ABSTRACT

DISSERTATION: Perinatal Complications as Predictors of Autism

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The reported diagnosis of autism has increased in the past two decades. The term autism does not refer to a specific diagnosis. Most research on autism involves individuals with one or more of the following diagnoses: autistic disorder, Asperger’s disorder, or pervasive developmental disorder not otherwise specified (PDD-NOS). The majority of research concerning this population has focused on etiology. Findings from this research suggest that both genetic and environmental factors play a major role. Despite numerous studies finding a link between perinatal complications and autism, a firm conclusion cannot be drawn due to the variation in methodology. The present study further investigated the relationship between perinatal complications and autism. Perinatal data were collected using the Maternal Perinatal Scale (MPS), a standardized measure with evidenced validity and reliability. There were three subject groups. The first group consisted of individuals previously diagnosed with autistic disorder. The second group consisted of individuals previously diagnosed with Asperger’s disorder. The third group was the control group, and it consisted of individuals with no history of neurologic or psychological diagnoses. Results of an ANOVA indicated individuals with autistic disorder had a significantly higher number of reported perinatal complications when compared to
individuals in the control group. Those diagnosed with Asperger’s disorder did not differ significantly from the individuals in the control group or the autistic individuals in terms of number of complications. A CART analysis yielded a prediction model that examined if a subject’s diagnosis could be predicted using solely his/her perinatal data. The model was only able to accurately predict a subject’s diagnosis 60% of the time. Although the model predicted better than chance (e.g., 33%), the results did not provide strong support for the sole use of perinatal factors for predicting a later diagnosis of autistic disorder or Asperger’s disorder.
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CHAPTER ONE

Introduction

The term autism was first coined in 1911 (Gupta, 2004). It was not used diagnostically until 1943. Leo Kanner (1943) used the term to describe children who sought social isolation, showed severe deficits in communication skills, and desired “sameness” in the environment. In addition, these patients had a preoccupation with objects and stereotyped play habits (Kanner, 1943, as cited in Wilkerson, 1992 and Gupta, 2004). Since 1943, autism has received a great deal of attention in the popular media as well as in the research literature. Currently, one particular area of concern is the increased prevalence rate of autism (Stokstad, 2001).

Psychologists and psychiatrists do not use autism as a diagnosis. Instead, they utilize a specific diagnosis outlined in the pervasive developmental disorder (PDD) section of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; APA, 2000). The PDD diagnoses included in DSM-IV-TR are: autistic disorder, Asperger’s disorder, childhood disintegrative disorder, Rett’s disorder, and pervasive developmental disorder not otherwise specified (PDD-NOS; APA, 2000). All of these conditions are characterized by severe and pervasive impairment in multiple areas of development including communication skills, reciprocal social interaction, and the presence of stereotyped behavior, activities, or interests (APA, 2000). The present study examined whether or not differences existed in the etiology of Asperger’s disorder and autistic disorder. These two disorders were selected because they are believed to be linked (Cederlund & Gillberg, 2004).

Autistic disorder is characterized by impairments in social interaction and language development as well as restricted, stereotyped, and repetitive behaviors, activities, and interests (APA, 2000). A delay or abnormal functioning is present in social interaction, language, or
imaginative play prior to three years of age. Epidemiologically, autistic disorder occurs in 5 to 13 per 10,000 children (Fombonne, 2006; APA, 2000). The prevalence of the diagnosis has dramatically increased from previous years (Stokstad, 2001). Autistic disorder is reported to occur more frequently in males with a male to female ratio of approximately 4:1 (Volkmar et al., 2004).

Asperger’s disorder is also characterized by difficulty with social interactions. Additionally, there are restricted and repetitive patterns of behavior, activities, and interests (APA, 2000). However, the prognosis for individuals diagnosed with Asperger’s disorder tends to be better than for individuals diagnosed with autistic disorder. Indeed, cognitive deficits or significant delays in language are rarely present in individuals with Asperger’s disorder (Carlson, 2005). Research has provided limited information regarding the epidemiology of Asperger’s disorder. It appears that this disorder occurs more frequently in males (APA, 2000).

Although autistic disorder and Asperger’s disorder fall under the PDD category, the Center for Disease Control (CDC) and numerous researchers have adopted another category for these diagnoses. Indeed, recent research concerning these disorders focuses on the subtypes that fall under Autism Spectrum Disorder (ASD; e.g., CDC, 2012; Mann, McDermott, Bao, Hardin, & Gregg, 2010; Reichenberg et al., 2006). ASD includes the following PDD diagnoses: autistic disorder, Asperger’s disorder, and pervasive developmental disorder not otherwise specified (PDD-NOS; Dawson & Faja, 2008). Studies typically use mixed samples of individuals who have one of those three diagnoses, rarely comparing the groups to each other. That is, they use a sample consisting of any individual who has a diagnosis considered to be an ASD (e.g., Bilder, Pinborough-Zimmerman, Miller, & McMahon, 2009; Herbert, 2010; Mann et al., 2009). Furthermore, it appears that in the research literature the term autism has become synonymous
with ASD (e.g., Yirmiya & Charman, 2010; Kolevzon, Gross, & Reichenberg, 2007; Reichenberg et al., 2006; Glasson et al., 2004).

The majority of research concerning the ASD diagnoses has focused on etiology and treatment. The reason to study the etiology is to help clinicians. If a clinician can identify a child as being at-risk for ASD, that child can then be monitored. That will likely result in an early diagnosis, which means early treatment. This is important because early treatment results in better long-term outcomes (e.g. Howling, Magiati, & MacLean, 2009; Majnemer, 1998). Relatively little is known about the etiology of ASD; however, research has suggested that both genetic and environmental factors play a role (Dawson, Glasson, Dixon, & Bower, 2009).

There have been a number of studies that investigated the particular genes related to PDDs (e.g. Geschwind, 2011; Muhle, Trentacoste, & Rapin, 2004). For example, research has suggested a strong relationship between genetic factors and autistic disorder (Muhle et al., 2004). Past twin and family studies support a strong genetic component (Bailey et al., 1995; Steffenburg et al., 1989). More recently, several chromosomal abnormalities have been linked to autistic disorder (Beaudet & Zoghbi, 2006; Bonora et al., 2006; Muhle et al., 2004). So too, a number of researchers have found a link between autistic disorder and other known genetic disorders, such as tuberous sclerosis and fragile X syndrome. This research provides further support of a genetic influence in the development of the disorder (Muhle et al., 2004).

