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THE NEUROPSYCHOLOGICAL ENDOPHENOTYPE OF
SPECIFIC LANGUAGE IMPAIRMENTS AND AUTISM SPECTRUM DISORDERS:
CATEGORY OR CONTINUUM?

by

Heather M. Anson

Dissertation

Submitted to the Department of Psychology

Eastern Michigan University

in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

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June 9, 2008

Ypsilanti, Michigan

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The Neuropsychological Endophenotype of
Specific Language Impairments and Autism Spectrum Disorders:
Category or Continuum?

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“Success is not a place at which one arrives, but rather the spirit with which one undertakes and continues the journey.” Without the support, encouragement, and sacrifice of my wonderful husband, Terry, I may not have had the courage to have embarked upon this educational endeavor. I am eternally grateful to him.

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ABSTRACT

The primary goal of this investigation was to illuminate variables of the specific language impairment (SLI) and autism spectrum disorders (ASD) neuropsychological endophenotypes and to clarify the nature of overlap between SLI and ASD. Group differences in cognitive functioning, epidemiological factors including proband comorbidity and health problems, and familial data in 39 SLI children and 89 ASD children who presented for clinical evaluation at Henry Ford Health System in Detroit were examined by retrospective chart review.

Cognitive data revealed that ASD probands performed more poorly on tests of perceptual-motor functioning and had higher rates of pragmatic language deficits than SLI probands. In addition, ASD probands had higher rates of pragmatic speech problems than SLI probands.

Proband comorbidity and health problem group differences were noted in several areas. SLI probands had higher rates of learning disorders, asthma, and stomach/digestion problems than the ASD probands. ASD probands had higher rates of mental retardation (MR) than the SLI probands.

Familial group differences were noted in parental education levels and family history of psychopathology. SLI parents were less likely to have obtained a high school diploma or GED than ASD parents. SLI probands had higher rates of first-degree maternal relatives with learning disorders than ASD probands. ASD probands had higher rates of first-degree maternal relatives with ASD and thought disorders than SLI probands.

In addition to significant findings between the diagnostic groups, differences between severity levels were also found. The severe groups performed more poorly on tests of academic functioning and visual attention than mild-moderate groups. In addition, the severe groups had higher rates of verbal communication content problems than the mild-moderate groups.

In terms of comorbidity, the mild-moderate groups had higher rates of learning disorders and ADHD than the severe groups. The severe groups had higher MR rates than the mild-moderate groups. Finally, familial data indicated that the mild-moderate groups had higher rates of parents employed in business/finance and engineering/science than the severe groups.

Overall, these findings provide valuable information on factors present in SLI and ASD neuropsychological endophenotypes and increase understanding on the nature of overlap between the two disorders.

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THE NEUROPSYCHOLOGICAL ENDOPHENOTYPE OF
SPECIFIC LANGUAGE IMPAIRMENTS AND AUTISM SPECTRUM DISORDERS:
CATEGORY OR CONTINUUM?

Chapter 1: Introduction and Background

The term *specific language impairment* (SLI) describes the unexplainable language acquisition difficulties in children (Bishop, 2001). Autism Spectrum Disorders (ASD) describe a spectrum of disorders that includes deficits in reciprocal social interaction skills, communication skills, and the presence of stereotyped behaviors, interests, and activities (American Psychiatric Association [APA], 2000). During the past several years, evidence has mounted to show that genes play an important role in both SLI and ASD aetiology (De Fossé et al., 2004). Unfortunately, the lack of information on the associated endophenotypes hinders researchers' ability to explain related genetics (Gottesman & Gould, 2003). Previous SLI studies are at a disadvantage given the fact that it is unclear whether researchers should look at SLI as a discrete disorder or a continuous variable. Complicating this issue is the fact that it is uncertain which measures ought to be used for identifying cases and the ambiguity of the number of SLI subtypes (Bishop, 2001). ASD research is slightly more advanced as investigators recognize the disorder as a spectrum and have begun to explore the broad autism phenotype (BAP). The BAP refers to the finding that relatives of individuals with ASD often have mild forms of autistic-like characteristics (Lainhart et al., 2002). Given evidence that ASD characteristics can extend to relatives widens the ASD continuum. The fact that communication and language difficulties are present in both SLI and ASD gives rise to

the question of whether SLI and ASD are truly categorical disorders or if they are actually part of a larger overlapping continuum.

Traditionally, researchers have had a tendency to focus on a single cause for disorders or for each subtype of a disorder. A better and more realistic way to study SLI and ASD may be to focus on multiple risk and protective factors, which is similar to the approach adopted in medicine (Bishop, 2001). Research on the BAP provides an example of how researchers have begun to move in this direction. Endophenotypic research will further propel the field in this direction.

Behavioral studies examining SLI and ASD are important for two main reasons. First, both SLI and ASD are heterogeneous and largely defined through exclusionary criteria. A successful search for genes implicated in SLI and ASD depends on a clear definition of the heritable phenotype. Second, the environment has a large influence over the presentation of a disorder, and behavioral studies can illuminate the dimensions of this control (Bishop, 2001). Michel and Moore (1995) have stated that the discovery of genetic influence on behavioral patterns ought to be seen as a new beginning for psychological investigation.

Chapter 2: Psychopathology

The psychopathology section will begin with a description of the psychological, social, and biological features SLI. Then it will move into a description of the psychological, social, and biological features of the ASD.

Psychological Features of SLI

Currently SLI is characterized by the inability to acquire accurate language expression and/or comprehension. An SLI diagnosis requires a speech or language impairment in the presence of normal cognitive skills. In addition, the impairments cannot be caused by neurological or physical abnormalities. Clinicians most commonly diagnose SLI during the preschool or the early elementary school years (Aram, Morris, & Hall, 1993; Botting & Conti-Ramsden, 2003; Dunn, Flax, Sliwinski, & Aram, 1996; Plante, 1998). Essentially, SLI is an exclusionary diagnosis. That is, the language difficulties are not associated with factors such as hearing loss, physical handicap, brain injury, pervasive developmental disorder, or general learning difficulties. The clinical variation associated with SLI may be diverse. Some children with SLI may have difficulties in comprehension and language production, and others may appear to understand well but have trouble producing language. It is possible for individuals to have difficulties with vocabulary, peculiarities in communication, or impairment in the production of speech sound sequences (Bishop, 2001).

SLI Diagnostics Criteria

The *Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision (DSM-IV-TR)* characterizes SLI under the broad category of communication disorders. The communication disorders encompass expressive language disorder, mixed

receptive-expressive language disorder, phonological disorder, stuttering, and communication disorder not otherwise specified (APA, 2000).

Expressive language disorder. Expressive language disorder is characterized by impairment in expressive language development. This impairment is demonstrated by an expressive language development level that is substantially below both nonverbal intellectual capacity and receptive language development (APA, 2000).

Mixed receptive-expressive language disorder. Mixed receptive-expressive language disorder is characterized by impairments in both receptive and expressive language development. These impairments are demonstrated by both receptive and expressive language development levels that are substantially below nonverbal intellectual capacity (APA, 2000).

Phonological disorder. Phonological disorder is characterized by a failure to use developmentally expected speech sounds appropriate for both age and dialect. This difficulty may include errors in sound production, use, representation, or organization.

Stuttering. Stuttering is characterized by a disturbance in the normal fluency and time patterning of speech (APA, 2000).

Communication disorder not otherwise specified (NOS). Communication disorder NOS includes disorders in communication that do not meet criteria for any of the specific communication disorders. An example for this category could consist of a voice disorder where there is an abnormality in pitch or tone (APA, 2000).

Epidemiology/Course of SLI

The prevalence rate of communication disorders varies with age. Language delays in children less than three years of age occur in 10 to 15 percent of the population. This

percentage decreases to 3 to 7 percent by school age (APA, 2000). Several studies report SLI to occur in males at higher rates than females. The estimated male-to-female ratio is 2:1 to 3:1 (Bishop, 1997; Flax et al., 2003; Lahey & Edwards, 1995; Rice, Haney, & Wexler, 1998; Shriberg, Tomblin, & McSweeny, 1999).

Behavioral-genetics researchers have shown SLI to have a highly heritable component. In general, behavioral-genetic study findings show monozygotic (MZ) twins having higher concordance rates for language-based learning disorders than dizygotic (DZ) twins (Bishop, North, & Donlan, 1995; Lewis & Thompson, 1992; Tomblin & Bucksalter, 1998). Bishop et al. (1995) found 70% concordance rates for MZ male twins on both articulation and language disorders compared to only 46% of DZ twins. Tomblin and Buckwalter (1998) also reported higher rates of concordance in language disorders. They found 96% concordance for poor language achievement in MZ twins and 69% in DZ twins. In addition to these findings, Dale et al. (1998) demonstrated that children with higher levels of impairment had stronger genetic involvement related to the problem.

Communication disorders usually come to the attention of parents and professionals when the child is between the ages of 2 to 4 years. However, milder forms may not be evident until the child reaches elementary school, where comprehension difficulties become noticeable, or the early teens, when language becomes more complex. The outcome of communication disorders is variable. Many children improve substantially. However, in some individuals SLI difficulties continue through adulthood. Clinical improvement in language can be quick and thorough. However, communication deficits and related cognitive difficulties may continue. In some instances these deficit

may be progressive. In addition, children with severe communication deficits are likely to develop learning disabilities (APA, 2000).

Comorbidity in SLI

As with most disorders, comorbidity is often present in SLI individuals. Even though reading impairments are not included in the criteria for SLI, approximately 50% of children with SLI eventually develop reading difficulties (Catts, Fey, Tomblin, & Zhang, 2002). Longitudinal research indicates that children who have trouble developing oral language during early childhood are at an increased risk for later language, reading, and general academic difficulties (Bishop & Adams, 1990; Scarborough, 1990; Aram & Hall, 1989; Tallal, Allard, Miller, & Curtiss, 1997). This is demonstrated in a study by McArthur, Hogben, Edwards, Heath, and Mengler (2000). Fifty-three percent of their sample could have been identified with either SLI or specific reading disability. Fifty-five percent of children with a specific reading impairment also had impaired oral language, and 51% of the SLI children had a reading disability. Findings such as these, where a large percentage of individuals can be classified as either SLI or reading disabled, have consequences for the criteria used to define either disorder and for conceptualizing each disorder's subgroups. Future research will need to work to determine whether these disorders are distinct or part of an overlapping continuum.

Developmental dyslexia and SLI are both disorders of language, but they differ in diagnostic criteria and outcome (Leonard, Eckert, Given, Virginia, & Eden, 2006). As discussed earlier, poor receptive and expressive oral language defines SLI. Even when dyslexic children do not meet formal diagnostic criteria for SLI, their ability to perceive speech can be impaired (Manis, Seidenberg, Doi, McBride-Chang, & Petersen, 1996;

Breier, Gray, Fletcher, Foorman, & Klaas, 2002). Tallal, Miller, and Fitch (1993) propose that the prevalence of oral language impairments in developmental dyslexia suggests that developmental dyslexia and SLI are not distinct categorical disorders but instead differ quantitatively along a dimension of severity.

Attention deficit/hyperactivity disorder (ADHD) has been documented in some children with speech and language disorders (Aram, Ekelman, & Nation, 1984; Goorhuis-Brouwer & Wijnberg-Williams, 1996; Redmond & Rice, 1998, Tallal, Townsend, Curtiss, & Wulfeck, 1991), and approximately two thirds of children with ADHD have SLI (Cantwell, 1996; Love & Thompson, 1988; Smalley, 1997). It is possible that ADHD could deter the development of speech and language, creating an inflated report of SLI individuals diagnosed with ADHD. However, Kovac, Garabedian, Du Souich, and Palmour (2001) showed that SLI children with a medical record of ADHD were significantly more likely to have a first-degree relatives with SLI than those without an ADHD record. Additionally, Tallal et al. (1991) found that SLI children with at least one SLI parent presented with higher rates of attention/hyperactivity behavioral problems.

Recent research indicates that SLI may occur with autoimmune disorders. Specifically, some researchers have reported higher rates of language-related disorders in individuals with autoimmune disorders, while others have suggested higher rates of autoimmune disorders in individuals with language disorders (Gilger, Pennington, Green, Smith, & Smith, 1992; Hugdahl, Synnevag, & Satz, 1990; Wood & Cooper, 1992).

Social Features of SLI

Children learn language by listening and interacting with others. Researchers previously assumed the development of language difficulties were the result of poor

language interactions on the part of a child's caregivers. Early correlation research showed certain environmental factors to differentiate SLI children from normally developing children. For example, children with SLI tended to be from families with lower socio-economic status (Fundudis, Kolvia, & Garside, 1979), were often the younger children from large families (Bishop, 1997), and their fathers generally had fewer years of formal education (Tomblin, Hardy, & Hein, 1991). Upon closer examination of these results, the problem of overgeneralizations arose, which hid variation within the SLI population. Many SLI children have highly educated parents of affluent households. In addition, research looking at the quality or quantity of mothers' speech directed to their children did not produce any reliable evidence to show inadequate communicative interactions from SLI mothers. The language interaction differences that have been consistently documented in SLI families include parents altering communicative styles as a result of a child's language impairment (Conti-Ramsden & Friel-Patti, 1984).

SLI Family Aggregation

Finding that environmental factors were not the sole cause of SLI, researchers shifted to examining other possible origins of SLI. Through familial aggregation and twin studies, researchers have repeatedly documented that genetic factors play an etiological role in SLI (Bishop et al., 1995; Lewis, Ekelman, & Aram, 1989; Neils & Aram, 1986; Rice et al., 1998; Tallal, Ross, & Curtis, 1989; Tomblin, 1989). Family aggregation studies gain data on the extent to which disorders run in families. Several studies show that SLI aggregates in families (Benasich & Spitz, 1999; Bishop et al., 1995; Lahey &

Edwards, 1995; Rice et al., 1998; Spitz, Tallal, Flax, & Benasich, 1997; Tallal et al., 2001; Tomblin & Buckwalter, 1998).

SLI occurs in the general population on an average of about 4% (Tomblin, 1996). In families with SLI, this percentage increases dramatically. SLI is estimated to occur in families with a history of the disorder at a rate of 20% to 40%. In addition, it appears that relatives of SLI children with expressive language disorder are at higher risk for SLI than relatives of children with mixed expressive-receptive language disorder (Lahey & Edwards, 1995).

Flax et al. (2003) report language impairments and reading impairments in two family aggregation studies. Their first study examined the occurrence of oral language impairments and reading impairments in SLI children. The second study included SLI probands and their nuclear and extended family members. Findings indicate that rates of oral language impairments and reading impairments were significantly higher in SLI proband family members than controls. In addition, affected SLI family members had higher levels of both oral language impairments and reading impairments than either impairment alone. Overall, 68% of SLI probands met reading impairment criteria, 25% of family members met language impairment criteria, and 23% of family members met reading impairment criteria. The researchers also found significant sex ratio differences, with more male than female offspring in SLI families, and more language-and-reading impaired males. Overall, these results indicate that oral language impairments are more likely to occur in SLI probands families, and these impairments often co-occur with reading impairments.

Choudhury and Benasich (2003) studied family aggregation in SLI using a unique sample of children. These researchers looked at children prior to 6 months of age from families with a history of SLI. At the time these children were selected, they did not have SLI diagnoses. Findings showed that 32% of these children were subsequently diagnosed with SLI by age three, which was significantly higher than the control group of children from families without SLI histories. By age three, children from the experimental group had lower scores on language comprehension and expression on the Receptive and Expressive scales of the Preschool Language Scale-3 (PLS-3), the Word Structure subtest of the Clinical Evaluation of Language Fundamentals-Preschool (CELF-P), and the Verbal Comprehension and Vocabulary scores of the Stanford-Binet Intelligence Scale, 4th edition (SB-4). There were no significant differences between the two groups on nonverbal reasoning measures. Another interesting finding indicated that the experimental group consisted of significantly more boys than girls diagnosed with SLI. Finally, the children from SLI families had higher rates of autoimmune diseases as well as a family history of autoimmune problems than control children. These researchers did not find differences between the groups on environmental risk factors such as socioeconomic status or parental education level. Overall, these results add to the evidence that children from families with a history of SLI are at a higher risk for developing a language delay than children from families without this history.

Familial aggregation in and of itself does not offer evidence for genetic influence as there are several other factors that must be considered. For example, cultural transmission or shared environmental influences may account for similar disorders among family members. Adding to this, parents of SLI children might be more attuned to

language problems occurring in relatives than parents of children without a disorder. For these reasons, aggregation studies of SLI cannot provide conclusive evidence for genetic influence, but they provide reason to conduct further research aiming to reveal genetic influences on SLI (Bishop, 2001).

