalence of personality disorders, as well as the

incidence of specific DSM-IV related personality traits, will be compared between both groups and against controls using ratings derived from the Structured Interview for DSM-IV Personality, (SIDP-IV; Pfohl, Blum, & Zimmerman, 1995), a semi-structured personality interview. In the same vein, similarities and differences in cognitive functioning will be assessed between schizophrenia relatives and bipolar relatives through comparison to the control group mean. Four measures of cognition, the Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004, 2008), the Wechsler Memory Scale, Third Edition (Wechsler, 1997b), the Penn Conditional Exclusion Test (Kurtz, Ragland, Moberg & Gur, 2004), and a version of the widely utilized Continuous Performance Test (MacDonald et al., 2005), will be used to assess components of attention, working memory, and executive functioning.

The following hypotheses are presented:

1) It is hypothesized that first-degree relatives of patients with schizophrenia (SCH-REL) will differ from a group of first-degree relatives of patients with bipolar I disorder (BP-REL) and a group of healthy controls (HC) with regard to personality traits as examined by the SIDP-IV, such that:
    a) The schizophrenia relative group (SCH-REL) will show more elevations on cluster A, or the schizophrenia-spectrum personality traits (i.e. paranoid, schizoid and schizotypal), than both the bipolar relative (BP-REL) and healthy control (HC) groups.
    b) The schizophrenia relative group (SCH-REL) will exhibit more elevations on avoidant personality traits than both the bipolar relative (BP-REL) and healthy control (HC) groups.

c) The bipolar relative group (BP-REL) will show more elevations on cluster B traits (i.e. histrionic, borderline, narcissistic and antisocial) than both the schizophrenia relative (SCH-REL) and healthy control (HC) groups.

d) The bipolar relative group (BP-REL) will exhibit more elevations on obsessive-compulsive personality traits than both the schizophrenia relative (SCH-REL) and healthy control (HC) groups.

2) It is hypothesized that a group of first-degree relatives of patients with schizophrenia (SCH-REL) will differ from a group of first-degree relatives of patients with bipolar I disorder (BP-REL) and a group of healthy controls (HC) with regard to cognitive functioning as examined by the BACS, WMS-III, PCET, and DPX-CPT such that:

a) Both the schizophrenia relative (SCH-REL) and the bipolar relative (BP-REL) groups will demonstrate impaired performance on all measures of cognitive functioning (BACS, WMS-III, PCET, and DPX-CPT) when compared to the healthy control (HC) group.

b) It is further predicted that the schizophrenia relative group (SCH-REL) will show greater impairment on measures of cognitive functioning (BACS, WMS-III, PCET and DPX-CPT) than the bipolar relative (BP-REL) group.

3) It is hypothesized that family type (schizophrenia or bipolar I disorder) can be predicted from the combined patterns of personality traits and cognitive functioning demonstrated by relatives of persons with schizophrenia and relatives of persons with bipolar I disorder, such that:

a) The schizophrenia relative (SCH-REL) group will demonstrate cluster A and avoidant personality traits and pronounced cognitive deficits.

b) The bipolar relative (BP-REL) group will demonstrate cluster B and obsessive-compulsive personality traits with less pronounced cognitive deficits.

CHAPTER II

Method

Participants

The study sample of 177 consisted of 59 relatives of persons diagnosed with schizophrenia (SCH-REL), 54 relatives of persons diagnosed with bipolar I disorder (BP-REL), and 64 healthy controls (HC) who participated in the ongoing multi-site study titled the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) at Wayne State University, School of Medicine (WSU-SOM). Some participants were recruited by and completed portions of the study at both the University of Michigan and Wayne State University, Schools of Medicine (n = 36). The remainder completed all portions of the study at WSU-SOM (n = 141). The B-SNIP study was reviewed and approved by the human investigation committees of each university. See Appendix A. All participants provided written informed consent and were monetarily compensated.

Participants in the B-SNIP study were classified into one of five groups: (1) probands diagnosed with schizophrenia (SZ), (2) probands diagnosed with bipolar I disorder (BP), (3) first-degree relatives of schizophrenia probands, (SCH-REL) (4) first-degree relatives of bipolar probands (BP-REL), and (5) healthy controls (HC). Because the probands were not the groups of focus in the present study, they are only briefly described herein. However, proband diagnosis and eligibility was important as it was used to determine the group membership of the relatives. Probands were required to meet DSM-IV-TR (APA, 2000) diagnostic criteria for schizophrenia, schizoaffective disorder, or bipolar I disorder based on the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 2002) following consent. Individuals interested in participating in the

study as probands were asked to refer at least one first-degree biological relative who was willing and eligible to participate in the study as well. All full siblings, biological parents and/or age-eligible biological children of probands who were referred to the study could participate if they met inclusion and exclusion criteria.

A small proportion of the proband sample also included individuals diagnosed with schizoaffective disorder. For purposes of grouping and analyses, these participants were included in either the schizophrenia proband group or the bipolar I disorder proband group based upon the sub-typing of their illness. Schizoaffective disorder is a heterogeneous diagnosis with poor reliability and stability (Kane, 2010). It has been conceptualized in various forms, including as a type of schizophrenia with prominent mood symptoms, a severe form of either bipolar or major depressive disorder with prolonged psychotic symptoms occurring outside of the mood episodes, or as a comorbid illness in which the patient is dually diagnosed with both schizophrenia and bipolar disorder (Abrams, Rojas, & Arciniegas, 2008; Keshavan et al., 2011). Given the debate surrounding the diagnosis of schizoaffective disorder, it has been suggested that it be included in the middle along the dimensional approach to diagnosing psychotic disorders (Abrams et al., 2008) as was previously reviewed in the introduction. DSM-IV-TR (APA, 2000) categorizes schizoaffective disorder into two sub-types: depressive and bipolar type. Treatment outcomes have been shown to be similar to schizophrenia for those with the depressive type of schizoaffective disorder and similar to bipolar I disorder for those with the bipolar type of schizoaffective disorder (Keck, McElroy, & Strakowski, 1996). Therefore, in the present study, individuals diagnosed with schizoaffective disorder, depressive type were included in the schizophrenia group. Individuals diagnosed with schizoaffective disorder, bipolar type

were included in the bipolar disorder group. Four participants (2.3% of the total sample) were related to probands who were diagnosed with schizoaffective disorder, depressive type. Comparably, six participants (3.4% of the total sample) were related to probands who were diagnosed with schizoaffective disorder, bipolar type. These individuals are included in the total sample as described above.

Some exclusion criteria were the same for all groups. Participants were required to meet age criteria of a range of 15 to 65 years. This age range was designated to reduce the impact of age-related changes on cognitive performance. Probands, relatives and healthy controls alike lacked a history of serious medical, neurological or severe head trauma (e.g. cancers, seizure disorders, and encephalopathy). Exclusion due to severe head trauma was determined on a case-by-case basis by psychiatric and neurological research team members, but no loss of consciousness exceeding five minutes was employed as a general standard. Participants were also excluded if they reported a history of mental retardation, current substance abuse (within 1 month), substance dependence within three months, extensive history of drug dependence (based on DSM-IV-TR criteria), or they obtained a positive urine test for illicit substance use following consent. In relation to psychiatric diagnoses, first-degree relatives participated in the study regardless of current or lifetime diagnosis of psychotic, mood or anxiety disorders. On the other hand, the participants enrolled in the healthy control group were without personal or family history (first- and second- degree relatives) of psychotic or major mood disorder (e.g. recurrent major depressive disorder or bipolar disorders of both types). Finally, all participants showed proficiency in English. Reading ability was based upon achieving a Wide Range Achievement Test, 4th Edition (WRAT4; Wilkinson & Robertson, 2006) standard score of ≥ 65. Given that the study

involved a comprehensive screening process, if a person revealed exclusionary information prior to consent they were typically not invited to participate. However, five relatives and four healthy controls were excluded from the study following consent due to the reasons described above and are not represented in the total sample of 177.

Demographic characteristics (in the form of means, standard deviations, and frequencies) of the three groups are presented in Table 1. Demographic information was collected on the demographic form and is based on the self-report of the participants. Participants were asked to describe their ethnicity as either not Hispanic or Latino in background or of Hispanic/Latino background (i.e. a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish origin. They were also asked to describe their race and could pick multiple groups (see Table 1 for categories).

Table 2 summarizes DSM-IV-TR lifetime diagnoses of the participants in the present study. Best estimate diagnoses were determined through SCID interviews and consensus diagnosis conferences for relative and controls. Diagnoses were based upon a lifetime history of mental illness, primarily as reported by the participant. In some cases collateral information was provided by family members or medical record. To aid in describing the clinical characteristics of the three groups (SCH-RELs, BP-RELs, and HCs), individual SCID (First et al., 2002) diagnoses were re-coded into diagnostic categories for the present study. Each participant was assigned a lifetime score (present vs. absent) for each of the diagnostic categories reflected in Table 2. Coding was based upon data contained on the B-SNIP Diagnosis Form, which was informed by the SCID (for any Axis I disorders), and the SIDP-IV ratings (for any Axis II disorders).

Table 1

Demographic Characteristics of the Relatives and Healthy Controls

	Schizophrenia Relatives (n = 59)		Bipolar Relatives (n = 54)		Healthy Controls (n = 64)	
Characteristic	*M*	*SD*	*M*	*SD*	*M*	*SD*
Age (years)	38	14.8	40	16.2	32	11.4
Education (years)	13	2.2	14	2.6	15	2.5
WRAT4 Reading SS[a]	94.0	13.5	100.3	15.0	100.3	15.2
	n	%	*n*	%	*n*	%
Gender[b]						
Male	15	25	16	30	22	34
Female	44	75	38	70	42	66
Ethnicity[b]						
Hispanic	0	0	2	4	5	8
Non-Hispanic	59	100	52	96	59	92
Race[c]						
Black/African American	42	71	18	33	27	42
White/Caucasian	16	27	35	65	32	50
Asian	0	0	1	2	3	5
American Indian	0	0	0	0	3	5
Other	1	2	0	0	1	2
Marital Status[b]						
Married/common-law	18	31	27	50	15	23
Widowed	2	3	0	0	1	2
Divorced/separated	11	19	7	13	7	11
Never married	28	48	20	37	41	64

Note. WRAT4 = Wide Range Achievement Test, 4th Edition by Wilkinson and Robertson in 2006; SS = Standard Score based on age-related norms published in the WRAT5 administration manual. [a]WRAT4 Reading standard score is based on blue version for 161 cases. Blue version data was missing for 3 individuals and green version standard score was substituted. Group sample sizes for WRAT4 are reduced due to missing values (n = 13) for the variable: per group, n = 52, 49, and 63 respectively. [b]Percentages are per group for the variables of gender, ethnicity, and marital status. [c]Race is reported as percent of the total sample (n = 177) answering "yes" to each category. The three groups were compared on each category and participants could indicate more than one racial identity. Therefore, frequencies per each racial category do not sum to 100%.

Lifetime prevalence of personality disorders scores were primarily based upon SIDP-IV ratings using the cut-off criteria per each scale as described by the authors of the measure (Pfohl et al., 1995). However, in cases where an individual was determined to meet at least minimum criteria for a personality disorder diagnosis based upon the SIDP-IV, this diagnosis was also confirmed during the case conference diagnostic meeting. In addition to the Axis I and Axis II diagnostic categories, each participant was assessed for lifetime history of at least one psychotic episode. This added a level of specificity to the diagnosis in addition to the categories. For example, an individual may have been diagnosed with a major depressive disorder, which would fall under the category of depressive disorder. However, they may have experienced a major depressive episode during their lifetime that included psychotic symptoms. Therefore, the history of psychosis was reflected separately in the lifetime history of psychosis item. For those relatives with a substance use disorder, the individual met remission criteria within the past one month (for abuse) and at least three months (for dependence). As previously described, persons actively using substances were excluded from participation. The category called “other Axis I disorders” represented Axis I disorders that did not fall into any other categories and occurred at low frequencies in the sample. These included eating disorders, body dysmorphia, conduct disorder, disruptive behavior disorder, bereavement, and ADHD.

Table 2

Lifetime Prevalence Rates (%) of DSM-IV-TR Diagnoses by Relative Type

	Schizophrenia Relatives (n = 54)		Bipolar Relatives (n = 49)		Healthy Controls (n = 63)	
Diagnostic Category	n[a]	%[b]	n[a]	%[b]	n[a]	%[b]
Lifetime History of Psychotic Episode	8	4.8	3	1.8	0	0.0
Any Diagnosis on Axis I	43	25.9	34	20.5	22	13.3
Schizophrenia Spectrum Disorder	7	7.1	0	0.0	0	0.0
Bipolar Disorder	0	0.0	3	1.8	0	0.0
Depressive Disorder	21	12.7	16	9.6	8	4.8
Anxiety Disorder	20	12.0	11	6.6	5	3.0
Substance Use Disorder	12	7.2	14	8.4	12	7.2
Adjustment Disorder	5	3.0	4	2.4	2	1.2
Other Axis I Disorder	3	1.8	4	2.4	4	2.4
Any Diagnosis on Axis II	12	7.2	9	5.4	4	2.4
Paranoid Personality Disorder	2	1.2	1	0.6	0	0.0
Schizoid Personality Disorder	2	1.2	0	0.0	1	0.6
Schizotypal Personality Disorder	0	0.0	1	0.6	0	0.0
Antisocial Personality Disorder	0	0.0	0	0.0	1	0.6
Borderline Personality Disorder	0	0.0	1	0.6	0	0.0
Histrionic Personality Disorder	1	0.6	0	0.0	0	0.0
Narcissistic Personality Disorder	0	0.0	0	0.0	1	0.6
Avoidant Personality Disorder	3	1.8	1	0.6	1	0.6
Obsessive Compulsive PD	1	0.6	4	2.4	0	0.0
More Than One Personality Disorder	3	1.8	1	0.6	0	0.0

Note. Diagnoses are based upon *Diagnostic and Statistical Manual of Mental Disorders* (APA, 2000) criteria in *Structured Clinical Interview for DSM-IV Axis I Disorders* (SCID) by First and colleagues in 2002.

[a]Number (n) of participants with lifetime prevalence scored as "present" for given diagnostic category. [b]Represents % of total sample of N = 166 as clinical data was missing for some participants.

Measures

During the course of the larger B-SNIP study, a battery of measures to collect pertinent background and demographic information, determine diagnosis, assess personality traits and assess domains of cognitive functioning were administered as part of the more extensive clinical and neuropsychological assessments. Those measures that were pertinent to the present study will be reviewed herein.

Demographic, psychiatric, medical and family history. A set of forms designed to collect demographic, psychiatric, medical and family history data while interviewing participants was developed by the B-SNIP consortium. Those forms were completed by clinical raters during semi-structured interviews with all participants including probands, relatives and controls. Originally developed as paper and pencil measures, the forms were incorporated into a Microsoft Access database that contained all scored clinical data. Raters had the option to enter data as they interviewed the participant or following the clinical assessment. See Appendices B and C for copies of these forms. Pertinent demographic information included age, gender, educational level of participant and each parent, as well as highest occupation for participant and each parent. The pertinent psychiatric information that was collected included history of psychiatric treatment, total number of hospitalizations, and age at onset of psychiatric symptoms. The presence or absence of a wide range of medical diseases, illness, and conditions was obtained for each participant on the medical history form. The family history form was designed to gather information regarding the distribution of probable and certain psychiatric illness and substance abuse/dependence among the participant's first-, second-, and third- degree relatives.

Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID; First et al., 2002). Every participant completed the SCID regardless of group membership. The SCID is a semi-structured interview that was developed in order to diagnose DSM-IV-TR Axis I disorders. It is appropriate for use with both psychiatric and general medical patients, as well as with individuals from the community even if no psychiatric diagnosis is expected. The interview was designed for use with individuals age 18 or older with at least an eighth grade education. It was administered by qualified researchers with training in the DSM-IV-TR diagnostic system (APA, 2000). The purpose of the use of the SCID in this study, as it is most often used, was to establish the presence (or absence) of DSM-IV-TR Axis I disorders. The patient edition (SCID-I/P) was used with all participants. The SCID-I/P contains 10 modules that are designed to assess respectively the presence of mood episodes, psychotic symptoms, psychotic disorders, mood disorders, substance use disorders, anxiety disorders, somatoform disorders, eating disorders, adjustment disorders and optional disorders. With the exception of the optional disorder module, all modules were administered to every participant. The SCID begins with a screening module which consists of 12 yes or no questions used to elicit basic information that may imply possible diagnoses. This information was used to guide administration of more probing questions that follow later in the interview. Each symptom in the SCID was rated on a scale of 1 to 3 (1 = symptom is absent; 2 = symptom is sub-threshold; 3 = symptom is present). Specific DSM-IV-TR Axis I diagnoses are suggested following the scoring of each module. Inter-rater reliabilities have been found to be excellent with kappa values ranging from .71 to .97 and an average kappa value of .85 (Ventura, Liberman, Green, Shaner & Mintz, 1998). SCID-I/P has also demonstrated high validity for the diagnosis of schizophrenia and bipolar disorder (Steiner,

Tebes, Sledge & Walker, 1995). Comparing SCID ratings to best estimate diagnoses made by psychiatrists on first-admission psychotic patients yielded good sensitivity (.89), specificity (.96) and agreement (.86) (Fennig, Craig, Lavelle, Kovasznay, & Bromet, 1994).

Structured Interview for DSM-IV Personality (SIDP-IV; Pfohl et al., 1995). The SIDP-IV is a comprehensive, semi-structured diagnostic interview for the assessment of the 10 major DSM-IV personality disorders. It contains non-pejorative questions that are organized into topical sections rather than by the individual personality disorders. These sections include: Interest and Activities, Work Style, Close Relationships, Social Relationships, Emotions, Observational Criteria, Self-perception, Perception of Others, Stress and Anger, and Social Conformity. Every symptom of each personality disorder falls into one of these sections and clinical raters are provided with a set of questions for each symptom to facilitate the interview and make a rating on that item. According to its authors, the structure of the SIDP-IV was designed to improve interview flow. In the present study, the SIDP-IV was completed following the SCID-I/P (First et al., 2002). Having already gathered information related to Axis I disorders helped clinical interviewers to distinguish longstanding behaviors from the more temporary states that would result from Axis I disorders.

SIDP-IV ratings are based on what Pfohl and colleagues (1995) describe as the "5-year rule." This rule recommends that behaviors, cognitions, and feelings that have predominated for the majority of the past five years are considered representative of the individual's long-term personality functioning. Each DSM-IV criterion is scored as absent (0), subthreshold (1), present (2) or strongly present (3). Administration time was approximately 60 to 90 minutes depending upon participant and interviewer variables. It was

recommended that another 20 to 30 minutes be allotted at the conclusion of the clinical assessment to review scoring on each item and transfer scores to the score sheet. This instrument allowed the rater to obtain quantitative scores for each personality trait, as well as arrive at a DSM-IV personality disorder diagnosis, if applicable. The score sheet specified the number of criteria which must be present (a rating of 2 or 3) to meet the threshold for personality disorder based on the personality being assessed. Although the SIDP-IV was initially designed (Pfohl et al., 1995) and traditionally has been used (Avila et al., 2006) to determine the presence or absence of the 10 personality disorders, some researchers have used it to provide dimensional ratings for each of the 10 personality types by summing individual item scores (Jane, Pagan, Turkheimer, Fiedler, & Oltmanns, 2006; Torgersen, et al., 2008). For the present study, dimensional scores were computed for each of the 10 personality types by summing together the item (symptom/trait) scores that comprised each scale. The ten scales contained seven, eight or nine items. The range of possible scores for each scale varied based upon the number of items that made up the scale. For example, the paranoid personality scale is comprised of seven items. Therefore, the dimensional score tabulated for the paranoid scale ranged from 0 to 21. Composite dimensional scores for each of the clusters (A, B, and C) were also computed by tabulating the total score for each of the personality type scale comprising the given cluster. For example, the cluster A personality scale is comprised of the paranoid, schizoid, and schizotypal scales, which are each comprised of seven to nine items. The total scores for the three personality type scales contained in cluster A were summed to obtain the cluster A total score (dimensional) which ranged from 0 to 69. Participants were also assigned a categorical score for each of the ten personality types (present/absent) based on the threshold scores previously described. For the

present study, the categorical SIDP-IV ratings were used to describe the clinical characteristics of the sample. In a study with an non-treatment seeking population of military recruits to determine interrater reliability of the SIDP-IV, Jane and colleagues (2006) found that reliability estimates based on dimensional scores (computed in same manner as described for the current study) were more reliable than reliability estimates based on categorical scores. In fact, kappa values ranged from .77 for histrionic personality disorder to .93 for avoidant personality disorder using this method.

At the beginning of the B-SNIP study inter-rater reliability was computed on the SIDP-IV ratings across sites following training sessions with a kappa value of greater than .85. These were consistent with previously published inter-rater reliabilities where kappa estimates exceeded .81 (Avila et al., 2006). Damen, DeJong, and VanderKroft (2004) reported kappa coefficients ranging from .76 to .93 for the individual SIDP-IV items, and from .66 to 1.00 at the level of diagnosis, specifically the presence or absence of the personality disorder diagnosis.

Brief Assessment of Cognition in Schizophrenia (BACS; Keefe et al., 2004). The BACS is a recent cognitive battery that was originally designed to be used in clinical trials to measure treatment-related changes in cognition with schizophrenia patients (Keefe et al., 2004). For this purpose it is also available in alternate forms. The BACS is primarily a paper and pencil test and was completed by the participants under the guidance of trained neuropsychology technicians. The BACS technicians were trained through a standardized process by the authors of the measure and Keefe and colleagues requested 1 of every 7 administrations to be faxed to their research lab for review and reliability. It is a brief assessment with an approximate completion time of 30 minutes. The BACS includes

assessments of four of the seven neurocognitive domains that were identified by the MATRICS group (Nuechterlein et al., 2004) including reasoning and problem solving, processing speed, verbal memory, and working memory.

The BACS consists of six subtests that correspond to the MATRICS group constructs. Scores were obtained for each of the six subtests. Keefe and colleagues (2004) recommended computing a composite score by averaging the standardized scores on the six subtests and then calculating the z-score for the composite. The composite score is highly correlated with the composite score on another 2.5 hours long neurocognitive test battery (CATIE; $r=.84$, $p<.001$). It also has shown high test-retest reliability in patients with schizophrenia and healthy controls (intraclass coefficients > .80) (Keefe et al., 2008). The brevity of the BACS also makes it an ideal measure in large scale studies. Descriptions of the six subtests are as follows:

1. *List learning* was designed to measure the construct of verbal memory. Participants were read a list of 15 words and asked to recall as many words as possible from the list, in any order. They were presented with the list five times. Scoring: the number of words recalled on each trial was summed and scores ranged from 0 to 75.
2. *Digit sequencing task* was designed to measure the construct of working memory. Participants were presented orally with sequences of numbers. They were asked to say the numbers back in order from lowest to highest. Sequences ranged in length from two numbers to eight numbers. Participants were presented with four trials per each sequence length. Participants moved to the next level if they correctly answered at least one of four items from the previous level. There were

a total of 28 trials. Scoring: number of correct responses was computed which ranged from 0 to 28.

3. *Token motor task* was designed to assess the construct of motor speed. The task asked participants to place 100 poker chips into a plastic container as quickly as possible. They were required to place the tokens into the container two at a time within 60 seconds. Scoring: total number of tokens correctly placed into the container with scores ranging from 0 to 100.
4. *Semantic and letter fluency* was designed to measure the construct of verbal fluency. A total score was obtained from three trials of 60 seconds each. In the first trial, participants were asked to name as many words as possible within a given category. In the second and third trials, participants were asked to say as many words as possible that began with a given letter. Scoring: total number of words generated for all three trials.
5. *Symbol coding* was designed to assess the constructs of attention and speed of information processing. Participants had 90 seconds to write the numbers 1 – 9 as they corresponded to symbols from a presented key. Scoring: total number of correct numerals which ranged from 0 to 110.
6. *Tower of London* was designed to measure executive functioning. In 20 trials, participants were shown two pictures of colored balls arranged on three pegs. They were asked to imagine moving the configuration of balls in one picture in order to make it match the configuration of balls in the other. Participants were repeatedly prompted to determine the lowest number of possible moves to achieve this goal. The degree of difficulty varied throughout the trials. However, Keefe

and colleagues (2004) reported a general tendency for later items to be more difficult. The task was discontinued after five consecutive errors. Two additional trials of greater difficulty were presented to the participant only if he or she correctly responded to all 20 trials. Participants had 20 seconds to respond per trial. Scoring: total number of correct responses (ranging from 0 – 22).