Asperger’s disorder, on the other hand, has limited research concerning its etiology in general, including genetic factors. This disorder has not had the major family or twin studies to the same extent as autistic disorder. However, the few studies that have investigated the heritability of the disorder do suggest a genetic component. For instance, there is a higher frequency of Asperger’s disorder among family members of a patient with the disorder compared...
to the family of those with no diagnosis (APA, 2000). Several clinical studies have suggested 30% to 60% of cases of Asperger’s disorder have a close relative with the disorder or similar symptoms (Gillberg & Coleman, 2000).

There appears to be a shared belief among researchers that there is a synergy of environmental and genetic factors in ASD diagnoses (e.g., Herbert, 2010; Muhle et al., 2004; Korvatska, Van de Water, Anders, & Gershwin, 2002). One of the environmental factors previously hypothesized to be related to a PDD diagnosis was immunizations received in early childhood (Dawson & Faja, 2008; Muhle et al., 2004). However, other research argues against the creditability of this conclusion (Madsen et al., 2002; Taylor et al., 2002). Many environmental factors have important roles in the development, and possibly the severity, of autism (Rodier & Hyman, 1998). Investigations concerning relevant environmental influences have included examining perinatal complications.

Perinatal complications, sometimes referred to as obstetric complications, can be defined as deviations from the expected course of events during pregnancy, labor, delivery, or the first 28 days of life (Gray, Dean, Joy, Sowles, & Sparzo, 1987). The significance of perinatal complications in relation to an individual’s functioning later in life has been investigated in numerous studies (e.g., Commey & Fitzhardinge, 1979; Field, Dempsey, & Shuman, 1981; Holmes, Reich, & Pasternak, 1984). For example, children who experience perinatal complications were more likely to display developmental abnormalities in multiple areas of functioning, including medical, mental, physical, motor, and behavioral (Field et al., 1981).

Other studies have also shown an association between developmental deviations and perinatal complications (e.g., Thompson et al., 2003; Dean & Davis, 2007). These deviations include neurological (Hill, Cawthorne, & Dean, 1998) as well as psychiatric outcomes.
Specifically, compromising events during the perinatal period of development have been implicated in the development of a number of disorders, such as learning difficulties (Colletti, 1979), speech problems (Gattie, Arceneaux, Dean, & Anderson, 1994), cerebral palsy (Drougia et al., 2007), mental retardation (Dammann & Leviton, 1997), psychiatric problems (Indredavik et al., 2010), and pervasive developmental disorders (Dean & Davis, 2007).

A number of researchers have argued in favor of potential environmental triggers for ASD disorders related to the earliest prenatal and perinatal experiences (Stein, Weizman, Ring, & Barak, 2006). The results of such studies have shown a higher number of these complications among individuals with autistic disorder than a normal cohort (Larsson et al., 2005). In fact, several perinatal factors have been implicated in relation to the development of autism. Advanced paternal age and maternal age have been linked to the disorder (Gardener, Speigelman, & Buka, 2009; Reichenberg et al., 2006; Burd Severud, Kerbeshian, & Klug, 1999). Another perinatal factor related to autism is maternal medication use during pregnancy (Gardener, Speigelman, & Buka, 2009; Wilkerson, Volpe, Dean, & Titus, 2002). Additional factors reportedly related to autism include intrauterine exposure to certain drugs, viral infections, maternal stress, congenital rubella, and birth weight (Kinney, Munir, Crowley, & Miller, 2008; Wilkerson, Volpe, Dean, & Titus, 2002; Burd, Severud, Kerbeshian, & Klug, 1999; Rodier & Hyman, 1998; Christianson, Chester, & Kromberg, 1994; Chess, Fernandez, & Korn, 1978). Despite numerous studies examining perinatal complications, a consistent set of perinatal risk factors for autism has not yet been established (Glasson et al., 2004).

Although the etiological research of Asperger’s disorder is sparse, it has been shown that perinatal complications are more likely in this population than in normal cohorts. For example,
Cederlund and Gillberg (2004) conducted a study comparing 100 males with Asperger’s disorder with typical counterparts. For those who had been diagnosed with Asperger’s disorder, they found that some mothers had experienced a major viral or bacterial infection during pregnancy. They also found that bleeding during the second or third trimester as well as incidences of jaundice were higher in individuals with Asperger’s disorder.

There are some issues with the studies investigating perinatal complications in autism. There is a tendency to use a sample of ASD without controlling for the individual diagnoses of ASD. Although Asperger’s has been linked clinically and genetically to autism (Cederlund & Gillberg, 2004), there are major symptomatic differences between the two. One such difference relates to language development; specifically, individuals with autism have a significant delay or impairment in this area (APA, 2000) and those with Asperger’s disorder do not. Additionally, there is a difference in the manifestation of the restricted, repetitive, and stereotyped behavior, activities, and interests (APA, 2000). The two disorders also differ in their developmental course. Indeed, patients with Asperger’s disorder typically have a significantly better prognosis than those with autistic disorder (APA, 2000). Additionally, there is a significant difference in age at diagnosis between the two conditions with Asperger’s disorder typically diagnosed at an older age (Mandell, Novak, & Zubritsky, 2005). Based on these disparities, one might conclude a significant difference exists in the etiology of the two disorders. The present study investigated potential differences between the disorders in terms of perinatal complications related to each disorder.

Very few investigations of perinatal development compare the individual conditions encompassed within the spectrum in order to see if they are in fact unique individual disorders. Therefore, further research is needed in order to consider the role of perinatal factors in the
development of autistic disorder as well as Asperger’s disorder. Although they are considered to be on the same symptomatological spectrum there seems to be a need for comparison between these groups. Clearly, there is little research on the etiology of Asperger’s disorder. Thus, it is difficult to conclude if it is in fact comparable to the etiology of autistic disorder. Perhaps, then, investigating the perinatal environmental factors related to each disorder would be useful, particularly whether a significant difference exists between them.