Biological Features of SLI

Similar to family aggregation studies, twin studies alone do not provide conclusive evidence in terms of genes. Researchers must keep in mind that MZ twins share environmental factors that are more similar than those shared by DZ twins, and these factors may affect language development (Bishop, 2002). Adoption studies assist in providing further understanding to the role of genetics versus environmental influence in SLI.

SLI adoption studies point to genetic influences. Research shows having a biological parent with SLI significantly increased the probability of a child developing speech problems. However, whether or not a child lived with an affected parent did not contribute to a stronger risk for the development of SLI (Bishop, 2001). These factors combined point to a biological basis for SLI. Brain imaging and genetic research provide additional support for a biological basis in SLI.

SLI and Brain Regions

Brain imaging studies have helped to illuminate cerebral areas of abnormality in individuals with SLI. Several studies have reported a decrease in the size of left hemisphere language structures (Gauger, Lombardino, & Leonard, 1997), generally reduced brain size (Preis, Jäncke, Schitter, Huang, & Steinmetz, 1998), or reversal of normal leftward asymmetry (Plante, Swisher, Vance, & Rapcsak, 1991; Jackson &

Plante, 1996; Herbert et al., 2005). There are exceptions to these findings. Preis et al. (1998) examined children with and without oral language impairments and did not find group differences in planar asymmetry. Herbert et al. (2003) found enlarged instead of reduced brain size in oral language-impaired children. Herbert et al. (2004) later found that this enlargement in brain size was attributed to a specific increase in intrahemispheric fiber pathways.

Foundas and colleagues (Foundas, 1995; Foundas, Leonard, Gilmore, Fennell, & Heilman, 1994; Foundas, Leonard, Gilmore, Fennell, & Heilman, 1996) showed anatomical asymmetries of the pars triangularis (PTR) and pars opercularis (POP) in the language-related cortex (Broca's area) to be associated with language laterality dominance in normal controls based on Wada tests. Moffat, Hampson, and Lee (1998) showed similar results based on dichotic listening tests. MRI and autopsy research shows the language region in the inferior frontal cortex (Broca's area) in right-handed typically developed individuals to be larger in the left hemisphere than in the right (Foundas, 1995; Foundas, Leonard & Heilman, 1995; Foundas, Eure, Luevano, & Weinberger, 1998; Watkins et al., 2001; Zetsche et al., 2001). Contrasting this, research with individuals who have developmental language disorders demonstrates either reduced or reversed asymmetry patterns in the language areas. For instance, in children with SLI, the pars triangularis of the inferior frontal cortex in the left hemisphere is smaller than in controls (Gauger et al., 1997). In addition, adults with developmental language disorders have an inferior frontal gyrus that often includes an extra sulcus when compared to typical controls (Clark & Plante, 1998).

Watkins et al. (2002) reported both speech- and motor-related brain region abnormalities in SLI-affected and unaffected individuals from the KE family and normal controls. SLI-affected probands had significantly different amounts of grey matter when compared with non-affected groups. Several regions, including the caudate nucleus, were abnormal bilaterally. In the SLI participants, the volume of the caudate nucleus was reduced bilaterally, most notably in the superior portion. In addition, the volume of the caudate nucleus was significantly correlated with the performance of affected SLI individuals on a test of oral praxis, a test of non-word repetition, and the coding subtest of the Wechsler Intelligence Scale. Findings such as this demonstrate the brain-behavior relationship in SLI individuals.

SLI and Genes

Even though SLI seems to run in families and specific brain regions appear to be affected, most pedigrees do not connect the disorder to a single gene (Bishop et al., 1999). The international SLI Consortium (2002) conducted the first SLI genome screen. The study included 98 families. Linkage analysis showed significant evidence for SLI phenotype linkage to 16q24 and 19q13. The SLI Consortium (2004) conducted a follow-up study with 86 different families and the 16q and 19q loci linkages were both replicated. Bartlett et al. (2002) conducted a study with five extended SLI families. Findings demonstrated evidence for linkage to 13q21 and suggested evidence for linkage to 2p22. A follow-up study (Bartlett et al., 2004) with a different sample of families replicated the linkage to chromosome 13, but linkage to the chromosome 2 locus was weak (Bartlett et al., 2004). In addition, O'Brien, Zhang, Nishimura, Tomblin, and

Murray (2003) found strong association of SLI to a marker on 7q31 in SLI children and their family members.

In order for molecular geneticists to make further progress in understanding the genes underlying SLI, researchers must first gain a stronger understanding as to which genes are heritable. Twin studies have been helpful in beginning to distinguish genetic influences from environmental influences. For example, Bishop et al. (1999) examined auditory processing and nonword repetition, which is considered an index of phonological short-term memory, in SLI twins. Findings indicated that SLI children had impairments on both measures, but these deficits had different origins. There was no evidence of genetic influence on auditory processing difficulties, but trouble with nonword repetition tasks was highly heritable. Given this information, SLI genetic studies may benefit from the use of measures targeting the underlying cognitive processes tapping into the behavioral phenotype, rather than using conventional psychometric definitions of disorder. Knowledge of these SLI cognitive factors will lead researchers toward a better understanding of how the associated genes operate (Bishop, 2002). This understanding may lead researchers to shift from relying on the DSM's categorical criteria, which is the current gold standard for identifying and grouping individuals, to focusing on disorders as more dimensional in nature.

SLI: Category or Continuum

A strongly debated question is whether SLI is a distinct disorder or on the tail end of a normal distribution for language ability. Currently, diagnosticians treat SLI as a categorical disorder. However, SLI is diagnosed based on quantitative test scores using cut-offs to distinguish normality from disorder. These cut-offs are both arbitrary and

unreliable (Cole, Schwartz, Notari, Dale, & Mills, 1995). In order to reveal SLI causes, it is necessary to look at both environmental and genetic influences, as well as the effects of their interactions. These factors will give researchers a clearer view of the SLI phenotype, which will in turn reveal the nature of the disorder: that is, to illuminate whether SLI is truly a categorical disorder or part of a continuum (Bishop, 2001).

Rationale for the ASD Comparison Group

The genetic involvement in ASD has been well documented both through twin studies and in researching the broad autism phenotype (BAP). In addition, there appear to be overlapping groups between the SLI and ASD disorders. For this reason, the current researchers plan to compare SLI and ASD groups. First, for a better understanding of ASD, the background and research on these topics, including psychological features, social features, and biological features, will be discussed.

Psychological Features of ASD

ASD describe a spectrum of disorders, which includes deficits in reciprocal social interaction skills, communication skills, and the presence of stereotyped behaviors, interests, and activities. The behaviors exhibited by individuals with ASD are unusual relative to developmental level. These atypical behaviors usually appear within the first few years of life. ASD encompass autistic disorder, Asperger's disorder, and pervasive developmental disorder not otherwise specified (PDD-NOS; APA, 2000).

ASD Diagnostic Criteria

Autistic disorder. Autistic disorder is characterized by developmental impairments in social interaction, communication, and range of interests and activities. The expression of the disorder varies greatly. Autism is a lifelong disorder. Over time,

the nature of symptoms may fluctuate, abate, change, and even disappear (APA, 2000; Dahl, Cohen, & Provence, 1986).

Asperger's disorder. Asperger's disorder is characterized by impairments in social interaction and a restrictive repertoire of interests and activities. The main distinguishing factor from autistic disorder is the typical development of language and communication skills aside from appropriate social communication (APA, 2000).

Pervasive developmental disorder not otherwise specified (PDD-NOS). PDD-NOS is a category used to denote an individual with marked impairments in reciprocal social interactions. The social impairment must be present in combination with either impaired communication skills or the presence of stereotyped, restrictive, or repetitive interests. This diagnosis is given when full criteria are not met for one of the specific pervasive developmental disorders, schizophrenia, or a personality disorder (APA, 2000).

Epidemiology/Course of ASD

ASD are lifelong neurological disorders and typically appear within the first three years of life. Autism is four times more likely to occur in males than in females (Kerrell, 2001). However, the male-to-female ratio decreases when greater degrees of cognitive impairment are present (Fombonne, 2005; Nicholas et al., 2008). The APA (2000) reported ASD rates to be 5 cases per 10,000 individuals based on epidemiological studies and reported rates to range from 2 to 20 per 10,000 individuals. However, the Center for Disease Control and Prevention recently reported the prevalence to be approximately 1 in 150 (Autism and Developmental Disabilities Monitoring Network et al., 2007). In addition, current estimates of relative risk in full siblings is now as high as 100 times that

of the general population (Pennington, 2002; Plomin, DeFries, McClearn, & Rutter, 1997)

Clearly, there has been a considerable rise in reported cases of ASD over the past few decades. This change in rates indicates a considerable rise in the incidence of these disorders. Many have suggested that the increase may be due to *in utero* or soon-after-birth environmental exposure to immunizations or toxins. However, there are not currently data to support this belief. Others argue that the increase is most likely due to factors related to higher rates of children receiving ASD diagnoses. Some of these factors include the broadening of the definition of autism, the increased demand and availability for ASD services, and physicians', teachers', and parents' increased awareness of ASDs (Bruey, 2004; Mash & Barkley, 2006). Unfortunately, it continues to be unclear whether higher reported rates are the result of changes in methodology or a true increase in the frequency of the disorder (APA, 2000). It is possible that a true increase in incidences along with more frequent use of ASD diagnoses are interacting, resulting in the extreme rise in prevalence rates (Mash & Barkley, 2006).

Folstein and Rutter (1977a, b) were some of the first researchers to propose the idea of a genetic basis in autism, based on findings from their twin study. These data demonstrated high rates of cognitive deficits, including reading and spelling deficits and language delays, in MZ co-twins of individuals with autism.

It is now clear that genetic links to autism exist (Hollander, King, Delaney, Smith, & Silverman, 2003). Based on several studies, the concordance rates for MZ twin pairs range from 36 to 91% (Bailey et al., 1995; Folstein & Rutter, 1977a, b; Steffenburg et al., 1989), and heritability estimates are above 90% (Bailey et al., 1995). MZ and DZ twin

studies clearly show that if a MZ twin has autism, the likelihood of autism or other neurodevelopmental difficulties affecting language and social interaction in the co-twin is greatly increased. In DZ twins, the risk for autism or neurodevelopmental difficulties is considerably lower than MZ twins (Bailey et al., 1995; Folstein & Rutter, 1977a, b).

Comorbidity in ASD

ASD often occur in combination with other developmental disorders, syndromes, and specific diseases. Mental retardation (MR) is the most common co-occurring condition, presenting in approximately 75% of cases (Bailey, Philips, & Rutter, 1996). Other frequent problems include epilepsy, tuberous sclerosis, motor incoordination, and severe allergies (APA, 2000; Ritvo et al., 1990). Sometimes, general medical conditions such as chromosomal abnormalities (e.g., fragile X), congenital infections, and central nervous system abnormalities are present (APA, 2000). As individuals with ASD reach adolescence, they are at risk for developing anxiety or depression, most likely due to difficulty in social situations (Freeman, 1997).

Some disorders share certain similar features with ASD but cannot co-occur with autism. For example, expressive and receptive language disorders involve language impairment, but unlike the ASD, they are not associated with qualitative impairment in social interaction and restricted, repetitive, and stereotyped behavior patterns (APA, 2000). Overactivity and inattention are frequent impairments present in ASD, but the DSM-IV-TR is ambiguous on whether a diagnosis of ADHD can be made if autism is present (APA, 2000). Recent research, however, indicates that the co-occurrence of clinically significant ADHD and ASD is common (Reiersen & Todd, 2008).

Social Features of ASD

Even though early researchers were not looking for a genetic basis in autism, they noted specific characteristics in parents. Kanner and Eisenberg (1957) reported many parents of children with autism to be perfectionists who had intensive interests in abstract ideas and lacked interest in developing close relationships with others. Sadly, these observations were misinterpreted to mean that particular personality characteristics combined with child-rearing practices resulted in autism. Several follow-up studies focusing on parent-child interactions consistently failed to support the hypothesis that certain parenting strategies could result in autism (Cantwell, Baker, & Rutter, 1976). Current research is providing evidence that suggests certain behavioral characteristics occur more frequently in the relatives of persons with autism than in the general population (Piven, Palmer, Landa, et al., 1997).

BAP

The BAP refers to the finding that relatives of individuals with ASD often have mild forms of autistic-like characteristics. These features include a set of subclinical personality characteristics and other behavioral deficits and excesses thought to index familiarity and/or genetic liability to autism (Lainhart et al., 2002). Several studies support the BAP idea, showing that relatives often experience communication problems, social difficulties, and stereotyped behaviors (Bishop et al., 2004; Bolton et al., 1994). These findings indicate that mild forms of autistic-like symptomology may occur in relatives of individuals with ASD (Bailey, Palferman, Heavey, & Le Couteur, 1998; Bradford et al., 2001; Landa et al., 1992; Yirmiya & Shaked, 2005). While a disturbance in parental behavior may be in response to the stress associated with raising an autistic

child (Wolf, Noh, Fisman, & Speechley, 1989), evidence for genetic involvement is extremely high (Rutter, 1991a). It is probable that some unusual features reported in parents of autistic children reflect the difficulties of raising a handicapped child, while other features represent a subtle expression of autistic traits.

Studies assessing relatives of individuals with ASD show familial difficulties in communication, socialization (MacLean et al., 1999; Silverman et al., 2002), and repetitive behaviors (Folstein et al., 1999; Silverman, et al., 2002; Spiker et al., 1994). A classic study by Bolton et al. (1994) compared families of individuals with autism to families of individuals with Down's syndrome. The findings indicated a broad phenotype in 20% of autism siblings as compared with only 3% of Down's syndrome siblings. Piven, Palmer, Jacobi, Childress, and Arndt (1997) furthered this research by including aunts, uncles, and grandparents in addition to parents of individuals with autism. Findings indicated that relatives had higher levels of social deficits, communication deficits, and repetitive behaviors than Down's syndrome parent controls. Several other family history studies report similar results (DeLong & Dwyer, 1988; Gilberg, 1989; Piven et al., 1991). A study by Szatmari et al. (1995), however, was unsuccessful in detecting personality characteristics, speech, or conversation skill differences in parents of individuals with ASD. These differences may be due in part to ASD being a more broadly defined condition than autism. ASD are both more common in the population and more likely to be etiologically heterogeneous than autism alone.

Several studies have suggested that in addition to the BAP, psychological disorders in the relatives of individuals with ASD occur at higher than expected rates. Researchers have found more depression and anxiety in relatives of individuals with

ASD. In addition, there appear to be higher rates of developmental and cognitive problems in comparison to control groups (Bolten, Pickles, Murphy, & Rutter, 1998; Micali, Chakrabarti, & Fombonne, 2004; Piven et al., 1990; 1991; Piven & Palmer, 1999; Smalley, McCracken, & Tanguay, 1995).

Biological Features of ASD

As previously stated, Folstein and Rutter (1977a, b) were some of the first researchers to propose the idea of a biological basis in autism based on findings from their twin study. As researchers have begun to look more closely at communication and social interaction difficulties in parents, siblings, and second-degree relatives of individuals with autism, evidence continues to point toward a biological basis for ASD. This suggests biological mediation between parents and their children with autism (Bishop et al., 2004).

ASD and Brain Regions

Cognitive testing combined with brain imaging allows researchers the opportunity to study brain behavior relationships in ASD. An early consistent finding in the neuropathology of autism has been decreased cerebellar volume (e.g., cerebellar hypoplasia) in ASD individuals when compared to typical controls (Bauman & Kemper, 1990; Courchesne, Yeung-Courchesne, Press, Hesselink, & Jernigan, 1988, Courchesne et al., 1994). Research has also indicated that persons with ASD show altered patterns of brain activity. For example, autistic individuals' brains showed significantly less brain activity in the frontal and parietal areas during a visual search task than controls. The Eyes Test, an emotion recognition test, elicited three areas (superior temporal sulcus (STS), left inferior frontal cortex, and amygdala) in a control group, whereas the autism

group showed significantly less activity in both the inferior frontal cortex and the amygdala (Baron-Cohen et al., 1999; Manjaly et al., 2003; Ring et al., 1999). These studies add important information to the theories of autism. Both brain activity and participant performance during tests assessing weak central coherence (referring to an individual's information processing bias of focusing on parts or details rather than the whole or gestalt) and theory of mind (referring to an individual's ability to take the perspective of others) demonstrate significant differences from controls (Dennett, 1978; Happé, Briskman, & Frith, 2001).