Wechsler Memory Scale, Third Edition (WMS-III), spatial span subtest (Wechsler, 1997b). The spatial span subtest from the WMS-III is a measure of working memory, specifically visual-spatial working memory. The overall purpose of this particular Wechsler subtest is to measure an individual's ability to hold a visual-spatial sequence in working memory and then physically reproduce it. According to Wechsler (1997b), the spatial span subtest loads on the primary working memory index of the WMS-III, which measures an individual's ability to remember and manipulate verbal and/or visual information. The spatial span subtest provides a measure of visual memory manipulation.

The spatial span subtest was administered to participants by a trained examiner. A three dimensional board consisting of ten blocks was used to create series of spatial patterns. The examiner tapped individual blocks at a rate of approximately one block per second. The series prompts for each step were provided in the administration manual. Following presentation of each series of block taps, the participant attempted to duplicate the pattern by tapping blocks in the same sequence from memory. The spatial span subtest consisted of two conditions: forward and backward. The forward condition was described. The backward condition is a variation wherein the presentation by the examiner of each series was the same, but the participant was required to attempt to duplicate the presented pattern in the reverse sequence. There were eight possible levels for each condition. Levels become increasingly

longer with a maximum number of block taps of eight. There were two patterns presented per level. Once the participant missed both attempts per level, the subtest was discontinued. This rule applied for both the forward and backward conditions. The participant was awarded one point per series in a level. The total number of possible points was 32. A maximum of sixteen points could be earned for each level. For the present study, raw scores for each condition were summed. Using age-related norms that were published in the administration and scoring manual, these scores were converted to scaled total scores.

In addition to the BACS and WMS-III, participants completed computerized cognitive tasks that were selected to assess cognitive domains that were not fully evaluated by the BACS. The computerized tests provided more detailed assessment of executive functioning, working memory, and attention. These included the Penn Conditional Exclusion Test (PCET; Kurtz et al., 2004) and the Dot Pattern Expectancy Continuous Performance Test (DPX-CPT; MacDonald et al., 2005).

Penn Conditional Exclusion Test (PCET). The PCET (Kurtz et al., 2004) is a computerized measure of executive functioning that is related to the Wisconsin Card Sorting Test. It is available in four forms and in fact was designed in order to meet the need for a measure of executive function that could be used to assess change in neurocognition over time with repeated trials. Studies assessing multiple administrations of commonly used measures of executive function, such as the WCST, have found significant practice effects across the test-retest interval. For example, in a study by Basso, Bornstein, and Lang (1999) the mean number of perseverative errors on the WCST between a 12-month long interval decreased by nearly 50%. The PCET was computerized for ease of administration and potential to use it conjunctly with neuroimaging studies. Kurtz and colleagues (2004)

describe it as a task that is based on Flowers and Robertson's (1985) "odd man out" paradigm that was designed for research into Parkinson's disease. Participants are asked to decide which of four objects does not belong with the other three. Objects are chosen based on three sorting principles and the participant needs to infer the correct sorting principle based on response feedback. Once the participant successfully completes 10 consecutive correct responses, the sorting principle is shifted. Each of the four versions of the PCET includes three sorting principles. For the present study, the PCET – Form 1 was used. The three sorting principles associated with this form were line thickness, shape and size. The participant was seated in front of a computer and presented with screens showing four figures oriented horizontally. For each trial, the participant was required to use the mouse to click on the figure that did not belong with the other three. Once the participant responded, the next screen provided feedback stating "correct" or "incorrect." Directions for the task were as follows:

> *In this task you will be shown four objects. You will need to determine which object does not belong with the other three. When you correctly choose the object that does not belong you will be told 'correct.' If you choose an incorrect item you will be told 'incorrect.'*

With each presentation of stimuli the subject reads and technician says aloud "Click on the object that does not belong." The PCET takes approximately 10 minutes to complete. If a participant could not master a single category the test was terminated automatically by the computer after 144 trials. The PCET yielded three major scores: categories achieved, total number of errors, and speed. Kurtz and colleagues (2004) have also demonstrated good convergent and divergent validity with similar measures on the WCST with a schizophrenia

population (*n*=32). Criterion-related validity was also established for both the PCET and WSCT as categories achieved and total errors on both measures were found to be related to measurements of cooperativeness on the job.

Dot Pattern Expectancy Continuous Performance Test (DPX-CPT; MacDonald et al., 2005). There is a wide variety of versions of the Continuous Performance Test, which is identified as a measure of sustained attention. Performance on the CPT has been shown to differentiate between patients with schizophrenia and healthy controls (Cornblatt, Lezenweger, & Erlenmeyer-Kimling, 1989), as well as identify persons vulnerable to schizophrenia (Cornblatt & Keilp, 1994). A more recent version included the dot pattern expectancy task. The CPT was first introduced by Rosvold, Mirsky, Sarason, Bransome and Beck in 1956 and included an X and an AX form. This original study asked participants to visually monitor a series of letters that was presented continuously for 10 minutes. In the X form, participants were instructed to press a response key whenever the letter "X' appeared in the string. The AX form was slightly more difficult as it required participants to press the response key whenever the "X" appeared, but not unless the letter "A" had appeared immediately prior to the X. Other versions have been put forth that include the identical pairs, as well as degraded stimulation (Borgaro et al., 2003). The dot pattern expectancy task (MacDonald et al., 2005) is a variation of the AX paradigm that has been found to assess not only impairments in sustained attention, but the more recent construct of context processing.

In the present study, the dot pattern expectancy CPT was administered via computerized testing with a game controller. The DPX-CPT used configurations of dots (from Braille font), rather than letters, as cues and probes. The use of dot patterns allowed researchers to decrease the amount of time in between presentation of stimuli since these are

unfamiliar and therefore less easily stored in working memory as compared to letters (Jones, Sponheim & MacDonald, 2010). DPX-CPT asked participants to decide whether each presented stimuli required a target (AX) or non-target (BX) response. Participants were instructed to accordingly press either the target or non-target button on the game controller. They were instructed to make the target response to an AX pattern sequence and press the non-target button for all other stimuli (BX). The entire task was approximately 15 minutes in duration and participants were provided with up to three practice sessions prior to the actual test, based upon their BX results. A BX accuracy below 75% suggested that the participant did not understand the task. Following the practice sessions, participants completed two blocks of 40 trials each. Trials were one of four conditions: AX (target cue followed by target probe), AY (target cue followed by non-target probe), BX (non-target cue followed by target probe) and BY (non-target cue followed by non-target probe). In each block 28 trials (70%) were of the AX condition, 5 trials (12.5%) were AY, 5 trials (12.5%) were BX, and 2 trials (5%) were BY. The computer program generated accuracy ratings (percent of correct responses) for each of the four conditions. AX accuracy and BX accuracy ratings were used as the performance measures in the present study. The ratings represented an average of the scores for two blocks.

Procedures

As previously mentioned, participants in the present study were drawn from the pool of individuals who took part in the B-SNIP study at Wayne State University. The B-SNIP study began in 2007 and Wayne State University was one of seven sites comprising this consortium of research groups throughout the United States. The B-SNIP was and continues to be supported by Grant Number R01MH078773 from the National Institute of Mental

Health. The overall goal of the B-SNIP study was to examine similarities and differences in the genetic and endophenotypic signatures within schizophrenia and bipolar families through obtaining a variety of measures of neurophysiology, neurocognition, and brain structure. In addition to the clinical and neuropsychological assessments featured in this small study based on the B-SNIP project, participants also took part in scans of their brains and eye-tracking and electrophysiological tasks. They were also asked to provide a sample of their blood for future genetic studies. IRB approval was obtained through the NIMH and the Human Investigation Committee at Wayne State University in 2007 and was consecutively renewed each year. The B-SNIP study was ongoing. However, for the purposes of the present study, a set of data was extracted from the database for analysis and investigation of research hypotheses. Data was extracted based upon the date of the proposal of this project, which occurred on November 20, 2011. Any data that has been collected since that time for the B-SNIP study was not included in the sample.

Recruitment of probands diagnosed with schizophrenia or bipolar I disorder was multi-faceted. They were recruited from inpatient units, outpatient units, and community hospitals and programs that were linked with the research group at Wayne State University. Community advertisements in the form of flyers, websites, newspaper ads, and radio interviews with the principle investigator were also utilized. Key personnel on the research team contacted local groups such as the National Alliance for Mental Illness, as well as mailings and phone calls to physicians who treated patients eligible for the study. Once a potential participant contacted research staff, a brief phone screening was completed in order to determine eligibility (e.g. age, absence of neurological disorder, and interest and availability of first-degree relatives). The screening process was approved by the Human

Investigation Committee at Wayne State University. Relatives were recruited through their family members who had already agreed to participate in the study. Potential participants were asked to either encourage their relatives to contact the research team or their consent was obtained for researchers to contact relatives to describe the study. Community control participants were recruited via the advertising methods described above, as well as recruitment from a control participant pool maintained by the WSU Department of Psychiatry.

Following the initial phone screening process, participants were scheduled to meet with the project coordinator to go over an extensive informed consent document. Participants under the age of 18 provided verbal assent, in addition to the written consent of their parent or legal guardian. All participants received a copy of their consent form and were advised that they could withdraw from the study at any time in the future. At this point, participants that were determined to be eligible for participation were assigned a research number to ensure confidentiality. Access to all data was limited and was stored under a unique ID number, separate from the signed consent form. The document that linked ID numbers to names was kept in a separate, locked filing cabinet and only accessible to one or two key personnel.

Once a participant agreed to take part in the study, a urine test to rule out illicit drug use was obtained. This initial step was designed to reduce the potential that substances could alter the participants' performance on certain tasks involved in the study, including neuropsychological testing. It also provided some clinical information with regard to the potential for a diagnosis of substance abuse or dependence. The demographic form was completed by the project coordinator and participant via brief interview. This was then

reviewed and confirmed by the clinical assessor. The project coordinator completed the reading subtest of the WRAT4 (Wilkinson & Robertson, 2006) with the participant to determine whether or not the participant read at a level sufficient enough to understand the questions and tasks involved in the study (SS $\geq$ 65). An alternate form of the WRAT4 was later completed by the neuropsychology technician for reliability purposes.

The participant met with a clinical assessor for approximately three hours to complete clinical measures including the SCID-I/P (First et al., 2002), SIDP-IV (Pfohl et al., 1995), the psychiatric, medical and family history forms, and a variety of other symptoms scales. There were approximately two clinical assessors designated at each site. Clinical assessors were experienced Masters' level clinicians, clinical psychologists, psychiatrists or advanced graduate students with extensive training. Following clinical assessment, information on each participant was reviewed in a best estimate diagnostic meeting based on findings from the clinical measures. A senior psychiatrist or psychologist guided the meeting. Cases were presented blind to the subject type (i.e. whether the participant was a proband, relative or control). In some cases it was necessary to obtain more information from the participant to reach a consensus diagnosis. As such, some participants were re-contacted. A monthly diagnostic conference call across the seven sites was conducted throughout the duration of the study to maintain ongoing inter-rater reliability and provide a forum to discuss difficult diagnostic cases. Clinical personnel completed extensive training using videotapes and observational methods of completing measures at the beginning of their involvement in the study.

Neuropsychological testing for scheduled for the same day or a second visit. This was dependent upon the availability of both the participant and the research lab. Research

staff was trained to adjust the timeframe of procedures on an individual basis with each participant based on factors of fatigue, boredom and emotional responses. The neuropsychological portion of the study was divided into two parts: BACS with WMS-III, and computerized testing. These could be administered in any order, but order was indicated on the neuropsychological testing form.

Participants were allotted a total of 8 to 10 hours to complete all study related procedures. For the most part, participation in the entire study took place over the course of several days. In rare cases, all procedures were completed in one day. All participants were compensated up to $200 for completing study related tasks.

All analyses of data were performed using the IBM Statistical Package for the Social Sciences, Version 20.0 (SPSS, 2011) program.

Protection of Human Participants

There was minimal risk posed to the participants in this study. Sensitive information regarding their psychiatric and substance abuse was discussed during clinical assessments and they may have felt embarrassed or upset. Assessors were trained clinicians who were trained to assist participants with these concerns, if any. They may have experienced boredom or fatigue during both the clinical and neuropsychological sections of the study. Participants were provided breaks at their request. Prior to joining the study, all key personnel were required to complete and pass a web-based training course on the Protection of Human Research Subjects that was administrated by the Institutional Review Board. This procedure also helped to protect participants against risks that could potentially occur due to a lack of awareness of the rights for research subjects, such as breaches in confidentiality.

CHAPTER III

Results

Demographic and Clinical Characteristics of the Sample

The demographic characteristics of the three groups (schizophrenia relatives, bipolar relatives, and healthy controls) are shown in Table 1. Descriptive statistics were analyzed in SPSS 20.0 to characterize the sample (N = 177) with regard to the demographic variables of age (in years), education (highest grade achieved), gender (male or female), ethnicity (Hispanic vs. Non-Hispanic), race (White/Caucasian, Black/African American, Asian, American Indian/Alaskan Native, and other racial group), and marital status (married/common-law relationship, widowed, divorced/separated, or never married). The three groups were compared on these variables using F tests for the continuous variables (age, education, and WRAT4 reading standard score) and chi-square tests for the categorical variables (gender, ethnicity, race and marital status).

Average age was significantly different among the three groups, $F(2, 174) = 5.68$, $p = .004$, with the mean ages of the groups ranging from 32 years (HC) to 38 years (SCH-REL) to 40 years (BP-REL). Significant differences in years of education were also found among the three groups, $F(2, 173) = 10.20$, $p < .001$. Significant differences in WRAT4 standard scores were revealed, $F(2, 161) = 3.30$, $p = .039$. However, post hoc comparison using Tukey's HSD showed that group differences only approached significance. The schizophrenia relatives' WRAT4 scores were lower than those of the bipolar relatives ($p = .081$) and healthy controls ($p = .058$). Regarding racial identity, significantly more family members identified themselves as African American in the SCH-REL group, $\chi^2(2, N = 177) = 18.11$, $p < .001$, and significantly more family members identified themselves as Caucasian

in the BP-REL group, $\chi^2(2, N = 177) = 16.48$, $p < .001$. The three groups differed on the demographic variable of marital status, $\chi^2(6, N = 177) = 14.08$, $p = .029$ with 31% of the SCH-REL group married, 50% of the BP-REL group married, and 23% of the HC group married. Groups were not significantly different on the variables of gender and ethnicity (Hispanic vs. non-Hispanic), nor the racial categories of Asian, American Indian/Alaskan Native, and other racial group.

The clinical characteristics of the sample by group (schizophrenia relative, bipolar relative, and healthy control) are shown in Table 2. Lifetime prevalence rates (scored as present vs. absent) for each of the diagnostic categories presented in Table 2 were compared among groups using chi-square analysis. By definition, the healthy control group was expected to show a very low incidence of any Axis I and II disorders. Therefore, the healthy control group was not included in the analyses. This allowed for 2 x 2 contingency tables to be used. Diagnostic information was missing for 10 individuals. The two groups when evaluating clinical characteristics, therefore, consisted of 54 schizophrenia relatives and 49 bipolar I relatives. There were no differences in lifetime history for any Axis I diagnosis among the two groups. Twenty-six individuals were classified as absent for this item and removed from further analysis of the specific types of Axis I diagnoses (yielding sample of 77 relatives with history of some Axis I disorder). Chi-square analysis revealed that a significantly greater proportion of schizophrenia relatives had a lifetime diagnosis of a schizophrenia spectrum disorder, $\chi^2(1, N = 77) = 6.09$, $p = .014$. A significantly greater proportion of bipolar I relatives had a lifetime diagnosis of any bipolar disorder, $\chi^2(1, N = 77) = 3.95$, $p = .047$. No differences in lifetime prevalence rates were noted between schizophrenia relatives and bipolar I relatives for the following Axis I disorders: lifetime

history of psychotic disorder, depressive disorders, anxiety disorders, substance use disorders, adjustment disorders, and the other category. Furthermore, the two groups were not different in the frequency of any Axis II disorder.

Overview of Methods for Testing Assumptions with Implications for Interpretation

Data screening procedures included identification of missing values, identification of outliers, and testing of the assumptions of normality, linearity, and homogeneity of variance-covariance (univariate and multivariate). These procedures will be specifically discussed prior to review of the results for each set of hypotheses.

Furthermore, to address a design issue with regard to independence of data, the results for each hypothesis will be discussed twice. One complication of the design of this study involved the violation of the assumption of independence of observations. There were 20 families (a total of 43 participants) where more than one relative of a single proband participated in the study and were therefore classified into the same family group. It cannot be assumed that data obtained from individuals belonging to the same family are independent of one another given that relatives interact with each other typically from an early age, as well as share common genes (Faraone et al., 2000; Fogelson et al., 2007). Hierarchical linear models are suggested to address problems of nonindependent data (Cone and Foster, 2006). However, these techniques were determined to be beyond the scope of this dissertation; therefore, an alternative analysis was followed. The multiple family members could have been randomly deleted so that only one family member per group remained in the analysis. This deletion would have resulted in smaller sample sizes per group which would result in a sacrifice of more power. The power analysis that was conducted prior to data analysis recommended that a minimum of 50 participants per group would yield power close to 80%

with a medium effect size and alpha value of .05. Therefore, it was determined that for the 20 families where several relatives were included in the sample, data was averaged for these members based upon the recommendation from Cone and Foster (2006). Analyses for each hypothesis are first presented for the full dataset, not taking into consideration the violation of nonindependence of data within families. Analyses for each hypothesis are next considered using an adjusted dataset where multiple family members' scores are averaged for each variable of interest. This approach is less sensitive than the first, but also more conservative. Therefore, it can be assumed that the true findings fall somewhere in the middle of each method. There were 17 families with two members included in the sample. There were three families with three members included in the sample. In cases where there was data for a given variable for only one family member, that participant's data was used to represent the family unit even if other variables for the family consisted of averaged data from multiple family members. The full dataset refers to a sample size of 177. The smaller, adjusted dataset, or family averaged dataset, refers to a sample size of 154. Group sizes for the second method following the data averaging of multiple family members are as follows: 46 SCH-RELs, 49 BP-RELs, and 59 HCs. These numbers are compared to 59 SCH-RELs, 54 BP-RELs, and 64 HCs in the full dataset as shown in Table 1.

Hypothesis 1: Group Comparisons of Personality Dimensions

Table 3 is presented to provide the reader with a summary of how the four personality trait variables of interest are measured based on SIDP-IV ratings. For the main analyses, SIDP-IV individual items were summed to obtain composite scores as presented in Table 3. The variable name (e.g. cluster A traits) and measure of variable (e.g. cluster A total score)

are used interchangeably herein. Individual item score rating scales were reviewed in the Methods section.

Table 3

Summary of the Four Personality Dependent Variables Derived from SIDP-IV

Variable name	SIDP-IV measurement	Score range
Cluster A Traits	Cluster A total score	0 – 69
Avoidant Traits	Avoidant total score	0 – 21
Cluster B Traits	Cluster B total score	0 – 99
Obsessive Compulsive Traits	Obsessive compulsive total score	0 – 24

Note. Score ranges for SIDP-IV measurements are dimensional. SIDP-IV = Structured Interview for DSM-IV Personality by Pfohl, Blum, and Zimmerman in 1995.

Analysis of full dataset (*N* = 177).

Data screening. The four main personality variables (Cluster A Total Score, Avoidant Total Score, Cluster B Total Score, and Obsessive-compulsive Total Score) were evaluated for missing data. There were eight cases with missing personality data (approximately 5% of the total sample). Therefore, these cases were removed from the analyses using listwise deletion in SPSS 20.0.

Frequencies, descriptive statistics, box-plots, and stem- and leaf- plots were examined to identify univariate outliers and their potential influence on the results for each of the personality dependent variables. The number of univariate outliers identified for each personality DV varied from zero to nine. These cases were examined for unusual patterns. There were three cases that produced outliers on more than one personality-related dependent variable. For these three cases, the participant had also been diagnosed with one or two personality disorders. Given that a personality disorder diagnosis represented an extreme

score on the SIDP-IV that was expected in this sample, these cases remained in the dataset. According to Tabachnick and Fidell (2001), MANOVA is particularly sensitive to outliers. Therefore, in order to reduce the impact of the outliers on multivariate statistics, the four main personality variables were recoded so that the values for these outliers were replaced with the accepted maximum value as shown by stem- and leaf- plots. This resulted in transformations of scores for six cases on cluster A total score, sixteen cases on avoidant total score, ten cases on cluster B total score, and three cases on obsessive compulsive total score.

To assess the potential impact of multivariate outliers, Mahalanobis distance critical values were calculated using procedures outlined by Tabachnick and Fidell (2001). For Hypothesis 1, a Mahalanobis critical value of 20.52 at an alpha level of .001 was computed. Three multivariate outliers were identified when analysis of Mahalanobis distance was based upon the variables of cluster A total score, avoidant total Score, cluster B total score, and obsessive-compulsive total score prior to their transformation to address univariate outliers. Following the variable transformation, no multivariate outliers were identified.

Univariate normality was assessed for every combination of independent variable level (SCH-REL, BP-REL, and HC) with each dependent variable (cluster A total score, avoidant total score, cluster B total score, obsessive compulsive total score) using histograms, normality plots and skewness and kurtosis values also based upon recommendations made by Tabachnick and Fidell (2001). Univariate normality was first assessed using the personality-related dependent variables prior to the data transformation to reduce the impact of outliers. These tests showed positive skewness for all 12 variable combinations with most falling outside of the recommended range of -1 to 1. Kurtosis values also suggested nonnormality for most variable combinations. Univariate normality was then

assessed following the data transformation of the personality-related dependent variables. Skewness and kurtosis values improved and variables fell within the recommended ranges for these values, with the exception of avoidant total score, which was positively skewed and showed distributions with leptokurtosis, which indicates that the distribution is overly peaked and has long, thin tails (Mertler & Vannatta, 2002). Although the avoidant total score variable violates the assumption of normality, it was not transformed. Tabachnick and Fidell (2001) suggest that MANOVA is fairly robust to violations of normality. Therefore, transformation may be unnecessary. Linearity was assessed by creating scatterplots of the dependent variables for Hypothesis 1, as well as calculating Pearson correlation coefficients between every combination of dependent variables. The variables appeared fairly linear. Homogeneity of variance-covariance was evaluated during the MANOVA procedure. Combined with fairly equal group sample sizes, a significant Box's Test revealed that equal variances could not be assumed, $F(20, 88714) = 2.20$, $p = .002$. Therefore, Pillai's trace will be interpreted as the MANOVA test statistic. Given that equal variances cannot be assumed Pillai's trace is recommended for interpreting MANOVA results (Mertler & Vannatta, 2002).

Main analyses. A one-way multivariate analysis of variance (MANOVA) was conducted to determine if there were differences in the three relative groups (schizophrenia vs. bipolar I disorder vs. healthy control) on a linear combination of cluster A personality traits, avoidant personality traits, cluster B personality traits, and obsessive compulsive personality traits. Data on all four dependent variables was missing for 11 participants and, therefore, deleted listwise from the analysis. Data were first transformed to eliminate outliers for all four of the dependent variables. See the description in the previous section for specific transformations. MANOVA results indicate significant group differences in relative

type with respect to personality traits, Pillai's Trace = 0.24, $F(8, 322) = 5.51$, $p < .01$, multivariate $eta^2 = .12$.