Other issues, aside from heterogenous samples, exist among the numerous investigations of perinatal factors related to ASD. In regards to specific complications, findings have been inconsistent (Gardener, Spiegelman, & Buka, 2009). This variability may be related to methods of collecting data, which varied from one study to the next and tended to be informal, with most studies relying solely on medical records. Methods of collecting perinatal information have differed between studies. One method involves examining medical records, which can provide relevant data concerning gestation and delivery. However, they may not be able to capture many of the maternal and paternal factors related to development, such as whether or not the mother smoked during the pregnancy. Not to mention, the utility of medical record reviews is questionable in light of our highly mobile society (Gray, Dean, & Lowrie, 1988; Gray, Dean, Rattan, & Betchel, 1988). Another, perhaps more convenient method is collecting the information from parents via interview. This method calls into question parents’ memory concerning events that may have occurred several years prior (Gray et al., 1987) and therefore may not be accurate.

The Maternal Perinatal Scale (MPS; Dean & Gray, 1985) is another method for collecting perinatal information. It is a standardized self-report measure that systematically assesses perinatal complications (Gray, Dean, & Rattan, 1987). The MPS examines a broad range of both
biological and environmental factors that have been shown to place an infant at risk for later neurological abnormality (Strom, 1991). It contains 47 items, which were written at a fourth grade reading level to ensure comprehension by the reader (Wilkerson, 1992). The items pertain to an infant’s gestation, birth, and first month of life as well as the mother’s medical history. Items on the measure were constructed based on established risk factors that occur during the perinatal period (Gray, Dean, & Rattan, 1987). Additionally, there were items included in the measure that had been implicated in early childhood development.

The items on the MPS were created so that mothers (or other informants) had to perform the simpler memory process of recognition as opposed to the more complex process of recall. This design feature helps reduce the potential problems of omission and confabulation associated with parent recall (Gray, Dean, & Rattan, 1987). The MPS has been shown to be both reliable and valid (Gray, Dean, & Rattan, 1985; Gray, Dean, Rattan, & Bechtel, 1987). Additionally, it has been used to investigate perinatal events in relation to several developmental outcomes, including emotional/behavior disorders (Batchelor, Dean, Gray, & Wenck, 1991), school achievement (Gray et al., 1992), mental retardation (Gray, Dean, Strom, Wheeler, & Brockley, 1987), sensory processing difficulties (2009), and infantile autism (Wilkerson, Volpe, Dean, & Titus, 2002).

Purpose of the Study

Previous research has found a relationship between perinatal complications and a number of later developmental deviations (e.g., Commey & Fitzhardinge, 1979; Field, Dempsey, & Shuman, 1981). Autistic and Asperger’s disorders are associated with developmental deviations, and therefore, may be related to perinatal complications. Indeed, numerous studies have investigated perinatal complications in ASD. One such study indicated the presence of
encephalopathy at birth was associated with the presence of ASD (Badawi et al., 2006). This line of research indicated that advanced paternal and maternal age increased the risk of a child being diagnosed with an ASD (Durkin et al., 2008; Gardener, Speigelman, & Buka, 2009). Aside from advanced age, other maternal factors related to ASD include prenatal medication use, bleeding, gestational diabetes, number of previous births, hypertension, previous fetal loss, proteinuria (excess protein in the urine), pre-eclampsia, and swelling (Gardener, Speigelman, & Buka, 2009).

However, the research investigating perinatal complications related to these disorders has yet to yield a firm conclusion about their etiological similarities. Indeed, research with autistic patients has produced inconsistent conclusions about the type and frequency of pertinent perinatal complications (Glasson et al., 2004). This may be attributed to differences in methodology, including samples and data collection. This study wanted to contribute to the research literature by further investigating the perinatal complications in Asperger’s disorder and autistic disorder by taking a different approach. First, perinatal data was collected using an established measure, Maternal Perinatal Scale (MPS; Dean & Gray, 1985), which is both structured and reliable. Second, a control group was utilized. The perinatal history of individuals in each of the diagnostic groups was compared to a group consisting of unrelated counterparts who had no history of neurologic or psychological diagnoses. Third, individuals with autistic group were in a separate group from those who had been diagnosed with Asperger’s disorder.

Autistic disorder and Asperger’s disorder, along with PDD-NOS, fall under the umbrella label of ASD (Dawson & Faja, 2008). This implies, yet to be shown empirically, that these disorders are similar in etiology and merely differ in severity of presentation. In fact, the newest edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V; APA, 2013) does
not differentiate these disorders, which supports the belief of similar etiology. Limited studies have examined the etiology of Asperger’s disorder, including perinatal factors. However, it has been shown that autistic disorder and Asperger’s disorder differ not only in clinical features but also in the frequency of perinatal complications (Dawson, Glasson, Dixon, & Bower, 2009). The present research examined similarities between autistic and Asperger’s disorders in terms of the number of perinatal complications.

Research Questions

The first research question examined the relationship between the number of perinatal complications experienced and a diagnosis of autistic disorder. This was investigated by comparing a control group within individuals diagnosed with autistic disorder on the number of reported perinatal complications.

The second research question examined the relationship between the number of perinatal complications experienced and a diagnosis of Asperger’s disorder. A control group was compared to individuals diagnosed with Asperger’s disorder in terms of the number of complications.

The third research question pertained to whether or not a difference exists in the etiology of Asperger’s disorder and autistic disorder. This involved comparing the two groups on the number of perinatal complications reported.

There was also a fourth research question. Could a later diagnosis of autistic disorder or Asperger’s disorder be predicted based solely on perinatal development? The perinatal data for the prediction model will be weighted based on the influence a specific complication has on later functioning.
Useful Definitions

There are terms relating to perinatal factors and their relationship with developmental outcomes that are of particular importance to this study. Many of these terms are defined below.

**Perinatal.** Perinatal, in general, refers to the development of an individual from conception throughout gestation, labor, delivery, and the first 28 days of life.

**Perinatal Complications.** These are deviations from an expected course of events, which involves both the mother and her child, during pregnancy, delivery, and the early neonatal period.

**Autistic Disorder.** Autistic disorder is a neurodevelopmental condition in which clinical features are present prior to three years of age. Features of this disorder include impairment in social interaction, impairment in communication, and the presence of restricted, repetitive behaviors, interests, and activities. These features could be manifested in the following manners: impairment in the use of nonverbal behaviors (e.g., eye contact), failure to form appropriate peer relationships, lack of seeking out shared enjoyment with others, inability to initiate or sustain conversation, lack of creative play, use of idiosyncratic language, inflexible adherence to routines or rituals, restricted range of interests, stereotyped and repetitive motor mannerisms, and a preoccupation with parts of objects (APA, 2000).