Language impairments are an inherent component of the theories of autism and represent a core deficit in ASD individuals (De Fossé et al., 2004). Some researchers have indicated language region abnormalities, including Broca's area, in autism. Abell et al. (1999) reported autistic adults as having decreased gray matter density in Brodmann area 45 (BA45) in the left inferior frontal gyrus. In addition, Herbert et al. (2002) observed rightward volumetric asymmetry of inferior frontal cortex pars opercularis in right-handed school-aged autistic children, which contrasted leftward asymmetry in a right-handed control group. De Fossé et al. (2004) reported asymmetry reversal of frontal language cortex in males with autism.

ASD and Genes

Given twin studies, information on the BAP, and brain imaging research, it is difficult to deny that genetic links to autism are present (Hollander, King, Delaney, Smith, & Silverman, 2003). As with virtually all of the behaviorally defined disorders, the mode of transmission is complex (Pennington, 2002). Some results from several molecular studies have emerged, although none are definitive (Lamb, Moore, Bailey, &

Monaco, 2000). Currently the strongest linkage finding for ASD is for a locus on chromosome 7q (International Molecular Genetic Study of Autism Consortium, 1998). This finding has now been replicated several times (Lamb et al., 2000). In addition, preliminary linkage results report loci on chromosomes 1p, 2q, 6q, 13q, 16p, 18p, and 19q (Lamb et al., 2000). Several of these linkages have been replicated, but further study is required.

As with SLI, most pedigrees do not connect ASD to a single gene. For progress to be made in understanding the genes underlying ASD, researchers must gain a better understanding of the genes that are heritable. This understanding could prompt researchers to look at multiple genetically related disorders as part of a dimension rather than distinct categories (Bishop, 2002).

ASD: A Spectrum of Disorders

The term *spectrum disorder* refers to the broad range of expression of a particular disorder or disorders along a hypothetical continuum of pervasiveness and severity (Freeman, 1997). Children with ASD can present with varying symptoms at any point along the continuum. The manifestation of symptoms can range from mild to severe. Social, communication, and behavioral impairments vary in category and severity (Freeman, 1997). Dahl et al. (1986) suggest that the ASD groups differ mainly in the degrees of impairment. For example, social impairments and restrictive or repetitive behaviors, interests, or activities are common to both autistic disorder and Asperger's disorder.

Any particular individual with ASD is likely to have various symptoms present along different points on the continuum (Cohen, Paul, & Volkmar, 1986). A child with

profound MR and multiple other handicaps, who displays a rather consistent pattern of profound impairments throughout the intellectual, adaptive, social, language, and motor functioning domains, falls at the most pervasive end of the continuum. Children at the least pervasive end of the continuum typically show impairments in only one domain (Mash & Barkley, 2006). Children with ASD fall at a variety of points between the two extremes. These children show uneven patterns of impairments across many of the domains. There are two large, overlapping ASD subgroups differing in developmental categories. Generally, one group has lower intelligence levels, significant motor stereotypes, sensory abnormalities, and severely impaired language and imitation skills. The second group tends to have higher intelligence, communicative speech that may include peculiar features and atypical prosody, and persistent perseverative behaviors (Stevens et al., 2000; Waterhouse et al., 1996). This second group may border on and in some cases overlap with many of the characteristics seen in severe SLI individuals.

Chapter 3: Overlap Between SLI and ASD

It can be difficult to distinguish ASD and SLI as many children fall into an overlapping group. The ASD and SLI groups share similar symptoms (Botting & Conti-Ramsden, 2003). For example, language functioning deficits are often an observed aspect of communication impairments in autism. Difficulties may vary from limited functional communication, to difficulties with phonological processing, vocabulary, syntax, and semantics (Lord & Paul, 1997; Tager-Flusberg, 2003). Kjelgaard and Tager-Flusberg (2001) conducted a large-scale study focusing on language in a heterogeneous group of autistic children. Findings indicated that the autistic group with impaired language skills had similar profiles to children with SLI.

A subgroup of children who fall between the ASD and SLI diagnostic groups have often been noted in the literature (Bishop, 1998; Bishop & Norbury, 2002; Botting & Conti-Ramsden, 1999). Botting and Conti-Ramsden (2003) have referred to this group of children as having primary pragmatic language impairment (PLI). These children are generally talkative and can produce complex sentences, but usually with errors. Unfortunately, they have poor comprehension of functional communication. For example, they have difficulties with turn-taking, have poor understanding of roles, are limited in their conversational topics, lack sensitivity with regard to social cues, and have a tendency to give inappropriate amounts of information.

Recent literature has emphasized three psycholinguistic tasks that denote language impairment. These tasks include non-word repetition, past tense knowledge, and sentence repetition. Using this information, Botting and Conti-Ramsden (2003) examined three groups of children with communication disorders including SLI, ASD,

and PLI groups. These researchers used a series of psycholinguistic markers in order to discover if certain tasks could identify children with varying language impairments and distinguish specific group membership. From their analysis, four groups emerged including the ASD group, the SLI group, and two distinct PLI groups. The two PLI groups consisted of a “pure” group and a PLI group with some autistic-like behaviors. The PLI “pure” group was characterized by severe pragmatic language and linguistic difficulties but did not present with autistic traits. The PLI group with some autistic-like behaviors included characteristics such as narrow interests, obsessions, and social difficulties but did not present with the linguistic difficulties found in the other three groups.

Group comparisons revealed that the SLI group scored significantly lower on the Children’s Non-Word Repetition (CNRep) than the other groups. In addition, data analysis showed that the PLI with autistic-like behaviors group could be accurately distinguished from the other groups as this group scored best on overall communication markers and performance IQ scores. Another interesting finding involved the CELF-P Recalling Sentences measure. This measure has been shown to efficiently discriminate SLI children. Botting and Conti-Ramsden (2003) revealed that Recalling Sentences may also be helpful in identifying other disorders involving communication impairments such as ASD as well as assisting in discriminating level of impairment within this group. Finally, these researchers noted that non-word repetition did not accurately identify either the PLI group or ASD group using any threshold, regardless of marked communication difficulties. This suggests different underlying mechanisms for the PLI and ASD groups than the SLI group.

Researchers investigating similarities and differences in SLI and ASD proband brain regions have produced interesting results. The planum temporale, including the ascending part bordered by the posterior ascending ramus, was larger in the right hemisphere for SLI children and larger on the left in a typical control group (Gauger et al., 1997). In adults with autism, left planum temporale was reduced in volume when compared with typical adults (Rojas, Bawn, Benkers, Reite, & Rogers, 2002). Herbert et al. (2002) focused on volumetric symmetry with a group of autistic children and found that their planum temporale had more extreme leftward asymmetry, with larger volume in the left hemisphere, than normal controls. Other research suggests posterior superior temporal abnormalities in both SLI and autism. For example, Plante et al. (1991) show SLI males as having atypical perisylvian asymmetries due to a larger right perisylvian area when compared to normal controls. Salmond, de Haan, Friston, Gadian, and Vargha-Khadem (2003) reported structural abnormalities in the amygdala in approximately half of the autistic children in their study, which highlights the heterogeneity present in autistic individuals (Aylward et al., 1999; Howard et al, 2000). De Fossé et al. (2004) added to these results with the finding that language impaired males with autism and SLI both have significant reversal of asymmetry in the frontal language-related cortex. Regions were larger on the right side for both language impaired groups, while in the unimpaired language groups' brain regions were larger on the left side. These findings strengthen evidence for a phenotypic link between SLI and ASD language-impaired individuals. In addition, findings suggest that Broca's area asymmetry reversal may be more highly related to language impairment than to a specific autism diagnosis.

The similar language impairments combined with similar brain abnormalities in individuals with ASD and SLI suggest possible genetic links (De Fossé et al., 2004). There are strong genetic bases for both ASD and SLI (Fisher, Lai, & Monaco, 2003; Santangelo & Folstein, 1999). As previously discussed, both family and twin studies show first-degree relatives of SLI probands to have higher levels of language skills deficits than the general population (Fombonne, Bolten, Prior, Jordan, & Rutter, 1997; Folstein et al., 1999; Bailey et al., 1995). In addition, siblings of ASD individuals are at higher risk for developing autism than the general population (Tomblin, Hafeman, & O'Brien, 2003).

Even though SLI often co-occurs with dyslexia, most of the common genetic effects appear to be with ASD language characteristics rather than dyslexia and related disorders (Smith, 2007). Genetic linkage studies suggest that there are overlapping regions on chromosome 7q (Barret et al., 1999; O'Brien et al., 2003) and chromosome 13q (Barrett et al., 1999; Bartlett et al., 2002) in SLI and ASD. In ASD genetic studies, loci on both chromosomes 7q and 13q significantly increase when linkage analyses are limited to ASD families with apparent language impairments (Alarcon, Cantor, Liu, Gilliam, & Geschwind, 2002; Bradford et al., 2001). Findings such as these propose that genetic abnormalities leading to developmental language disorders phenotype (Fisher, Lai, & Monaco, 2003) might overlap with the genetic alterations, which are liability factors for autism (De Fossé et al., 2004).

Diagnosing SLI versus ASD

In clinical practice, different professionals often give children who do not meet straightforward diagnostic criteria for SLI or ASD varying labels. This problem is

heightened by the lack of known diagnostic markers. Professionals diagnose these children by the exclusion of other possibilities instead of identification of certain characteristics the children possess (Botting & Conti-Ramsden, 2003).

Chapter 4: Endophenotype Description

Discovering genetic determinants of complex brain-related disorders is crucially important. The genetic and phenotypic complexity has hampered the search for genes predisposing individuals to particular illnesses and therefore has led researchers and clinicians to rely on qualitative diagnostic systems (Glahn, Thompson, & Blangero, 2007), which is the case for SLI and ASD. Endophenotypes are emerging as important concepts in the study of complex neuropsychiatric diseases (Gottesman & Gould, 2003). Endophenotypes are indicators of processes mediating between genotype and phenotype (Glahn et al., 2007). They may be neurophysiological, biochemical, endocrinological, neuroanatomical, cognitive, or neuropsychological in nature. Endophenotypes represents straightforward clues to the genetic underpinnings of a disorder (Gottesman & Gould, 2003). They are genetically correlated markers with disease liability and can be measured in all individuals (Glahn et al., 2007). Given this, endophenotypic information can provide assistance in genetic analysis. In turn, they can assist in clarifying classification and diagnosis of a particular disorder as well as helping to resolve questions about etiological models. Outcomes of endophenotypic analysis would include stronger understanding in relation to psychopathology, neurobiology, and genetics (Gottesman & Gould, 2003). In addition, new insights into biological mechanisms predisposing individuals to particular illnesses may lead to new therapies, thereby reducing the burden and improving lives of affected individuals (Glahn et al., 2007).

Endophenotype Clinical Implications

Rutter (1991a, b) addresses the numerous misconceptions regarding genetic disorders and the resulting implications for treatment outcome. Clinicians often assume

genetic disorders are unwavering and untreatable. This is a misconception. Once the genes underlying a disorder are understood, many possibilities arise. For example, biological treatments become a feasible possibility, and behavioral interventions can be extremely effective. Opposing popular belief, genes do not limit potential. This is because environment plays a large and important role. For example, in populations where individuals contact different environmental experiences, there is likely to be lower heritability than in a more uniform environment. When evidence shows limited natural environmental influence on the language skills, making a difference requires the development of specific interventions to target the underlying problems (Bishop, 2001). In dimensional disorders, it is important to remember that each of the impairments can occur in widely varying degrees of severity and take many different forms (Wing & Potter, 2002). As such, researchers recommend clinicians treat the differing groups along a range that may require different treatment approaches.

Chapter 5: Study Purpose

As seen, there is currently a great deal of evidence that genes are involved in the etiology of SLI and ASD. However, a specific gene does not connect most cases. Before molecular genetics can make additional progress, researchers need a stronger understanding of the heritable SLI and ASD characteristics. Further progress in revealing the role genes play in the underlying causes of these disorders is limited without a strong understanding of the SLI and ASD endophenotypes (Bishop, 2001; Bishop, 2002). The goals of the current study were to illuminate factors involved in the SLI and ASD neuropsychological endophenotypes and clarify the nature of overlap between SLI and ASD.

Specific Aim I

Examine group differences with respect to cognitive functioning (academic, motor, perceptual-motor, memory, and attention/executive functioning) in participants with SLI and ASD. In addition, examine qualitative information on pragmatic speech and language functioning.

Hypothesis 1

It was hypothesized that four distinct profiles based on group differences from the SLI and ASD groups would emerge, including a mild-moderate SLI group, a severe SLI group, a mild-moderate ASD group, and a severe ASD group.

Specific Aim II

Examine group differences with respect to comorbid psychopathology rates and health problems in SLI and ASD participants in order to identify potential endophenotypic subtypes.

Hypothesis 1

It was hypothesized that the SLI participants would have higher rates of learning disorders, ADHD, and autoimmune disorders. It was hypothesized that the ASD participants would have higher rates of MR/global developmental disorder (GDD)/developmental disorder (DD).

Specific Aim III

Determine parental education levels, parental occupations, and the frequency of psychopathology in first-degree relatives of participants with SLI and ASD in order to identify potential endophenotypic subtypes for subsequent genetic linkage or association studies.

Hypothesis 1

It was hypothesized that parental education levels of SLI and ASD participants would be similar.

Hypothesis 2

It was hypothesized that the parental occupations of SLI and ASD participants would be similar.

Hypothesis 3

It was hypothesized that SLI participants' first degree maternal and paternal relatives would have higher rates of SLI, ADHD, and learning disorders. It was hypothesized that ASD participants' first degree maternal and paternal relatives would have higher rates of anxiety disorders, mood disorders, ASD, MR, and epilepsy.

Specific Aim IV

Based on the aforementioned results, cognitive functioning, pragmatic speech and language functioning, and comorbid diagnosis in mild-moderate SLI, severe SLI, mild-moderate ASD, and severe ASD participants, as well as psychopathology in first degree relatives, parental education levels, and parental occupations were examined in predicting group membership. The aim was more exploratory in nature.

Hypothesis 1

Factors were combined to predict group membership to diagnostic group (SLI or ASD) and severity level (mild-moderate or severe).

Chapter 6: Method

Participants

Participants included children with SLI (N = 39, 28 males; Mean age = 6.63 years) and ASD (N = 89, 70 males; Mean age = 6.35 years) who presented for clinical evaluation at Henry Ford Health System, Detroit, Michigan, between 1997 and 2005 due to developmental delay and to assist in diagnosis. Inclusion criteria for participants with SLI required a diagnosis of either expressive language disorder or mixed receptive-expressive language disorder and a standardized speech and language score one standard deviation below their standardized measure of nonverbal intellectual capacity/receptive language development (APA, 2000). Inclusion criteria for participants with ASD required an autistic disorder, Asperger's disorder, or PDD-NOS diagnosis based on the DSM-IV-TR (APA, 2000) and/or a Child Autism Rating Scale Score (CARS) of ≥ 30 (Schopler, Reichler, & Renner, 1998). All ethical guidelines related to conducting research with human subjects, as outlined by the American Psychological Association (2002), were followed (see Appendices A and B).

SLI and ASD participants were divided into severity level groups. These groups included a mild-moderate SLI group, a severe SLI group, a mild-moderate ASD group, and a severe ASD group. The mild-moderate SLI group was defined by speech scores 1 to 2 standard deviations below the mean, while the severe SLI group was defined by speech scores greater than 2 standard deviations below the mean (Zimmerman, Steiner, & Pond, 1992). The mild-moderate ASD group was defined by an existing CARS rating of 30 to 35. The severe ASD group was defined by an existing CARS rating of ≥ 36 (Schopler et al., 1998). For ASD participants without a CARS score, a predicted score

based on their full scale intelligence quotient (FSIQ) was computed. First, bivariate correlation between FSIQ and existing CARS scores was computed. Subsequent regression equations were then conducted to predict the CARS for participants with missing scores. If the predicted CARS score ranged from 30 to 35 and the participant had a PDD-NOS or Asperger's disorder diagnosis, the participant was placed in the mild-moderate ASD group. If the predicted CARS score was ≥ 36 and the participant had an autistic disorder diagnosis, the participant was placed in the severe ASD group.

Neuropsychological Procedures/Protocol

Each participant underwent a comprehensive neuropsychological/developmental battery. The testing was performed by a clinical neuropsychologist, postdoctoral fellow in neuropsychology, or master's level psychologist. Diagnosis was based on DSM-IV-TR clinical criteria (APA, 2000) and the CARS when available (Schopler et al., 1988). Data were obtained by retrospective chart review. In addition, information that had been provided by parents on the child's historical data as well as paternal and maternal level of education, occupation, and history of psychopathology was retrieved from the database or child's clinical chart.