Analysis of variance (ANOVA) was conducted on each dependent variable as a follow-up test to MANOVA. Relative type (schizophrenia, bipolar I disorder, healthy control) group differences were significant for cluster A total score, $F(2, 163) = 15.25$, $p < .001$, partial $eta^2 = .16$. Relative type group differences were significant for avoidant total score, $F(2, 163) = 3.41$, $p = .035$, partial $eta^2 = .04$. Relative type group differences were significant for cluster B total score, $F(2, 163) = 3.47$, $p = .034$, partial $eta^2 = .04$. Relative type group differences were significant for obsessive compulsive total score, $F(2, 163) = 5.17$, $p = .007$, partial $eta^2 = .06$. These results suggest that although significant differences were found on all multivariate and univariate analyses, effect sizes were below .20, which could be considered small (Ferguson, 2009). Table 4 presents means and standard deviations for the personality variables by relative group. Furthermore, Table 4 summarizes results of the follow-up ANOVAs to assess group differences on each personality variable

The Bonferroni post hoc analysis specified the following relative type group differences. The cluster A total score for the schizophrenia relatives significantly differed from both the bipolar I relative and healthy control groups (both at $p < .001$). This supports Hypothesis 1a and suggests that relatives of patients with schizophrenia demonstrate more schizophrenia-spectrum personality traits than bipolar I relatives or healthy controls. On avoidant total score, the only significant ($p = .032$) differences were between the schizophrenia relative and healthy control groups. This partially supports Hypothesis 1b and suggests that relatives of patients with schizophrenia demonstrate more avoidant personality traits than healthy controls, but did not differ from the bipolar I relatives on this dimension.

On cluster B total score, the only significant (p = .039) differences were between the schizophrenia relative and healthy control groups. Therefore, Hypothesis 1c is not supported. On obsessive-compulsive total score, the only significant (p = .002) differences were between the bipolar I relative and healthy control groups. This finding partially supports 1d and suggests that relatives of patients with bipolar I disorder demonstrate more obsessive compulsive personality traits than control subjects, but did not differ on this dimension from relatives of patients with schizophrenia..

Table 4

Means and Standard Deviations for SIDP-IV Personality Measures by Relative Group with Statistical Analysis of Group Differences Using ANOVA for Full Dataset

	Schizophrenia Relatives (n = 53)		Bipolar Relatives (n = 50)		Healthy Controls (n = 63)			
Dependent Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	$F(2, 163)$	*p*
Cluster A Total Score	7.30_a	4.03	4.28_b	3.74	3.57_b	3.59	15.25	.000
Avoidant Total Score	2.30_a	3.42	$1.46_{a,b}$	2.23	1.05_b	2.01	3.41	.034
Cluster B Total Score	5.87_a	4.51	$5.38_{a,b}$	3.86	3.94_a	4.01	3.47	.035
OBCMP Total Score	$3.47_{a,b}$	2.93	4.56_a	3.28	2.86_b	2.24	5.17	.007

Note. Means sharing a common subscript in each row do not differ significantly at p < .05 according to Bonferroni correction procedure for multiple comparisons. SIDP-IV = Structured Interview for DSM-IV Personality (Pfohl et al., 1995); ANOVA = Analysis of Variance; OBCMP = Obsessive Compulsive.

Analysis of adjusted dataset (N = 154). The reader is again referred to Table 3, which summarizes the four SIDP-IV (Pfohl et. al., 1995) personality trait measures.

Data screening. Prescreening of data after scores on the dependent variables were averaged for multiple members per family resulted in similar results as to the screening of data for Hypothesis 1 that occurred previously. Missing data on the personality variables

existed for seven cases, which represented less than 5% of the sample. Therefore, these cases were deleted using the listwise default function in SPSS 20.0. As MANOVA is particularly sensitive to outliers, the four main personality variables were re-coded to reduce the impact of outliers on the multivariate statistics. The values that represented outliers per each of the four variables were replaced with the accepted maximum value that was shown by stem- and leaf- plots. This resulted in transformations of scores for six cases on cluster A total score, eight cases on cluster B total score, 14 cases on avoidant total score, and three cases on obsessive compulsive total score. Following variable transformation no multivariate outliers were revealed using Mahalanobis distance calculation. Normality was first visually assessed using histograms. This revealed positive skewness for all variables. However, kurtosis and skewness values fell within the accepted range (-1 to 1) for all variables. Combined with the knowledge that MANOVA is fairly robust to violations of normality (Tabachnick & Fidell, 2001), these values indicated that no transformations were necessary to improve normality. Linearity was assessed via scatterplots of the dependent variables. These appeared fairly linear. Finally, homogeneity of variance-covariance was evaluated during the MANOVA procedure. Combined with fairly equal group sample sizes, a nonsignificant Box's Test revealed that equal variances could be assumed, $F(20, 66021) = 1.37$, $p = .13$. Therefore, Wilk's Lambda could be interpreted as the MANOVA test statistic.

Main analyses. A one-way multivariate analysis of variance (MANOVA) was conducted to determine if there were differences in the three relative groups (schizophrenia vs. bipolar I disorder vs. healthy control) on a linear combination of cluster A personality traits, avoidant personality traits, cluster B personality traits, and obsessive compulsive personality traits. This MANOVA was conducted on the sample of participants wherein the

dependent variable scores for multiple members of one family were averaged to obtain one score for each redundant family, reducing the original dataset from 177 to 154 participants. Groups remained fairly equal in size with 46 SCH-RELs, 49 BP-RELs, and 59 HCs. Data on all four dependent variables was missing for seven participants and therefore, deleted from the analysis. As previously described, data were first transformed to address multivariate outliers for each of the four dependent variables. MANOVA results indicate significant group differences in relative type with respect to personality traits, Wilk's Lambda = 0.81, $F(8, 282) = 3.89$, $p < .001$, multivariate $eta^2 = .10$.

Analysis of variance (ANOVA) was conducted on each dependent variable as a follow-up test to MANOVA. Relative type (schizophrenia, bipolar I disorder, healthy control) group differences were significant for cluster A total score, $F(2, 144) = 9.20$, $p < .001$, partial $eta^2 = .11$. Relative type group differences were significant for avoidant total score, $F(2, 144) = 3.66$, $p = .012$, partial $eta^2 = .05$. Relative type group differences were significant for cluster B total score, $F(2, 144) = 4.54$, $p = .028$, partial $eta^2 = .06$. Relative type group differences were significant for obsessive compulsive total score, $F(2, 144) = 6.03$, $p = .003$, partial $eta^2 = .08$. These results suggest that although significant differences were found on all multivariate and univariate analyses, effect sizes were below .15, which could be considered small (Ferguson, 2009). Table 5 presents means and standard deviations for the personality variables by relative group. Furthermore, Table 5 summarizes results of the follow-up ANOVAs to assess group differences on each personality variable.

Table 5

Means and Standard Deviations for SIDP-IV Personality Measures by Relative Group with Statistical Analysis of Group Differences Using ANOVA for Adjusted Dataset

	Schizophrenia Relatives (n = 43)		Bipolar Relatives (n = 46)		Healthy Controls (n = 58)			
Dependent Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	$F(2, 163)$	*p*
Cluster A Total Score	9.02_a	6.18	5.85_b	6.71	3.96_b	4.86	9.20	.000
Avoidant Total Score	1.84_a	2.01	$1.32_{a,b}$	1.58	0.91_b	1.56	3.66	.028
Cluster B Total Score	8.45_a	7.81	$7.09_{a,b}$	7.11	4.50_b	5.45	4.54	.012
OBCMP Total Score	$3.59_{a,b}$	2.90	4.72_a	3.31	2.80_b	2.23	6.03	.003

Note. Means sharing a common subscript in each row do not differ significantly at $p < .05$ according to Bonferroni correction procedure for multiple comparisons. SIDP-IV = Structured Interview for DSM-IV Personality (Pfohl et al., 1995); ANOVA = Analysis of Variance; OBCMP = Obsessive Compulsive.

The Bonferroni post hoc analysis specified the following group differences. The cluster A total score for the schizophrenia relatives significantly differed from both the bipolar I relative and healthy control groups. Significance values were at levels of $p = .036$ and $p < .001$, respectively. This supports Hypothesis 1a and suggests that relatives of patients with schizophrenia demonstrate more schizophrenia-spectrum personality traits than bipolar I relatives or healthy control groups. On avoidant total score, the only significant ($p = .023$) differences were between the schizophrenia relative and healthy control groups. This partially supports Hypothesis 1b and suggests that relatives of patients with schizophrenia demonstrate more avoidant personality traits than controls, but did not differ from relatives of patients with bipolar I disorder on this dimension. On cluster B total score, the only significant ($p = .012$) differences were between the schizophrenia relative and healthy control

groups. Therefore, Hypothesis 1c was not supported. On obsessive compulsive total score, the only significant (p = .002) differences were between the bipolar I relative and healthy control groups. This finding partially supports Hypothesis 1d and suggests that relatives of patients with bipolar I disorder demonstrate more obsessive compulsive personality traits than healthy control participants, but did not differ on this dimension from relatives of patients with schizophrenia.

Hypothesis 2: Group Comparisons of Cognitive Functioning

Table 6 is presented to provide the reader with a summary of performance measures (dependent variables) used to assess cognitive functioning in the domains of attention, working memory, and executive functioning in Hypothesis 2. Where normative data was available, raw scores were converted to *z*-scores (BACS; Keefe et al., 2008) or subtest scaled scores (WMS-III; Wechsler, 1997b) prior to analysis.

Analysis of full dataset (*N = 177*).

Data screening. The eight cognitive variables as described were evaluated for missing data. There was more missing cognitive data than had previously been found in the personality data, and as such, the patterns of missing data were examined. Nineteen participants were missing all cognitive data, which represented 10.7% of the total sample. In the majority of these cases, it appeared that the participant had completed the first part of the study (the clinical evaluation), but did not return to complete the cognitive assessment. An additional ten individuals (5.7% of the total sample) had completed the BACS assessment, but had missing computerized data (PCET only, CPT only, or both measures). In the majority of these cases, records indicated that the computer had malfunctioned. Therefore, missing data for the cognitive variables ranged from 10.7% to 16.4% of the total sample.

Table 6

Summary of the Eight Cognitive Dependent Variables

Cognitive Task	Performance Measure	Domain
BACS Symbol Coding	No. correct symbols copied in 90 seconds (*z*-score)	Attention
DPX- CPT AX Accuracy	% of correct responses to AX trials[a] on CPT	Attention
DPX-CPT BX Accuracy	% of correct responses to BX trials[b] on CPT	Attention
BACS Digit Sequencing	No. of correct responses converted to *z*-score	Working Memory
WMS-III Spatial Span Scale Score	No. of correct responses (forwards and backward)	Working Memory
BACS Tower of London	No. of correct responses converted to *z*-score	Executive Functioning
PCET Categories	No. of total categories achieved on PCET	Executive Functioning
PCET Errors	No. of total errors on PCET	Executive Functioning

Note. BACS = Brief Assessment of Cognition (Keefe et al., 2004, 2008); DPX-CPT = Dot Pattern Expectancy Continuous Performance Test (MacDonald et al., 2005); WMS-III = Wechsler Memory Scale, Third Edition (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).
[a]AX trials are trials during which a target cue is followed by a target probe. [b]BX trials are trials during which a non-target cue is followed by a target probe.

Based upon recommendations from Mertler and Vannatta (2002), the Hypothesis 2 analyses were conducted using two alternative approaches to the missing data. The 29 participants were deleted from the analyses using listwise deletion in SPSS 20.0, which resulted in a reduction in sample size (n = 148) and thereby power. The analyses were then also run by replacing the missing values with the series mean for that variable, rather than using deletion. Both analyses yielded similar results. Therefore, only the first alternative (i.e. deleting the cases via listwise deletion) will be reported.

Frequencies, descriptive statistics, box-plots, and stem- and leaf- plots were examined to identify univariate outliers and their potential influence on results for each of the cognitive dependent variables. The number of univariate outliers identified for each cognitive DV varied from zero to fifteen. As MANOVA is particularly sensitive to outliers (Tabachnick and Fidell, 2001) cognitive variables with outliers were recoded so that the values for these outliers were replaced with the accepted maximum value as shown by stem- and leaf- plots. This resulted in transformations of scores for eleven cases on CPT AX Accuracy, fifteen cases on CPT BX Accuracy, one case on BACS Digit Sequencing, seven cases on BACS Tower of London, and five cases on PCET Categories. To assess the potential impact of multivariate outliers, Mahalanobis distance critical values were calculated using procedures outlined by Tabachnick and Fidell (2001). For Hypothesis 2, a Mahalanobis critical value of 26.13 at an alpha level of .001 was computed. This identified one multivariate outlier and this case was deleted from the dataset prior to analysis.

Univariate normality was assessed for every combination of independent variable level (SCH-REL, BP-REL, and HC) with each cognitive dependent variable (BACS Symbol Coding, CPT AX accuracy, CPT BX accuracy, BACS Digit Sequencing, WMS-III Spatial

Span, BACS Tower of London, PCET categories, and PCET errors) using histograms, normality plots and skewness and kurtosis values also based upon recommendations made by Tabachnick and Fidell (2001). Univariate normality was assessed following outlier transformation. Skewness and kurtosis values fell within the recommended range (-1 to 1) for most of the cognitive variables. CPT BX accuracy was negatively skewed for all three family groups, with skewness values around -1.2. The PCET categories variable was similarly negatively skewed for the healthy control group. Although these variables suggest violations of the assumption of normality, they were not transformed as MANOVA is fairly robust to violations of normality (Tabachnick & Fidell, 2001). Linearity was assessed by creating scatterplots of the dependent variables for Hypothesis 2, as well as calculating Pearson correlation coefficients between every combination of dependent variables. The variables appeared fairly linear. Homogeneity of variance-covariance was evaluated during the MANOVA procedure. Combined with fairly equal group sample sizes, a nonsignificant Box's Test revealed that equal variances could be assumed, $F(72, 52455) = 1.18$, $p = .136$. Therefore, Wilk's Lambda will be interpreted as the MANOVA test statistic.

Main analyses. A one-way multivariate analysis of variance (MANOVA) was conducted to determine if there were differences in the three relative groups (schizophrenia vs. bipolar I disorder vs. healthy control) on a linear combination of attention (measured by BACS Symbol Coding, CPT AX accuracy, and CPT BX accuracy), working memory (measured by BACS Digit Sequencing and WMS-III Spatial Span), and executive functioning (measured by BACS Tower of London, PCET categories, and PCET errors). MANOVA results indicate significant group differences in relative type with respect to

cognitive functioning, Wilk's Lambda = 0.77, $F(16, 274) = 2.38$, $p = .002$, multivariate $eta^2 = .12$.

Analysis of variance (ANOVA) was conducted on each dependent variable as a follow-up test to MANOVA. Relative type (schizophrenia, bipolar I disorder, healthy control) group differences were significant for BACS Symbol Coding score, $F(2, 144) = 10.64$, $p < .001$, partial $eta^2 = .13$. Relative type group differences were significant for the WMS-III Spatial Span score, $F(2, 144) = 9.57$, $p < .001$, partial $eta^2 = .12$. Relative type group differences were significant for the BACS Tower of London score, $F(2, 144) = 3.24$, $p = .042$, partial $eta^2 = .04$. Relative type group differences were significant for PCET errors, $F(2, 144) = 5.13$, $p = .007$, partial $eta^2 = .07$. Relative type group differences were not significant for CPT AX Accuracy, CPT BX Accuracy, the BACS Digit Sequencing score and PCET Categories. These results suggest that although significant differences were found on all multivariate and univariate analyses, effect sizes were below .15, which could be considered small (Ferguson, 2009). Table 7 presents the means and standard deviations for the personality variables by relative group. Furthermore, Table 7 summarizes results of the follow-up ANOVAs to assess group differences on each cognitive variable.

The Bonferroni post hoc analysis specified the following relative type group differences. The BACS Symbol Coding score for the schizophrenia relatives differed significantly ($p = .005$) from the healthy control group, but was not significantly different from the bipolar I relative group. Similarly, the BACS Symbol Coding score for bipolar I relatives differed significantly ($p < .001$) from the healthy control group, but was not significantly different from the schizophrenia relative group. These findings support Hypothesis 2a suggesting that both schizophrenia and bipolar I relatives show impairments

on one measure of attention when compared to healthy controls. However, these findings do not support Hypothesis 2b as the schizophrenia relative group did not show significantly greater impairment when compared to the bipolar relative group.

Table 7

Means and Standard Deviations for Cognitive Performance Measures by Relative Group with Statistical Analysis of Group Differences Using ANOVA for Full Dataset

	Schizophrenia Relatives (n = 47)		Bipolar Relatives (n = 43)		Healthy Controls (n = 57)			
Dependent Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	F^a	*p*
BACS Symbol Coding[b]	-0.19_a	0.99	0.02_a	0.95	0.64_b	0.95	10.64	.000
DPX-CPT AX Accuracy[b]	94.26	4.57	94.87	4.83	95.98	4.35	1.91	.152
DPX-CPT BX Accuracy[b]	89.10	14.27	89.71	13.76	92.54	12.69	0.97	.381
BACS Digit Sequencing[b]	-0.46	0.92	-0.15	0.98	-0.15	1.00	1.58	.209
WMS-III Spatial Span[b]	7.68_a	3.35	10.00_b	3.37	10.32_b	3.07	9.57	.000
BACS Tower of London[b]	-0.33_a	1.04	$0.08_{a,b}$	0.98	0.12_b	0.88	3.24	.042
PCET Categories[b]	2.34	0.67	2.40	0.73	2.60	0.59	2.20	.115
PCET Errors[c]	35.79_a	15.92	$29.21_{a,b}$	16.33	24.63_b	19.91	5.13	.007

Note. Means sharing a common subscript in each row do not differ significantly at $p < .05$ according to Bonferroni correction procedure for multiple comparisons. Bonferroni multiple comparisons are only shown for significant *F* tests. BACS = Brief Assessment of Cognition (Keefe et al., 2004, 2008); DPX-CPT = Dot Pattern Expectancy Continuous Performance Test (MacDonald et al., 2005); WMS-III = Wechsler Memory Scale, Third Edition (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]*df* = 2, 144. [b]Lower scores are indicative of worse performance on the cognitive measure. [c]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

The WMS-III Spatial Span scaled score for the schizophrenia relative group differed significantly from both the bipolar I relative ($p = .003$) and healthy control ($p < .001$) groups. These findings lend partial support to both Hypothesis 2a and 2b suggesting that only schizophrenia relatives demonstrate impaired performance on one measure of working memory when compared to bipolar I relatives and healthy controls.

The follow-up ANOVA revealed relative type group differences on the BACS Tower of London. However, post host analysis showed that the score for schizophrenia relatives as compared to healthy controls only approached significance ($p = .058$). This finding does not support either Hypothesis 2a or 2b for this particular measure of executive functioning.

PCET errors for the schizophrenia relatives differed significantly ($p = .005$) from the healthy control group. This partially supports Hypothesis 2a, but not Hypothesis 2b suggesting that only schizophrenia relatives show worse performance on a measure of executive functioning when compared to healthy controls.

Analysis of adjusted dataset ($N = 154$). The reader is again referred to Table 5 which summarizes the eight performance measures (dependent variables) used to assess cognitive functioning in the three main domains of attention (A), working memory (WM), and executive functioning (EF).

Data screening. As had also occurred in the analysis of the full dataset for the second hypothesis (previous section), it was noticed that there was more missing cognitive data than had been found in the personality data, and as such, patterns of missing data were examined. Fourteen participants were missing all cognitive data, which represented 9.1% of the total sample. In the majority of these cases, it appeared that the participant had completed the first part of the study (the clinical evaluation), but did not return to complete the cognitive

assessment. An additional eight individuals (5.2% of the total sample) had completed the BACS assessment, but had missing computerized data (PCET only, CPT only, or both measures). In the majority of these cases, records indicated that the computer had malfunctioned. Therefore, 14.3% of the total sample had missing data on at least two and up to all eight of the cognitive variables. Based upon recommendations from Mertler and Vannatta (2002), the Hypothesis 2 analyses to address nonindependence were conducted using two alternative approaches to the missing data. The 22 participants were deleted from the analyses using listwise deletion in SPSS 20.0, which resulted in a reduction in sample size (n = 132) and thereby power. The analyses were then also run by replacing the missing values with the series mean for that variable, rather than using deletion. Both analyses yielded the same results. Therefore, only the first alternative (i.e. deleting the cases) will be reported.

Frequencies, descriptive statistics, box-plots, and stem- and leaf- plots were examined to identify univariate outliers and their potential influence on results for each of the cognitive dependent variables. The number of univariate outliers identified for each cognitive DV varied from zero to thirteen. As MANOVA is particularly sensitive to outliers (Tabachnick and Fidell, 2001) cognitive variables with outliers (five of eight variables) were recoded so that the values for these outliers were replaced with the accepted minimum or maximum value as shown by stem- and leaf- plots. This resulted in transformations of scores for ten cases on CPT AX accuracy, thirteen cases on CPT BX accuracy, one case on BACS Digit Sequencing, three cases on BACS Tower of London, and four cases on PCET categories. To assess the potential impact of multivariate outliers, a Mahalanobis distance critical value was calculated using procedures outlined by Tabachnick and Fidell (2001). For the Hypothesis 2

re-analysis, a Mahalanobis critical value of 26.13 at an alpha level of .001 was computed. No multivariate outliers were identified using this approach.

Univariate normality was assessed for every combination of independent variable level (SCH-REL, BP-REL, and HC) with each cognitive dependent variable (BACS Symbol Coding, CPT AX accuracy, CPT BX accuracy, BACS Digit Sequencing, WMS-III Spatial Span, BACS Tower of London, PCET categories, and PCET errors) using histograms, normality plots and skewness and kurtosis values also based upon recommendations made by Tabachnick and Fidell (2001). Univariate normality was assessed following outlier transformation. Skewness and kurtosis values fell within the recommended range (-1 to 1) for all of the cognitive variables, suggesting no obvious violations of normality. Linearity was assessed by creating scatterplots of the dependent variables for the Hypothesis 2 re-analysis, as well as calculating Pearson correlation coefficients between every combination of dependent variables. The variables appeared fairly linear. Homogeneity of variance-covariance was evaluated during the MANOVA procedure. Combined with fairly equal group sample sizes, a nonsignificant Box's Test revealed that equal variances could be assumed, $F(72, 41174) = 1.25$, $p = .075$. Therefore, Wilk's Lambda was interpreted as the MANOVA test statistic.

Main analyses. A one-way multivariate analysis of variance (MANOVA) was conducted to determine if there were differences in the three relative groups (schizophrenia vs. bipolar I disorder vs. healthy control) on a linear combination of attention (measured by BACS Symbol Coding, CPT AX accuracy, and CPT BX accuracy), working memory (measured by BACS Digit Sequencing and WMS-III Spatial Span), and executive functioning (measured by BACS Tower of London, PCET categories, and PCET errors).

MANOVA results indicate significant group differences in relative type with respect to cognitive functioning, Wilk's Lambda = 0.74, $F(16, 244) = 2.50$, $p = .001$, multivariate $eta^2 = .14$.

Analysis of variance (ANOVA) was conducted on each dependent variable as a follow-up test to MANOVA. Relative type (schizophrenia, bipolar I disorder, healthy control) group differences were significant for BACS Symbol Coding score, $F(2, 129) = 12.30$, $p < .001$, partial $eta^2 = .16$. Relative type group differences were significant for the WMS-III Spatial Span score, $F(2, 129) = 10.38$, $p < .001$, partial $eta^2 = .14$. Relative type group differences were significant for the BACS Tower of London score, $F(2, 129) = 3.82$, $p = .024$, partial $eta^2 = .06$. Relative type group differences were significant for PCET Errors, $F(2, 129) = 4.02$, $p = .020$, partial $eta^2 = .06$. Relative type group differences were not significant for CPT AX accuracy, CPT BX accuracy, the BACS Digit Sequencing score and PCET categories. These results suggest that although significant differences were found on all multivariate and univariate analyses, effect sizes were below .20, which could be considered small (Ferguson, 2009).

The Bonferroni post hoc analysis specified the following relative type group differences. The BACS Symbol Coding score for the schizophrenia relatives differed significantly ($p < .001$) from the healthy control group, but was not significantly different from the bipolar I relative group. Similarly, the BACS Symbol Coding score for bipolar I relatives differed significantly ($p = .004$) from the healthy control group, but was not significantly different from the schizophrenia relative group. These findings support Hypothesis 2a suggesting that both schizophrenia and bipolar I relatives show impairments on one measure of attention when compared to healthy controls. However, these findings do

not support Hypothesis 2b as the schizophrenia relative group did not show significantly greater impairment when compared to the bipolar I relative group.