**Asperger’s Disorder.** Asperger’s disorder is a condition involving impairment in social interaction. Unlike autistic disorder, there is no delay in the acquisition of developmental milestones related to language. Additionally, features of the disorder do not need to be present before a specific age. Like autistic disorder, there is the presence of restricted and repetitive patterns of behavior, interests, and activities. The features of this disorder could manifest in the following manners: restricted range of interests, inflexible adherence to routines or rituals,
stereotyped and repetitive motor mannerisms, preoccupation with parts of objects, impairment in nonverbal social behaviors (e.g., facial expression), failure to develop appropriate peer relationships, lack of social or emotional reciprocity, and lack of seeking shared enjoyment (APA, 2000).

**Pervasive Developmental Disorder (PDD).** PDD is an umbrella term that refers to a group of disorders characterized by severe and pervasive impairment in multiple areas of development, including communication skills, reciprocal social interaction, or the presence of stereotyped behavior, activities, or interests. Both autistic disorder and Asperger’s disorder are a subtype of PDD (APA, 2000).
CHAPTER TWO

Review of the Literature

This chapter is divided into four major sections. The correlation between perinatal complications and a number of negative developmental outcomes is discussed in the first section. A discussion of the Maternal Perinatal Scale including previous research utilizing this measure is featured in the second section. An overview of pervasive developmental disorders, particularly autistic disorder and Asperger’s disorder, is provided in the third section. The fourth section discusses the findings of previous investigations concerning perinatal complications in relation to pervasive developmental disorders.

Perinatal Complications and Developmental Outcomes

Events occurring during the perinatal period have been shown to be related to children’s long-term developmental functioning (e.g., Commey & Fitzhardinge, 1979; Dean & Davis, 2007; Field, Dempsey, & Shuman, 1981; Holmes, Reich, & Pasternak, 1984). Research has indicated that infants who experience perinatal complications are more likely to display developmental delays. For instance, Field, Dempsey, and Shuman (1981) showed that children who experience perinatal complications exhibit differences in the areas of medical, physical, mental, motor, and behavioral development throughout the first two years of life compared to normals. Thompson and his colleagues (2003) examined perinatal factors related to early developmental delay or disability in children. Their results indicated a significant association between a child having a developmental delay and/or a disability before the age of three and low birthweight, maternal tobacco use, prenatal care, complications of labor and delivery, previous pregnancy experience, and congenital anomalies. Numerous studies have shown a significantly greater incidence of mild handicaps (e.g., mild mental retardation, learning difficulties, behavior problems) for
premature/low birth weight and anoxic samples than control children (Telzrow, 1991). Overall, the impact of perinatal complications can be serious in nature and long-lasting.

Two earlier studies showed a relationship between perinatal complications and motor development (Field, Dempsey, and Shuman, 1981; Gatten, Arceneaux, Dean, and Anderson 1994). Specifically, they found birth weight, labor and delivery (e.g. child’s color at birth, type of anesthesia used during delivery), and pregnancy (i.e. viral infection, tranquilizer use) were predictors of later motor functioning. They also showed that these complications were predictors of speech development. Perinatal factors have been linked to cerebral palsy (Dammann & Leviton, 1997; Drougia et al., 2007), which is “an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of its development” (Mutch et al., 1992). Thus, cerebral palsy often involves abnormal motor functioning. Specific perinatal problems associated with cerebral palsy include small for gestational age, perinatal asphyxia, and periventricular leukomalacia (Drougia et al., 2007).

Research also suggests negative mental health outcomes are related to perinatal complications. For example, Indredavik and colleagues (2010) found a relationship between perinatal factors and psychiatric disorders among adolescents born with very low birth weight. Their results indicated three perinatal factors were shown to be the most predictive. Specifically, lower birth weight, shorter gestation period, and intraventricular hemorrhage were found to be the clearest indicators. In a literature review, Dean and Davis (2007) outlined perinatal complications related to several common childhood disorders. They examined perinatal factors associated with learning disabilities, autism, Attention-Deficit Hyperactivity Disorder (ADHD), and anxiety disorders. Research has also shown perinatal complications are related to mood
disorders and disruptive behavior disorders (Fryer, Crocker, & Mattson, 2008) as well as mental retardation (Dammann & Leviton, 1997).

Earlier research indicates that the strongest perinatal predictors of later psychiatric outcomes are obstetrical complications that result in damage or alteration of the brain (Holmes, Reich, & Pasternak, 1984). This is not surprising given that during postnatal development, brain impairment increases vulnerability to psychopathology (McCurry, Silverton, & Mednick, 1991). There are numerous perinatal threats to the integrity of the brain. Some specific threats include oxygen deprivation (anoxia), reduction in available oxygen (hypoxia), intracranial hemorrhage, physical trauma associated with delivery, and prenatal exposure to toxins, drugs, or infectious agents (Chelune & Edwards, 1981).

Some research has demonstrated a relationship between perinatal events and cognitive functioning (Commey & Fitzhardinge, 1979; Dammann & Leviton, 1997; Field, Dempsey, & Shuman, 1981). In one particular study, events occurring during perinatal development were linked with intellectual functioning in middle childhood (Gray et al., 1987). The results of this study indicated that approximately 96% of the variability in children’s patterns of cognitive functioning could be accounted for by perinatal variables related to prenatal care and labor. A study by Camp, Broman, Nichols, and Leff (1998) examined risk factors associated with mental retardation in seven-year-old children. Their findings showed there was a negative relationship between prenatal complications and later intellectual functioning. Specifically, low maternal weight gain (less than 10 pounds), low hematocrit, and urinary tract infection were related to mental retardation.