Procedures/Protocol

Cognitive Testing/Surveys. Participants underwent neuropsychological testing, which included assessments of intellectual/cognitive, speech and language, academic, motor, perceptual-motor, memory, and attention/executive functioning. In addition, parent, teacher, and self-report measures were used to assess social and emotional functioning. Table 1 lists the general domains sampled and the measures employed (Boston Naming Test; Kaplan, Goodglass, & Weintraub, 1983; BSID-2; Bayley, 1993;

CARS; Schopler et al., 1988; CELF; Semel, Wiig, & Secord, 2003; Grooved Pegboard; Tiffin, 1968; Leiter-R; Roid & Miller, 1997; Mullen Scales of Early Learning; Mullen, 1995; NEPSY; Korkman, Kirk, & Kemp, 1998; PLS-3; Zimmerman et al., 1992; PPVT-III; Dunn & Dunn, 1997; SB-4; Thorndike, Hagen, & Sattler, 2003; TOKEN; DiSimoni, 1978; TOMAL; Reynolds & Bigler, 1994; VMI-4; Beery, 1997; WCST; Heaton, Chelune, Talley, Kay, & Curtis, 1993; WISC-III; Wechsler 1991; WJ-III; Woodcock, McGrew, & Mather, 2001; WPPSI-R; Wechsler, 1989; WRAT-3; Wilkinson, 1993 (see Footnote 1)).

Table 1

General Domains Sampled and Measures Employed

General Domain	Test(s) of	Source
Intellectual/Cognitive	<ul style="list-style-type: none"> • Bayley Scales of Infant Development 2nd Ed. (BSID-2) • Leiter International Performance Scale, Revised (Leiter-R) • Mullen Scales of Early Learning • Stanford-Binet Intelligence Scale, 4th ed. (SB-4) • Wechsler Intelligence Scale for Children-III (WISC-III) • Wechsler Preschool and Primary Scale of Intelligence, Revised Ed. (WPPSI-R) 	

¹ Full descriptions of acronyms are in Table 1.

General Domain	Test(s) of	Source
Speech & Language		<ul style="list-style-type: none"> • Boston Naming Test • Clinical Evaluation of Language Fundamentals (CELF) • Developmental Neuropsychological Assessment (NEPSY): Language Domain • Peabody Picture Vocabulary Test 3rd Ed. (PPVT-III) • Preschool Language Scale 3 (PLS-3) • Token Test for Children (TOKEN)
Academic	Reading	<ul style="list-style-type: none"> • Composite: Wide Range Achievement Test-3 (WRAT-3) Word Reading Subtest / Woodcock Johnson Psycho-Educational Battery Test 3rd Ed. (WJ-III) Letter-Word-Identification Subtest
	Spelling	<ul style="list-style-type: none"> • Composite: WRAT-3 Spelling Subtest / WJ-III Spelling Subtest
	Mathematics	<ul style="list-style-type: none"> • Composite: WRAT-3 Math Computation Subtest / WJ-III Calculation Subtest
Motor		<ul style="list-style-type: none"> • Grooved Pegboard (Dominant) • Grooved Pegboard (Nondominant)
Perceptual-Motor		<ul style="list-style-type: none"> • The Beery-Buktenica Developmental Test of Visual-Motor Integration 4th Ed. (VMI-4)
Memory	Verbal Memory	<ul style="list-style-type: none"> • Test of Memory and Learning (TOMAL): Memory-for-Stories (MFS) Subtest • TOMAL: Word Selective Reminding (WSR)
	Visual Memory	<ul style="list-style-type: none"> • TOMAL: Facial Memory (FM) Subtest • TOMAL: Visual Selective Reminding (VSR) Subtest
Executive Functioning & Attention	Executive Functioning	<ul style="list-style-type: none"> • Wisconsin Card Sorting Test (WCST): Conceptual Level • WCST: Perseverative Responses

General Domain	Test(s) of	Source
	Visual Attention	• NEPSY: Visual Attention Domain
	Auditory Attention	• NEPSY: Auditory Attention and Response Set Domain

Data Analysis

Exploration of the Neuropsychological Data

Parametric tests were used to explore the neuropsychological data. Parametric tests are based on four basic assumptions, which must be met to be accurate. First, it is assumed that the data are from normally distributed populations. Second, homogeneity of variance, which means that the variances are the same throughout the data, is assumed. Third, it is assumed that interval data are measured at the interval level (meaning that the distance between points on an interval scale is equal at all parts along the scale). Fourth, the data from each participant are independent. Normality and homogeneity were formally tested. The following measures were used to test the assumption of normally distributed data and homogeneity of variance (Field, 2005).

Testing for normally distributed data. Testing for normality involved two main steps. Step 1 consisted of completing an examination of the distributional qualities of the neuropsychological data. Histograms for the neuropsychological domain scores/composites were generated. This allowed for examination of distributional differences and identification of potential outliers. Step 2 consisted of exploring the distribution of the variables further by generating descriptive statistics and boxplots, including values of kurtosis and skewness. In addition, the Kolmogorov-Smirnov and

Shapiro-Wilk tests were run to determine whether each distribution deviated from comparable normal distributions (Field, 2005).

Testing for homogeneity of variance. Homogeneity of variance within the neuropsychological data was tested using Levene's test. Levene's test examines whether the variances in groups are equal. When Levene's test is not significant (i.e., $p > .05$) the difference between the variances is zero, meaning the variances are nearly equal and the assumption of homogeneity of variance is reasonable. When Levene's test is significant ($p \leq .05$), then the variances are significantly different, meaning that the assumption of homogeneity of variances has been violated (Field, 2005).

Formal Test of Specific Aim I

The goal of specific aim I was to examine group differences with respect to cognitive functioning (academic, motor, perceptual motor, memory, and attention/executive functioning) and qualitative pragmatic speech and language data in participants with SLI and ASD.

Hypothesis 1: neuropsychological data. MANOVAs and ANOVAs were used to test the difference between diagnostic group (SLI or ASD) and severity level (mild-moderate or severe) on domains/composites of academic, motor, perceptual-motor, memory, and attention/executive functioning. Initially, reliability analyses were run on scores within each domain to determine whether to collapse domain scores into one composite. A MANOVA was then run on domains/composites with a reasonable number of subjects in each cell (≥ 7).

Conducting the MANOVA involved three main steps. Step 1 involved examination of the data based on MANOVA assumptions. The MANOVA has four basic

assumptions. First, it is assumed that the data are statistically independent. Second, the data should be randomly sampled and measured at an interval level. Third, it is assumed that the dependent variables, collectively, have multivariate normality within each group. Fourth, homogeneity of variance is assumed for each variable and the correlation between any two dependent variables is the same in all groups. Aside from the assumption of homogeneity of covariance matrices, each assumption will have been explored in the preliminary data analysis. Box's test was used to test the assumption of equality covariance matrices for the MANOVA (Field, 2005).

Once assumptions were met, Step 2 consisted of examining the MANOVA for significance. The MANOVA produces four test statistics (Pillai's Trace, Wilks's Lambda, Hotelling's Trace and Roy's Largest Root). The four tests are the same if there is only one underlying variate, which is uncommon. These test statistics differ if there are multiple underlying variates. For small and moderate sample sizes, the four test statistics are similar in regards to power. When group differences are concentrated on the first variate, Roy's statistic is usually most powerful, followed by Hotelling's trace, Wilks's lambda, and Pillai's trace. However, when groups differ along more than one variate, then the power ordering is the reverse. All four test statistics are comparatively robust to violations of multivariate normality. However, Roy's root is affected by platykurtic distributions and is not robust when the homogeneity of covariance matrix assumption is untenable. When sample sizes are equal, the Pillai-Bartlett trace is the most robust to violations of assumptions, but when sample sizes are unequal, it is affected by violations of the assumption of equal covariance matrices. However, as long as Box's test is non-significant, the assumption is that Pillai's trace is accurate (Field, 2005).

Step 3 involved examination of the residual sum of squares and cross-product matrices (SSCPs). The SSCP is useful for obtaining information on the pattern of the data and for inspecting the cross-products values to indicate dependent variable relationships. The SSCP is also helpful in assessing the extent of the error in the model (Field, 2005).

To follow up the MANOVA, ANOVAs were conducted for each dependent variable within the MANOVA. This is a traditional approach, as ANOVAs that follow a significant MANOVA are hypothetically protected. The overall multivariate test protects against Type I errors, but only for the dependent variable for which group differences exist (Field, 2005).

Following a MANOVA with ANOVAs assumes that the significant MANOVA is due to the dependent variables. It does not take into account that significance may be due to the possibility that the dependent variables may represent a set of underlying dimensions that differentiates the groups. For this reason, discriminant analysis can also follow MANOVAs. Discriminant analysis finds the linear combination or combinations of the dependent variables that best discriminates the groups. This test is helpful in revealing the relationship between the dependent variables and group membership (Field, 2005). For one-way MANOVAs with significant results on multiple dependent variables, a discriminant analysis should be run.

Conducting a discriminant analysis involves four steps. Step 1 consists of analyzing the covariance matrices. The covariance matrices include the variances of each dependent variable for each group. These values are useful as they provide information on the way the relationship between dependent variables changes from group to group.

Step 2 involves examining Wilk's lambda to determine significant variates. Significant variates provide information on any underlying dimensions that result in group differences in the MANOVA. Step 3 consists of examining the standardized discriminant coefficients to determine the relative contribution of each variable to the variates. Additionally, the structure matrix should be looked at to examine the relationship between the dependent variables and discriminant variates. The structure matrix gives the canonical variate correlation coefficients, which indicate the substantive nature of the variates. Step four consists of examining the variate centroid values for each group. The centroids are the mean variate scores for each group. This information further illuminates the relationship between the variates and the groups (Field, 2005).

In addition to the MANOVA, two-way ANOVAs were run on each domain/composite due to sample size issues. A factorial ANOVA is used when two or more independent variables are present. Like MANOVAs, ANOVAs also rely on the assumption of a normal distribution, which is required for all parametric tests. As such, data should be from a normally distributed population, the variables in each experimental condition should be fairly similar, observations should be independent, and the dependent variable should be measured on an interval scale (Field, 2005).

Hypothesis 1: qualitative pragmatic speech and language data. In order to analyze pragmatic language differences between the groups, information on pragmatic speech and language was extracted from the historical data in participants' neuropsychological reports. Based on available information, four dichotomous pragmatic categories were defined and coded based on the absence or presence of any problems in the specified area. Two categories included pragmatic verbal information, and two

categories included pragmatic nonverbal information. The two verbal categories were divided into a verbal communication quality variable and a verbal communication content variable. The verbal communication quality variable consisted of presence or absence of any problems such as intonation, prosody, and affect. The verbal communication content variable consisted of presence or absence of any problems such as echolalia, pallalalia, scripted language, idiosyncratic speech, or repetitive speech, as well as presence or absence of any difficulties such as responding to greetings, initiating conversations, or turn taking in conversations. The pragmatic nonverbal categories were divided into a nonverbal communication withdrawal/isolation variable and a nonverbal communication disruption/aggression variable. The nonverbal communication withdrawal/isolation variable consisted of presence or absence of any problems such as self-stimulatory behaviors, or lack nonverbal social behaviors such as eye contact, joint attention, socially appropriate facial expressions, gestures, or social play. The nonverbal communication disruption/aggression variable consisted of presence or absence of any problems with transitions, inappropriate touching, proxemics (body distance) based on setting, tantrums, or aggressive play/interaction.

Bivariate correlations were used to examine the relationship between diagnostic category (SLI or ASD) and severity level (mild-moderate or severe) with verbal communication quality, verbal communication content, nonverbal communication withdrawal/isolation, and nonverbal communication disruption/aggression. A bivariate correlation is a correlation between two variables conducted to measure the linear relationship between variables (Field, 2005)

Chi-squares were used to follow up the significant severity level correlations in order to examine relationships within each group based on severity level. Pearson's chi-square test is used to examine relationships between two categorical variables. It is a statistic based on comparing observed frequencies in certain categories to the expected frequencies by chance in those categories. Conducting a chi-square test involves five main steps (Field, 2005).

Step 1 of the chi-square test involves examination of the data based on its assumptions. The chi-square test has two basic assumptions. First, for the test to be meaningful, each subject can contribute to only one cell of the contingency table. Second, the expected frequencies should be greater than five. However, in larger contingency tables, 20% of frequencies can be below five, but this results in a loss of statistical power. No expected frequencies should be below one (Field, 2005).

Step 2 involves examination of the chi-square tests to determine any significant relationships. Step 3 involves inspection of the crosstabulation table to explore the nature of the relationship between the variables. Step 4 involves examination of additional statistical tests, which measure the strength of association. These tests included phi, Cramer's V, and contingency coefficient. These statistics are based on modifying the chi-square statistic in order to take account of sample size and degrees of freedom. In addition, they attempt to restrict the range of the test statistic from 0 to 1. When variables have more than two categories, Cramer's V and contingency coefficient are most useful. Finally in Step 5, the odds ratio is used to calculate the effect size, which provides additional information on the strength of association (Field, 2005).

Formal Test of Specific Aim II: Chi-square

The goal of specific aim II was to examine group differences with respect to comorbid psychopathology rates and health problems in SLI and ASD participants in order to identify potential endophenotypic subtypes.

Hypothesis 1. Several chi-squares were used to test comorbid psychopathology rate and health problem differences in the diagnostic groups (SLI and ASD) and severity levels (mild-moderate and severe). Rates of learning disorders, ADHD, autoimmune disorders, health problems, and MR/GDD/DD in each group were examined. Conducting the chi-squares involved the previously described steps.

Formal Test of Specific Aim III: Chi-square

The goal of specific aim III was to determine parental education levels, parental occupations, and the frequency of psychopathology in parents of SLI and ASD participants in order to identify potential subtypes for subsequent genetic linkage or association studies.

Hypothesis 1. Chi-square analyses were used to determine the frequency of the diagnostic groups' parental education levels. Parental education variables included less than 12 years of education, high school diploma or GED, 1 to 4 years of college, and more than four years of college. Mothers and fathers were rated separately. Conducting the chi-squares involved the previously described steps.

Hypothesis 2. Chi-square analyses were used to determine frequency of the diagnostic groups' parental occupations. Parental occupation variables included unemployed, homemaker, self-employed/owner, unskilled, semi-skilled, skilled, business/finance, engineer/science, health care, education, professional, and social

services. Mothers and fathers were rated separately. Conducting the chi-squares involved the previously described steps.

Hypothesis 3. Several chi-squares were used to determine frequency of the diagnostic groups' first-degree relatives' psychopathology. Psychopathology variables included SLI, ADHD, learning disorders, anxiety disorders, mood disorders, ASD, MR, epilepsy, and thought disorders. Conducting the chi-squares involved the previously described steps.

Formal Test of Specific Aim IV: Logistical Regression

Based on the results of the previously described analyses, cognitive functioning and comorbid diagnosis in participants, as well as psychopathology in participants' first degree relatives, parental education, and parental occupation were examined in predicting group membership. This aim was more exploratory in nature.

Hypothesis 1. Logistic regression tests based on results from the previously described analyses were used to predict group membership to the diagnostic groups (SLI or ASD) and severity levels (mild-moderate or severe).

Logistical regression is multiple regression with an outcome variable that is a categorical dichotomy and predictor variables that are continuous or categorical. Essentially, it tests a model or group of variables' ability to predict group membership. This membership is defined by some categorical dependent variable. It predicts the probability, varying from 0 to 1, that membership occurs (Field, 2005; Mertler & Vannatta, 2002).

When conducting logistical regression, SPSS has problems if data are not available for all combinations of variables. Therefore, the data will be checked using crosstabulation tables before running the analysis (Field, 2005).

The logistic regression output includes three parts. The first part involves statistics for overall model fit. The overall fit of the final model is shown by the $-2 \times \log$ -likelihood statistic and its associated chi-square statistic. If the significance of the chi-square statistic is less than .05, then the model is a significant fit of the data. The second part of the output includes the classification table. The classification table presents the percent of cases correctly classified with the generated model. It indicates how well the model predicts group membership. The third part of the output provides summary of model variables. The summary of model variables provides several variable statistics that indicate variable contribution to the model (Field, 2005; Mertler & Vannatta, 2002).

In order to identify cases that may influence the logistic regression model, standardized residuals will be examined. There are two main purposes for examining residuals in logistic regression. The first is to isolate points for which the model fits poorly. The second is to isolate points that exert an undue influence on the model (Field, 2005).

Given that logistic regression is prone to the biasing effects of collinearity, it is essential to test for this. Since SPSS does not have an option for producing collinearity diagnostics in logistic regression, statistics such as the tolerance and variance inflation factor (VIF) will be obtained through a linear regression analysis using the same outcome and predictors (Field, 2005). Menard (1995) suggests that a tolerance value less than .1

indicates serious collinearity problems. Myers (1990) suggests that a VIF value greater than 10 is cause for concern.