The WMS-III Spatial Span scaled score for the schizophrenia relative group differed significantly from both the bipolar I relative ($p = .001$) and healthy control ($p < .001$) groups. The bipolar I relative and healthy control groups were not significantly different from one another. These findings lend partial support to both Hypothesis 2a and 2b suggesting that only schizophrenia relatives demonstrate impaired performance on this measure of working memory when compared to bipolar I relatives and healthy controls.

The BACS Tower of London score for the schizophrenia relative group differed significantly ($p = .029$) from the healthy control group, but was not significantly different from the bipolar I relative group. Significant differences were not shown between the bipolar I relative and healthy control groups. Therefore, these findings lend partial support to Hypothesis 2a suggesting that schizophrenia relatives show impairments on one measure of executive functioning when compared to healthy controls, yet bipolar I relatives do not. Furthermore, these findings do not support Hypothesis 2b as the schizophrenia relative group did not show significantly greater impairment when compared to the bipolar I relative group.

PCET errors for the schizophrenia relatives differed significantly ($p = .016$) from the healthy control group. This partially supports Hypothesis 2a, but not Hypothesis 2b suggesting that only schizophrenia relatives show worse performance on a measure of executive functioning when compared to healthy controls. Table 8 presents the means and standard deviations for the cognitive variables by participant group. Table 8 also summarizes results of the follow-up ANOVAs to assess relative type group differences on each cognitive variable.

Table 8

Means and Standard Deviations for Cognitive Performance Measures by Relative Group with Statistical Analysis of Group Differences Using ANOVA for Adjusted Dataset

Dependent Variable	Schizophrenia Relatives (n = 38) *M*	*SD*	Bipolar Relatives (n = 42) *M*	*SD*	Healthy Controls (n = 52) *M*	*SD*	F^a	*p*
BACS Symbol Coding[b]	-0.26_a	.94	0.05_a	.93	0.70_b	.95	12.30	.000
DPX-CPT AX Accuracy[b]	94.13	4.58	94.84	4.99	95.94	4.57	1.70	.188
DPX-CPT BX Accuracy[b]	87.87	14.48	88.75	14.52	92.36	12.84	1.37	.259
BACS Digit Sequencing[b]	-0.38	.85	-0.18	1.01	-0.10	.98	0.95	.390
WMS-III Spatial Span[b]	7.59_a	3.06	10.08_b	3.18	10.46_b	3.09	10.38	.000
BACS Tower of London[b]	-0.39_a	.94	$0.07_{a,b}$	.97	0.13_b	.88	3.82	.024
PCET Categories[b]	2.35	.67	2.35	.75	2.60	.59	2.10	.126
PCET Errors[c]	34.92_a	15.53	$29.47_{a,b}$	15.57	24.50_b	19.56	4.02	.020

Note. Means sharing a common subscript in each row do not differ significantly at $p < .05$ according to Bonferroni correction procedure for multiple comparisons. Bonferroni multiple comparisons are only shown for significant *F* tests. BACS = Brief Assessment of Cognition (Keefe et al., 2004, 2008); DPX-CPT = Dot Pattern Expectancy Continuous Performance Test (MacDonald et al., 2005); WMS-III = Wechsler Memory Scale, Third Edition (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).
[a]*df* = 2, 144. [b]Lower scores are indicative of worse performance on the cognitive measure.
[c]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

Hypothesis 3: Predictions of Group Membership

Introduction to the results for the third hypothesis. The third hypothesis of the present study addresses the question of whether or not group membership, or more specifically, relative type can be predicted from a combination of variables that have been assessed in the previous two hypotheses. It was initially planned that a total of twelve variables would be chosen as predictor variables for this final hypothesis: four personality variables and eight cognitive variables. However, MANOVA results from the second hypothesis revealed that significant group differences did not exist for four of the cognitive variables. Therefore, these cognitive variables (BACS Digit Sequencing Standard Score, CPT AX accuracy, CPT BX accuracy, and PCET categories achieved) were dropped from the analyses in the final hypothesis. It is important to note that at least one of each type of cognitive measure (i.e. attention, working memory, and executive functioning) was retained and represented in the following analyses.

Analysis of the third hypothesis proceeds in four parts. Both a discriminant function analysis and logistic regression analysis are conducted to address the final hypothesis in two ways. Both analyses are reported using the full dataset (N = 177). The analyses were also conducted with the smaller dataset (N = 154) where families with multiple members are represented by a single "member" of averaged data for that family group. The discriminant function analyses are first presented to attempt to predict membership into all three groups. Logistic regression analyses may better represent the overall findings and are therefore presented second. Some potential violations of assumptions (especially related to homogeneity of variance and covariance) were involved with the discriminant function analysis. The same assumptions are not of the same level of concern with regard to the

logistic regression analyses. Details regarding the violations of assumptions will be discussed along with results of the analyses. For the logistic regression, relative type includes only the schizophrenia relative and bipolar I relative groups. The control group could not be included due to the binary structure of logistic regression, which required defining relative type as a dichotomous variable.

Discriminant function analysis of full dataset (*N* = 177). A discriminant analysis was conducted to determine whether eight variables (four personality and four cognitive)—cluster A total score, avoidant total score, cluster B total score, obsessive compulsive total score, BACS Symbol Coding standard score, WMS Spatial Span total scaled score, BACS Tower of London standard score, and PCET total errors—could predict relative type (schizophrenia relative, bipolar relative, or healthy control) for a participant in the present study. Table 9 presents the means, standard deviations and ANOVA results of the predictor variables that were simultaneously entered into the analysis.

Prior to discriminant analysis, missing values were explored, and outliers and assumptions of normality, linearity and homogeneity of variance and covariance were assessed. Only those assumptions that may be problematic for this particular analysis will be discussed herein as they have already been discussed with regard to these variables for the previous hypotheses. Some missing values were present for all variables. Listwise deletion in SPSS 20.0 reduced the original sample size to 149, which included 46 in the SCH-REL group, 46 in the BP-REL group, and 57 in the HC group.

Table 9

Means, Standard Deviations, and Group Differences Among Discriminant Function Analysis Predictor Variables as a Function of Relative Type for Full Dataset

	Schizophrenia Relatives (n = 46)		Bipolar Relatives (n = 46)		Healthy Controls (n = 57)			
Predictor Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*F*	*p*
Cluster A Total Score[a]	9.67	8.14	5.74	6.91	4.00	4.41	9.85	.000
Avoidant Total Score[a]	2.43	4.22	1.50	2.50	1.14	2.09	2.43	.092
Cluster B Total Score[a]	9.57	9.93	7.91	9.18	4.68	5.26	4.79	.010
OBCM Total Score[a]	3.63	3.37	4.63	3.51	2.82	2.03	4.68	.011
BACS Symbol Coding[b]	-0.18	1.00	-0.01	0.90	0.64	0.95	10.68	.000
WMS-III Spatial Span[b]	7.67	3.39	10.13	3.36	10.32	3.07	9.84	.000
BACS Tower of London[b]	-0.40	1.21	0.03	1.00	-0.02	1.16	2.08	.129
PCET Errors[c]	35.59	16.05	29.28	16.29	24.00	19.13	5.67	.004

Note. N = 149. OBCM = Obsessive Compulsive; BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004); WMS = Wechsler Memory Scale (Wechsler et al., 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Higher scores are indicative of more extreme responding for personality variable. [b]Lower scores are indicative of worse performance on the cognitive measure. [c]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

Identification of univariate outliers for the eight predictor variables was accomplished through assessment of stem-and-leaf plots and *z*-scores following listwise deletion. Values for *z*-scores on the variables that exceeded an absolute value of four were considered univariate outliers based upon recommendation by Mertler and Vannatta (2002). The authors suggested that for larger sample sizes (n > 100) the requirements for assessing *z*-scores for univariate outliers can be extended to an absolute value of four instead of three. Using this

approach, univariate outliers were only identified for two of the four personality variables (cluster A total score and avoidant total score). The number of outliers per personality variable was one and three, respectively. Additionally, three multivariate outliers were identified using a Mahalanobis distance critical value of 26.13 for eight predictors. The assumption of normality was discussed in the previous hypotheses as it was evaluated for all personality and cognitive variables. The interested reader is referred to that section for greater detail. All variables were positively skewed with the avoidant total score being the most skewed and also exhibiting leptokurtosis. Although some outliers were identified and the personality variables, in particular, were found to be non-normal in their distributions, no variables were transformed. A sample size of 177 may be large enough to be robust to these violations (Tabachnick & Fidell, 2001). Homogeneity of variance-covariance was evaluated during the discriminant analysis using Box's $M = 137.83$, $F(72, 55356) = 1.76$, $p < .001$. The significant results from Box's Test suggest that the assumption of homogeneity of covariance matrices has not been met. However, according to Leech, Barrett and Morgan (2005), non-normality, which is present for some of the predictor variables, can strongly influence the results of Box's Test. Logistic regression is recommended as an alternative to discriminant function analysis when violations of assumptions are of concern. The results of Box's test will be taken into consideration when interpreting the discriminant function analysis results. It may be more prudent to base general conclusions for the third hypothesis more heavily upon the logistic regression analysis as opposed to discriminant function analysis results.

According to Tabachnick and Fidell (2001), discriminant function analysis is also sensitive to high correlations among predictor variables, resulting in multicollinearity.

Therefore, a bivariate correlation matrix was first assessed to identify any high correlations among the eight predictor variables. All bivariate correlations were below .70, which was the cut off value recommended by Tabachnick and Fidell for evaluating variable redundancy. The highest bivariate correlation (Pearson's $r = .65$, $p < .001$) was between the cluster A total score and cluster B total score variables. A preliminary multiple regression was also conducted prior to the logistic regression in order to further evaluate multicollinearity among the eight predictors as recommended by Mertler and Vannatta (2002). Since tolerance statistics for all eight predictors were above 0.1, multicollinearity did not appear to pose a problem for interpretation.

The discriminant function analysis was conducted using the enter method in SPSS 20.0, which enters all predictors into the model simultaneously. The analysis generated two functions with a combined Wilk's Lambda = 0.69, $\chi^2(16) = 53.91$, $p < .001$. After removal of the first function, there was still a strong association between groups and predictors, Wilk's Lambda = 0 .88, $\chi^2(7) = 18.71$, $p = .009$. These results lend support to Hypothesis 3, indicating that both functions of personality and cognitive predictors significantly differentiated between schizophrenia relatives, bipolar relatives, and healthy controls. Regarding effect size, the two discriminant functions accounted for 22% and 12% respectively of the function variance explained by relative type.

Table 10 presents the standardized function coefficients and correlation coefficients for both functions. Consideration of both of these types of coefficients informs interpretation of each function. Based upon the standardized coefficients, BACS Symbol Coding is the predictor that contributes the most to both function 1 and function 2 with loadings of -.55 and -.70, respectively. For function 1, cluster A total score and BACS Tower of London are the

next best contributors. For function 2, obsessive compulsive total score and WMS Spatial Span are the next best contributors. Based upon the correlation coefficients provided by the structure matrix, greater differences in the two functions are revealed. BACS Symbol Coding is the predictor most related to function 1 with a loading of -.69, followed by cluster A total score and WMS Spatial Span. In contrast, obsessive compulsive total score is the predictor most related to function 2 with a loading of .59, followed by WMS Spatial Span (in the opposite direction from function 1) and BACS Symbol Coding. Examination of the scores in Table 10, per function, suggests that findings from this analysis partially support Hypothesis 3. Consideration of the sign (positive vs. negative) of the coefficients with knowledge of the predictor variables is consistent with some of the hypothesized relationships. Function 1 differentiates an individual with higher scores (indicative of more traits in these areas) on the personality variable of cluster A total score, as well as scores in the direction of worse performances on the BACS Symbol Coding task in particular, but also on WMS Spatial Span.. Function 2 differentiates an individual with higher scores (indicative of more traits in this area) on the personality variable of obsessive compulsive total score, as well as scores in the direction of better performances on the WMS Spatial Span task., and worse performance on BACS Symbol Coding.

Classification results (as presented in Table 11) revealed that the original grouped cases were classified with 57.7% overall accuracy. Healthy controls were classified with the best accuracy at 71.9%. Schizophrenia relatives and bipolar I relatives were classified at similar rates to one another, respectively 50.0% and 47.8%. Group means for function 1 indicated that schizophrenia relatives had a mean of .68, bipolar I relatives had a mean of .04,

and healthy controls had a mean of -.58. For function 2, group means for the schizophrenia relatives, bipolar I relatives, and healthy controls were -.27, .55, and -.23, respectively.

Table 10

Correlation of Predictor Variables with Discriminant Functions and Standardized Discriminant Function Coefficients for Full Dataset

	Correlation with discriminant functions		Standardized discriminant function coefficients	
Predictor Variable	Function 1	Function 2	Function 1	Function 2
Cluster A Total Score[a]	.68	-.20	.51	-.32
Avoidant Total Score[a]	.34	-.11	.08	-.20
Cluster B Total Score[a]	.48	.12	.06	.21
OBCM Total Score[a]	.24	.59	-.03	.61
BACS Symbol Coding[b]	-.69	-.32	-.56	-.70
WMS-III Spatial Span[b]	-.62	.43	-.36	.50
BACS Tower of London[b]	-.26	.26	.39	.32
PCET Total Errors[c]	.53	-.03	.20	-.09

Note. *N* = 149. OBCM = Obsessive Compulsive; BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004); WMS = Wechsler Memory Scale (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Higher scores on personality measure are indicative of more extreme responding. [b]Lower scores on cognitive measure are indicative of worse performance. [c]Higher scores on cognitive measure are indicative of worse performance (specifically, more errors).

Table 11

Classification Analysis for Relative Type for Full Dataset

		Predicted Group Membership					
		Schizophrenia Relatives		Bipolar Relatives		Healthy Controls	
Actual Group Membership	*n*	*n*	%	*n*	%	*n*	%
Schizophrenia Relatives	46	23	50.0	12	26.1	11	23.9
Bipolar Relatives	46	10	21.7	22	47.8	14	30.4
Healthy Controls	57	11	19.3	5	8.8	41	71.9

Note. N = 149. Overall percentage of correctly classified cases = 57.7%

Discriminant function analysis of adjusted dataset (N = 154). A discriminant analysis was conducted to determine whether eight variables (four personality and four cognitive)—cluster A total score, avoidant total score, cluster B total score, obsessive compulsive total score, BACS Symbol Coding standard score, WMS Spatial Span total scaled score, BACS Tower of London standard score, and PCET total errors—could predict relative type (schizophrenia relative, bipolar relative, or healthy control) for a participant in the present study sampled from the dataset of 154 participants to account for the violation of the assumption of non-independence. Table 12 presents the means, standard deviations and ANOVA results of the predictor variables that were simultaneously entered into the analysis.

Prior to discriminant analysis, missing values were explored, and outliers and assumptions of normality, linearity and homogeneity of variance and covariance were assessed. Some missing values were present for all variables. Listwise deletion in SPSS 20.0 reduced the original sample size to 131, which included 37 in the SCH-REL group, 42 in the BP-REL group, and 52 in the HC group.

Table 12

Means, Standard Deviations, and Group Differences Among Discriminant Function Analysis Predictor Variables as a Function of Relative Type for Adjusted Dataset

	Schizophrenia Relative (n = 37)		Bipolar Relative (n = 42)		Healthy Control (n = 52)			
Predictor Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*F*	*p*
Cluster A Total Score[a]	9.75	7.94	6.05	7.14	3.89	4.36	8.93	.000
Avoidant Total Score[a]	2.64	3.82	1.61	2.58	1.09	1.91	3.40	.036
Cluster B Total Score[a]	8.90	9.01	8.15	9.51	4.58	5.19	3.95	.022
OBCM Total Score[a]	3.76	3.41	4.81	3.56	2.76	1.99	5.51	.005
BACS Symbol Coding[b]	-0.25	0.95	0.03	0.91	0.69	0.96	11.88	.000
WMS-III Spatial Span[b]	7.58	3.10	10.15	3.24	10.46	3.09	10.26	.000
BACS Tower of London[b]	-0.44	1.09	0.06	0.99	0.05	1.00	3.05	.051
PCET Errors[c]	34.64	15.66	28.83	15.42	23.81	18.68	4.48	.013

Note. N = 131. OBCM = Obsessive Compulsive; BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004); WMS = Wechsler Memory Scale (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Higher scores are indicative of more extreme responding for personality variable. [b]Lower scores are indicative of worse performance on the cognitive measure. [c]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

The violations of assumptions that were described for the discriminant function analysis using the full dataset applied here as well, even though this is a smaller dataset. The interested reader is referred to the section on the discriminant function analysis for the full dataset for an in-depth discussion of how these violations of assumptions were identified and addressed. The same procedure was adopted for this secondary discriminant function analysis. Some differences to note were the identification of fewer outliers, albeit on the

same variables. Univariate outliers were only identified for two of the four personality variables (cluster A total score and avoidant total score). The number of outliers per personality variable was one and two, respectively. Two multivariate outliers were revealed. Homogeneity of variance-covariance was evaluated and determined to again be violated using Box's M = 122.75, $F(72, 39783) = 1.55$, $p = .002$. Due to this violation, results will be interpreted cautiously. Multicollinearity did not appear to be a problem: bivariate correlations and tolerance statistics were within expected ranges.

The discriminant function analysis was conducted using the enter method in SPSS 20.0, which enters all predictors into the model simultaneously. The analysis generated two functions with a combined Wilk's Lambda = 0.66, $\chi^2(16) = 52.46$, $p < .001$. After removal of the first function, there was still a strong association between groups and predictors, Wilk's Lambda = 0.87, $\chi^2(7) = 17.51$, $p = .014$. These results lend support to Hypothesis 3, indicating that both functions of personality and cognitive predictors significantly differentiated between schizophrenia relatives, bipolar I relatives, and healthy controls. Regarding effect size, the two discriminant functions accounted for 25% and 12% respectively of the function variance explained by relative type.

Table 13 presents the standardized function coefficients and correlation coefficients for both functions. Consideration of both of these types of coefficients informs interpretation of each function. Based upon the standardized coefficients, the three highest predictors that contribute to function 1 are BACS Symbol Coding, cluster A total score, and WMS-III Spatial Span. Based upon the standardized coefficients, the three highest predictors that contribute to function 2 are obsessive compulsive total score, BACS Symbol Coding, and WMS-III Spatial Span. Based upon the correlation coefficients provided by the structure

matrix, greater differences in the two functions are revealed. BACS Symbol Coding is the predictor most related to function 1 with a loading of .74, followed by cluster A total score and WMS Spatial Span. In contrast, obsessive-compulsive total score is the predictor most related to function 2 with a loading of .63, followed by WMS Spatial Span, and BACS Symbol Coding (in the opposite direction of function 1). Examination of the scores in Table 13, per function, suggests that findings from this analysis partially support Hypothesis 3. Consideration of the sign (positive vs. negative) of the coefficients with knowledge of the predictor variables is consistent with some of the hypothesized relationships. Function 1 differentiates an individual with lower scores (indicative of less traits in these areas) on the personality variable of Cluster A Total Score, as well as scores in the direction of better performances on the BACS Symbol Coding task in particular, but also on WMS Spatial Span and BACS Tower of London. Function 2 differentiates an individual with higher scores (indicative of more traits in this area) on the personality variable of Obsessive Compulsive Total score, as well as scores in the direction of worse performance on the BACS Symbol Coding, and scores in the direction of better performance on the WMS Spatial Span task.

Table 13

Correlation of Predictor Variables with Discriminant Functions and Standardized Discriminant Function Coefficients for Adjusted Dataset

	Correlation with discriminant functions		Standardized discriminant function coefficients	
Predictor Variable	Function 1	Function 2	Function 1	Function 2
Cluster A Total Score[a]	-.65	-.15	-.49	-.32
Avoidant Total Score[a]	-.40	-.11	-.18	-.20
Cluster B Total Score[a]	-.41	.21	.09	.31
OBCM Total Score[a]	-.29	.63	-.04	.64
BACS Symbol Coding[b]	.74	-.24	.67	-.61
WMS-III Spatial Span[b]	.64	.44	.38	.44
BACS Tower of London[b]	.33	.30	-.34	.38
PCET Total Errors[c]	-.46	-.03	-.02	-.10

Note. N = 131. OBCM = Obsessive Compulsive; BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004); WMS = Wechsler Memory Scale (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Higher scores on personality measure are indicative of more extreme responding. [b]Lower scores on cognitive measure are indicative of worse performance. [c]Higher scores on cognitive measure are indicative of worse performance (specifically, more errors).

Classification results (as presented in Table 14) revealed that the original grouped cases were classified with 59.5% overall accuracy. Healthy controls were classified with the best accuracy at 69.2%. Schizophrenia relatives and bipolar relatives were classified at similar rates to one another, respectively 51.4% and 54.8%. Group means for function 1 indicated that schizophrenia relatives had a mean of -.77, bipolar relatives had a mean of -.08, and healthy controls had a mean of .61. For function 2, group means for the schizophrenia relatives, bipolar relatives, and healthy controls were -.32, .56, and -.22, respectively. The pattern of these function means per group lend further support to Hypothesis 3. It appears positive scores on function one best identify healthy controls, whereas negative score on function 1 identify schizophrenia relatives and bipolar relatives fall somewhere in between. Comparably, positive scores on function two seem to best identify bipolar relatives. Negative scores on function two are associated with both schizophrenia relatives and healthy controls, but the schizophrenia relatives show the lowest.

Table 14

Classification Analysis for Relative Type for Adjusted Dataset

		Predicted Group Membership					
		Schizophrenia Relatives		Bipolar Relatives		Healthy Controls	
Actual Group Membership	*n*	*n*	%	*n*	%	*n*	%
Schizophrenia Relatives	37	19	51.4	12	32.4	6	16.2
Bipolar Relatives	42	8	19.0	23	54.8	11	26.2
Healthy Controls	52	11	21.2	5	9.6	36	69.2

Note. $N = 131$. Overall percentage of correctly classified cases = 59.5%

Logistic regression analysis of full dataset (*N* = 113). Direct logistic regression was conducted to determine which personality and cognitive variables (cluster A total score, avoidant total score, cluster B total score, obsessive compulsive total score, BACS Symbol Coding, WMS Spatial Span, BACS Tower of London, and PCET total errors) were predictors of relative type (schizophrenia relative or bipolar relative). The control group was removed for this analysis to create a dichotomous variable for relative type. Therefore, the sample size was decreased to 113 which included 59 SCH-RELs and 54 BP-RELs. Missing data existed for all predictor variables. Cases with missing data (n = 21) were removed using listwise deletion in SPSS 20.0. Data from 92 relatives remained available for the logistic regression analysis: 46 SCH-RELs and 46 BP-RELs. Outliers were identified for some of the predictor variables. Tabachnick and Fidell (2001) advise that the presence of extreme values (both univariate and multivariate) can contribute to a poor fitting model in logistic regression analysis. To address this potential limitation, separate analyses were conducted, first using raw data, and second using variables that had been altered to reduce the impact of the outliers. Results are first reported without any changes to the predictor variables. Following presentation of the initial logistic regression results, both the adjustments made to the variables and the differences that were observed when the extreme values were addressed will be discussed.

According to Tabachnick and Fidell (2001), logistic regression can be sensitive to high correlations among predictor variables, resulting in multicollinearity. Therefore, a correlation matrix (see Table 15) was first assessed to identify any high correlations among the eight predictor variables. All bivariate correlations were below .70, which was the cut off value recommended by Tabachnick and Fidell for evaluating variable redundancy.