Despite differing in etiology, learning disabilities tend to have common neurofunctional commonalities (Dean & Woodcock, 2003). One such commonality among children with a
learning disorder is often the slower learning rate compared to their peers. A study by Hill, Cawthorne, and Dean (1998) revealed that prepregnancy, prenatal, and birth and delivery factors contributed most to the ability to correctly distinguish between children with learning problems and their normal counterparts. In fact, using a stepwise discriminate analysis of perinatal factors, the authors were able to correctly sort individuals into their corresponding group with 92.5% accuracy. Another study by Colletti (1979) supported a link between perinatal complications and the later development of learning disabilities. This study compared learning disabled children with a normative group. The results indicated the learning disabled group experienced significantly more perinatal problems, including anoxia, poor circulation, and respiratory distress.

ADHD is one of the most common disorders occurring during childhood, and as a result, it has been frequently researched. Epidemiological investigations have indicated a genetic component of the disorder, and have implicated perinatal complications are a strong environmental component related to ADHD (Biederman, 2005). Milberger et al. (1997) found a relationship between perinatal complications and ADHD. Specifically, they found maternal bleeding, smoking, family problems, and drug use during pregnancy were more likely to occur in children who developed ADHD symptoms. Linnet et al. (2005) provided further evidence of a link between smoking during pregnancy and the development of ADHD symptoms, particularly hyperactivity. In a comparison of children with ADHD and their unaffected siblings, Amor et al. (2005) found that children with ADHD had a greater number of perinatal complications compared to their unaffected siblings. Particularly, the children with ADHD had higher rates of problems associated with hypoxia. Indredavik et al. (2010) found lower birth weight was a risk factor for ADHD symptoms as well as perinatal intraventricular hemorrhage.
Riikonen et al. (2005) conducted a study of children with fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE). An interesting outcome of the study was the fact that all of the children were found to have ADHD, which suggested a relationship between alcohol use during pregnancy and the acquisition of ADHD symptoms. Attention deficits are common among children with Fetal Alcohol Spectrum Disorder (FASD), and are considered hallmark features of prenatal alcohol exposure (Fryer, Crocker, & Mattson, 2008). Maternal alcohol consumption has also been linked to other disruptive behavior disorders, such as Oppositional Defiant Disorder and Conduct Disorder (Fryer et al., 2007). Conduct problems have also been associated with intrauterine exposure to nicotine (Maughan, Taylor, Caspi, & Moffit, 2004) as well as lead (Dietrich et al, 2001).

Other research provides evidence of a link between anxiety disorders and complications occurring during the perinatal period. Specifically, a study conducted by Hirshfeld-Becker et al. (2004) showed an association between perinatal complications and childhood anxiety disorders. Specifically, they found that children who were exposed to multiple perinatal complications were at an increased risk for developing an anxiety spectrum disorder. These perinatal complications included maternal bleeding necessitating bed rest, maternal infection, and maternal preeclampsia.

Research has also revealed a relationship between mood disorders and perinatal events. O’Connor (2001) found that prenatal alcohol exposure was a significant risk factor of depressive symptomatology at 6 years of age. Furthermore, elevated rates of depressive disorders were observed in children who had been exposed to alcohol during gestation (Fryer et al., 2007). Preti et al. (2000) compared the perinatal histories of individuals with a diagnosis of depression and normal healthy controls. The outcome indicated that the depression patient group had experienced a greater frequency of obstetric complications than their normal counterparts.
The Maternal Perinatal Scale

Although there is ample research investigating developmental outcomes of perinatal complications (e.g., Commey & Fitzhardinge, 1979; Field, Dempsey, & Shuman, 1981), it is difficult to draw conclusions from it. Methods utilized by researchers for collecting perinatal information vary from one study to the next. Additionally, most employ methods that are informal in nature, such as an unstandardized parent interview. Even those studies using more objective techniques, such as medical records, may be missing critical information from an individual’s perinatal history. Furthermore, the majority of studies fail to consider the interaction of multiple perinatal complications. That is, the data are analyzed in a univariate fashion. Overall, there are a few techniques for collecting perinatal data; however, they all have issues that could lead to inaccurate results. There is clearly a need for an objective, reliable measure to capture relevant perinatal information.

One of the more popular techniques for identifying an at-risk child is using their Apgar score. This scale is a rating system developed by Virginia Apgar (Apgar, 1953). It is used to assess an infant’s physical condition at one and five minutes following birth. Specifically, it examines heart rate, respiratory effort, reflex irritability, muscle tone, and color. Each of these five characteristics are rated 0, 1, or 2. Higher scores designate better physical condition with 10 being the highest possible score. A score falling between 4 and 6 indicates the newborn requires assistance in establishing breathing and other vital signs. An infant with a score of 3 or lower is in danger and requires emergency medical attention. Apgar scores help identify infants who require immediate medical attention. These scores have been shown to be related to neonatal mortality; however, the predictive ability of low Apgar scores is debatable. Some studies found that Apgar scores were not predictive of later cognitive and motor functioning (Nelson &
Ellenberg, 1981; Silverman, Suidan, Wasserman, Antoine, & Young, 1985). Other studies support a relationship between Apgar scores and neurologic difficulties (Drage, Kennedy, Berendes, Schwartz, & Weiss, 1966; Moster, Lie, Irgens, Bjerkedal, & Markestad, 2001), learning problems, behavioral problems and minor motor difficulties (Moster, Lie, & Markestad, 2002). Thus, more research is needed in order to establish the utility of Apgar scores for predicting later development.

Another technique for identifying an at-risk child involves the review of medical records/charts. Medical records, in general, provide an ample amount of relevant information related to gestation and delivery. However, most children are not seen by a neuropsychologist until a number of years after these records were completed. Furthermore, these records are often not able to capture many of the maternal and paternal factors related to development, such as maternal smoking during pregnancy. As mentioned above, nicotine exposure during gestation has been shown to be related to many problems later in life for an infant, particularly difficulty with attention (Milberger et al., 1997). Indeed, mothers who smoked during pregnancy were more likely to engage in other behaviors that are related to complications. Furthermore, medical records are questionable in their clinical utility given our highly mobile society (Gray, Dean, & Lowrie, 1988; Gray, Dean, Rattan, & Betchel, 1988). Perinatal data has commonly been obtained through an informal interview with a child’s mother. This manner of collecting data is problematic because of the lack of structure. Furthermore, it involves the mother recalling information concerning events that may have occurred several years earlier (Gray et al., 1987).