Chapter 7: Results

Several steps were required prior to formal testing of the specific aims and hypotheses. First, FSIQ was analyzed as a predictor of CARS scores. Second, reliability analyses were performed on the neuropsychological domain composites. Third, the neuropsychological domain composites were tested for normally distributed data. Fourth, the neuropsychological domain composites were tested for homogeneity of variance. Finally, specific aims along with hypotheses were formally tested. An alpha level of .05 was used for all statistical tests.

Prediction of CARS

Participants' FSIQ composite scores were converted to z -scores to ensure all scores were on the same scale. Z -scores were converted based on the means and standard deviations of the original IQ measures, not based on the distribution of the sample. The ASD participants' FSIQ z -scores were depressed ($M = -1.47$, $SD = 1.48$, $N = 86$), and their CARS scores ranged from 30 to 51.5 ($M = 37.40$, $SD = 5.96$, $N = 44$). The bivariate correlation of FSIQ and existing CARS scores was significant, $r(41) = -.55$, $p < .001$. Subsequent simple regression analysis revealed that FSIQ was a significant predictor of CARS scores, $b = -2.38$, $t(41) = 24.82$, $p < .001$. FSIQ also explained a significant proportion of variance in CARS scores, $R^2 = .30$, $F(1, 41) = 17.57$, $p < .001$.

Development of Composite Scores

Initially, the neuropsychological domain scores were converted to z -scores based on the means and standard deviations of the sample. Reliability analyses were then conducted on the scores within each neuropsychological domain composite. For reliability analyses, Field (2005) recommends an overall Cronbach's alpha, α , magnitude

of .7 to .8 and correlations between each item and the total score for the composite to be above .3.

Academic domain. The academic domain composite (consisting of three scores including the reading composite, spelling composite, and mathematics composite) *corrected item-total correlations* were above .3. *Cronbach's α* = .77, and none of the items would have increased the reliability if they were deleted.

Motor domain. The motor domain composite (consisting of two scores including dominant and nondominant grooved pegboard) *corrected item-total correlations* were above .3. *Cronbach's α* = .91.

Memory domain. The memory domain composite (consisting of eight scores including immediate and delayed scores for the TOMAL: MFS subtest, TOMAL: WSR subtest, TOMAL: FM subtest, TOMAL: VSR subtest) *corrected item-total correlations* ranged from .01 to .55. *Cronbach's α* = .65. The TOMAL: FM subscales had correlations of less than .3, and results indicated *Cronbach's α* would increase if deleted. Therefore, the TOMAL: FM subscales were deleted from the composite. The modified memory domain composite (consisting of six scores including immediate and delayed scores for the TOMAL: MFS subtest, TOMAL: WSR subtest, TOMAL: VSR subtest) *corrected item-total correlations* were above .3. *Cronbach's α* = .71, and none of the items would have increased the reliability if they were deleted.

Attention/executive functioning domain. The attention/executive functioning domain composite (consisting of four scores including the WCST: conceptual level, WCST: perseverative responses, NEPSY: visual attention domain, and NEPSY: auditory attention response set domain) *corrected item-total correlations* ranged from .11 to .57.

Cronbach's α = .79. The NEPSY visual attention domain and auditory attention and response set domain had *corrected item-total correlations* of less than .3, and results indicated *Cronbach's α* would increase if deleted. Therefore, the NEPSY: visual attention and auditory attention and response set scores were deleted from the composite. The modified executive functioning domain (consisting of two scores including the WCST: conceptual level, WCST: perseverative responses) *corrected item-total correlations* were above .3. *Cronbach's α* = .93, and none of the items would have significantly increased the reliability if they were deleted.

Means of the scores within the academic, motor, memory, and executive functioning domains were then calculated to create composite scores. The perceptual-motor domain, visual attention domain, and auditory attention domain each consisted of only one score.

Testing for Normally Distributed Data

Initially the distributional qualities of the seven domain composites/scores (academic, motor, perceptual-motor, memory, executive functioning, visual attention, and auditory attention) were examined. The academic composite, perceptual-motor scores, memory composite, executive functioning composite, visual attention scores, and auditory attention scores skewness and kurtosis *z*-scores were below an absolute value of 1.97. This indicates nonsignificant values of skewness and kurtosis. For the motor composite, both the skewness and kurtosis *z*-scores were greater than an absolute value of 3.29, which is significant at $p < .001$. This indicated that the motor composite had a significantly positive skew, and the kurtosis score indicated a pointy distribution.

To follow up the analysis for skewness and kurtosis, the Kolmogorov-Smirnov and Shapiro-Wilk tests were run to determine whether each distribution deviated from comparable normal distributions. The academic composite, motor composite, perceptual-motor scores, memory composite, executive functioning composite, and visual attention scores were not significantly non-normal. As noted, the motor composite skewness and kurtosis were significantly non-normal. However, given that the Kolmogorov-Smirnov test was not significantly non-normal, the motor composite distribution did not deviate from comparable normal distributions. Therefore, the motor composite did not require data transformation. Kolmogorov-Smirnov tests indicated that the auditory attention score, $D(44) = .14, p < .05$, was significantly non-normal. Based on the sample size, the auditory attention domain scores were not transformed; instead a more conservative p value was adopted for this score.

Testing for Homogeneity of Variance

Levene's test was used to examine homogeneity of variance within the academic composite, motor composite, perceptual-motor scores, memory composite, executive functioning composite, visual attention scores, and auditory attention scores. Results were non-significant for all the domain composites/scores, indicating the variances were nearly equal and the assumption of homogeneity was reasonable.

Analysis of Specific Aim I

MANOVAs were used to test group differences on measures of academic and perceptual-motor functioning. Due to low availability of neuropsychological data in the severe ASD group within the other domain composites/scores, ANOVAs were used to test group differences on measures of motor, memory, executive functioning, visual

attention, and auditory attention. Finally, bivariate correlations were used to examine qualitative information on pragmatic speech and language functioning.

Hypothesis 1: MANOVA

It was hypothesized that distinct profiles based on cognitive data would emerge, including cognitive differences in the diagnostic groups (SLI and ASD) and severity levels (mild-moderate and severe).

Academic composite and perceptual-motor scores. A two-way MANOVA was conducted to determine the effect of diagnostic category (SLI or ASD) and severity level (mild-moderate or severe) on the two dependent variables of academic functioning and perceptual-motor functioning. Means and standard deviations are presented in Table 2. MANOVA results, presented in Table 3, indicated a significant difference in severity level (Wilks' $\Lambda = .837$, $F(2, 42) = 4.08$, $p < .05$, $\eta^2 = .16$) on the combined DV of academic functioning and perceptual-motor functioning. However, multivariate effect size is small. MANOVA results indicate that diagnostic category (Wilks' $\Lambda = .953$, $F(2, 42) = 1.05$, $p = .36$) and interaction of diagnostic category and severity level (Wilks' $\Lambda = .944$, $F(2, 42) = 1.25$, $p = .30$) did not show significant differences on the combined DV of academic functioning and perceptual-motor functioning. ANOVAs were conducted as follow-up tests. ANOVA results indicated that severity level resulted in significant differences on academic functioning measures ($F(1, 43) = 8.21$, $p < .01$, $\eta^2 = .16$), with participants in the mild-moderate groups performing significantly better on measures of academic functioning than those in the severe groups. However, univariate effect size is small. ANOVA results indicate that diagnostic category did not show significant differences on measures of academic functioning ($F(1, 43) = 0.00$, $p = .98$). In addition,

ANOVA results indicate that diagnostic category ($F[1, 43] = 1.80, p = .19$) and severity level ($F[1, 43] = 0.69, p = .41$) did not show significant difference on the perceptual-motor functioning measure. Finally, ANOVA results indicate that the interaction between diagnostic category and severity level did not significantly differ for academic functioning ($F[1, 43] = 2.56, p = .12$) or perceptual motor functioning ($F[1, 43] = 0.55, p = .46$).

Table 2

Mean Scores and Standard Deviations for Measures of Cognitive Functioning (Academic and Perceptual Motor) as a Function of Diagnosis and Severity Level

Group	Cognitive Functioning Measure			
	Academic		Perceptual-Motor	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
SLI				
Mild-moderate	.01	.75	.35	.84
Severe	-.30	.46	.32	.91
ASD				
Mild-moderate	.40	.80	.18	.91
Severe	-.69	.96	-.27	.98

Note. All cognitive data were converted to z-scores prior to analyses.

Table 3

Multivariate and Univariate Analyses of Variance for Cognitive Functioning

Source	Multivariate <i>F</i> (2, 42)	Univariate	
		Academic <i>F</i> (1, 43)	Perceptual-Motor <i>F</i> (1, 43)
Diagnosis (D)	1.05	0.00	1.80
Severity Level (S)	4.08*	8.21**	0.69
D × S	1.25	2.56	0.55

Note. Multivariate *F* ratios are Wilks' approximation of *F*s.

* $p < .05$. ** $p < .01$.

Discriminant analyses are appropriate following a one-way MANOVA for the purpose of revealing relationships between dependent variables and group membership (Field, 2005). However, based on the current data, a discriminant analysis was not warranted for two reasons. First, it was not appropriate as a two-way MANOVA was conducted given the division of groups, and discriminant analysis relies on one predictor variable only. Second, discriminant analysis was not needed as a significant difference was found on only one dependent variable.

Hypothesis 1: ANOVAs

Although MANOVAs were used to test group differences on measures of academic and perceptual-motor functioning, sample size was decreased due to several participants having scores on only one of the measures. Therefore, in order to increase the power to detect differences, two-way ANOVAs were also run for the academic composite and perceptual-motor scores. Due to low availability of neuropsychological

data in the severe ASD group on areas of motor, memory, executive functioning, visual attention, and auditory attention, a MANOVA on these domain composites/scores could not be run. Therefore, ANOVAs were used as the primary means to test group differences on measures of motor, memory, executive functioning, visual attention, and auditory attention.

Two-way ANOVAs were conducted to investigate diagnostic category and severity level differences in academic, motor, perceptual-motor, memory, executive functioning, visual attention, and auditory attention. Means and standard deviations are presented in Table 4. Three significant findings emerged from the analyses (see Table 5). First, ANOVA results showed a significant main effect for severity level difference in academic functioning, $F(1, 67) = 16.22, p < .001$, partial $\eta^2 = .20$, with the participants in the mild-moderate groups performing significantly better on academic tasks than those in the severe groups. However, univariate effect size is small. This finding is consistent with the MANOVA results. Second, ANOVA results also indicated a significant main effect for diagnostic category in perceptual-motor functioning, $F(1, 59) = 8.44, p < .01$, partial $\eta^2 = .13$, with participants in the SLI diagnostic group performing significantly better on perceptual-motor tasks than those in the ASD diagnostic groups. However, univariate effect size is small. This is in contrast to MANOVA results where significance levels were not reached for perceptual-motor measures. This difference in findings is likely due to the increased sample size for the ANOVA. Although bordering on significance, main effect for severity level, $F(1, 59) = 3.57, p = .06$, and interaction between factors, $F(1, 59) = 3.11, p = .08$, did not reach significance. Third, ANOVA results showed a significant main effect for severity level in visual attention, $F(1, 44) = 5.06, p < .05$,

partial $\eta^2 = .10$, with participants in the mild-moderate groups performing significantly better on visual attention tasks than those in the severe groups. However, univariate effect size is small. ANOVAs did not produce significant results in other areas (see Table 5).

Table 4

Mean Scores and Standard Deviations for Seven Cognitive Functioning Measures as a Function of Diagnosis and Severity Level

Variable	SLI: Mild-Mod		SLI: Severe		ASD: Mild-Mod		ASD: Severe	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Academic	.02	.75	-.42	.45	.49	.72	-.62	.91
Motor	.12	1.37	-.27	.75	-.20	.63	.32	1.51
Perceptual-Motor	.38	.81	.35	.75	.11	.91	-.78	1.17
Memory	-.01	.65	-.17	.58	.04	.86	-.35	.38
Executive Functioning	-.49	.95	.37	1.04	.25	.85	-.28	1.41
Visual Attention	.03	1.04	-.69	.83	.35	1.00	-.36	.89
Auditory Attention	.00	.92	-.26	1.24	.26	.86	-.86	1.31

Note. All cognitive data were converted to z-scores prior to analyses, Mod = moderate.

Table 5

Two-Way Analyses of Variance for Quantitative Cognitive Data

Variable and source	<i>df</i>	<i>MS</i>	<i>F</i>	partial η^2
Academic				
Diagnosis (D)	1	0.27	0.51	.01
Severity Level (S)	1	8.71	16.22***	.20

Variable and source	<i>df</i>	<i>MS</i>	<i>F</i>	partial η^2
D × S	1	1.61	3.00	.04
Error	67	0.54		
Motor				
Diagnosis (D)	1	0.15	0.15	.01
Severity Level (S)	1	0.03	0.03	.00
D × S	1	1.73	1.69	.04
Error	44	1.03		
Perceptual-Motor				
Diagnosis (D)	1	7.36	8.44**	.13
Severity Level (S)	1	3.11	3.57	.06
D × S	1	2.71	3.11	.05
Error	59	0.87		
Memory				
Diagnosis (D)	1	0.04	0.07	.00
Severity Level (S)	1	0.64	1.21	.03
D × S	1	0.10	0.19	.00
Error	47	0.53		
Executive Functioning				
Diagnosis (D)	1	0.01	0.01	.00
Severity Level (S)	1	0.17	0.19	.01
D × S	1	2.97	3.35	.09
Error	35	0.89		
Visual Attention				
Diagnosis (D)	1	0.99	1.06	.02

Variable and source	<i>df</i>	<i>MS</i>	<i>F</i>	partial η^2
Severity Level (S)	1	4.75	5.06*	.10
D \times S	1	0.00	0.00	.00
Error	44	0.94		
Auditory Attention				
Diagnosis (D)	1	0.21	0.21	.01
Severity Level (S)	1	3.60	3.57	.09
D \times S	1	1.43	1.42	.04
Error	36	1.01		

Note. partial η^2 = effect size.

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

ANOVA results summary. Overall, ANOVA results indicated significant diagnostic category group differences on measures of perceptual-motor functioning, with the SLI group performing better than the ASD group. Results also indicated significant severity level group differences on measures of academic functioning and visual attention functioning, with the mild-moderate group performing better than the severe group on both measures.

Hypothesis 1: bivariate correlations and chi-squares

Bivariate correlations were conducted to investigate the relationship between diagnostic category and severity level with the participants' qualitative pragmatic data. The qualitative data had a threshold of 1, which indicated the presence of any problems. Bivariate correlations indicated that diagnostic category was significantly correlated with verbal communication quality problems, $r(108) = .31, p < .01$, verbal communication content problems, $r(107) = .44, p < .001$, nonverbal communication withdrawal/isolation

problems, $r(111) = .60, p < .001$, and nonverbal communication disruption/aggressiveness problems, $r(107) = .29, p < .01$. These results indicated that the ASD participants had more pragmatic problems in all areas than the SLI group. Severity level was significantly correlated with verbal communication content problems, $r(107) = .20, p < .05$, indicating that the severe groups had more verbal communication content problems than the mild-moderate groups. There was not a significant correlation between severity level and problems in verbal communication quality, nonverbal communication withdrawal/isolation, or nonverbal communication disruption/aggressiveness.

To further examine the severity level differences in verbal communication content, participants were divided into the SLI and ASD groups by severity level. Chi-squares were then conducted to determine whether the SLI or ASD group was driving the severity level finding. Chi-squares, presented in Tables 6 and 7, indicated a significant relationship between verbal communication content problems and severity level in the ASD group, $\chi^2(1, N = 70) = 9.51, p < .01$, but not in the SLI group. Based on the odds ratio, verbal communication content problems were present in the severe ASD group 5.58 times more often than in the mild-moderate ASD group. There was not a significant relationship between verbal communication content problems and severity level in the SLI group, $\chi^2(1, N = 39) = 0.30, p = .58$.

Table 6

Qualitative Pragmatic Problem Rates Among ASD groups by Severity Level

	ASD: Mild-Mod	ASD: Severe		
Qualitative Pragmatic Problem	(<i>n</i> = 41)	(<i>n</i> = 29)	χ^2 (1)	<i>p</i>
Verbal communication quality	19	18 (<i>n</i> = 30)	1.30	.26
Verbal communication content	19	24	9.51**	.01
NVC withdrawal/isolation	41 (<i>n</i> = 43)	30 (<i>n</i> = 31)	0.09	.76
NVC disruption/aggression	21 (<i>n</i> = 40)	20 (<i>n</i> = 30)	1.42	.23

Note. NVC = nonverbal communication, Mod = moderate.