Table 15

Intercorrelations for Relative Type (Two Groups) and Predictor Variables for Full Dataset

Measure	1	2	3	4	5	6	7	8	9
1. Relative Type[a]	--								
2. Cluster A Total Score[b]	.26*	--							
3. Avoidant Total Score[b]	.14	.45***	--						
4. Cluster B Total Score[b]	.09	.65***	.31**	--					
5. OBCM Total Score[b]	-.15	.26*	.23*	.38***	--				
6. BACS Symbol Coding[c]	-.09	-.10	-.03	-.03	-.06	--			
7. WMS Spatial Span[c]	-.35**	-.32**	-.01	-.08	.06	.43***	--		
8. BACS Tower London[c]	-.19	-.31*	-.04	-.10	-.01	.47***	.51***	--	
9. PCET Total Errors[d]	.19	.08	.04	.08	-.01	-.48***	-.29	-.32**	--

Note. Sample (n = 92) comprised of only two groups[a] for relative type. OBCM = Obsessive-Compulsive; BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004; WMS = Wechsler Memory Scale (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Relative Type coded as 0 = Bipolar I relative, 1 = Schizophrenia relative. [b]Higher scores are indicative of more extreme responding for personality variable. [c]Lower scores are indicative of worse performance on the cognitive measure. [d]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

*p < .05. **p < .01. ***p < .001.

The highest bivariate correlation (Pearson's $r = .65$, $p < .001$) was between the cluster A total score and cluster B total score variables. A preliminary multiple regression was also conducted prior to the logistic regression in order to further evaluate multicollinearity among the eight predictors as recommended by Mertler and Vannatta (2002). Since tolerance statistics for all eight predictors were above 0.1, multicollinearity did not appear to pose a problem for interpretation. The logistic regression was conducted using the enter method in SPSS 20.0, which enters all predictors into the model simultaneously.

A test of the full model with all eight predictors against a constant-only model was statistically significant, $\chi^2(8, N = 92) = 21.02$, $p = .007$, indicating that the predictors, as a set, reliably distinguished between schizophrenia and bipolar relatives. However, regression results assessing overall model fit were fairly large (*-2 Log Likelihood* = 106.52) suggesting that the goodness-of-fit for the model may be questionable. Estimation of the variance that can be predicted from the combination of eight predictors can be evaluated using Nagelkerke's R square = .27 (Leech et al., 2005). This value suggests that roughly 27% of the variation in relative type could be explained by the logistic model. Overall prediction success for the model was 70%, with 67% of the schizophrenia relatives and 72% of the bipolar I relatives correctly predicted. These findings were an improvement over what would be predicted by chance alone (a 50% success rate for equal groups of 46). In other words, a researcher would be correct 50% of the time had they only guessed that all 92 relatives belonged to the SCH-REL group without using prior knowledge of the predictors. This first set of findings from the logistic regression analysis supports Hypothesis 3. Relative type (schizophrenia relative or bipolar I relative) can be reliably predicted from a model combining measures of personality traits and cognitive functioning.

Table 16 presents regression coefficients, standard errors, Wald Statistics, and odds ratios for each of the eight predictors. According to Tabachnick and Fidell (2001), the Wald statistic is quite conservative. Therefore, a more liberal significance level ($p < 0.10$) was applied when interpreting these results. The Wald criterion demonstrated that both WMS Spatial Span ($p = .022$) and obsessive compulsive total score ($p = .081$) made significant contributions to the prediction of relative type. The odds ratio indicates that membership in the schizophrenia relative group is 19% less likely with a one unit increase in WMS Spatial Span score. The odds ratio indicates that membership in the schizophrenia relative group is 13% less likely with a one unit increase in obsessive compulsive total score.

The second set of findings from the logistic regression analysis (presented in Table 16) partially supports Hypothesis 3. Obsessive-compulsive traits were the only personality measure to contribute significantly in distinguishing schizophrenia relatives from bipolar relatives. Consistent with Hypothesis 3, obsessive compulsive personality traits that were more pronounced more likely predicted membership in the bipolar relative group. Inconsistent with hypothesized relationships, higher levels of cluster A and avoidant personality traits were not found to significantly contribute to predicting membership into the schizophrenia relative group. Also, cluster B personality traits were not found to significantly contribute to predicting membership into the bipolar relative group. WMS Spatial Span Total score (a measure of working memory) was the only cognitive measure to contribute significantly in distinguishing schizophrenia relatives from bipolar relatives. Consistent with Hypothesis 3, higher scores on the WMS Spatial span task (suggestive of less pronounced cognitive deficits) more likely predicted membership in the bipolar relative group. Inconsistent with hypothesized relationships, worse performances on the remaining

cognitive variables (including measures of attention and executive functioning) did not significantly contribute to distinguishing schizophrenia relatives from bipolar relatives.

Table 16

Summary of Logistic Regression Analysis Predicting Relative Type for Full Dataset

Predictor Variable	*B*	*SE*	Wald statistic (*df* =1)	*p*	Odds Ratio
Cluster A Total Score[a]	.07	.05	1.65	.199	1.07
Avoidant Total Score[a]	.06	.08	0.68	.411	1.07
Cluster B Total Score[a]	-.004	.04	0.01	.914	1.00
Obsessive Compulsive Total Score[a]	-.14	.08	3.05	.081	0.87
BACS Symbol Coding[b]	.39	.35	1.28	.259	1.48
WMS Spatial Span[b]	-.21	.09	5.28	.022	0.81
BACS Tower of London[b]	.01	.26	0.001	.982	1.01
PCET Total Errors[c]	.03	.02	2.11	.146	1.02

Note. *N* = 92. Relative Type coded as 0 = BP-REL, 1 = SCH-REL. BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004); WMS = Wechsler Memory Scale (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Higher scores are indicative of more extreme responding for personality variable. [b]Lower scores are indicative of worse performance on the cognitive measure. [c]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

As previously stated, the logistic regression analysis was also conducted following adjustment of some of the predictor variables in order to determine to what extent any outliers influenced the results. Outliers were evaluated following listwise deletion of 21 participants in SPSS 20.0 yielding a sample of 92. Identification of univariate outliers was accomplished through assessment of stem-and-leaf plots and *z*-scores. Values for *z*-scores on predictor variables that exceeded an absolute value of three were considered univariate outliers based upon recommendation by Mertler and Vannatta (2002) for sample sizes of roughly 100. Univariate outliers were identified for the following variables: all four personality variables (cluster A total score, avoidant total score, cluster B total score, and obsessive compulsive total score) and one cognitive variable (BACS Tower of London). To conserve sample size, rather than delete participants, predictor variables that might be influenced by univariate outliers were adjusted to reduce potential impact. Tabachnick and Fidell (2001) recommended lowering the outlying values to a value one higher than the next closest to the outliers. One univariate outlier was identified on each predictor variable of concern, with the exception of the avoidant total score where there were three. One multivariate outlier had been identified prior to these transformations (using a Mahalanobis distance critical value of 26.13 for eight predictors), but it disappeared once the univariate outliers were reduced.

The logistic regression was conducted a second time with the eight predictors, and where applicable, included the adjusted predictor variables as described above. Results were similar. The test of the full model against the constant-only model remained statistically significant, $\chi^2(8, N = 92) = 20.56$, $p = .008$, indicating that the predictors, as a set, reliably distinguished between schizophrenia and bipolar relatives. Overall prediction success for the

model was very similar at 70%. The classification rates for the two groups improved slightly for the schizophrenia relative group (to 74%), but decreased for the bipolar group (to 67%). The same predictor variables (WMS Spatial Span and obsessive compulsive total score) again emerged as significant contributors to the eight-predictor model. Interpretation of the odds ratios for these predictors produced the same results for the outlier adjusted model as compared to the untransformed dataset.

Logistic regression analysis of adjusted dataset (*N* = 95). Direct logistic regression was conducted to determine which personality and cognitive variables (cluster A total score, avoidant total score, cluster B total score, obsessive compulsive total score, BACS Symbol Coding, WMS Spatial Span, BACS Tower of London, and PCET total errors) were predictors of relative type (schizophrenia relative or bipolar relative). The control group was removed for this analysis to create a dichotomous variable for relative type. Therefore, the sample size was decreased to 95 which included 46 schizophrenia relatives and 49 bipolar I relatives. Missing data existed for all predictor variables. Cases with missing data (n = 16) were removed using listwise deletion in SPSS 20.0. Data from 79 relatives remained available for the logistic regression analysis: 37 SCH-RELs and 42 BP-RELs.

Outliers were identified for some of the predictor variables. Tabachnick and Fidell (2001) advise that the presence of extreme values (both univariate and multivariate) can contribute to a poor fitting model in logistic regression analysis. To address this potential limitation, separate analyses were conducted, first using raw data, and second using variables that had been altered to reduce the impact of the outliers. Results are first reported without any changes to the predictor variables. Following presentation of the initial logistic

regression results, both the adjustments made to the variables and the differences that were observed when the extreme values were addressed will be discussed.

According to Tabachnick and Fidell (2001), logistic regression can be sensitive to high correlations among predictor variables, resulting in multicollinearity. Therefore, a correlation matrix (see Table 17) was first assessed to identify any high correlations among the eight predictor variables. All bivariate correlations were below .70, which was the cut off value recommended by Tabachnick and Fidell for evaluating variable redundancy. The highest bivariate correlation (Pearson's $r = .69$, $p < .001$) was between the cluster A total score and cluster B total score variables. A preliminary multiple regression was also conducted prior to the logistic regression in order to further evaluate multicollinearity among the eight predictors as recommended by Mertler and Vannatta (2002). Since tolerance statistics for all eight predictors were above 0.1, multicollinearity did not appear to pose a problem for interpretation. The logistic regression was conducted using the enter method in SPSS 20.0, which enters all predictors into the model simultaneously.

A test of the full model with all eight predictors against a constant-only model was statistically significant, $\chi^2(8, N = 79) = 19.22$, $p = .014$, indicating that the predictors, as a set, reliably distinguished between schizophrenia and bipolar relatives. However, regression results assessing overall model fit were fairly large (*-2 Log Likelihood* = 89.98) suggesting that the goodness-of-fit for the model may be questionable. Estimation of the variance that can be predicted from the combination of eight predictors can be evaluated using Nagelkerke's R square = .29 (Leech et al., 2005). This value suggests that roughly 29% of the variation in relative type could be explained by the logistic model.

Table 17

Intercorrelations for Relative Type (2 Groups) and Predictor Variables for Adjusted Dataset

Measure	1	2	3	4	5	6	7	8	9
1. Relative Type[a]	--								
2. Cluster A Total Score[b]	.24*	--							
3. Avoidant Total Score[b]	.16	.43***	--						
4. Cluster B Total Score[b]	.04	.69***	.34**	--					
5. OBCM Total Score[b]	-.15	.26*	.19	.42***	--				
6. BACS Symbol Coding[c]	-.15	-.14	-.08	-.09	-.10	--			
7. WMS Spatial Span[c]	-.38**	-.32**	-.07	-.06	.04	.47***	--		
8. BACS Tower London[c]	-.23*	-.31**	-.07	.12	-.05	.49***	.52***	--	
9. PCET Total Errors[d]	.19	.08	.04	.17	-.02	-.56***	-.31**	-.32**	--

Note. Sample (n = 79) comprised of only two groups[a] for relative type. OBCM = Obsessive-Compulsive; BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004; WMS = Wechsler Memory Scale (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Relative Type coded as 0 = Bipolar I relative, 1 = Schizophrenia relative. [b]Higher scores are indicative of more extreme responding for personality variable. [c]Lower scores are indicative of worse performance on the cognitive measure. [d]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

*p < .05. **p < .01. ***p < .001.

Overall prediction success for the model was 68%, with 62% of the schizophrenia relatives and 74% of the bipolar relatives correctly predicted. These findings were an improvement over what would be predicted by chance alone (a 53% success rate based upon group sizes). In other words, a researcher would be correct 53% of the time had they only guessed that all 79 relatives belonged to the schizophrenia relative group without using prior knowledge of the predictors. This first set of findings from the logistic regression analysis supports Hypothesis 3. Relative type (schizophrenia relative or bipolar relative) can be reliably predicted from a model combining measures of personality traits and cognitive functioning.

Table 18 presents regression coefficients, standard errors, Wald Statistics, and odds ratios for each of the eight predictors. According to Tabachnick and Fidell (2001), the Wald statistic is quite conservative. Therefore, a more liberal significance level ($p < 0.10$) was applied when interpreting these results. The Wald criterion demonstrated that only WMS Spatial Span ($p = .034$) made a significant contribution to the prediction of relative type. The odds ratio indicated that membership in the schizophrenia relative group is 19% less likely with a one unit increase in WMS Spatial Span score. No other variables were found to contribute significantly to the overall prediction.

The second set of findings from the logistic regression analysis (presented in Table 18) partially supports Hypothesis 3. WMS Spatial Span Total score (a measure of working memory) was the only measure to contribute significantly in distinguishing schizophrenia relatives from bipolar relatives. Consistent with Hypothesis 3, higher scores on the WMS Spatial span task (suggestive of less pronounced cognitive deficits) more likely predicted membership in the bipolar I relative group. Inconsistent with hypothesized relationships,

worse performances on the remaining cognitive variables (including measures of attention and executive functioning) did not significantly contribute to distinguishing schizophrenia relatives from bipolar relatives, nor did higher levels of the four personality measures.

As was the case for the logistic regression analysis with the full dataset, a second logistic regression to address outliers was conducted for the dataset containing only one representative per family group. The same rationale and procedures for outlier identification and adjustment were followed. The reader is referred to the logistic regression for the full dataset for that description. The only difference was that six rather than five predictor variables needed to be adjusted in order to reduce the potential impact of extreme values on the results. For this analysis, univariate outliers were identified for all four personality variables (cluster A total score, avoidant total score, cluster B total score, and obsessive compulsive total score) and two cognitive variables (BACS Symbol Coding and BACS Tower of London). The number of univariate outliers per predictor variable varied from zero to three. One multivariate outlier had been identified prior to these transformations (using a Mahalanobis distance critical value of 26.13 for eight predictors), but it disappeared once the univariate outliers were reduced.

The logistic regression was then conducted a second time with the eight predictors, and where applicable, included the adjusted predictor variables as described above. Results were similar to the first logistic regression with the sample of 79 relatives. The test of the full model against the constant-only model remained statistically significant, $\chi^2(8, N = 79) = 19.19$, $p = .014$, indicating that the predictors, as a set, reliably distinguished between schizophrenia and bipolar relatives.

Table 18

Summary of Logistic Regression Analysis Predicting Relative Type for Adjusted Dataset

Predictor Variable	*B*	*SE*	Wald statistic (*df* =1)	*p*	Odds Ratio
Cluster A Total Score[a]	.07	.06	1.38	.240	1.07
Avoidant Total Score[a]	.10	.09	1.10	.295	1.10
Cluster B Total Score[a]	-.02	.04	0.28	.595	0.98
Obsessive Compulsive Total Score[a]	-.14	.09	2.42	.120	0.87
BACS Symbol Coding[b]	.29	.42	0.48	.490	1.33
WMS Spatial Span[b]	-.22	.10	4.48	.034	0.81
BACS Tower of London[b]	.09	.30	0.09	.771	0.92
PCET Total Errors[c]	.02	.02	1.20	.274	1.02

Note. *N* = 79. Relative Type coded as 0 = Bipolar I relatives, 1 = Schizophrenia relatives. BACS = Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004); WMS = Wechsler Memory Scale (Wechsler, 1997b); PCET = Penn Conditional Exclusion Test (Kurtz et al., 2005).

[a]Higher scores are indicative of more extreme responding for personality variable. [b]Lower scores are indicative of worse performance on the cognitive measure. [c]Higher scores are indicative of worse performance (specifically, more errors) on the cognitive measure.

Overall prediction success for the model following outlier adjustment was reduced by one percentage point to 67%. The classification rate for the bipolar relative group remained the same at 74%, while the rate for the schizophrenia relative group decreased by two percentage points to 60%. The same predictor variable, WMS Spatial Span, again emerged as the only significant contributor to the eight-predictor model. Interpretation of the odds ratio for this predictor showed was also similar. The odds ratio indicated that membership in the schizophrenia relative group is 21% less likely with a one unit increase in WMS Spatial Span score (compared to 19% in the analysis that did not adjust outliers).

Exploratory Post Hoc Comparisons

Given that the personality variable of cluster B traits did not significantly contribute to the prediction model in distinguishing bipolar I relatives from the other two groups (as was hypothesized), a post hoc analysis of the personality scales comprising the cluster B total score was undertaken. This was only completed for the full dataset. Also, this analysis seemed particularly important to conduct because the cluster B mean score was surprisingly higher in schizophrenia relatives as compared to bipolar I relatives (albeit, non significantly). These findings will be interpreted as preliminary because they were not planned nor did the scales adhere well to assumptions of normality and homogeneity of variance-covariance (i.e. Box's M was significant). However, the post hoc analyses were conducted in order to investigate in a preliminary way what groupings of personality traits may have been contributing to the variation among groups.

One-way MANOVA was conducted to determine relative type (schizophrenia vs. bipolar I disorder vs. healthy control) differences in antisocial total score, borderline total

score, histrionic total score, and narcissistic total score from the SIDP-IV (Pfohl et al., 1995). Significant group differences were found on the multivariate level, Pillai's Trace = 0.46, $F(8, 322) = 2.74$, $p = .006$, partial $eta^2 = .06$. On follow-up ANOVA for individual dependent variables, relative type group differences were significant for borderline total score and histrionic total score. Significant group differences were not found for the antisocial and narcissistic total scores. Schizophrenia relatives had significantly higher scores on borderline total score compared to the healthy control group. Bipolar relatives showed significantly higher scores on histrionic total score compared to the healthy control group. ANOVA and Bonferroni post hoc analysis results are provided in Table 19.

Table 19

Post Hoc Analysis of Cluster B Total Score by Relative Group Displaying Follow-up ANOVAs to MANOVA Based on Full Dataset

	Schizophrenia Relatives (n = 53)		Bipolar Relatives (n = 50)		Healthy Controls (n = 63)				
Cluster B Scale	*M*	*SD*	*M*	*SD*	*M*	*SD*	F^a	*p*	eta^2
Antisocial TS	0.94	1.78	0.68	1.58	0.56	1.50	0.84	.431	.01
Borderline TS	3.09_a	3.70	$2.08_{a,b}$	3.14	0.92_b	1.51	8.36	.000	.09
Histrionic TS	$2.26_{a,b}$	3.00	2.42a	2.77	1.17_b	1.69	4.28	.015	.05
Narcissistic TS	2.96	3.60	2.58	3.45	1.95	2.72	1.44	.239	.02

Note. Means sharing a common subscript in each row do not differ significantly at $p < .05$ according to Bonferroni correction procedure for multiple comparisons. TS = Total Score.
[a]$df = 2, 163$

Exploratory post-host analysis was also conducted to determine the relationship between the overall logistic regression analysis findings and some specific demographic variables. Determining the extent to which demographic factors might contribute to the prediction model for the two relative groups was not a planned component of the present

study. However, in light of observed significant differences among the relative groups with regard to the demographic variables of age, education level, and race (specifically Caucasian and African American), logistic regression analyses were also conducted including these variables as co-variates in the prediction model. The reader is referred to Table 1 for the descriptive demographic characteristics and to the first section of the Results chapter for a review of group comparisons of these variables.

A preliminary correlation matrix was created between the eight original predictor variables (four personality and four cognitive) used in the logistic regression analyses, and the additional four demographic variables used a co-variates. The demographic variable of age was significantly correlated with BACS Symbol Coding (r = -.353, p = .001) and PCET total errors (r = .270, p = .009). The demographic variable of education level (highest grade achieved in years) was significantly correlated with WMS Spatial Span (r = .231, p = .027) and BACS Tower of London (r = .286, p = .006). The demographic variable of Caucasian race (present vs. absent) was significantly correlated with cluster A total score (r =-.375, p < .001), BACS Symbol Coding (r = .274, p =. 008), WMS Spatial Span (r = .497, p < .001), and BACS Tower of London (r = .509, p < .001). The demographic variable of African American race (present vs. absent) was significantly correlated with cluster A total score (r =.365, p < .001), BACS Symbol Coding (r = -.274, p =. 008), WMS Spatial Span (r = -.529, p < .001), and BACS Tower of London (r = -.508, p < .001).

Given that there were some significant correlations among demographic and prediction model variables, the logistic regression was conducted to explore how the overall findings might be impacted using 12 predictor variables (four personality, four cognitive, and four demographic). The full dataset (N = 113) was used which included 59 SCH-RELs and

54 BP-RELs. A test of the full model against a constant-only model was statistically significant, $\chi^2(12, N = 92) = 25.77$, $p = .012$, indicating that the predictors, as a set, reliably distinguished between schizophrenia and bipolar relatives. Nagelkerke's R square value suggested that approximately 33% of the variance in relative type could be explained by the model. A more liberal significance level ($p < 0.10$) was used for interpretation of the contribution role of each of the 12 predictor variables given that the Wald criterion is quite conservative (Tabachnick & Fidell, 2001). WMS Spatial Span was a significant predictor at $p = .071$. Obsessive-compulsive total score approached significance at $p = .147$. PCET total errors also approached significance at $p = .110$. No other variables were shown to make significant contributions to the prediction model. Findings from this post-hoc analysis suggest that although demographic variables differ among the two groups and are correlated to some of the main predictor variables, WMS Spatial Span, in particular, is still a significant predictior of relative type when controlling for these variables.

CHAPTER IV

Discussion

The purpose of this study was to compare the personality traits and cognitive functioning among a group of relatives of persons diagnosed with schizophrenia and a group of relatives of persons diagnosed with bipolar I disorder. Establishing that these relative groups exhibited personality functioning that looked different from individuals in the population without a family history of either disorder (the healthy control group) was of particular interest as well.

Relatives of persons diagnosed with both schizophrenia and bipolar I disorder have been found to show "softer" signs of the major mental illnesses as can be reflected in personality traits, as well as cognitive deficits in areas such as attention, working memory, and executive functioning. Awareness of these subtler features and deficits can aid in early and more specific diagnosis, improve psychiatric and psychological treatment for both patients and family members, and allow researchers and clinicians alike to increase their understanding of the major mental illnesses. The family members of persons diagnosed with schizophrenia and bipolar I disorder have long been the focus of scientific research with regard to these two areas of investigation, yet there has been less research focused upon comparing the two groups on both personality traits and cognitive deficits within the same study, as well as compared to a healthy control group. Additionally, the present study sought to add to the current literature by using the Structured Interview for DSM-IV Personality (SIDP-IV; Pfohl et al., 1995) in a trait-dimensional, rather than primarily categorical manner. This methodology was selected in order to add to the trend in the scientific community toward conceptualizing personality disorders and personality traits, in general, in a more

dimensional as opposed to purely categorical approach (Skodol et al., 2011). The ultimate goal of the study was to determine a set of personality and cognitive variables that could best be used to predict membership into either the schizophrenia-relative or bipolar I disorder relative groups.

A Note on Methodology

Before discussing specific personality results as related to group differences, it is important to point out the methodology used in the present study. Prior research has suggested that it is difficult to evaluate personality traits by just looking at the incidence of personality disorders in a sample of the population (Jane et al., 2006). Although there was notable incidence of maladaptive traits in the current sample of schizophrenia and bipolar I relatives, very few met full diagnostic criteria for personality disorders. For the present study, the overall incidence of any personality disorder in the total sample was 15.0%. When this was broken down into the personality disorders that comprised the clusters of traits that were of interest, that rate decreased substantially. For example, the rates of the personality disorders comprising cluster A were only 1.8, 1.8, and 0.6% of the total sample for the paranoid, schizoid and schizotypal personalities respectively. The same measure, the SIDP-IV, that was used to assess the lifetime prevalence of the personality disorders, was also used to assess traits in a dimensional manner for the primary hypotheses. Looking at the frequencies of personality disorders in the current sample, one would not expect to see much data related to personality traits, but that was the benefit of the dimensional approach. Differences were able to be observed when the groups were compared on dimensional trait scores. Most of the lifetime prevalence rates for the ten personality disorders (by group) were less than 1% and many were zero. The highest was obsessive-compulsive personality

disorder at 2.4% for the bipolar I relative group, and avoidant personality disorder at 1.8% for the schizophrenia relative group. Interestingly, findings from the prevalence rates alone, even though small, seemed to support hypothesized groupings. Considering the results of the study, clearly, the dimensional manner allowed for better group comparisons. Jane and colleagues (2006), found that using the SIDP-IV in a dimensional manner, also with a nonclinical population, improved the reliability of the measure in diagnosing personality disorders. For the present study, it is important to note that different conceptualizations of personality are being discussed. Personality disorders are a set of traits that have risen to a level that is substantial enough to suggest significant pathology in that area (APA, 2000). The present study focused upon specific elevations in traits, and not diagnosed disorders, in order to compare the two relative groups and controls. Because differences in personality functioning among groups represent softer signs of mental illnesses, in other words, very subtle differences, this seemed like an appropriate approach that is in fact supported by the current findings.