Due to the questionable accuracy of recalled information, including omissions and confabulations, this type of data collection is inadequate for clinical investigations (Gray, Dean, & Lowrie, 1988; Gray, Dean, Rattan, & Betchel, 1988).
The Maternal Perinatal Scale (MPS; Dean & Gray, 1985) offers a highly structured method for collecting past perinatal information. The MPS is a systematic self-report measure completed by an individual’s mother or knowledgeable informant (Gray, Dean, & Rattan, 1987). It examines a broad range of biological and environmental perinatal factors that would put an infant at risk for later neurological dysfunction (Strom, 1991). Items for the MPS were constructed based on established risk factors that occur during the perinatal period (Gray, Dean, & Rattan, 1987). Particularly, the measure appraises factors that occur during an infant’s gestation, birth, and first month of life as well as the mother’s medical history (Dean & Gray, 1985). Additionally, there are items included in the measure that had been implicated in early childhood development. Some of the items on the measure pertain to characteristics of the infant’s parents, including age, medical history, previous pregnancies, and stress. The specific factors assessed by the MPS are shown in the Appendix.

The MPS contains a total of 47 items, which were selected following a review of all the initially selected items by members of the medical community. Specifically, 26 of these items pertain to the pregnancy, birth/delivery, and early neonatal period of a child. The other 21 items address the mother’s health prior to the pregnancy as well as her health during gestation. These items are binary in nature; either the condition was present or it was absent. All of the items on the MPS were written at a fourth grade reading level and were constructed in a multiple-choice format (Gray, Dean, & Rattan, 1987). This type of format allows respondents to perform the simpler memory process of recognition as opposed to the more complex process of recall. The structured design of the MPS reduces the potential for errors of omission, selective memory, and unconscious confabulations (Strom, 1991). The MPS has been used to investigate the relationship between perinatal complications and several developmental outcomes, including but
not limited to, infantile autism (Wilkerson, Volpe, Dean, & Titus, 2002), emotional/behavioral disorders (Batchelor, Dean, Gray, & Wenck, 1991), school achievement (Gray et al., 1992) mental retardation (Gray et al., 1987), and sensory processing difficulties (Crepeau-Hobson, 2009).

Psychometric data showed that the information collected with the MPS was consistent with medical records; correlation coefficients ranged from .42 to 1.00 with 91% of the coefficients exceeding an $r$ of .90 (Gray, Dean, Rattan, & Bechtel, 1988). Additional research has provided further evidence the MPS is a reliable measure. Specifically, Gray, Dean, and Rattan (1987) looked at the test-retest reliability of the MPS. They found significant agreement between the two different administrations with the coefficients ranging from .85 to 1.00 for the various items of the measure. The results of testing item stability indicated the socioeconomic status of the mother did not appear to affect the reliability of the information gathered by the MPS (Gray, Dean, & Rattan, 1987). Thus, research has provided adequate evidence that the MPS is a structured, reliable measure that provides information comparable to that found in medical records/charts.

One potential limitation of the MPS was it had to be interpreted in terms of individual items. Moreover, it lacked standardized scoring procedures. However, Trammell (2012) created an empirically based scoring system for the MPS, which weights the individual items in terms of risk. This scoring system was designed to help clinicians determine if a child is at-risk for developmental or cognitive deficits. A population-based approach was utilized for developing the scoring procedures. That is, data from the CDC on children born in 2006 were used. Specifically, the CDC collected certain data regarding perinatal history of these children. Trammell compared the items used by the CDC with all 47 items from the MPS. Eighteen items
from the MPS matched those used by the CDC. All 18 items were from the section of the MPS that pertains to the pregnancy, birth/delivery, and early neonatal period of a child’s development. Trammell utilized those 18 matching items to develop the MPS scoring system. She organized them into two subscales, the Maternal Subscale and the Labor/Neonatal Subscale.

Once the items from the MPS were selected, relative risk ratios for later developmental deviations were calculated for the responses within each of the items. Next, a logistic regression was conducted. The logistic regression yielded beta weights, which were then applied to the scoring system. Each response for each of the 18 items was given a point value based on its associated beta weight. The weights represent the influence a perinatal complication has on later functioning. Each of the items has a referent that represents the ideal option for that particular item. The ideal option was determined by a review of previous findings. Ideal options were given a weight of zero. Non-ideal options were assigned a weight based on the results of a logistic regression analysis. Less ideal options have higher weights. The weights, and their corresponding scores, for the items included in the MPS scoring system as developed by Trammell (2012) are illustrated in the Appendix.

When scoring responses on the MPS, one determines the points for each item and then adds the points of all the items together. This can result in three different scores. The first is the Maternal Subscale score. To calculate this score, one adds the points for each response to the seven MPS items that are included in this subscale. The second score one can achieve using the scoring system is the Labor/Neonatal Subscale score. This is calculated the same way as the Maternal Subscale score. The points for each response to the 11 MPS items on that subscale are added up. The third possible score is the overall score. This is the sum of the two subscale scores.
or the sum of all the points of the responses to the 18 MPS items included in the scoring system. High scores on the MPS suggest a child is at-risk for developmental or cognitive deficits.

The scoring system provides cutoff scores for whether or not a child should be considered at-risk. There is an Overall cutoff score as well as a Maternal Subscale cutoff score and a Labor/Neonatal Subscale cutoff score. If a child’s total on the MPS exceeds the Overall cutoff score, then he/she would be considered at-risk. The subscale cutoff scores indicate which factors put the child at-risk. Rather than designating an arbitrary cutoff score, Trammell tested which score would be the best. Percentage scores were used. That is, what percentage of the population would be identified as not at-risk. For example, a percentage score of 70% would result in 70% of the population being identified as not at-risk and 30% of the population being identified as at-risk. Three percentages were compared: 70%, 75%, and 80%. Those three percentages were used to calculate the Overall cutoff score, the Maternal Subscale cutoff score, and the Labor/Neonatal Subscale cutoff score. The calculated cutoff scores were tested to determine which one had the best predictive ability for identifying a child as at-risk. Using a sample consisting of both children known to have later developmental deviations and children known to have normal development, Trammell examined which score was best at accurately classifying the children as at-risk or not at-risk. This meant being able to capture those with risks of developmental problems without having a high number of false-positives. In the end, the 80% cutoff scores for the overall and the subscales were recommended. Those scores can be found in the Appendix.