***p* < .01.

Table 7

Qualitative Pragmatic Problem Rates Among SLI groups by Severity Level

	SLI: Mild-Mod.	SLI: Severe		
Qualitative Pragmatic Problem	(<i>n</i> = 22)	(<i>n</i> = 17)	χ^2 (1)	<i>p</i>
Verbal communication quality	6	2	1.41	.23
Verbal communication content	4	2	0.30	.58
NVC withdrawal/isolation	9	8	0.15	.70
NVC disruption/aggression	5	6	0.75	.39

Note. NVC = nonverbal communication, Mod = moderate.

Analysis of Specific Aim II

Chi-squares were performed to examine the relationship between diagnostic category (SLI or ASD) and comorbid psychopathology/health problems. Additional chi-square analyses were then conducted to examine the relationship between severity level (mild-moderate or severe) and comorbid psychopathology.

Hypothesis 1

It was hypothesized that the SLI group would have higher rates of learning disorders, ADHD, and autoimmune disorders. It was hypothesized that the ASD group would have higher rates of MR/GDD/DD.

Comorbid psychopathology/health problems and diagnostic category. Chi-squares, presented in Table 8, indicated four significant relationships between participant comorbid psychopathology/health problem rates and diagnostic group (see Table 8). First, chi-squares indicated a significant relationship between learning disorder comorbidity and diagnostic category, $\chi^2(1, N = 128) = 4.85, p < .05$. Based on the odds ratio, learning disorder comorbidity was present in the SLI group 2.56 times more often than in the ASD group. Second, chi-squares indicated a significant relationship between asthma and diagnostic category, $\chi^2(1, N = 121) = 6.14, p < .05$. Based on the odds ratio, asthma was present in the SLI group 4.17 times more often than in the ASD group. It should be noted that the expected frequency for asthma in the SLI group was below 5, which resulted in a loss of statistical power. Third and interestingly, chi-squares indicated a significant relationship between frequent stomach/digestion problems and diagnostic category, $\chi^2(1, N = 115) = 7.24, p < .01$. Based on the odds ratio, frequent stomach/digestion problems were present in the SLI group 11.66 times more often than in

the ASD group. It should be noted that the expected frequency for frequent stomach/digestion problems in the SLI and ASD groups was below 5, which resulted in a loss of statistical power. Fourth, chi-squares indicated a significant relationship between MR/GDD/DD comorbidity and diagnostic category, $\chi^2(1, N = 128) = 23.13, p < .001$. Based on the odds ratio, MR/GDD/DD was present in the ASD group 18.11 times more often than in the SLI group. There were no other significant relationships between participant comorbid psychopathology/health problems and diagnostic group.

Table 8

Comorbidity Rates Among SLI and ASD Groups

Comorbidity type	SLI	ASD	$\chi^2 (1)$	<i>p</i>
	(<i>n</i> = 39)	(<i>n</i> = 89)		
Learning disorders	14	16	4.85*	.03
ADHD	14	26	0.56	.45
Health Problems				
Autoimmune disorder composite	9	17	0.16	.69
	(<i>n</i> = 38)	(<i>n</i> = 83)		
Asthma	8	5	6.14*	.01
	(<i>n</i> = 38)	(<i>n</i> = 83)		
Stomach/digestion problems	5	1	7.24**	.007
	(<i>n</i> = 38)	(<i>n</i> = 77)		
MR/GDD/DD	2	44	23.13***	.000

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

Comorbid psychopathology/health problems and severity level. Chi-squares, presented in Table 9, indicated three significant relationships between participant

comorbid psychopathology/health problem rates and severity level. First, chi-squares indicated a significant relationship between learning disorder comorbidity and severity level, $\chi^2(1, N = 113) = 3.98, p < .05$. Based on the odds ratio, learning disorder comorbidity was present in the mild-moderate groups 2.59 times more often than in the severe groups. Second, chi-squares indicated a significant relationship between ADHD comorbidity and severity level, $\chi^2(1, N = 113) = 3.76, p < .05$. Based on the odds ratio, ADHD comorbidity was present in the mild-moderate groups 2.39 times more often than in the severe groups. Third, chi-squares indicated a significant relationship between MR/GDD/DD and severity level, $\chi^2(1, N=113) = 19.13, p < .001$. Based on the odds ratio, MR/GDD/DD was present in the severe groups 6.43 times more often than the mild-moderate groups. There were no other significant relationships between participant comorbid psychopathology/health problems and severity level.

Table 9

Comorbidity Rates Among Severity Level

Comorbidity type	Mild-Mod.	Severe	$\chi^2 (1)$	<i>p</i>
	(<i>n</i> = 65)	(<i>n</i> = 48)		
Learning disorders	20	7	3.98*	.05
ADHD	23	9	3.76*	.05
Health Problems				
Autoimmune disorder composite	9	12	2.31	.13
	(<i>n</i> = 61)	(<i>n</i> = 45)		
Asthma	6	5	0.05	.83
	(<i>n</i> = 61)	(<i>n</i> = 45)		

Comorbidity type	Mild-Mod.	Severe	χ^2 (1)	<i>p</i>
	(<i>n</i> = 65)	(<i>n</i> = 48)		
Stomach/digestion problems	3	3	0.16	.69
	(<i>n</i> = 59)	(<i>n</i> = 43)		
MR/GDD/DD	11	27	19.13***	.000

Note. Mod. = Moderate

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

To further examine comorbid psychopathology rates and severity level, participants were divided into the SLI and ASD groups by severity level. Chi-squares were then conducted to determine whether the SLI or ASD group was driving the severity level finding. Three significant relationships between participant comorbid psychopathology rates and ASD level emerged (see Table 10). First, chi-squares indicated a significant relationship between learning disorder comorbidity and severity level in the ASD group, $\chi^2(1, N = 74) = 11.37, p < .01$. The odds ratio was unable to be calculated as there were no ASD participants in the severe group with a comorbid diagnosis of learning disorder. Second, chi-squares indicated a significant relationship between ADHD comorbidity and severity level in the ASD group, $\chi^2(1, N = 74) = 6.22, p < .05$. Based on the odds ratio, ADHD comorbidity was present in the mild-moderate ASD group 4.87 times more often than in the severe ASD group. Third, chi-squares indicated a significant relationship between MR/GDD/DD comorbidity and severity level in the ASD group, $\chi^2(1, N = 74) = 21.86, p < .001$. MR/GDD/DD comorbidity was present in the severe ASD group 4.17 times more often than in the mild-moderate ASD group. There were no significant relationships between comorbid psychopathology rates and severity level in the SLI group (see Table 11).

Table 10

Comorbidity Rates Among ASD Groups by Severity Levels

Comorbidity type	ASD: Mild-Mod	ASD: Severe	χ^2 (1)	<i>p</i>
	(<i>n</i> = 43)	(<i>n</i> = 31)		
LD	13	0	11.37**	.001
ADHD	15	3	6.22*	.01
MR/GDD/DD	11	25	21.86***	.000

Note. Mod. = moderate.

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

Table 11

Comorbidity Rates Among SLI Groups by Severity Levels

Comorbidity type	SLI: Mild-Mod.	SLI: Severe	χ^2 (1)	<i>p</i>
	(<i>n</i> = 22)	(<i>n</i> = 17)		
LD	7	7	0.37	.55
ADHD	8	6	0.01	.96
MR/GDD/DD	0	2	2.73	.10

Note. Mod. = moderate.

Summary of comorbid psychopathology/health problem findings. Overall, chi-square results indicated significantly more learning disorders, asthma, and frequent stomach/digestion problems in the SLI diagnostic category than the ASD diagnostic category. MR/GDD/DD occurred significantly more often in the ASD diagnostic category than the SLI diagnostic category. Chi-square results also indicated that learning

disorders and ADHD occurred significantly more often in the mild-moderate groups, while MR/GDD/DD occurred significantly more often in the severe groups. In all instances of severity level significance, findings were primarily driven by ASD severity level group differences.

Analysis of Specific Aim III

Chi-squares were used to examine group differences with respect to parental education levels, parental occupations, and the frequency of psychopathology in participants' parents in order to identify potential subtypes for subsequent genetic linkage or association studies.

Hypothesis 1

It was hypothesized that parental education levels in SLI and ASD participants would be similar.

Chi-squares, presented in Table 12, indicated a significant relationship between maternal education levels and diagnostic category, $\chi^2(3, N = 114) = 8.88, p < .05$. Chi-squares, presented in Table 13, also indicated a significant relationship between paternal education levels and diagnostic category, $\chi^2(3, N = 108) = 9.34, p < .05$. In both instances, significant results were driven by the less-than-12-years of education variable, indicating that there were significantly more SLI parents who did not earn a high school diploma or GED than ASD parents. It should be noted that 2 and 1 cells, respectively, in the maternal and paternal education level analysis, had an expected count of less than 5, which resulted in a loss of statistical power.

Table 12

Maternal Education Levels Among SLI and ASD Groups

	SLI	ASD		
Maternal Education Levels	(<i>n</i> = 35)	(<i>n</i> = 79)	χ^2 (3)	<i>p</i>
< 12 years	6	3	8.88*	.03
HS graduate or GED	8	19		
1-4 years of college	16	52		
> 4 years of college	5	5		

**p* < .05.

Table 13

Paternal Education Levels Among SLI and ASD Groups

	SLI	ASD		
Paternal Education Levels	(<i>n</i> = 32)	(<i>n</i> = 76)	χ^2 (3)	<i>p</i>
< 12 years	8	4	9.34*	.03
HS graduate or GED	9	23		
1-4 years of college	9	33		
> 4 years of college	6	16		

**p* < .05.

Hypothesis 2

It was hypothesized that the parental occupations of SLI and ASD participants would be similar.

Chi-squares, presented in Table 14, did not indicate a significant relationship between maternal occupation and diagnostic category, $\chi^2(10, N = 113) = 16.89, p = .08$. Additionally, the chi-squares, presented in Table 15, did not indicate a significant relationship between paternal occupation and diagnostic category, $\chi^2(10, N = 102) = 5.04, p = .88$. It should be noted that in both analyses, 15 cells had expected counts of less than 5, which resulted in loss of statistical power.

Table 14

Maternal Occupation Among SLI and ASD Groups

Maternal Occupation	SLI (<i>n</i> = 34)	ASD (<i>n</i> = 79)	χ^2 (10)	<i>p</i>
Unemployed	3	0	16.89	.08
Homemaker	6	30		
Unskilled	7	6		
Semi-skilled	4	10		
Skilled	1	3		
Business/finance	4	15		
Engineer/science	3	3		
Health care	4	5		
Education	0	1		
Professional	1	3		
Social services	1	3		

Table 15

Paternal Occupation Among SLI and ASD Participants

Paternal Occupation	SLI (<i>n</i> = 28)	ASD (<i>n</i> = 74)	χ^2 (10)	<i>p</i>
Unemployed	2	2	5.04	.88
Homemaker	0	1		
Self-employed/owner	0	2		
Unskilled	5	12		
Semi-skilled	7	15		
Skilled	4	12		
Business/finance	4	9		
Engineer/science	4	7		
Education	0	2		
Professional	2	11		
Social services	0	1		

Additional chi-squares were conducted to explore the relationship between parental occupation and group severity levels. Chi-square analysis, presented in Table 16, indicated a significant relationship between maternal occupation and severity level, $\chi^2(10, N = 98) = 19.51, p < .05$. Significant results were driven by the unskilled, business/finance, and engineer/science variables, indicating that mothers in the severe groups were involved in unskilled occupations more often than those in the mild-moderates groups, while mothers in the mild-moderate groups were involved in business/finance and engineer/science careers more often than in the severe groups. Chi-square analysis, presented in Table 17, also indicated a significant relationship between paternal

occupation and severity level, $\chi^2(10, N = 88) = 17.49, p < .05$. Significant results were driven by the engineer/science variable, indicating that fathers in the mild-moderate groups were involved in engineer/science careers more often than those in the severe groups. To further examine parental occupation and severity level findings, participants were divided into the SLI and ASD groups by severity level. Chi-squares were then conducted to determine whether the SLI or ASD group was driving the severity level findings. Chi-squares, presented in Table 18, indicated a significant relationship between paternal occupation and severity level in the ASD group, $\chi^2(1, N = 60) = 18.90, p < .05$, indicating that fathers in the mild-moderate ASD group were involved in engineer/science careers more often than fathers in the severe ASD group. There was not a significant relationship between paternal occupation and severity level in the SLI group, $\chi^2(1, N = 28) = 5.93, p = .43$. Neither was there a significant relationship between maternal occupation and severity level in the SLI group, $\chi^2(1, N = 34) = 15.65, p = .08$, or the ASD group, $\chi^2(1, N = 64) = 8.67, p = .47$. It should be noted that in all analyses, more than 10 cells had expected counts of less than 5, which resulted in a loss of statistical power.

Table 16

Maternal Occupation Among Severity Level Groups

Maternal Occupation	Mild-Mod.	Severe	χ^2 (10)	<i>p</i>
	(<i>n</i> = 56)	(<i>n</i> = 42)		
Unemployed	3	0	19.51*	.03
Homemaker	17	15		
Unskilled	3	10		

Maternal Occupation	Mild-Mod.	Severe	χ^2 (10)	<i>p</i>
	(<i>n</i> = 56)	(<i>n</i> = 42)		
Semi-skilled	5	7		
Skilled	1	2		
Business/finance	10	3		
Engineer/science	5	1		
Health care	5	4		
Education	1	0		
Professional	2	0		
Social services	4	0		

Note. Mod. = moderate

**p* = < .05.

Table 17

Paternal Occupation Among Severity Level Groups

Paternal Occupation	Mild-Mod.	Severe	χ^2 (10)	<i>p</i>
	(<i>n</i> = 51)	(<i>n</i> = 37)		
Unemployed	0	1	17.49*	.04
Homemaker	1	2		
Self-employed/owner	0	2		
Unskilled	8	8		
Semi-skilled	8	13		
Skilled	9	2		
Business/finance	7	3		
Engineer/science	10	1		

Paternal Occupation	Mild-Mod.	Severe	χ^2 (10)	<i>p</i>
	(<i>n</i> = 51)	(<i>n</i> = 37)		
Education	1	0		
Professional	7	5		

Note. Mod. = moderate

**p* < .05.

Table 18

Paternal Occupation Among ASD by Severity Level

Paternal Occupation	Mild-Mod.	Severe	χ^2 (10)	<i>p</i>
	(<i>n</i> = 51)	(<i>n</i> = 37)		
Unemployed	0	1	18.90*	.03
Homemaker	0	1		
Self-employed/owner	0	2		
Unskilled	7	4		
Semi-skilled	4	10		
Skilled	6	1		
Business/finance	4	2		
Engineer/science	7	0		
Education	1	0		
Professional	5	5		

Note. Mod. = moderate

**p* < .05.

Hypothesis 3

It was hypothesized SLI participants' first degree maternal and paternal relatives would have higher SLI, ADHD, and learning disorder rates. It was hypothesized that ASD participants' first degree maternal and paternal relatives would have higher rates of anxiety disorders, mood disorders, ASD, MR, and epilepsy.

Chi-squares, presented in Table 19, indicated three significant relationships between maternal psychopathology family history and diagnostic category. First, chi-squares indicated a significant relationship between maternal learning disorder family history and diagnostic category, $\chi^2(1, N = 121) = 5.16, p < .05$. Based on the odds ratio, maternal learning disorder family history was present in the SLI group 3.09 times more often than in the ASD group. Second, chi-squares indicated a significant relationship between maternal ASD family history and diagnostic category, $\chi^2(1, N = 121) = 3.77, p < .05$; $LR(1, N=121) = 6.09, p < 01$. The odds ratio was unable to be calculated as there were no SLI participants with a maternal history of ASD. This resulted in a loss of statistical power. Third and interestingly, chi-squares indicated a significant relationship between maternal thought disorder family history and diagnostic category, $\chi^2(1, N = 121) = 6.59, p < .05$. Based on the odds ratio, maternal thought disorder family history was present in the ASD group 6.50 times more often than in the SLI group. It should be noted that the expected frequency for maternal thought disorder family history in the SLI group was below 5, which resulted in a loss of statistical power. There were no other significant relationships between maternal psychopathology family history and diagnostic category. There were no significant relationships between paternal psychopathology family history and diagnostic category (see Table 20).