Personality Dimensions of the Relative Groups and Healthy Controls (Hypothesis 1)

It was hypothesized that first-degree relatives of patients with schizophrenia would differ from a group of first-degree relatives of patients with bipolar I disorder, and a group of healthy controls with regard to personality traits as examined by the SIDP-IV. Overall this hypothesis was supported. Differences among the three groups were observed on each of the four personality variables focused upon in the present study: cluster A traits, avoidant traits, cluster B traits, and obsessive compulsive traits. The groupings of traits in these four areas will be termed “personality styles” herein, so as not to confuse things by suggesting that they

represent disorders, but to distinguish that the relative groups showed clustering of traits as was hypothesized.

Without exception, both the schizophrenia relative and bipolar I relative group showed higher mean scores on all four personality styles of interest as compared to the healthy control group, although not all group comparisons were significant. This lends support to prior research that suggests relatives exhibit more pathology in personality functioning than persons without a family history of either schizophrenia or bipolar I disorder (Maier et al., 1994, 1995; Savitz & Ramesar, 2006).

In consideration of the results, it will be helpful to bear in mind what traits the personality styles investigated in this study represent as per the DSM-IV-TR (APA, 2000). The traits included in the cluster A personalities refer to individuals who may appear "odd and eccentric." This cluster included the paranoid, schizoid and schizotypal personalities. The traits included in the cluster B personalities refer to individuals who present as "dramatic, emotional or erratic." This cluster included the antisocial, borderline, histrionic, and narcissistic personalities. Two personalities outside of these clusters were also hypothesized to distinguish schizophrenia and bipolar relatives as well (based upon review of the literature; Maier et al., 1995; Fogelson et al., 2007; Keshavan, Diwadkar, et al., 2005). Avoidant personalities, which belong to the cluster C or "anxious-fearful" grouping, are described as socially inhibited individuals who experience prominent feelings of inadequacy and hypersensitivity to negative evaluations. Obsessive compulsive personalities, which also belong to the anxious-fearful group, are described as being preoccupied with orderliness, perfection and control.

The following findings were supported as hypothesized. Compared to the healthy control group, relatives of probands diagnosed with schizophrenia appeared more odd and eccentric (cluster A traits), and showed more social inhibition and feelings of inadequacy and hypersensitivity (avoidant traits). These seem like sensible descriptions of a schizophrenia relative group given that in some ways their functioning might be conceptualized as a variation (albeit not as pronounced) of schizophrenia. Schizophrenia as a mental illness, in addition to prominent symptoms such as delusions and hallucinations (which do represent eccentricities on a grander scale), is also characterized by serious deficits in social functioning. When compared to the bipolar I relative group, the schizophrenia relative group appeared more odd and eccentric. The avoidant dimension was not significantly different in bipolar I relatives versus schizophrenia relatives as was hypothesized (rather, the mean scores on this measure were nearly as equally elevated). These findings could suggest that bipolar I relatives demonstrate functioning in the avoidant personality style that is similar to schizophrenia relatives and could be indicative of subtle psychosocial difficulties. It has been found in previous research that the relative groups, in general, show more elevations on many of the personality styles (Gilvarry et al., 2001; Reichborn-Kjennerud, 2008), but perhaps this finding is also due to the fact that the bipolar I relative group consisted of the relatives of probands who primarily had been diagnosed with *psychotic* bipolar I disorder. Previous research (Fogelson et al., 2007; Keshavan et al., 2005) has suggested that it could be the psychosis component that leads to impairments in social functioning along the lines of the avoidant traits.

Findings related to schizophrenia relatives. Personality findings from the present study as related to the schizophrenia relative group, in particular, are consistent with the

literature in a few ways. First, in comparison studies of schizophrenia relatives with healthy controls, schizophrenia relatives tend to be diagnosed with paranoid, schizoid and schizotypal personality disorders at a greater incidence (Maier, Lichtermann, Minges, & Heun, 1994). Second, a main line of inquiry in the present study was whether or not schizophrenia relatives appeared different from bipolar I relatives with regard to personality. Schizophrenia relatives only presented with personality traits that were more odd and eccentric than bipolar I relatives, so there is some partial support for this hypothesis, which is consistent with findings from studies such as the one by Maier and colleagues (1994). Third, it is well accepted that there is a greater incidence of schizotypal traits in family members of patients with schizophrenia (Kendler et al., 1996; Appels et al., 2004) compared with any other group. Although the results of the present study are not focused upon schizotypal traits, specifically per se, these are reflected in the cluster A personality measure, and therefore, these findings would be somewhat consistent with previous research. However, when looking at the rates of lifetime prevalence of diagnosed personality disorders in the current sample (15.0% overall), only one individual (0.6% of the total sample) was diagnosed with schizotypal personality disorder, and this individual belonged to the bipolar I relative group and not the schizophrenia relative group. This particular finding could raise concerns about the composition of the current sample along the lines of diagnosis. It could also suggest that even though the two groups may exhibit different personality styles, in general, there is still a degree of overlap when we consider that personality traits may best be described as presenting dimensionally. Fourth, personality findings for the schizophrenia relative group with regard to avoidant traits are consistent with previous studies such as the study by Fogelson and colleagues in 2007. Both the present study and Fogelson and

colleagues' study in 2007 found more avoidant traits when schizophrenia relatives were compared to healthy controls. Similarly, Silberschmidt and Sponheim (2008) also found avoidant trait elevations in schizophrenia relatives when compared to healthy controls. Consistent with the present study, the bipolar I disorder relatives in their study did not exhibit elevations when compared to healthy controls with regard to avoidant traits. In summary, schizophrenia relatives presented with more maladaptive personality traits as compared to healthy controls along the odd and eccentric and avoidant dimensions. They presented with more maladaptive personality traits as compared to bipolar I relatives as well, but only along the odd and eccentric dimension.

Findings related to bipolar I relatives. Compared to the healthy control group, the relatives of probands diagnosed with bipolar I disorder appeared to be more preoccupied with orderliness, perfection and control (obsessive-compulsive traits). Adding further to this finding, the incidence of a lifetime diagnosis of obsessive compulsive personality disorder was the highest in the bipolar I relative group as well. Maier and colleagues (1995) observed similar results. Not only were bipolar relatives diagnosed with obsessive compulsive personality disorder at a greater incidence than healthy controls, but they were also found to score higher on a measure of rigidity, which the authors noted was a component of obsessive compulsive personality. An interesting finding that emerged in the present study is that although the relatives of bipolar I patients showed higher mean scores on all four personality variables when compared with healthy controls, significant differences in trait elevations were only observed with regard to the preoccupation with orderliness, perfection and control. Schizophrenia relatives when compared with bipolar I relatives show higher mean scores on cluster A, avoidant, and cluster B traits, but only significantly differ on cluster A. The only

personality variable, therefore, that seems to differentiate the bipolar I relative group from the schizophrenia relative group in the present study is cluster A. Schizophrenia relatives were not able to be differentiated from bipolar I relatives with regard to obsessive-compulsive personality traits as might have been expected. These findings suggest that the differences between the relative groups' personality functioning are finite and may call for a more sensitive methodology that could better clarify these differences.

Findings related to cluster B traits. One of the most striking personality findings was revealed when comparing the three groups along the cluster B trait dimension. It was hypothesized that bipolar I relatives would exhibit more emotional-dramatic-erratic traits than any other group. Rather, the bipolar I relative group looked similar to the schizophrenia relative group in this regard (mean scores were similar) and although the mean score on the measure of cluster B traits was elevated in the bipolar I relative group as compared to the healthy control group, significant differences were not observed. No hypotheses regarding the schizophrenia relative group versus the healthy control group were put forth. However, this is where significant differences were found. When compared to healthy controls, it was the schizophrenia relative group and not the bipolar I relative group that showed more elevations suggesting emotional, dramatic and erratic personality traits.

These results contrast with previous work by Silberschmidt and Sponheim (2008) who found elevated levels of emotional dysregulation in bipolar relatives when compared to both healthy controls and schizophrenia relatives. However, their bipolar relative group consisted primarily of relatives of probands diagnosed with primarily non-psychotic bipolar disorder, whereas the bipolar relative group in the present study consisted primarily of relatives of probands diagnosed with psychotic bipolar I disorder. The results could also be

considered inconsistent with previous research that has shown a higher level of cluster B characteristics in first-episode non-schizophrenia patients compared to first-episode schizophrenia patients (Keshavan, Duggal, et al., 2005).

To follow up on cluster B trait findings in the present study, exploratory post hoc analyses were conducted. Comparison of the three groups on the four personality styles (antisocial, borderline, histrionic, and narcissistic) comprising cluster B showed that personality patterns of impulsivity and emotional and interpersonal instability (the borderline total score) distinguished the schizophrenia relatives from the healthy controls. Whereas personality patterns of excessive emotionality and attention-seeking (the histrionic total score) distinguished the bipolar I relatives from the healthy controls. No cluster B personality styles, in particular, distinguished the two relative groups.

Consideration of the individual items of the borderline scale suggested that schizophrenia relatives may show higher mean scores (as compared to the bipolar I relative group) on many items. Group differences were not investigated statistically, so specific conclusions about group differences cannot be made. However, observations about the direction of these potential differences could inform future studies. It was interesting to note that schizophrenia relatives had elevated mean scores compared to bipolar I relatives on an item assessing impulsivity in self-damaging areas and on an item assessing difficulty controlling anger and frequently experiencing intense anger. These observations, albeit exploratory, could suggest a degree of emotional distress that is common for both schizophrenia relatives and bipolar I relatives. Furthermore, it is possible that the elevations observed in the schizophrenia relative group on cluster B traits, in general, reflect not only

the emotionally erratic behavior associated with cluster B, but also the paranoid component of the borderline scale.

Findings related to cluster B trait elevations in the schizophrenia relative group may be further explained in consideration of results from the study by Laurent and colleagues in 2002. The authors compared the personality functioning (using the Eysenck Personality Questionnaire; EPQ; as cited in Laurent et al., 2002) among relatives of schizophrenia patients and relatives of affective-psychotic patients. Males in the schizophrenia relative group scored significantly higher than males in the affective-psychotic group on the psychoticism scale. The authors described individuals with high scores on this scale as "solitary, not caring for people, hostile to others, with a liking for odd and unusual things, often troublesome and possibly cruel, with no empathy, feelings of guilt or sensitivity to others" (Laurent et al., 2002, p. 242). Not only do these descriptors characterize traits found in cluster A personality styles, but they seem to also describe some traits better associated with cluster B when personality is conceptualized along the DSM system. The descriptor "with a liking for odd and unusual things" is consistent with schizotypal features. However, although the descriptor "with no empathy, feelings of guilt, or sensitivity to others" shares some similarities with paranoid personality style, it may be better related to DSM descriptions of antisocial and narcissistic personalities. Interestingly, when discussing the limitations of their study, Laurent and colleagues commented that previous research has suggested that the psychoticism scale of the EPQ is also consistent with behavior and traits that are more consistent with psychopathy as opposed to psychosis. Elevations in cluster B traits for the schizophrenia relatives in the current study, therefore, could also be reflecting characteristics of psychoticism scale that represent overlapping areas between the cluster A

and cluster B personality styles. Similarly, Keshavan, Duggal, et al. (2005) found higher levels of antisocial personality traits in a schizophrenia patient group compared to a group of patients with "nonschizophrenia" psychotic disorders.

An additional finding with regard to cluster B traits was that throughout the study, when the variables of interest were correlated with one another, the highest correlations were between the cluster A and cluster B variables (at $r = .64$). This could suggest that both variables may share a common factor that is being measured. No other personality variables were correlated as highly. What may be emerging as a common factor is a level of emotional distress that is prominent for both clusters of personality styles. One possible explanation for these findings relates to the potential presence of co-morbid Axis I disorders. Higher rates of a lifetime prevalence of depression and anxiety were observed between the schizophrenia relative and bipolar I relative groups. Schizophrenia relatives showed a rate of 12.7% of the total sample for a lifetime history of a depressive disorder compared to 9.6% of total sample for the bipolar I relatives. Schizophrenia relatives had a rate of 12.0% for a lifetime history of anxiety disorders compared to 6.6% for the bipolar I relatives. It was beyond the scope of the current study to determine whether or not the Axis I disorders were present at the time of personality assessment, and therefore, some participants with a lifetime history of depression or anxiety may have been experiencing "current" mood symptoms. Therefore, findings related to the presence of lifetime depression and anxiety may help to explain why the cluster B traits were elevated for schizophrenia relatives as compared to healthy controls. It is possible that the comorbid affective Axis I disorders present in the schizophrenia relative group could be artificially inflating their scores on cluster B personality style scales. When scoring the SIDP-IV, raters are instructed to not consider axis I symptomatology when rating

for personality traits. However, it could be difficult to consistently differentiate axis I and axis II symptomatology while rating a person's functioning. Given that assessments were typically completed in one setting (and personality traits are clinical diagnoses that are easier to make over a longer time frame), some of the axis I symptoms may have been included in these ratings. Future studies could be designed that control for a confounding variable such as lifetime or current history of comorbid affective illness.

Another explanation for the findings related to cluster B traits, is that the SIDP-IV composite scale used in the present study may represent a measure of pathology that is not unique to either the schizophrenia relative or bipolar I relative groups. The lack of support for Hypothesis 1c could be indicative of the difficulties in specific diagnosis, especially when considering that the SIDP-IV was used in a dimensional rather than categorical manner, and very subtle areas of psychological functioning are being examined at one moment in time and not in repeated sessions. Furthermore, individuals in the schizophrenia relative group, consistent with the literature (Kendler et al., 1993; Silberschmidt & Sponheim, 2009), may show pathology in general personality functioning that is at a greater magnitude than the bipolar I relative group on multiple dimensions, not just the areas that are typically found to be elevated in the literature (Appels et al., 2004; Fogelson et al., 2007; Kendler et al., 1993), in other words the cluster A and avoidant personalities.

Summary of personality findings. The overall results for this first hypothesis provide support for the following ideas. First, schizophrenia relatives when compared with healthy controls are quite different in personality functioning which includes presentations that are odd and eccentric, socially awkward, and emotionally erratic. Second, odd and eccentric traits best distinguish schizophrenia relatives from bipolar I relatives. Third,

personality functioning that is marked by perfectionism and control distinguish bipolar I relatives from healthy controls. Fourth, distinguishing schizophrenia relatives from bipolar I relatives with regard to both avoidant and emotionally erratic (cluster B) traits becomes quite muddy. That is, if one considers the personality styles assessed in the present study as existing on a dimensional scale, avoidant and cluster B personality traits fall somewhere in the middle.

However, it is important to bear in mind that the results related to the avoidant and cluster B traits could also be due to methodological issues. Of all the personality variables the avoidant total score was the least normal (it was the personality variable that showed the most skewness). For the emotional and dramatic (cluster B) traits, there is the potential that the presence of a lifetime history of axis I disorders proved to be a confounding variable. The cluster B traits, in fact, could be the area of greatest interest in distinguishing the schizophrenia and bipolar I relative groups in future studies. The similarities between the groups on these personality styles may be related to characteristics of the present sample in that it included some individuals with non-psychotic bipolar disorder and schizoaffective disorder.

Furthermore, if one considers the specific traits comprising the avoidant and emotional-dramatic-erratic personalities, they appear quite different. The avoidant personality style characterizes an individual who is socially awkward, hypersensitive to criticism, and quiet. Cluster B is characterized by dramatic and emotionally erratic traits. When considering what these two styles might have in common, one idea that emerges is psychosocial impairment in general. Perhaps psychosocial impairment is a prominent component of all the four personality styles of interest in this study. The current results may

suggest that psychosocial impairment is the main construct that dimensionally distinguishes the two relative groups with regard to personality functioning. Those with primarily odd and eccentric (cluster A) personalities may have the most difficult time in social settings. Those with primarily avoidant or cluster B traits may experience a fair amount of social impairment that at times can be severe, but is less frequent. Finally, those with primarily obsessive compulsive personalities experience social impairments at times, but that is not the most prominent aspect of their personality functioning. Therefore, when differentiating schizophrenia and bipolar I relatives with regard to personality functioning, the cluster A and obsessive-compulsive personality styles may fall at either end of the spectrum and the avoidant and cluster B personality styles may fall somewhere in the middle.

Cognitive Functioning of the Relative Groups and Healthy Controls (Hypothesis Two)

The second main pursuit of the present study was to compare the cognitive functioning profiles for each of the three groups. Cognitive functioning was assessed using a variety of tasks that tapped into three main domains of cognition: attention, working memory, and executive functioning. Attention describes the cognitive process that allows an individual to select and concentrate on information (Mirksy et al,. 1995). Working memory allows an individual to "simultaneously store and process information" (Baddeley, 1992, p. 556). Executive functioning, in general, is the cognitive process wherein an individual engages in reasoning and problem solving (Nuechterlein et al. 2004). These three areas of cognitive functioning, in particular, were selected for the present study as they are considered by some to be the most important for daily functioning (Trivedi et al, 2008), and therefore, may have clinical implications.

It was hypothesized that both the relatives of probands diagnosed with schizophrenia and the relatives of probands diagnosed with bipolar I disorder would demonstrate impaired performance when compared to a group of individuals without any family history of either disorder on cognitive tasks measuring attention, working memory, and executive functioning. It was further hypothesized that the performance of bipolar relatives on these tasks would not appear as impaired as the schizophrenia relative group. Six cognitive tasks were utilized, providing eight measures of performance. On four of the selected measures (two CPT accuracy ratings, BACS digit sequencing, and the PCET categories achieved item) significant differences among the three groups were not detected. Some deficits in cognitive functioning were observed on the other four measures, but mainly for the schizophrenia relative group. Contrary to what was hypothesized, bipolar I relatives did not exhibit many deficits.

Looking at mean scores per group for each of the eight measures that were evaluated in the present study, the hypothesized directions for performance were exhibited. In other words, the bipolar I relatives' performance fell in between the schizophrenia relative and healthy control groups with the schizophrenia relatives achieving the lowest mean scores and the healthy controls achieving the highest mean scores. However, in many instances the group "differences" were so mild that significance testing did not suggest that it could be concluded there were any real differences in the patterns of functioning. Overall, nonsignificant findings could speak to the subtle nature of the type of performances that are being studied since relatives, again, are thought to show "softer" signs of schizophrenia and bipolar I disorder. Conversely, it could be concluded that although research has suggested that bipolar relatives demonstrate deficits in cognitive functioning (Bora et al., 2009; Glahn

et al., 2010) the present study may not have assessed the specific areas of functioning where impairments are most often observed.

Some patterns of group differences in cognitive functioning did emerge. When compared to healthy controls, the schizophrenia relatives showed significantly lower performance on four of the eight cognitive measures and at least one of these potential deficits occurred for each of the three domains of cognitive functioning. This finding was consistent with the literature. It has been fairly well established that schizophrenia relatives do exhibit a variety of cognitive deficits in comparison to persons from the general population (Keefe et al., 2004; Faraone et al., 2000). When compared to healthy controls, relatives of bipolar I disorder probands showed significantly lower performance only on a task that measured attention. This finding was partially consistent with the literature. On the one hand, deficits in attention have been found among bipolar relatives when compared to healthy controls (as reviewed in the meta-analysis by Bora and colleagues in 2009), so this finding supports past research. On the other hand, deficits in cognitive functioning when comparing bipolar relatives to healthy controls have also been found in working memory (Glahn et al., 2010; Trivedi et al., 2008) and executive functioning (Bora et al., 2009). Therefore, the findings from the present study regarding bipolar relatives do not tend to support the past research that has observed deficits in working memory and executive functioning. However, the results of the present study perhaps could be considered more consistent with past research than it might first appear. An overarching theme that emerged during the literature review was that cognitive studies comparing bipolar relatives to healthy controls show mixed results (e.g. Bora et al., 2009). Oftentimes these heterogeneous findings are due to the variety of methodologies that are employed, be it sample characteristics or

assessment measures used. For example, some studies include only relatives of bipolar I patients, whereas other studies include bipolar I, II, and unipolar depression in one group designated relatives "at risk for affective disorders" (Laurent et al., 2002; Meyer & Blechert, 2005).

Findings related to attention. Both schizophrenia relatives and bipolar I relatives exhibited deficits in attention when compared to healthy controls. The deficits were observed on the symbol coding subtest of the Brief Assessment of Cognition in Schizophrenia (BACS; Keefe et al., 2004). During this timed subtest, study participants copied numbers that corresponded to symbols in a presented key. Both relative groups correctly copied fewer symbol-number pairs than healthy controls. Based on norm referenced z-scores for this measure, the bipolar relatives' performance (M = 0.02, SD = 0.95) was better than that of the schizophrenia relatives (M = -0.02, SD = 0.99), but not significantly so. Keefe and colleagues (2004) describe the BACS symbol coding subtest as not only a measure of attention, but one that also involves processing speed. Glahn and colleagues (2010) observed impairments on a symbol coding task when comparing "unaffected" bipolar relatives with a healthy control group. Notably, they focused upon the idea that the symbol coding task was more of a measure of processing speed rather than attention, and therefore concluded that deficits in processing speed may represent vulnerability markers for bipolar disorder. Both relative groups, as well as patients with these illnesses, have shown deficits in processing speed (Daban et al. 2012; McIntosh, Harrison, Forrester, Lawrie, & Johnstone, 2005).

With regard to the findings of the present study, it seems important to qualify the results in consideration of findings such as those by Glahn and colleagues (2010). Both

schizophrenia relatives and bipolar I relatives demonstrated deficits on a symbol coding task, which is a measure of both attention *and processing speed*. Given that findings from this study suggest that deficits in processing speed may have been a component that helped to differentiate the relative groups from healthy controls, it is also important to consider the possibility that medication use by participants may have contributed to lower scores on the BACS symbol coding subtest. Research has shown that deficits in processing speed for relative groups can still be observed when controlling for medication use (Glahn et al., 2010; Daban et al., 2012). Other studies have suggested it may play a role in psychomotor slowing to some extent (Bora et al., 2009). Given that the sample in the present study consisted of some individuals with histories of mental illnesses that may require medication, possible medication effects cannot be ruled out. Medication use was evaluated during the parent BSNIP study, but it was not a focus of the present study. Therefore, conclusions regarding the role of processing speed are exploratory and would need to be further addressed in future studies.

Neither relative group showed impairments when compared to the healthy controls on the Dot Pattern Expectancy Continuous Performance Test (DPX-CPT). These findings were surprising in that the CPT is widely used in research focused upon cognitive deficits in schizophrenia (Reichenberg, 2010). As a measure, versions of the CPT have been shown to elucidate impairments in sustained attention among schizophrenia relatives when compared to healthy controls (e.g. Avila et al., 2006). In fact, the CPT was recommended by the MATRICS group as a purer measure of attention than some other cognitive tasks, as it reduces the overlap in attention and working memory by focusing more upon this sustained attention component (Nuechterlein et al., 2004). Review of the CPT literature related to both

patient and relative groups for schizophrenia and bipolar disorder could shed some light on the lack of significant findings for the CPT in the present study. There are not only many versions of the task used throughout the literature, but a variety of indices that are assessed (Fleck, Sax, & Strakowski, 2001). Accuracy for target responses (AX trials), as well as accuracy for non-target responses (BX trials) were the indices focused upon in the present study, but these may not be the indices that could most readily differentiate the two relative groups from one another and healthy controls.