Overall, there are many advantages to using the MPS. It is a reliable and structured method for collecting perinatal data. The MPS provides clinicians with a standardized scoring procedure for estimating whether a child is at risk for future developmental deviations. Additionally, previous research on adverse outcomes of perinatal events has mainly focused on
individual complications and not the interaction. The MPS assesses perinatal data in a multivariate fashion, which could help clarify the contribution of obstetrical complications to the development of several different disorders.

**Overview of Pervasive Developmental Disorders**

Pervasive developmental disorder (PDD) is an umbrella term for a group of disorders characterized by severe and pervasive impairment in multiple areas of development: communication skills, reciprocal social interaction, or the presence of stereotyped behavior, activities, or interests (APA, 2000). In the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR), a diagnostic tool for clinicians, there are five subtypes of PDD: autistic disorder, Asperger’s disorder, childhood disintegrative disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Rett’s disorder (APA, 2000). While these disorders have commonalities, they also have key symptoms that differentiate them from one another.

Autistic disorder has been referred to as a number of terms: early infantile autism, childhood autism, or Kanner’s autism (APA, 2000). It is seen as a neurodevelopmental disorder characterized by impairments in social interaction and language development as well as the appearance of restricted, stereotyped, and repetitive patterns of behaviors, activities, and interests (Bonora et al., 2006). The term autism is of Greek origin and means “living in the self”; Eugen Bleuler, a Swiss psychiatrist, coined it in 1911 (Gupta, 2004). Then, in 1943, Dr. Leo Kanner utilized this term to describe a group of children who shared a number of the same symptoms: social isolation, severe deficits in communication skills, desire to maintain “sameness” in the environment, preoccupation with objects, and stereotyped play habits (Kanner, 1943 as cited in Wilkerson, 1992 and Gupta, 2004).
Autistic disorder occurs more frequently in males than females. The male to female ratio of autism is approximately 4:1 (Volkmar et al., 2004). A review of 37 surveys yielded a range of prevalence estimates of autism from 0.7/10,000 to 72.6/10,000 (Fombonne, 2006). After restricting the review to studies published since 1987, and then taking the midpoint of a new conservative estimation range, Fombonne (2006) adopted the prevalence rate of 13/10,000 for autism. Another source indicated the median rate of the disorder in epidemiological studies was 5 cases per 10,000 (APA, 2000). It has been reported that the prevalence of autism has increased dramatically. In fact, the U.S. Department of Developmental Services reported a 556% increase from 1991 to 1997 (Stokstad, 2001). However, this increase may be partially accounted for by increasing awareness of the disorder and the inclusion of similar disorders when investigating autism (Dawson & Faja, 2008; Muhle, Trentacoste, & Rapin, 2004).

Increasingly in the research literature the term autism has become synonymous with autistic spectrum disorder (ASD; e.g., Yirmiya & Charman, 2010; Kolevzon, Gross, & Reichenberg, 2007; Reichenberg et al., 2006; Glasson et al., 2004). ASD includes autistic disorder, Asperger’s disorder, and PDD-NOS (Dawson & Faja, 2008). When calculating the prevalence rate for autism, the Center for Disease Control (CDC) utilizes the ASD label. The CDC refers to ASDs as “a group of developmental disabilities that can cause significant social, communication, and behavioral challenges,” and estimates that in the United States an average of 1 in 88 children has an ASD (CDC, 2012).

According to the DSM-IV-TR, an important diagnostic feature of autistic disorder is the presence of a delay or abnormal functioning present in social interaction, language (as used in social communication), or symbolic or imaginative play prior to the age of three (APA, 2000). The impairment in reciprocal social interaction seen in autistic disorder is chronic and can
manifest in a variety of ways. This may involve marked impairment in the use of nonverbal behaviors including eye contact, facial expression, and gestures. Another manifestation could be the failure to form peer relationships appropriate to developmental level. The individual may not spontaneously seek out sharing enjoyment, achievements, or interests with others, which can be indicated by a lack of showing, bringing, or pointing out objects of interests (APA, 2000).

There are various communication deficits seen in individuals with autistic disorder. For example, there could be a delay in, or total lack of, the development of spoken language. Individuals who have adequate speech can still meet the diagnostic criteria for autistic disorder because the other manifestations do not pertain to language acquisition. For instance, one manifestation is marked impairment in the ability to initiate or sustain conversation with other people. Another is the use of idiosyncratic language or stereotyped and repetitive language usage. Impairment in communication could also entail lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level (APA, 2000).

As previously indicated, restricted, repetitive, and stereotyped patterns of behavior, interests, and activities is a diagnostic feature of autistic disorder. There may be an inflexible adherence to specific, nonfunctional routines or rituals (APA, 2000). Individuals with autistic disorder may insist on sameness and show resistance to or distress over changes in their physical environment and/or routines. Another possible manifestation of this diagnostic feature is an encompassing fixation with one or more stereotyped and restricted patterns of interest, which is abnormal either in focus or intensity (APA, 2000). That is, individuals display a strikingly restricted range of interests, and they usually are preoccupied with one narrow interest. Autistic disorder may present with stereotyped and repetitive motor mannerisms that include the hands (e.g., flapping) or the whole body (e.g., rocking; APA, 2000). There may also be a persistent
preoccupation with parts of objects (APA, 2000). Individuals with autistic disorder may show a fascination with movement and/or an attachment with an inanimate object.

Other features often associated with autistic disorder that are not considered in the diagnostic criteria for the disorder. Abnormal cognitive functioning is one such feature. Some individuals’ global intellectual ability falls within the mentally retarded range. Additionally, regardless of overall intelligence, there is a trend for verbal abilities to be weaker than nonverbal abilities (APA, 2000). Interestingly, despite autism occurring more frequently in males, females with this disorder are more likely to exhibit more severe mental retardation (APA, 2000). Occasionally there is a distinction made in the literature between high and low functioning autism. Unfortunately, few sources provide the criteria used in partitioning the groups. One approach for assessing level of functioning potentially involves examining nonverbal intelligence and social behavior. Specifically, the classification high functioning refers to children with a nonverbal IQ (intelligence quotient) above 65 who seek social interactions but in odd and eccentric ways. On the other hand, low-functioning children have a nonverbal IQ under 65, and they avoid social contact, except to fulfill need, and show poor attachment behaviors (Gupta, 2004).