Table 19

First-Degree Maternal Relative Psychopathology Rates

Maternal Family History	SLI	ASD	χ^2 (1)	<i>p</i>
	(<i>n</i> = 37)	(<i>n</i> = 84)		
SLI	3	14	1.56	.21
ADHD	7	13	0.22	.64
Learning disorders	10	9	5.16*	.02
Anxiety disorders	5	15	0.35	.55
Mood disorders	10	25	0.09	.76
ASD	0	8	3.77*	.05
MR	2	7	0.34	.56
		(<i>n</i> = 83)		
Epilepsy	1	9	2.18	.14
Thought Disorders	1	13	4.10*	.04

**p* < .05.

Table 20

First-Degree Paternal Relative Psychopathology Rates

Paternal Family History	SLI	ASD	χ^2 (1)	<i>p</i>
	(<i>n</i> = 34)	(<i>n</i> = 81)		
SLI	4	15	0.79	.37
ADHD	2	11	1.46	.23
		(<i>n</i> = 80)		
Learning disorders	7	15	0.07	.78
Anxiety disorders	1	2	0.02	.89

	SLI	ASD		
Paternal Family History	(<i>n</i> = 34)	(<i>n</i> = 81)	χ^2 (1)	<i>p</i>
Mood disorders	4	13	0.35	.56
ASD	0	4	1.74	.19
MR	1	3	0.04	.84
Epilepsy	1	2	0.02	.89
Thought Disorders	1	6	0.84	.36

Summary of psychopathology family history findings. Overall, chi-square results indicated significantly more learning disorders in first-degree maternal relatives for the SLI group. Results indicated significantly more ASD and thought disorders in first-degree maternal relatives for the ASD group. Chi-squares did not reveal significant first-degree paternal relative psychopathology differences in the diagnostic categories.

Analysis of Specific Aim IV

Based on the aforementioned results, cognitive functioning, comorbid diagnosis, and health problems in the participants, as well as familial variables, were examined in predicting group membership. This aim was more exploratory in nature.

Hypothesis 1

Logistic regression was used to combine factors to predict group membership to diagnostic group (SLI or ASD) and severity level (mild-moderate or severe).

Forward logistic regression was conducted to determine which independent variables (verbal communication quality, verbal communication content, nonverbal communication withdrawal/isolation, nonverbal communication disruption/aggression, learning disorder comorbidity, MR comorbidity, asthma, frequent stomach/digestion

problems, maternal family history of learning disorders, maternal family history of ASD, and maternal family history of thought disorders) are predictors of diagnostic category (SLI or ASD). Perceptual-motor scores were not entered into the analysis as this would have substantially decreased sample size. In addition, parental education variables were not entered into the analysis as the four levels of the variable would have complicated the analyses. Regression results indicated that the overall model fit of five predictors (verbal communication quality, nonverbal communication withdrawal/isolation, nonverbal communication disruption/aggression, mental retardation comorbidity, and frequent stomach/digestion problems) was questionable ($-2 \text{ Log Likelihood} = 62.33$) but was statistically reliable in distinguishing between diagnostic categories; $\chi^2(5) = 80.58, p < .001$). The model correctly classified 90.3% of the cases. Regression coefficients are presented in Table 21. *Wald* statistics indicated that verbal communication quality, nonverbal communication social withdrawal/isolation, nonverbal communication disruption/aggression, MR comorbidity, and frequent stomach/digestion problems significantly predict diagnostic category. However, data were extremely variable.

Table 21

Summary of Logistic Regression Analysis Predicting Diagnostic Group

Variable	<i>B</i>	<i>SE</i>	Odds ratio	<i>Wald</i>
VC quality	-2.04	.78	.13	6.89**
NC withdrawal/isolation	-4.00	.95	.02	17.81***
NC disruption/aggression	-1.82	.68	.16	7.21**
MR comorbidity	-3.63	1.08	.03	11.30**
Stomach/digestion probs.	3.28	1.40	26.51	5.49*

Variable	<i>B</i>	<i>SE</i>	Odds ratio	<i>Wald</i>
Constant	3.96	1.79	52.25	4.89*

Note. VC = verbal communication, NC = nonverbal communication, probs = problems.

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

Forward logistic regression was also conducted to determine which independent variables (MR comorbidity, learning disorder comorbidity, ADHD comorbidity, and verbal communication content) are predictors of diagnostic category (SLI or ASD). The academic and visual attention variables were not entered into the analysis as this would have substantially decreased sample size. In addition, parental occupation variables were not entered into the analysis as the 11 levels of the variables would have complicated the analyses. Regression results indicated that the overall model fit of one predictor (MR comorbidity) was questionable ($-2 \text{ Log Likelihood} = 112.62$) but was statistically reliable in distinguishing between diagnostic categories; $\chi^2(1) = 19.52, p < .001$). The model correctly classified 73.2% of the cases. Regression coefficients are presented in Table 22. *Wald* statistics indicated that MR comorbidity significantly predict diagnostic category. However, data were extremely variable.

Table 22

Summary of Logistic Regression Analysis Predicting Severity Level

Variable	<i>B</i>	<i>SE</i>	Odds ratio	<i>Wald</i>
MR comorbidity	-2.09	.51	0.12	16.75***
Constant	1.15	.43	3.14	6.96**

Note. VC = verbal communication, NC = nonverbal communication, probs = problems.

** $p < .01$. *** $p < .001$

Chapter 8: Discussion

Several significant findings emerged from the investigation. In this section each aim and hypothesis is discussed. Then, limitations of the study and future research to rectify these problems are identified. Finally, overall importance of the findings is discussed for the significant results.

Specific Aim I

The first aim was to examine group differences with respect to cognitive functioning in the SLI and ASD groups. Information on the qualitative aspects of pragmatic speech and language functioning was also examined.

Hypothesis 1

The hypothesis that four distinct profiles based on group differences from the SLI and ASD groups would emerge was not supported. Results indicated limited cognitive differences in diagnostic category, while some differences appeared primarily due to severity level. In regards to diagnostic category differences, the only quantitative cognitive distinction between the SLI and ASD groups was on the perceptual-motor measure. SLI participants performed significantly better on perceptual-motor tasks than ASD participants, although effect size was small. This finding is consistent with previous literature documenting motor coordination problems in high-functioning children with autism and Asperger's syndrome (Ghaziuddin, Tsai, & Ghaziuddin, 1992a, 1992b; Gilberg & Gillberg, 1989; Klin, 1994; Klin & Volkmar, 1995; Szatmari, 1991; Szatmari, Tuff, Finlayson, & Bartolucci, 1990; Tantam, 1988; Wing, 1981). In addition, Mayes and Calhoun (2003) found depressed VMI scores in ASD individuals regardless of IQ score.

Results also indicated diagnostic category differences in all qualitative pragmatic speech and language areas sampled, with ASD groups having significantly more pragmatic difficulties than SLI groups. Previous research has also indicated pragmatic language difficulties in ASD individuals (Bishop & Baird, 2001; Geurts et al., 2004; Philofshky, Fidler, & Hepburn, 2007; Verté et al., 2006). In addition, ASD groups have been characterized as having higher levels of pragmatic difficulties than SLI groups (Whitehouse, Barry, & Bishop, 2007). Taken together, the categorical differences in perceptual-motor functioning and pragmatic language skills may indicate neuropsychological endophenotypic markers within ASD individuals. However, future research with larger sample sizes and quantitative pragmatic language data will be required to obtain larger effect sizes and stronger generalizability.

Severity level differences were found in academic functioning and visual attention, with mild-moderate groups performing significantly better than severe groups in both domains; however, effect sizes were small. The academic functioning findings are consistent with previous literature, which shows achievement score differences within ASD individuals based on their IQ level (Mayes & Calhoun, 2003), as well as high incidences of learning disorders in SLI individuals (Bishop & Adams, 1990; Scarborough, 1990; Aram & Hall, 1989; Tallal et al., 1997). The visual attention findings are likely related to ADHD comorbidity, attention problems in both SLI and ASD individuals (Cantwell, 1996; Corbett & Constantine, 2006; Love & Thompson, 1988; Reiersen & Todd, 2008; Smalley, 1997), and persistent joint visual attention difficulties in ASD individuals (Naber et al., 2007). It is possible that attention difficulties mark

subtypes within each group. Future research is needed to further explore attention difficulties' effect on severity levels in SLI and ASD individuals.

Finally, severity level differences were found in the pragmatic speech and language area of verbal communication content. This finding was primarily driven by the ASD group, with problems in verbal communication content occurring more often in the severe ASD group. This finding is consistent with literature indicating psycholinguistic markers can distinguish groups along the SLI/ASD continuum (Botting & Conti-Ramsden, 2003). The current results add to previous literature by revealing that verbal communication content problems such as echolalia, pallalalia, or repetitive speech may be important in distinguishing severity in ASD individuals and may help distinguish these diagnostic groups in more severe cases. These problems may also suggest the presence of underlying motor difficulties related to language functioning, as evidenced by the presence of echolalia, pallalalia, and/or repetitive speech (Christman, Boutsen, & Buckingham, 2004). Future research is required to understand the brain regions that may be involved in motor and language difficulties that underlie verbal communication content difficulties. The lack of significant differences in the other pragmatic speech and language categories (verbal communication quality, nonverbal communication withdrawal/isolation, and nonverbal communication disruption/aggressive) in the mild-moderate and severe ASD groups highlight the heterogeneity present in ASD (Freeman, 1997).

Specific Aim II

The second aim was to examine comorbid psychopathology and health problem differences in SLI and ASD individuals in order to identify potential endophenotypic subtypes.

Hypothesis 1

The hypothesis that SLI participants would have higher rates of learning disorders, ADHD, and autoimmune disorders was supported, in part. SLI participants had significantly higher rates of learning disorders than ASD participants. This result is consistent with previous research indicating that approximately half of individuals with SLI also have a learning disorder (Catts et al., 2002). The results also indicated that the mild-moderate groups, driven primarily by the mild-moderate ASD group, had significantly higher rates of learning disorders than the severe groups. This finding demonstrated similarities in mild-moderate ASD participants and the SLI group. This finding adds to previous literature indicating similar symptoms in SLI and ASD (Botting & Ramsden, 2003) and gives further credence to conceptualizing SLI and ASD as continuous rather than categorical disorders.

There was not a significant relationship between the diagnostic groups' ADHD rates. Research indicates that the majority of children diagnosed with ADHD also have a comorbid diagnosis of SLI (Cantwell, 1996; Love & Thompson, 1988; Smalley, 1997) and ADHD symptoms have been widely reported in ASD children (Corbett & Constantine, 2006; Reiersen & Todd, 2008). These previous findings may explain the similar and possibly elevated rates for both groups within the current sample. Interestingly, results indicated that the mild-moderate groups, driven primarily by the

mild-moderate ASD group, had significantly higher rates of ADHD than the severe groups. The ADHD severity level finding in the ASD group is also likely to be a result of the high occurrence of MR/GDD/DD in the severe ASD group. This finding indicates that the mild-moderate ASD group's difficulties in regards to attention problems may be more similar to the SLI groups than the severe ASD group. Overall, these findings suggest that SLI and ASD disorders may lie on a continuum, at least in regards to attention problems. As the current study did not include a control group, it will be important for future research to examine the relationship between SLI and ASD individuals' ADHD comorbidity rates in comparison to a control population.

There was not a significant relationship for autoimmune disorders (defined by a composite including allergies, asthma, and eczema) rates. Increased rates of autoimmune disorders have been reported in SLI (Gilger et al., 1992; Hugdahl et al., 1990; Wood & Cooper, 1992) and proposed as a link to ASD conceptualization (Becker, 2007), which may explain the lack of significant relationship between the two groups. Rates of each type of autoimmune disorder within the composite were subsequently analyzed along with other health problems. Results indicated that SLI participants had significantly higher asthma rates than ASD participants. This finding is in line with previous research indicating that autoimmune disorders may occur more often in SLI (Gilger et al., 1992; Hugdahl et al., 1990) and expands previous finding by specifying the type of autoimmune disorder that occurs more often when compared to ASD individuals. This may be an important distinction in understanding the SLI and ASD endophenotypes.

Unexpectedly, SLI participants also had significantly higher rates of frequent stomach and digestion problems than ASD participants. Niehus and Lord (2006) found

that ASD children have significantly more medical problems, as well as a nonsignificant trend toward more chronic gastrointestinal problems, than typically developing children. Given this information, the current results are even more unexpected. Taken together, both SLI and ASD groups may present with GI distress, but with etiological differences. Future research will be required to determine the role of frequent stomach and digestion problem in SLI and ASD individuals.

The hypothesis that mildly-moderately and severely autistic participants would have higher rates of MR was supported. ASD participants had significantly higher MR rates than SLI participants. This is consistent with the existing literature indicating that MR is the most common comorbid diagnosis in ASD individuals (Bailey et al., 1996). In addition, results indicated that the severe groups, driven primarily by the severe ASD group, had significantly higher rates of MR than the mild-moderate groups. This finding is also consistent with literature indicating that autistic individuals dually diagnosed with MR often have many maladaptive behaviors and few adaptive skills, resulting in higher severity ratings on tests of adaptive functioning (Kraijer, 2000).

Specific Aim III

The third aim was to determine parental education levels, parental occupations, and the frequency of psychopathology in parents of SLI and ASD participants in order to identify potential endophenotypic subtypes for subsequent genetic linkage or association studies.

Hypothesis 1

The hypothesis that parental education levels of mild-moderate and severe SLI and mild-moderate and severe autistic participants would be similar was not supported.

Results indicated significant relationships between SLI and ASD participants' maternal and paternal education levels. This result was primarily driven by the less-than-12-years-of-education variable. SLI participants had higher than expected rates, and ASD participants had lower than expected rates, of parents who did not complete high school or a GED. As evidenced by the current data, as well as by previous research (Flax et al., 2003), first-degree relatives of SLI individuals have higher rates of learning disorders. Therefore, it is likely that the higher rates of first-degree relatives' learning disorders in this sample contributed to the difference in parental education levels. Additional research will be required to further examine factors related to lower levels of education, particularly at the K-12 level, in parents of SLI individuals.

Hypothesis 2

The hypothesis that the parental occupations of SLI and ASD participants would be similar was supported. Results did not indicate significant relationships between SLI and ASD participants' maternal or paternal occupations. However, a significant relationship between severity level and parental occupation emerged. For maternal occupation, differences were concentrated on the business/finance, engineer/science, and unskilled variables. It appears that mothers of less severely affected SLI and ASD individuals are more likely to be involved in business/finance or engineering science, while mothers of more severely affected SLI and ASD individuals are more likely to be involved in unskilled occupations. For fathers, occupation differences were concentrated on the engineer/science variable, with these findings being primarily driven by the ASD severity levels. These results are consistent with previous research indicating that ASD fathers are overrepresented in engineering, accounting, and science occupations when

compared to the typical population (Wheelwright & Baron-Cohen, 2001) The current results extend these findings by showing that fathers of less severely affected ASD individuals are more likely to have careers in engineering and science than fathers with severely affected ASD children.

Hypothesis 3

The hypothesis that mild-moderate and severe SLI participants' first degree maternal and paternal relatives would have higher rates of SLI, ADHD, and learning disorders was partially supported. SLI participants' first degree maternal relatives had significantly higher learning disorder rates than ASD participants' first degree maternal relatives. This is consistent with the findings of Flax et al. (2003) where reading impairments were significantly higher in proband family members when compared to controls. The current study has extended previous findings by demonstrating that learning disorders occur more often in maternal first-degree SLI relatives than in maternal first-degree ASD relatives. Future research is required to determine whether specific types of learning disorders in maternal relatives are important in SLI versus ASD participants. Contrary to the hypothesis, there was not a significant relationship between first-degree paternal relatives' learning disorder rates. This indicates a possibility for higher heritability of risk on the maternal side, and requires further research.

There was not a significant relationship between first-degree maternal or paternal relatives' SLI and ADHD rates. At first glance this finding appears to be in contrast with several studies indicating that SLI aggregates in families (Benasich & Spitz, 1999; Bishop et al., 1995; Lahey & Edwards, 1995; Rice, Haney, & Wexler, 1998; Spitz et al., 1997; Tallal et al., 2001; Tomblin & Buckwalter, 1998) and the hypothesis that the high

comorbidity of ADHD in SLI individuals (Aram et al., 1984; Cantwell, 1996; Goorhuis-Brouwer & Wijnberg-Williams, 1996; Love & Thompson, 1988; Redmond & Rice, 1998; Smalley, 1997; Tallal et al., 1991) would lead to higher rates of ADHD in first-degree relatives due to the high heritability rates in ADHD (Albayrak, Friedel, Schimmelmann, Hinney, & Hebebrand, 2008). However, the counts in first-degree relatives with SLI and ADHD (see Tables 19 and 20) indicate that rates in both groups' first-degree relatives may have been elevated, especially in relation to the general population. Future research will be important in illuminating whether there are higher rates of similar psychopathologies in both SLI and ASD relatives than in the general population.