In their meta-analysis, Bora and colleagues (2009) found that both bipolar patients and their relatives showed deficits in target detection on the CPT using an index that was similar to the CPT AX accuracy index. In contrast, other studies have found that schizophrenia relatives show impairments in sustained attention on multiple indices of the CPT, but especially in false alarming and target sensitivity (Sitskoorn et al., 2004). These aspects are related to accuracy in responding to non-targets, which was measured by the CPT BX accuracy index in the present study. These two indices of the CPT failed to differentiate the bipolar and schizophrenia relatives as hypothesized, so the findings of Bora and colleagues and Sitskoorn and colleagues are not supported. However, both sets of authors reflected on the fact that the CPT indices used, as well as the versions of the CPT measures, are often varied. Fleck et al. (2001) also supported this point and suggested that reaction time indices could be used with CPT measures of sustained attention as a way to enhance the ability to discriminate among groups, again commenting on the role of processing speed in studies of attention.

Findings related to working memory. Schizophrenia relatives exhibited deficits in working memory when compared to both the bipolar I relative and healthy control groups.

Performances by the bipolar I relatives as compared to the healthy controls did not differ. The deficits in working memory were demonstrated by the schizophrenia relative group on the spatial span subtest of the Wechsler Memory Scale, Third Edition (WMS-III; Wechsler, 1997b). During this task, study participants tapped blocks in response to patterns of blocks that were presented by the examiner. Because the subtest included both a forward and backward condition, this task required both maintenance and manipulation of visual spatial information. Schizophrenia relatives, as a group, were not as successful at duplicating the patterns when compared to both bipolar I relatives and healthy controls. These results are similar to other findings in the literature that suggest spatial working memory is impaired in schizophrenia groups. Sitskoorn and colleagues (2004) reported that in 18 of the 37 studies included in their meta-analyses assessing cognitive deficits in schizophrenia probands and relatives, WAIS or WMS versions of the digit and spatial span subtests were utilized to assess working memory. This underscores the role of working memory deficits in the cognitive profiles of schizophrenia patients and relatives.

The WMS-III spatial span subtest emerged as the only task in the present study where schizophrenia relatives were as impaired when compared to bipolar I relatives as they were compared to healthy controls, suggesting this may be the area of greatest impairment for the schizophrenia relative group, at least for the current sample. Significant impairment on spatial working memory, in particular, for schizophrenia relatives has been demonstrated throughout the literature (Glahn et al., 2010; Horan et al., 2008). The findings from the present study corroborate these findings. Glahn and colleagues (2010) have also suggested that it is higher order working memory processes such as those utilized in the spatial span tasks, rather than the digit span task, which better distinguish schizophrenia relatives from

healthy controls. Interestingly, the present study also included the digit sequencing subtest from the BACS. Significant differences failed to be found on this measure among any groups. This finding may lend further support to the notion that spatial working memory is of most interest when considering working memory impairments in schizophrenia relatives.

Although it was hypothesized that bipolar I relatives would also show impaired performance on measures of working memory, the lack of significant findings could probably be considered consistent with the literature. Findings regarding the cognitive functioning of the bipolar I relatives tend to be marked by heterogeneity. In a meta-analysis to investigate neurocognitive endophenotypes among relatives of bipolar patients, Balanzá -Martinez and colleagues (2008) evaluated six studies assessing verbal working memory and six studies assessing spatial working memory. Only one study found the bipolar relative group to be impaired in either of these areas of functioning.

Findings related to executive functioning. Schizophrenia relatives demonstrated deficits in executive functioning when compared to the healthy control group on two tasks. Performances by the bipolar I relatives on both of these tasks fell between the schizophrenia relative and healthy control groups, yet failed to reach statistical significance when compared to either group for both tasks. Such a finding does not support previous research that has shown deficits on the Wisconsin Card Sorting Test, in particular, for bipolar relatives when compared to healthy controls (Trivedi et al., 2008).

On the Penn Conditional Exclusion Test (PCET; Kurtz et al., 2004), a computerized version of the Wisconsin Card Sorting Test, schizophrenia relatives exhibited more perseverative errors when compared to healthy controls. This is indicative of difficulties in set shifting (Trivedi et al., 2008). On the BACS Tower of London, a complex task requiring

the participants to manipulate pictures in their mind and determine the most efficient way to construct a tower of pegs in a specified order, schizophrenia relatives were less accurate than the healthy control group. Given these results, it can be concluded that schizophrenia relatives demonstrate difficulties in reasoning and problem solving, which require not only intact lower level processes, but also abilities to engage in complex decision making and planning (Nuechterlein et al., 2004). Findings from the present study add to the body of research that suggests schizophrenia relatives, to a lesser degree than patients with the illness, demonstrate impairments in executive functioning (Reichenberg, 2010).

Summary of cognitive findings. The overall results for this second hypothesis provide support for the following ideas. First, as hypothesized, schizophrenia relatives showed deficits when compared to healthy controls in all three of the domains focused upon in the present study. Second, the hypothesis that bipolar I relatives would demonstrate impairments in cognitive functioning to a lesser extent than the schizophrenia relatives was not supported. Third, both schizophrenia relatives and bipolar I relatives exhibited impaired performance when compared to the healthy control group on a symbol coding task that measured attention, but this measure notably included a processing speed component as well. Fourth, schizophrenia relatives were impaired when compared to both the bipolar relative and healthy control groups, who themselves performed at virtually the same level, on a measure of spatial working memory. This pattern of working memory findings suggests that spatial working memory deficits are the most pronounced for schizophrenia relatives and most readily distinguish schizophrenia relatives from bipolar I relatives. Finally, schizophrenia relatives are impaired in their ability to reason and problem solve when compared to healthy controls. Bipolar I relatives do not exhibit similar impairments.

Impairments in cognitive functioning for patients with bipolar disorder have generally been found to show similar patterns albeit to a lesser extent as compared to schizophrenia relatives (Murray et al., 2004; Daban et al., 2006). Extending this line of reasoning to bipolar relatives as compared to schizophrenia relatives has also been of interest. Unfortunately, the patterns of cognitive functioning for both the patient and relative bipolar groups remain much less clear when compared to the schizophrenia literature. The current study failed to show convincing impairments for the bipolar I relative group. Continued research may prove that impairments do not in fact exist. However, the difficulty in identifying specific impairments seems hampered by both heterogeneity in the bipolar illness itself, as well as heterogeneity in studies examining cognitive deficits in this group.

Prediction of Group Membership (Hypothesis 3)

It was hypothesized that whether a relative belonged to a family of a proband diagnosed with schizophrenia or a family of a proband diagnosed with bipolar I disorder could be predicted from the combined patterns of personality traits and cognitive functioning demonstrated by the relatives themselves. Results from the second hypothesis influenced the analyses for prediction of group membership in this final hypothesis. The cognitive measures that failed to detect differences among the three groups were not included in the prediction analyses as was originally planned. Therefore, group membership was predicted based upon a set of four personality and four cognitive variables. In general, findings from the analyses for the third hypothesis provide support for the main goal of this study. It does appear that whether or not a relative belongs to a schizophrenia versus bipolar I disorder family can in fact be predicted based upon knowledge of that individual's personality and cognitive functioning. However, the third hypothesis is not as well supported when it comes

to consideration of the specific components that were hypothesized to play a role in the prediction of group membership. Only two of the four styles of personality traits that were of primary focus in the present study seemed to play a role in the prediction. Similarly, cognitive functioning was an important component in the prediction, but levels of impairment when comparing schizophrenia and bipolar I relatives did not play as much of a role in the prediction as had been expected.

Prediction of group membership was investigated both through discriminant function and logistic regression analyses. Inclusion of the healthy control group in the discriminant function analysis complicated interpretation of those results. However, using both types of analyses provided the opportunity to focus first upon how the control group can best be differentiated from the relative groups via discriminant function analyses that included all three groups. Logistic regression was then used to further determine what variables best distinguished the two relatives groups from one another. Discriminant function analysis results were more informative, yet findings from the logistic regression analyses can be considered more conservative as there was less concern with regard to violations of statistical assumptions. These were previously described in detail throughout the Results section.

Prediction findings from the discriminant function analysis. Some variation in the composition of the two functions per each discriminant analyses (full dataset vs. adjusted dataset) was observed. Interestingly, what stands out from both versions of the analyses is that group membership is being predicted primarily along the same three dimensions: odd and eccentric personality traits (cluster A), obsessive compulsive traits, and performance on a cognitive task measuring attention and speed of processing. Performance on a spatial working memory task also played a role in the predictions for both analyses, but not as

strongly. Neither the avoidant nor emotional-dramatic-erratic (cluster B) traits contributed strongly to the two functions. This held true for analyses of both the full and adjusted data sets. Prediction results with regard to executive functioning were mixed between the two discriminant function analyses, but what was clear is that in both analyses no measure of executive functioning contributed very strongly to the model. The results are probably to be expected based upon the pattern of group differences observed in Hypothesis 2. Deficits in performance on these measures were only observed in the schizophrenia group. It may be that the schizophrenia relatives' performance, although impaired, is not as impaired when compared to deficits in other areas of functioning that would better add predictive power to the model.

When results from both discriminant function analyses (full and adjusted datasets) are considered together, it was revealed that schizophrenia relatives were best predicted from higher levels of odd and eccentric personality traits coupled with low scores on a task measuring attention and processing speed. Bipolar I relatives were best predicted from higher levels of obsessive compulsive personality traits coupled with higher scores on a spatial working memory task, but lower scores on a measure of attention and processing speed. Healthy controls were best predicted from lower levels of odd and eccentric personality traits coupled with higher scores on measures of both spatial working memory and attention and processing speed. Obsessive compulsive traits have previously been shown to distinguish bipolar I relatives from healthy controls, so this finding is consistent with the literature (Maier et al., 1995).

Interestingly, the odd and eccentric traits appear to be the most important personality style in differentiating schizophrenia relatives from healthy controls, but not a primary

component of the function that discriminated bipolar I relatives from the schizophrenia relatives. Schizophrenia relatives showed significantly higher levels of odd and eccentric traits when compared to bipolar I relatives, but this did not emerge as an important contributor in distinguishing the two groups. Results from the first hypothesis did not suggest there were significant differences among the schizophrenia and bipolar I relative groups with regard to obsessive compulsive traits, yet it emerged as the personality factor that best differentiated the two groups in the prediction model.

Furthermore, schizophrenia relatives were shown in the analyses for the second hypothesis to exhibit cognitive deficits (when compared to controls) on all four of the cognitive variables that were used in the prediction model. Only one of these (the measure of attention and processing speed) strongly predicted schizophrenia relative group membership. Conversely, predicting membership in the bipolar I relative group required both lower scores on the attention and processing speed task, as well as higher scores on the spatial working memory task. Two measures of cognition were needed to differentiate, respectively, the bipolar I relative group first from healthy controls, and secondarily from the schizophrenia relatives. The prediction model, therefore, would suggest that bipolar I relatives do not show deficits on the spatial working memory task. It was hypothesized that bipolar I relatives would show less pronounced deficits than the schizophrenia relatives on all measures of attention, working memory, and executive functioning. These results were not supported, and in fact, it might be concluded that bipolar I relatives do not exhibit general deficits in cognitive functioning, but rather deficits in very specific areas that are at or near the level exhibited by schizophrenia relatives. Findings from this study would suggest that one of these deficits is in the area of attention and processing speed (perhaps specifically on the

BACS symbol coding subtest). Other specific areas were not identified in the present study and would need to be further investigated. Gilvarry, Russell, Hemsley, and Murray (2001) reported a similar pattern when they concluded that the prevalence of schizophrenia spectrum traits was similar in the relatives of schizophrenia patients compared to the relatives of affective psychosis patients (defined as being diagnosed with schizoaffective and psychotic bipolar disorders), yet they found that affective psychosis relatives showed fewer deficits on a battery of cognitive tests.

Discriminant function analysis findings could also provide support to the dimensional conceptualization of personality functioning among schizophrenia and bipolar I relatives that was proposed when interpreting the personality results related to the first hypothesis. It was previously suggested that the odd and eccentric traits fall at one end of a general personality spectrum for these two types of relatives, and obsessive compulsive traits fall at the other end. Discriminant function analysis results seem consistent with such a proposal given that these were the only personality styles to emerge as significant contributors to the prediction model. In that context, therefore, it is not surprising that the avoidant and cluster B traits were not significant contributors to the model. As was previously discussed, there may be more overlap in the level of avoidant traits between schizophrenia relatives and bipolar I relatives, as well as the level of cluster B traits. As such, neither personality style would be able to provide enough discrimination between the two relative groups. An alternative explanation would involve the personality scales that make up the cluster B composite. More personality trait variables may have proved to be significant contributors to the prediction model if variables such as the borderline and histrionic scales from the SIDP-IV had been used instead of cluster B. Post hoc comparisons suggested that schizophrenia relatives

appeared different than bipolar I relatives along these two dimensions. These differences may have been unnoticeable in the prediction models when the two were combined into the cluster B composite.

Prediction findings from the logistic regression analysis. Results from the logistic regression also indicated that the set of personality and cognitive variables was able to reliably distinguish between relatives in the schizophrenia and bipolar I disorder relative groups. However, fewer variables (as compared to the discriminant function analyses) emerged as significant contributors to the prediction of relative type. For the logistic regression analysis of the full dataset, both spatial working memory (measured by the WMS-III) and obsessive compulsive traits made significant contributions to the prediction of relative type. The odds of being classified in the schizophrenia relative group decreased with performance improvements (higher scores) on the WMS-III, and decreased with higher levels of obsessive compulsive traits. Logistic regression analysis results for the adjusted dataset only included performance on the spatial working memory task (WMS-III) as a significant contributor to the prediction of relative type. Again, the probability of being classified in the schizophrenia relative group decreased with performance improvements on the spatial working memory task. On the one hand, the logistic regression results are not as informative as those from the discriminant function analysis since fewer significant predictors were identified. On the other hand, logistic regression may help to underscore what variables are the most strongly associated with differentiating the relative groups since one emerged for each major area of functioning that was investigated.

Classifying schizophrenia and bipolar I relatives. The discriminant function and logistic regression analyses employed to address the third hypothesis suggest that accurate

classification of schizophrenia relatives and bipolar I relatives can be improved over chance alone based upon knowledge of personality traits and cognitive functioning. For the three group discriminant function analysis, assuming roughly equivalent group sizes, roughly 33% accuracy would be expected by chance alone. Overall accuracy using the functions to predict group membership fell between 57.7 and 59.5%. For the two group logistic regression, assuming equivalent group sizes, 50% accuracy would be expected by chance alone. Overall prediction accuracy fell between 68 and 70%. Classification rates using the prediction models are not substantial improvements over chance alone. However, it is clinically difficult to distinguish schizophrenia from bipolar I disorder. Given that the present study is not distinguishing patient groups from one another, but *relative groups* who demonstrate softer signs of these illnesses, classification rates that improve by approximately 20% when individuals are classified based on personality and cognitive features would be useful. However, the utility of these prediction models would have to be considered in the context of what the classification would be used for given that there is still a fair amount misclassification possible. If one was using the information to label an individual with a particular diagnosis or impairment this probably would not be a reasonable risk, but if one used the information to inform treatment decisions (for a form of treatment with minimal associated risks), it may be worthwhile.

The prediction models, on average, explain approximately 30% of the variance in relative type. This can be considered a small to moderate effect size (Ferguson, 2009). Given that both schizophrenia and bipolar I disorder are quite heterogeneous diagnoses, it seems safe to assume that it would be difficult to find a model that explains much more of the variance. However, in attempting to explain the other approximately 70% of variance in

relative type, it is highly probable that other important predictors of relative type were not considered in planning the present study. With regard to personality variables, it might have been a better approach to split up the cluster scores and use some of the specific personality styles that comprised these, such as schizotypal, borderline and histrionic personalities. Psychosocial impairment, as was previously discussed with regard to elevations on cluster B traits for both relative groups, may help to account for more variance in relative type. Inclusion of a measure of psychosocial impairment in future studies may aid the prediction.

Summary of prediction findings. As hypothesized, prediction of group membership was reliably accomplished through discriminant function and logistic regression models wherein measures of personality traits and cognitive functioning were used as predictors. In general, higher levels of obsessive compulsive personality traits predicted membership in the bipolar I relative group. Personality traits that emphasize preoccupation with orderliness, rigidity, perfection and control, therefore, seem to best distinguish bipolar I relatives from schizophrenia relatives. Pronounced deficits in performance on a spatial working memory task predicted membership in the schizophrenia relative group. These two factors emerged as the most significant predictors of group membership. The design of the current study provided an improvement over the prediction model described by Laurent and colleagues in 2002. The authors used both personality scales and measures of attention and executive functioning. However, rather than predict group membership, personality functioning was used to predict performance on the cognitive tasks (e.g. high vs. low scorers among the relatives). The present study is viewed as an improvement over the work of Laurent and colleagues (2002) because personality traits and cognitive functioning appear to be separate constructs. In fact, both personality traits and cognitive functioning may be separate

vulnerability markers for developing either disorder as has been suggested in previous research (Keshavan, Diwadkar, et al., 2005). Taken together, as was done in the present study, personality traits and specific areas of cognitive functioning may help to predict group membership, but is seems less important, as well as less likely, that they would predict one another.

Clinical Implications

An important concept that continually emerged in discussing the results of the present study was the dimensional conceptualization of personality and cognitive functioning for the relative groups. Results of this study seem to underscore the dimensional approach to personality especially. These findings are timely and have implications for clinical practice particularly because they are consistent with the newest version of the manual used in clinical practice for diagnosing mental illnesses. Therefore, one clinical application of the present study would be to think about the findings in the context of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013) because it is now the manual recommended for use in clinical practice.

With the recent introduction of DSM-5 an increasingly dimensional approach is being taken toward diagnosis in the clinical practice of both psychology and psychiatry. DSM-5 remains primarily categorical in its organizational structure, albeit reordered to be less so (e.g. the removal of the five axes of diagnosis). The authors stress throughout the manual that a more dimensional approach to diagnosis should be a future goal, and in some areas categories have been removed. The personality disorders chapter was kept intact from the previous version. However, a chapter in Section 3 of the DSM-5 provides an "alternative 'hybrid' model" (APA, 2013, p. xliii) that is intended to inform future research towards a

more dimensional diagnosis of personality disorders. This model focuses less upon distinct personality disorders and more upon overlapping traits and levels of impairment. In describing the proposed model for personality disorders the authors state, “impairment in personality functioning predicts the presence of a personality disorder, and the severity of impairment predicts whether an individual has more than one personality disorder or one of the more typically severe personality disorders” (APA, 2013).

Results of the current study are consistent with these concepts from the DSM-5. When considering avoidant and cluster B personality traits, especially, the idea that overlapping traits contributed to the pattern of findings was presented. The concept of elevated traits rather than impairment to the point of personality disorder diagnosis was also a recurrent theme. The alternative model for personality disorders in DSM-5 quantifies personality functioning on a continuum for impairment which ranges from no impairment to mild to moderate to severe (APA, 2013; Skodol et al., 2011). Therefore, clinicians who use the DSM-5 alternative model for personality disorders might be better able to describe and possibly diagnose the relatives of schizophrenia and bipolar I patients. It was observed in the present study, in general, that when the relatives presented with maladaptive traits these were mild. Both DSM-5 and the personality findings from this study recommend less focus upon distinct personality disorders and more upon traits and specific levels of impairments.

Diagnosis is certainly an important component of clinical practice and the DSM-5 may facilitate better diagnosis. The present study, at least with regard to treating individuals who might be relatives of persons diagnosed with schizophrenia and bipolar I disorder, highlights the heterogeneity inherent in diagnosis. An important point that should be made regarding the application of this study to clinical practice is that it should not be assumed that

a person who is related to persons with either schizophrenia or bipolar disorder would necessarily meet diagnostic criteria for any disorder. A clinician should not automatically assume that relatives would present with the personality styles described. In fact, if treating a patient who is a first-degree relative of a person diagnosed with either disorder, a clinician may want to be even more careful in diagnosing a personality disorder in light of the present study which underscored the subtle nature of these signs.

That said, the patterns of personality traits and cognitive functioning observed in the relatives, whether or not diagnosable, can inform development of treatment plans with these individuals. For example, if a clinician is treating a patient who has either of the family histories investigated in this study, awareness of potential personality traits can assist the clinician earlier in the course of treatment to identify specific strategies for promoting a positive therapeutic alliance. With regard to cognitive interventions, if a clinician notices any of the subtle cognitive difficulties or a patient complains of difficulties in school or at work that could be suggestive of deficits in attention, working memory, or executive functioning, strategies to track, as well as reduce the impact of impairment in these areas could be introduced. The BACS, which was useful in identifying some potential deficits in both relative groups during this study and has published norms (Keefe et al., 2008) could be used in clinical practice. It exists in alternate forms; therefore, it might be utilized to track the cognitive functioning of an at risk patient. If it was determined that subtle cognitive difficulties were present for a clinician's relative-patient, cognitive remediation programs could be introduced. This is proving to be a promising mode of treatment with a recent study showing significant improvement nine months following a three month long treatment (Poletti et al., 2010). In the case of young patients, awareness of the patterns of personality

and cognitive functioning investigated in the present study can lead to earlier interventions with at risk individuals. Strategies recommended for treatment of the early course of schizophrenia might be applied for relatives from both groups at least with regard to psychotherapy, psychoeducation, family communication, social skills training, and cognitive remediation (Keshavan, Roberts, & Wittman, 2006).

A final clinical application of the present study would be in designing psychoeducation programs that could involve patients (of either type) and their immediate family. An important component of treatment for the serious mental illnesses is psychoeducation for both patients and their family members. It may be challenging for family members without diagnoses of schizophrenia or bipolar I disorder to understand the difficulties experienced by their patient-relatives. However, in general, people can often more readily understand and appreciate the experiences of others when similarities are drawn to their own personal experiences. Therefore, psychoeducation programs could be designed for family members that review the symptoms experienced by their patient-relatives in a way that is personally relevant. Knowledge of the patterns of personality and cognitive functioning that are present for schizophrenia and bipolar I disorder patients, and to a lesser extent for their relatives, could inform the design of this hypothetical program. More specifically, a therapist could present samples of cognitive tasks that assessed attention, working memory, or executive functioning to family members. After trying the tasks, the therapist could invite the group of family members to discuss any difficulties they may have experienced in completing the tasks. Next, using the words of the family members, the therapist could explain how the patient-relatives experience those same difficulties, but to larger extent and discuss how such experiences are a symptom of the patients' illness.

Following this exercise, strategies for helping the patient-relatives with these cognitive difficulties could be discussed. Such an intervention could grow out findings from the present study, and similar studies, that increase understanding of the softer signs of schizophrenia and bipolar I disorder.

Limitations

A variety of limitations to the present study can be identified. One main limitation has been described in depth throughout this paper—the assumption of independence of observations was violated. Multiple members from single families were included in the sample. Members of the same family cannot be considered independent observations due to shared genetics and environment. Rather than delete these individuals, which would have resulted in decreased sample size and less power, all participants were retained. A solution to this violation was to run the main analyses addressing each of the three hypotheses with the full dataset, secondarily with an adjusted dataset wherein the data from multiple participants from the same family was averaged (per Cone and Foster, 2006). It was recognized that the real results would therein fall in between the two sets of results, and in fact, significant findings were generally consistent between the full dataset and adjusted dataset with regard to both the personality and cognitive findings. This was a reasonable solution, yet a similar study could be devised that uses more sophisticated statistical techniques to address the problem of nonindependence of observations. For example, Fogelson and colleagues (2007) included family membership as random effects in statistical models. Faraone and colleagues (2000) addressed the issue with a formula to adjust variance estimates for clustered data. Both of these techniques were determined to be beyond the

expertise and scope of the researcher and project, but would be a reasonable improvement over the current methodology.

On a related point, considerations regarding the conservation of power and sample size drove many decisions that were made in designing the methodology of the current study. For one, the study was limited by the fact that data was used from an ongoing larger scale study and to some extent the design of the BSNIP project influenced, the measures used and characteristics of the sample. The measures tended to be some newer instruments such as the BACS , the PCET, and the DPX-CPT that were specifically designed for use with schizophrenia populations, which was a strength of the design. However, newer instruments are not as well researched. Awareness of the literature suggested limiting group membership based on a variety of demographic and clinical variables (e.g., only including relatives without a history of psychosis or without any history of Axis I disorders). These decisions, unfortunately, would have resulted in reduction in sample size. Including only relatives without any history of Axis I disorders would have been a strategy that enabled this researcher to control for the modifying influence of current or past episodes of Axis I syndromes, which may in fact have influenced results. The study, using the same dataset could also be conducted that included some measure of axis I symptomatology as a covariate.