The hypothesis that mild-moderate and severe ASD participants' first degree maternal and paternal relatives would have higher rates of anxiety disorders, mood disorders, ASD, MR, and epilepsy was partially supported. ASD participants' first degree maternal relatives had significantly higher ASD rates than SLI participants' first degree maternal relatives. This finding is not surprising given the high heritability of ASD (Bailey et al., 1995). Contrary to the hypothesis, there was not a significant relationship between first-degree paternal relatives' ASD rates. This is consistent with Lajiness-O'Neill and Menard's (2007) findings indicating that higher rates of psychopathology, such as anxiety and mood disorders, in ASD family members occurs on the maternal side.

There was not a significant relationship between first-degree maternal or paternal relatives' anxiety disorders, mood disorders, MR, or epilepsy rates. This is in contrast to research indicating higher rates of depression, anxiety, and cognitive problems in ASD family members than in controls (Bolten et al., 1998; Lajiness-O'Neill & Menard, 2007; Micali et al., 2004; Piven et al., 1990; 1991; Piven & Palmer, 1999; Smalley et al., 1995).

As seen with the SLI and ASD counts in first-degree relatives (see Table 19 and 20), it appears that both SLI and ASD participants' first degree relatives have elevated rates of anxiety and mood disorders. Higher rates of anxiety and depressive symptoms, not appearing to be due to impoverished environments, have recently been found in SLI adolescents than in controls (Conti-Ramsden & Botting, 2008), suggesting possible family history of emotional health problems. Future research will be important in determining whether there are higher rates of mood and anxiety disorders in both SLI and ASD relatives than in controls.

Unexpectedly, ASD participants' first degree maternal relatives had significantly higher thought disorder rates than SLI participants' first degree maternal relatives. Mouridsen, Rich, Isager, and Nedergaard (2008) reported higher rates of psychiatric disorders in individuals who had been diagnosed with infantile autism as children than a normal control group. Stahlberg, Soderstrom, Rastam, and Gillberg (2004) reported higher than expected thought disorder comorbidity in an ASD sample. These increased incidence rates in ASD individuals, along with the high heritability rate of thought disorders (Greenwood et al., 2007), help to explain the current findings. In addition, very recent research using a large sample of 1,227 ASD subjects and 30,693 control subjects indicated that thought disorders occur in ASD parents more often than controls (Daniels et al., 2008). The current study extends these findings by indicating higher rates of thought disorders in ASD first-degree maternal relatives than the SLI group. This may be an important factor for genetic linkage and association studies.

Specific Aim IV

The fourth aim was to examine results from the analyses used in specific aims 1 to 3 in order to determine whether significant variables (from previous analyses) would be useful in predicting group membership. This aim was exploratory in nature. Unfortunately, due to poor ratio between predictor variables and cases, power to detect differences was poor.

Hypothesis 1

Factors were combined to predict group membership to diagnostic category and severity level. Results indicated that variables including verbal communication quality, nonverbal communication withdrawal/isolation, nonverbal communication disruption/aggression, MR comorbidity, and frequent stomach/digestion problems were most successful in predicting group membership; however, overall data was extremely variable. Results also indicated that the MR comorbidity variable was most successful in predicting severity level, but once again data were extremely variable.

Limitations

The study has a number of limitations. The use of clinical retrospective data can be restrictive, especially in relation to missing data. Missing data was most problematic in regards to the quantitative cognitive data. Missing data on the motor composite, memory composite, executive functioning composite, visual attention scores, and auditory attention scores limited analyses that could be conducted and also resulted in a loss of statistical power. Even though significant results were obtained based on three cognitive areas, effect size was small. A larger sample size would have allowed for greater power to detect differences and increased generalizability of findings.

Another limitation regarding the use of retrospective data was the restriction on the type of data available. In order to gather pragmatic data for the current study, it had to be extracted from the historical sections of the participants' neuropsychological reports. This resulted in data that were not clinically validated. Lack of clinical validation limited the areas of pragmatic language functioning that could be analyzed. As a result, generalizability was greatly decreased. In future research, it will be important to gather clinically validated pragmatic data to determine whether pragmatic differences found in the current study can be replicated, and to further illuminate areas of pragmatic differences in SLI and ASD individuals.

The psychopathology family history data were based on parent report. The use of data based on parent report is a limitation as it is possible that parents had incorrect information about first-degree family relatives. For example, parents may have reported bipolar disorder as a thought disorder rather than a mood disorder. Even still, the differences in maternal psychopathology family history in the areas of learning disorders, ASD, and thought disorders will be helpful in future research. Future prospective research verifying proband first-degree relatives' psychopathology is needed to confirm results of the current study.

The lack of a typical control group was also a limitation of the current study. Significance between the diagnostic categories was not found on variables such as comorbid ADHD and family history of anxiety and depression, but counts in each group may have been higher than in the typical population. Future research will be important in examining whether SLI and ASD taken together differ from the typical population on specific variables such as comorbidity and family psychopathology history.

Finally, the logistic regression analyses were very limited due to number of predictors relative to sample size. This problem resulted in the need to delete variables from the analysis as well as extremely low odds ratios. In sum, the logistic regression was not powerful enough to make a meaningful contribution to the study.

Importance of Findings

The goals of the current study were to illuminate factors involved in the SLI and ASD neuropsychological endophenotypes and to clarify the nature of overlap between the two disorders. Several significant results emerged from the analysis, indicating that SLI and ASD are not necessarily categorical or continuous disorders (see Figure 1). Instead, the two disorders can be classified along both categorical and continuous dimensions based on some distinct characteristics and by severity.

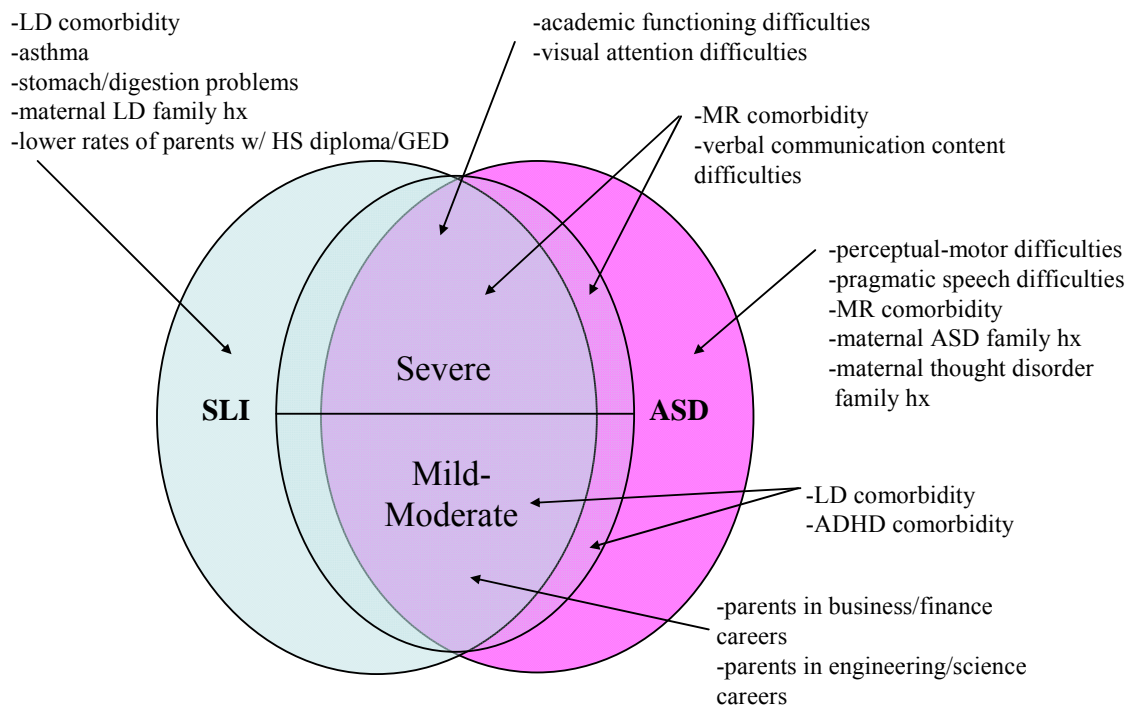


Figure 1. Diagram of diagnostic category and severity level findings.

In specific aim I, cognitive data revealed that perceptual-motor functioning and pragmatic language problems distinguished between the broad diagnostic categories of SLI and ASD, with the ASD group performing significantly poorer in both areas. Cognitive data also indicated differences in severity levels on measures of academic functioning, visual attention, and the pragmatic variable of verbal communication content, revealing lower functioning in the severe groups for both diagnostic categories. Taken together, the combination of these variables demonstrates two very specific differences between the broad diagnostic categories, but the vast majority of findings suggest that a continuum is present. These findings support the idea of SLI and ASD as continuous disorders with significant degrees of overlap, which adds additional information to previous literature indicating SLI and ASD similarities in speech and language functioning (Bishop, 1998; Bishop & Norbury, 2002; Botting & Conti-Ramsden, 1999; Botting & Conti-Ramsden, 2003; Kjelgaard & Tager-Flusberg, 2001).

In specific aim II this categorical versus continuous question was posed further by examining epidemiological variables such as comorbid psychopathology and health problems in the proband to explore other possible endophenotypic variables. Analyses indicated higher rates of learning disorders, asthma, and frequent stomach/digestion problems in the SLI group, while the ASD group had higher rates of MR. In addition, LD and ADHD were found to be more prevalent in the mild-moderate ASD group, while MR was found to occur more often in the severe ASD group. Comorbidity differences between the SLI and ASD groups and within the ASD severity levels will be helpful in identifying endophenotypic subtypes in SLI and ASD for subsequent genetic linkage or association studies.

The combined finding in specific aims I and II of higher levels of perceptual motor difficulties in the ASD group, lack of differences between SLI and ASD groups in the motor composite, and greater rates of ADHD comorbidity in the mild-moderate groups, specifically in the mild-moderate ASD, gives rise to the possibility of another overlap along the SLI-ASD continuum, possibility involving ADHD. Previous reports indicate attention problems in both SLI and ASD diagnostic groups (Cantwell, 1996; Corbett & Constantine, 2006; Love & Thompson, 1988; Reiersen & Todd, 2008; Smalley, 1997), and recent literature indicates motor difficulties in both ADHD and ASD, with ASD individuals having significantly more trouble with motor movements involving orientation and pragmatic language skills such as gesturing (Dewey, Cantell, & Crawford, 2007). The possibility exists that there may be overlap between all three groups, particularly in the area of motor skills, but this hypothesis requires further research.

In specific aim III, familial variables contributing to the SLI and ASD endophenotypes were explored. Parental education levels, parental occupations, and the frequency of psychopathology in parents of participants with SLI and ASD revealed several significant findings. First, the parental education differences, driven by the SLI group having fewer parents with high school degrees, was likely due to higher rates of learning disorders in SLI relatives (Flax et al., 2003) and the finding that SLI maternal first-degree relatives in the current sample also had higher rates of learning disorders than ASD maternal relatives. Interestingly, all significant findings regarding psychopathology differences in proband relatives occurred on the maternal side. In addition to higher rates of learning disorders in SLI maternal relatives, ASD maternal relatives had higher rates

of ASD and thought disorders. The parental differences found between the SLI and ASD groups are important for identification of endophenotypic subtypes as these factors may be important for genetic linkage and association studies.

Finally, there were no differences between parental occupation and diagnostic categories. However, significant relationships based on severity level were noted, with mild-moderate groups' parents more likely to be in engineering/science and business/finance careers than the severe groups. Previous research has indicated that ASD fathers are overrepresented in engineering, accounting, and science occupations when compared to the typical population (Wheelwright & Baron-Cohen, 2001), providing some evidence for the theory that autism is an extreme form of the male brain (Baron-Cohen & Hammer, 1997). The current study extends these results by specifying the importance of severity level within groups and indicating that mothers in both SLI and ASD groups may be more likely to be involved in certain occupations than the typical population. However, future research is required to determine whether occupations in SLI and ASD mothers differ from the typical population. Even still, the differences found based on severity level within diagnostic groups further supports SLI and ASD as continuous rather than discrete disorders. The severity level differences in parent occupation also suggest that mildly-moderately affected developmentally disabled off-spring of parents with extreme abilities, such as the strong spatial skills required of engineers, inherit these abilities, but at the loss of language skills. This possibility refers to the nontraditional inheritance concept of "anticipation," where a genetic disease displays an earlier age of onset and has a more severe expression in later generations (Goldstein & Reynolds,

1999). This is a large leap from the current data but is an important issue that will be critical to explore in future research.

In specific aim IV, specific cognitive data, epidemiological factors, and familial variables significantly predicted group membership for both diagnostic category and severity level. However, the extreme variability of the data resulted in significant results not being very meaningful or useful. Part of the difficulty was the poor predictor to subject ratio, especially in predicting group membership to diagnostic category. Additionally, there may be problems in predicting group membership for SLI and ASD individuals as the groups are not distinctive enough to have clear predictors. Further research with larger sample sizes is required to explore whether clear predictors exist for categorical distinction by diagnosis and severity level. Based on the current data, however, the groups do not have clear predictors for group membership, giving additional evidence that SLI and ASD are continuous rather than distinctly categorical disorders.

These combined findings have several important implications. They provide valuable information on factors present in SLI and ASD neuropsychological endophenotypes. They also increase understanding on the nature of overlap between the two disorders. Finally, results allow for a greater understanding of familial characteristics, leading to a stronger understanding of heritability.

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APPENDICES

APPENDIX A
Human Subjects Review Approval (EMU)



EASTERN MICHIGAN UNIVERSITY

September 25, 2007

Heather Anson
Department of Psychology

Dear Heather Anson:

The Human Subjects Institutional Review Board (IRB) of Eastern Michigan University has reviewed and approved as exempt research your proposal titled, "The Neuropsychological Endophenotype of Specific Language Impairment (SLI) and Autism Spectrum Disorders (ASD): Category or Continuum?". The IRB determined that the rights and welfare of the individual subjects involved in this research are carefully guarded.

Exempt research does not require reporting of continuation one year after approval if the project continues. However, should the sample or procedures change as to have an impact on human subjects, then UHSRC should be notified by using the *Minor Modification to Research Protocol* or the *Request for Human Subjects Approval* form depending upon the scope of the changes (see the forms online).

On behalf of the Human Subjects Committee, I wish you success in conducting your research.

Sincerely,

A handwritten signature in black ink that reads "Deb de Laski-Smith".

Deb de Laski-Smith, Ph.D.
Interim Dean
Graduate School
Administrative Co-Chair
University Human Subjects Review Committee

Reference # 070906

APPENDIX B

Human Subjects Review Approval (HFHS)



RESEARCH ADMINISTRATION

January 9, 2008

Research Administration

CFP-Basement 046
 2799 West Grand Boulevard
 Detroit, MI 48202-2689
 (313) 916-2024 Office
 (313) 916-2018 Fax

To: Renee Lajiness
 Neuropsychology
 Heather Anson (hanson@emich.edu)

Fm: Timothy Roehrs, Ph.D., Chair
 Tom Mikkelsen, M.D., Vice Chair
 Institutional Review Board (IRB)

Re: **“The Neuropsychological Endophenotype of Specific Language Impairment (SLI) and Autism Spectrum Disorders (ASD): Category or Continuum?”**, (IRB #: 4842)

Period of IRB Approval: 01/08/08 – 01/07/09

At a meeting on January 08, 2008, Institutional Review Board reviewed the above-referenced protocol. The IRB approved the project and the submitted consent form.

The Institutional Review Board and Federal Regulations require that each research proposal involving human subjects be reviewed at intervals appropriate to the degree of risk but not less than once per year and that a final report be submitted at the termination of the project.

A continuation or final report for this proposal is due in one year. The report must be approved by the IRB by January 07, 2009 to avoid a lapse in your approval. As the Principal Investigator, you are ultimately responsible for timely submissions of continuation and final reports. You are encouraged to create a tracking mechanism to ensure timely submissions.

Revisions to the protocol must be approved by the IRB prior to implementation. In addition, our IRB is expected to review all documents and activities that bear directly on the rights and welfare of the participants in the research project. This includes, but is not limited to advertisements used to recruit subjects

Moreover, **unexpected events and serious adverse effects** relating to subjects must be reported to the IRB as soon as possible; supplemental information may be appended to the notification form.

A copy of the signed & stamped application indicating approval by the IRB is enclosed for your files. Please be sure to keep copies of the signed informed consent forms on file. One convenient method is to duplicate each signed consent form, leaving the original with the patient's medical record and filing the copy together with all other consent forms for that project. Be sure to give the study subject a copy of the signed consent.

Forms for progress reports, final reports, modification and adverse/unexpected event are available on the Henry Ford website (<http://henry.hfhs.org/body.cfm?id=3323>). Please contact the IRB Coordinator at 916-2024 if you have questions regarding these matters.