There are additional limitations with regard to sample characteristics. Participants were randomly sampled through a variety of advertising approaches described in the Methods section, yet inclusion and exclusion criteria may have contributed to the creation of a sample that was not necessarily representative of a larger population of schizophrenia and bipolar I disorder families. During the course of recruitment, a number of individuals (primarily probands) volunteered to participate in the study, but could not due to the lack of a

willing first-degree relative. Decompensation into psychosis, as well as a chronic history of serious mental illness, is often associated with a lack of contact with family members. As such, results are not entirely generalizable. There may be significant differences in functioning on the variables studied between the probands who participated compared to the group of potential probands who were unable to participate because they could not provide a relative. Similarly, participating relatives might be different on the variables studied compared to the relative group that was not assessed due to unwillingness or lack of contact with their proband family member. The latter groups for each comparison are not contained in the current sample. Family members who did participate in the study may themselves possess better coping mechanisms and psychological resources and related to these characteristics (although not necessarily as a consequence), show less impairment in cognition and personality pathology. Given that this is a natural feature of the population, it may be difficult to design a study that better accommodates this potential limitation, but it is important to point out. One could recruit a small sample of patients without a first degree relative to use as a comparison group to the larger proband group in order to determine if any significant differences in demographic or clinical variables exist.

This was also a genetic study wherein the relatives groups were defined as being *first-degree* relatives of the probands. However, the relative status was determined primarily on self-report from the family members. There is a distinct possibility that there are individuals included in the current sample as relatives, who in fact, are not relatives. Better procedures for assessing degree of relatedness could have been employed, e.g. birth certificates and other forms of identification or collateral information that established the familial relationship between two participants.

Groups were not well matched on all demographic characteristics. Average age was significantly different between the schizophrenia relative and bipolar relative group, as well as the schizophrenia relative and healthy control groups. Schizophrenia relatives tended to be younger than the other two groups, with bipolar relatives and healthy controls fairly well matched in age, mean of 38 and 40 years, respectively. Years of education differed among the three groups with schizophrenia relatives reporting fewer years than healthy controls. The racial composition of the sample, in which Caucasians were over-represented in the bipolar relative group, and African Americans were over-represented in the schizophrenia relative group, is likely not representative of the larger population and may serve to confound group differences in personality and cognitive functioning.

Clinical characteristics of the proband groups also provide some potential limitations. There were some cases identified during outlier analysis of the personality variables that may have represented a proband who was misclassified (e.g. bipolar relatives with high ratings on the SIDP-IV). The cases were retained because they may not represent outliers, but rather interesting cases where overlapping traits against the hypothesized directions were actually observed. Careful diagnostic procedures were followed and probably cannot be improved upon, rather this speaks to the difficulty in making clear categorical diagnoses. Best estimate diagnoses were always the aim. Furthermore, some relatives of probands diagnosed with schizoaffective disorder and non-psychotic bipolar were included in the present sample. The incidence of this was low. As such, those individuals could have been removed from the sample, but again this would result in a reduction in sample size.

Finally, it is important to point out that when considering these results and the accompanying interpretations both effect sizes and design issues should be taken into

account. Effect sizes for the personality, cognitive and group membership prediction findings ranged from fairly small to medium (Ferguson, 2009). This suggests that the magnitude of the differences between the groups is not great and the findings, therefore, may not have a lot of practical significance. Put another way, the differences in relatives groups may not be easily observed in other samples. However, small effect sizes seem reasonable given that, again, this was a study investigating *subtle* differences among individuals.

In general, results from the present study seem to underscore the need for more consistency in measure selection when assessing cognition in schizophrenia and bipolar disorder. This study attempted to this follow recommendations by the MATRICs group (Nuechterlein et al., 2004) especially in the selection of the Brief Assessment of Cognition in Schizophrenia (Keefe et al, 2008).

Directions for Future Research

The present study leaves an opening for multiple avenues for future research. Some of these will be discussed, but the list is certainly far from exhaustive. A major area of refinement would be including a measure of Axis I symptomatology as a covariate. DSM-5 (APA, 2013) removed the multiaxial component of diagnosis that was present in DSM-IV-TR (APA, 2000). The change reflected the idea that there is a fair amount of overlap in both types of mental disorders (APA, 2013). As such, this would be an important component of future studies as results from the present study remain unclear as to the extent that Axis I symptomatology influenced the results. Consideration of changes to the diagnostic system implemented by DSM-5, could inform future studies in another way. A similar study that attempted to predict group membership for the two types of relatives could be designed using the alternative model of personality traits and disorders that is described in Section 3 of

DSM-5, rather than DSM-IV-TR conceptualizations. As DSM-5 reduced the number of personality disorders from ten to five. Therefore, the main personality styles to be focused on in future research would be borderline, obsessive compulsive, avoidant, antisocial and narcissistic. The current study was primarily focused upon clusters, but seeing that some of the personalities included in both cluster A and cluster B were removed from DSM-5, this could call for a new study that focused upon those styles. The authors of the DSM-5 particularly encourage future research that investigates these personality styles along dimensions. Constructing a new study that was focused upon the personalities of the DSM alternative model, would also allow future researchers to further investigate traits that could explain unexpected results of the present study. For instance, what traits of the borderline style differentiated schizophrenia relatives from bipolar I relatives? What traits of the antisocial style differentiated schizophrenia relatives from bipolar I relatives?

On obsessive compulsive personality traits, the relative groups were not significantly different when analyses of group comparisons were conducted. However, obsessive compulsive traits proved to be the main personality variable that distinguished the two groups in the prediction model. A future study could be developed that improved methodology in order to better evaluate group differences on these traits. The improved methodology might consist of (a) more specific definitions of the relative groups, (b) controlling for Axis I symptomatology, and (c) determining trait differences between the groups and designing follow-up analyses or additional studies to explain these findings.

It was speculated when discussing the results of the current study that psychosocial impairment may play an unmeasured role in the patterns of groups differences observed. Therefore, a future study that included a measure of psychosocial impairment in the

prediction model could be designed. Avoidant personality certainly has components of psychosocial impairment (APA, 2000). However, the traits that comprise avoidant personalities represent forms of psychosocial impairment that are too specific, especially if investigating more than just a schizophrenia relative group. Fogelson and colleagues (2007), in the context of discussing avoidant personality traits in schizophrenia relatives makes the point that level of social functioning is one of the best predictors of adapting to illness following onset of psychosis. This idea could be expanded to include bipolar relatives as well, taking into consideration the idea that bipolar relatives would likely express different psychosocial difficulties when compared to schizophrenia relatives. Therefore, it may be advantageous to identify and incorporate into future studies a general measure of psychosocial functioning that would assess an appropriate range of psychosocial difficulties.

Research related to cognitive functioning of bipolar relatives, in general, is under-researched when compared to schizophrenia relatives. The present study adds to the literature in that regard, but there is merit for ongoing study of bipolar relatives' cognitive functioning that will identify specific areas of impairment, if they exist at all. For one, it has been suggested that deficits are state-dependent. The ability to draw conclusions about trait- versus state-dependent deficits could be incorporated into future studies. As more specific areas of potential cognitive deficits are identified and replicated in the research, these areas should be applied to future studies with designs that are similar to the present study in attempting to predict membership into the two relative groups. Medication use and its potential influence on cognitive performances by the two groups should also be incorporated into future studies. Conclusions could not be drawn in this regard for the present study because it was beyond the scope of the study to investigate the influence of medication use.

Carefully collecting information on medication use, even for relatives, would help in this regard.

Differences in demographic characteristics were observed between the two groups. Although the design of the study aimed to include relative groups who were well matched on all demographic variables, some differences were observed at the time of analysis with regard especially to age, education level, and race (Caucasian and African American). It was beyond the scope of this study to investigate these demographic differences when designing the prediction model, but future research should take these patterns into account given findings from the present study.

Finally, the design of the current study was complicated by the composition of the two groups primarily around defining these groups based upon proband diagnosis. Future studies could replicate the design of the present study, but conduct separate analyses wherein the groups are defined differently. Some examples would include comparing both relatives of psychotic bipolar I patients and then relatives of non-psychotic bipolar I patients with schizophrenia relatives. Relatives of schizoaffective probands could also be investigated, although this would be more difficult as that group size tends to be low. However, the Schizobipolar Scale (SBS) that was developed by Keshavan and colleagues (2011) could help in this regard.

Specifically, it may have been more interesting for the present study to include a separate group of relatives of patients diagnosed with schizoaffective disorder. However, there were too few probands diagnosed with this variation of psychotic illness to create a group that would be comparable in size to the schizophrenia and bipolar I relative groups. A future study could do away with using the SCID diagnoses to determine group membership

and instead use the Schizobipolar scale (Keshavan et al., 2011). Relatives could be classified into three groups based upon dimensional ratings, rather than specific diagnosis, for the probands on this scale. They would belong to groups based on the following proband SBS scores, relatives of (a) probands scoring in the schizophrenia end of the scale, (b) probands scoring in the schizoaffective (or middle area of the scale), and (c) probands scoring in the bipolar end of the scale. The SBS was developed by Keshavan and colleagues in 2011 based on some of the multisite B-SNIP data. The interested reader is referred to his study for further details regarding the construction and properties of the SBS. A study of relative's personality traits that utilized the SBS to determine the groups could be considered more consistent with the dimensional approach that is recommended by the DSM-5 task force for future research (APA, 2013).

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APPENDIX A

WSU Institutional Review Board Approval for BSNIP Project

WAYNE STATE UNIVERSITY

HUMAN INVESTIGATION COMMITTEE
101 East Alexandrine Building
Detroit, Michigan 48201
Phone: (313) 577-1628
FAX: (313) 993-7122
http://hic.wayne.edu

NOTICE OF FULL BOARD CONTINUATION APPROVAL

To: Nashaat Boutros
Psychiatry
9B UHC

From: James Chinarian, M.D. J. Chinarian (Rmp)
Chairperson, Medical Pediatric Institutional Review Board (MP2)

Date: July 08, 2010

RE: HIC #: 093307MP2F
Protocol Title: Bipolar & Schizophrenia Network on Intermediate Phenotypes B-SNIP
Sponsor: ° NATIONAL INSTITUTE OF MENTAL HEALTH
Protocol #: 0709005198

Expiration Date: July 07, 2011

Risk Level / Category: Pediatric: 45 CFR 46.406 - Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condi

Adult: Research involving greater than minimal risk, presenting no prospect of direct benefit, but likely to yield generalizable knowledge about the participant's condition

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Continuation for the above-referenced protocol and items listed below (if applicable) were **APPROVED** following Full Board review by the Wayne State University Institutional Review Board (MP2) for the period of 07/08/2010 through 07/07/2011. This approval does not replace any departmental or other approvals that may be required.

- Research Informed Consent Form with HIPAA Authorization (Revision dated 06/14/2010)
- Research Informed Consent for MRI and Electrophysiology Only with HIPAA Authorization (Revision dated 06/14/2010)
- Assent Form (Revision dated 06/14/2010)
- Assent Form for MRI and Electrophysiology Only (Revision dated 06/14/2010)
- Telephone Screening Interview (dated 09/26/2008)
- Study Brochure (2)
- Study Flyers (2)

° Federal regulations require that all research be reviewed at least annually. You *may* receive a *"Continuation Renewal Reminder"* approximately two months prior to the expiration date; however, it is the Principal Investigator's responsibility to obtain review and continued approval ***before*** the expiration date. Data collected during a period of lapsed approval is unapproved research and can never be reported or published as research data.

° All changes or amendments to the above-referenced protocol require review and approval by the HIC **BEFORE** implementation.

° Adverse Reactions/Unexpected Events (AR/UE) must be submitted on the appropriate form within the timeframe specified in the HIC Policy (http://www.hic.wayne.edu/hicpol.html).

NOTE:

1. Upon notification of an impending regulatory site visit, hold notification, and/or external audit the HIC office must be contacted immediately.
2. Forms should be downloaded from the HIC website at **each** use.

APPENDIX B

BSNIP Demographic Questionnaire

61172

B-SNIP
PARTICIPANT DEMOGRAPHIC

DATE OF RATING: ☐☐ / ☐☐ / ☐☐☐☐

SUBJECT INITIALS: ☐☐ - ☐ RATER ID: ☐☐

SUBJECT ID: ☐☐ ☐☐☐☐ RATER INITIALS: ☐☐ - ☐

Notes:

Was form filled out? ○ Yes, some or all of data ○ No data at all If Not, Please Specify:

Last Name: **First Name:**

Social Security Number: ###-##-☐☐☐☐ (Last 4 digits required only)

DOB (MM/DD/YYYY) ☐☐ / ☐☐ / ☐☐☐☐ **Sex:** ○ Male ○ Female

Ethnicity:

○ Not Hispanic or Latino

○ Hispanic or Spanish Origin or Latino (A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish Origin)

○ Unknown/Not ascertainable

Race: (Mark one or more of the following:

○ White / Caucasian ○ Other, not specified above ○ American Indian or Alaska Native ○ Asian

○ Native Hawaiian or Other Pacific Islander ○ Black or African American ○ Unknown/Missing

Handedness: ○ Left ○ Right ○ Ambidextrous ○ N/A, Unknown

Marital Status: ○ Presently Married (or in sustained conjugal relationship) ○ Divorced/Separated

○ Widowed ○ Never Married (Single)

HOLLINGSHEAD 2-FACTOR SOCIAL ECONOMIC RATING SCALE

EDUCATION/OCCUPATION OF PARTICIPANT

Special Education: ○ Yes ○ No ○ Unknown Highest Grade Achieved in Years ☐☐ (GED=12 yrs., 99=missing)

☐ Highest Occupation (Participant response, if ascertainable)

Highest Occupation Category (Clinician evaluation) ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 Never worked in paid employment ○ 9 Not ascertained

EDUCATION/OCCUPATION OF PARTICIPANT'S MOTHER

Special Education: ○ Yes ○ No ○ Unknown Highest Grade Achieved in Years ☐☐ (GED=12 yrs., 99=missing)

☐ Highest Occupation (Participant response, if ascertainable)

Highest Occupation Category (Clinician evaluation) ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 Never worked in paid employment ○ 9 Not ascertained

EDUCATION/OCCUPATION OF PARTICIPANT'S FATHER

Special Education: ○ Yes ○ No ○ Unknown Highest Grade Achieved in Years ☐☐ (GED=12 yrs., 99=missing)

☐ Highest Occupation (Participant response, if ascertainable)

Highest Occupation Category (Clinician evaluation) ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 Never worked in paid employment ○ 9 Not ascertained

APPENDIX C

BSNIP Psychiatric, Medical, and Family History Questionnaire

12020

B-SNIP
PSYCHIATRIC, MEDICAL AND FAMILY HISTORY FORM

DATE OF RATING: ☐☐ / ☐☐ / ☐☐☐☐

SUBJECT INITIALS: ☐☐ - ☐ RATER ID: ☐☐

SUBJECT ID: ☐☐ ☐☐☐☐ RATER INITIALS: ☐☐ - ☐

Notes:

Was form filled out? ○ Yes, some or all of data ○ No data at all If Not, Please Specify:

PSYCHIATRIC HISTORY

ONSET OF ILLNESS

1. How old was the subject at the first onset of any psychiatric illness?
   a. Age: ☐☐ ; b. Specify probable DSM-IV diagnosis (if possible) ☐☐☐.☐☐
   c. Specify Treatment, if any:
2. How old was the subject at the beginning of first Schizophrenia/Bipolar Disorder symptoms?
   a. Age: ☐☐ ; b. Specify probable DSM-IV diagnosis (if possible) ☐☐☐.☐☐
3. How old was the subject at the time of first psychiatric hospitalization?
   a. Age: ☐☐ ; b. Specify probable DSM-IV diagnosis (if possible) ☐☐☐.☐☐
4. How many times has the subject been hospitalized for psychiatric illness? # of times: ☐☐
5. Has the subject ever made a suicide attempts? ○ Yes ○ No ○ Not Ascertainable
6. Has the subject ever received an ECT? ○ Yes ○ No ○ Not Ascertainable

FAMILY HISTORY

7. Has any member of your family ever been hospitalized for a psychiatric problem or a nervous breakdown?
   ○ Yes ○ No ○ Not Ascertainable
8. Has any member of your family taken medicines to treat a psychiatric problem?
   ○ Yes ○ No ○ Not Ascertainable
9. Has any member of your family lived in a group home or supervised housing?
   ○ Yes ○ No ○ Not Ascertainable
10. Does any member of your family receive SSI or disability benefits?
    ○ Yes ○ No ○ Not Ascertainable
11. Is any member of your family odd or eccentric? ○ Yes ○ No ○ Not Ascertainable
    Use the information provided in item 11 for recruitment of relatives with schizophrenia spectrum personality disorders.
    If yes, ask: a. Is he/she withdrawn? ○ Yes ○ No ○ Not Ascertainable
    b. Does he/she talk to himself/herself? ○ Yes ○ No ○ Not Ascertainable

12020

B-SNIP PSYCHIATRIC, MEDICAL AND FAMILY HISTORY FORM
continued

SUBJECT ID: ☐☐☐☐☐☐

☐☐ 12a. Number of first degree relatives with a probable schizophrenia/bipolar spectrum disorders (DSM-IV Axis I and Axis II): schizophrenia, schizoaffective disorder, bipolar disorders, major depressive disorder, cluster A and cluster B personality disorders.

☐☐ 12b. Number of second degree relatives (e.g. grandparents, grandchildren, aunts, uncles,) with a probable schizophrenia/bipolar spectrum disorders (DSM-IV Axis I and Axis II): schizophrenia, schizoaffective disorder, bipolar disorders, major depressive disorder, cluster A and cluster B personality disorders.

☐☐ 12c. Number of third degree relatives (e.g. great-grandparents) with a probable schizophrenia/bipolar spectrum disorders (DSM-IV Axis I and Axis II): schizophrenia, schizoaffective disorder, bipolar disorders, major depressive disorder, cluster A and cluster B personality disorders.

13. Draw Family Tree if cases of schizophrenia/bipolar spectrum disorders are reported.

MEDICAL HISTORY: Medical History from medical chart within last 6-months is acceptable.	History of: 1=No History of 2=Yes, does NOT EXCLUDE 3=Yes, EXCLUDES	*If YES or NOT EVALUATED, explain or describe below.
1. Allergies-Drugs	○ 1 ○ 2 ○ 3 ○ 9	
b) Allergies-Others ☐	○ 1 ○ 2 ○ 3 ○ 9	
2. HEENT Disorder	○ 1 ○ 2 ○ 3 ○ 9	
3. Cardiovascular Disorder		
a) Coronary Artery Disease	○ 1 ○ 2 ○ 3 ○ 9	
b) Hypertension	○ 1 ○ 2 ○ 3 ○ 9	
c) Other ☐	○ 1 ○ 2 ○ 3 ○ 9	
4. Renal Disorder	○ 1 ○ 2 ○ 3 ○ 9	
5. Hepatic Disorder	○ 1 ○ 2 ○ 3 ○ 9	
6. Pulmonary Disorder	○ 1 ○ 2 ○ 3 ○ 9	
7. Gastrointestinal Disorder	○ 1 ○ 2 ○ 3 ○ 9	
8. Musculoskeletal Disorder	○ 1 ○ 2 ○ 3 ○ 9	
9. Neurologic Disorder	○ 1 ○ 2 ○ 3 ○ 9	
10. Dermatologic Disorder	○ 1 ○ 2 ○ 3 ○ 9	
11. Metabolic Disorder		
a) Diabetes	○ 1 ○ 2 ○ 3 ○ 9	
b) Hyperlipidemia	○ 1 ○ 2 ○ 3 ○ 9	
12. Hematologic Disorder	○ 1 ○ 2 ○ 3 ○ 9	
13. Endocrine Disorder	○ 1 ○ 2 ○ 3 ○ 9	
14. Genitourinary Disorder	○ 1 ○ 2 ○ 3 ○ 9	
15. Infectious Disease	○ 1 ○ 2 ○ 3 ○ 9	
16. Other ☐	○ 1 ○ 2 ○ 3 ○ 9	
17. Other ☐	○ 1 ○ 2 ○ 3 ○ 9	

ABSTRACT

PERSONALITY DIMENSIONS AND COGNITIVE FUNCTIONING OF RELATIVES OF PERSONS DIAGNOSED WITH SCHIZOPHRENIA AND BIPOLAR I DISORDER: A COMPARATIVE AND PREDICTIVE STUDY

by

JULIE PAAVOLA

December 2013

Advisor: Judy McCown, Ph.D.

Major: Psychology (Clinical)

Degree: Doctor of Philosophy

The purpose of this study was to determine a set of personality and cognitive variables that could best be used to predict membership into either a schizophrenia or bipolar relative group. A group of relatives of persons diagnosed with schizophrenia (n = 59) and a group of relatives of persons diagnosed with bipolar I disorder (n = 54) were compared along four dimensions of personality and eight dimensions of cognitive functioning. Relative group comparison with a healthy control group (n = 64) along the same personality and cognitive dimensions was a secondary goal. Dimensions of personality were measured using the Structured Clinical Interview for *DSM-IV-TR* Personality (SIDP-IV) from which trait scores were derived for the cluster A, cluster B, avoidant and obsessive-compulsive personalities. Cognitive functioning was assessed within the domains of attention, working memory, and executive functioning using a variety of measures.

The schizophrenia relative group was best distinguished from the bipolar I relative group on cluster A traits, whereas the bipolar I relative group was best distinguished from the

healthy control group on obsessive-compulsive traits. As was hypothesized, the schizophrenia relative group showed deficits in cognitive functioning in all three domains when compared to healthy controls. The bipolar I relative group did not show impairments in cognitive functioning that were to a lesser extent than the schizophrenia relative group (which was contrary to hypotheses). Rather, deficits were similar to the schizophrenia-relative group or no impairment was observed along cognitive domains for the bipolar relative group. Both discriminant function analyses and logistic regression analyses were utilized to develop prediction models for group membership. Relative type was best predicted by the variables of WMS-III Spatial Span (a measure of spatial working memory) and obsessive-compulsive traits. Results of the present study underscore the use of dimensional models in personality conceptualization and provide further evidence in supporting subtle differences in both personality and cognitive functioning between family members of patients diagnosed with the major mental illnesses. Treatment implications are discussed in the context of assisting the family unit in the treatment of schizophrenia and bipolar I disorder.

AUTOBIOGRAPHICAL STATEMENT

Julie Nicole Paavola

EDUCATION

University of Detroit Mercy, Detroit, Michigan
Doctor of Philosophy in Clinical Psychology (2013)
Master of Arts in Clinical Psychology (2009)

Kalamazoo College, Kalamazoo, Michigan
Bachelor of Arts in Psychology (2002)

SELECTED PROFESSIONAL EXPERIENCE

10/2010 – 3/2013	Research Assistant Department of Psychiatry & Behavioral Neurosciences Wayne State University School of Medicine, Detroit, Michigan
9/2009 – 8/2010	General Psychology Pre-doctoral Intern Department of Psychiatry & Behavioral Neurosciences Wayne State University School of Medicine, Detroit, Michigan
2/2008 – 8/2009	Research Assistant Department of Psychiatry & Behavioral Neurosciences Wayne State University School of Medicine, Detroit, Michigan
9/2006 – 8/2007	Life Stress Center Practicum Student Detroit Receiving Hospital, Detroit, Michigan
8/2005 – 8/2006	Center for Forensic Psychiatry Practicum Student Saline, Michigan
9/2004 – 8/2005	Student Clinic Director Psychology Clinic of University of Detroit Mercy Detroit, Michigan

SELECTED ACADEMIC ACTIVITIES

Psychoanalytic Psychotherapy Fellowship Program at the Michigan Psychoanalytic Institute (9/2007 – 6/2008)

Paavola, J. (2006, October). *To use or not to use? An introduction to the Personality Assessment Inventory (PAI) in forensic practice.* Paper presented to the Department of Psychology, Center of Forensic Psychiatry.