Individuals with autistic disorder also differ in behavioral functioning. That is, there is a range of behavioral symptoms associated with the disorder. A child with autistic disorder may appear to have ADHD due to hyperactivity, impulsivity, and having a short attention span (APA, 2000). These symptoms are frequently seen in patients with autism; however, currently, the diagnosis of ADHD should not be given if autistic disorder is present (APA, 2000). An individual with autism may engage in self-injurious behavior, such as head banging or wrist wringing. Another possible behavior symptom is an odd response to sensory stimuli, including
exaggerated reactions to light or odors. There may be abnormalities in sleep patterns as well as eating behaviors (e.g., Pica). Other behavioral symptoms include abnormalities of mood or affect, aggressiveness, excessive fearfulness of harmless objects, and lack of fear response to real dangers (APA, 2000).

Gupta (2004) argued that the etiology of autism is heterogeneous in nature. Epidemiological reports have provided evidence of a genetic component to the development of the disorder (Bonora et al., 2006). Specifically, twin studies have offered evidence of autism, in part, having a genetic relationship. Findings revealed a concordance rate of >60% for classic autism (i.e. autistic disorder) in monozygotic (identical) twins, and no concordance was found between dizygotic (fraternal) twins (Bailey et al., 1995; Steffenburg et al., 1989). Additionally, family studies suggest the rate of occurrence in siblings with autism is 2% to 8%, which is much higher than the prevalence rate in the general population (Chakrabarti & Fombonne, 2001). Interestingly, research has suggested that undiagnosed relatives show elevated rates of autism-related symptoms (Bailey et al., 1995). Studies have since been trying to identify a model of genetic susceptibility for autism. It is believed there are multiple genes that interact in some manner to increase susceptibility to autism (Dawson & Faja, 2008; Bonora et al., 2006; Muhle, Trentacoste, & Rapin, 2004). Several chromosomal abnormalities have been linked to autism, including chromosome 15, 2, and 7 as well as the X chromosome (Beaudet & Zoghbi, 2006; Bonora et al., 2006; Muhle, Trentacoste, & Rapin, 2004).

Additional support for a genetic component in autism comes from its linkage with known genetic disorders, including tuberous sclerosis complex (TSC) and fragile X syndrome (FXS; Muhle, Trentacoste, & Rapin, 2004). It is estimated that as many as 25% of patients with TCS have autism (Baker, Piven, & Sato, 1998; Smalley, 1998). TSC arises from genetic mutations
that can lead to lesions in the brain called tubers (Muhle, Trentacoste, & Rapin, 2004). The haphazard distribution of these tubers in concert with metabolic changes is believed to be related to autism or epilepsy in some individuals with TSC (Asano et al., 2001). It should be noted that the incidence of TSC in individuals with autism is low, approximately 1% (Wong, 2006). However, that rate is 30% higher than that of TSC in the general population (Wong, 2006). FXS is an X-linked genetic disorder, and approximately 30% of individuals with this condition are on the autism spectrum (Rogers, Wehner, & Hagerman, 2001).

There are several other genetic conditions comorbid with autism. For example, untreated phenylketonuria (PKU) has been shown to be strongly related to the disorder (Baieli, Pavone, Meli, Fiumara, & Coleman, 2003). Some of the other genetic syndromes that have been associated with autism include Down syndrome, Prader Willi syndrome, Angelman syndrome, Hypomelanosis of Ito, Williams syndrome, XYY syndrome, Duchenne muscular dystrophy, Cornelia de Lange syndrome, neurofibromatosis, Mobius syndrome, and Joubert syndrome (Gupta, 2004). Another condition with genetic, as well as nongenetic, roots commonly observed in individuals with autism is epilepsy. In fact, seizures may develop in as many as 25% of individuals with autistic disorder, particularly in adolescence (APA, 2000).

The search for specific genetic factors related to autism has included examining differences in genes that regulate the corresponding endogenous metabolites related to successful pharmacologic interventions (Muhle, Trentacoste, & Rapin, 2004). Indeed, serotonin reuptake inhibitors have been shown to have favorable effects on the behavioral symptoms of autism (McDougle & Posey, 2002). Serotonin is critical to brain development; too little or too much seem related to abnormalities, which may account for some of the symptoms seen in individuals with autism (Chugani, 2002). It has been shown that some individuals with autism have 30% to
50% increase in platelet serotonin levels (Schain & Freedman, 1961). However, the physiologic source for this difference is still unknown. The success of serotonin reuptake inhibitors suggests the genes that code for receptors or neurotransmitters of this substance could contribute to the development of autism. Other neurotransmitters have also been found to be related to the disorder. For instance, it is believed dopamine may play a role because dopamine-blocking agents have been established as effective for treating the core symptoms of autism (McDougle & Posey, 2002). Acetylcholine is another neurotransmitter that, according to evidence, may be associated with autism (Muhle, Trentacoste, & Rapin, 2004).

Animal research has suggested endogenous opiates influence sociability. One of the core symptoms of autism is impaired sociability, which has led to interest in opiates in relation to the disorder (Muhle, Trentacoste, & Rapin, 2004). Specifically, research with rats have shown enhanced social play when administered exogenous morphine agonists, and treatment with antagonists reduces it (Vanderschuren, Niesink, & Van Pee, 1997). However, the sociability impairment in autism is often associated with a high threshold for pain, which suggests the individual would have abnormally high levels of endogenous opiates (Muhle, Trentacoste, & Rapin, 2004). Therefore, further research is needed to understand the relevance of opiates to autism. Oxytocin (OT) may also be relevant to the impaired sociability characteristic of autism. It has been shown to affect social behavior in animals (Muhle, Trentacoste, & Rapin, 2004). The results of one study with humans found children with autism had significantly lower overall plasma OT levels compared to age-matched control subjects (Modahl et al., 1998). Other findings indicated the ratio of the inactive OT precursor (OT-X) to active OT peptide was significantly higher in autistic youth than their control counterparts (Green et al., 2001).
Autism has a wide variety of both genetic and nongenetic causes (Muhle, Trentacoste, & Rapin, 2004). The lack of 100% concordance among genetically identical individuals (monozygotic twins) supported the notion that genes are not solely responsible for the development of the disorder and that there could be environmental factors involved. Furthermore, the variability in autism, even in children with the same genetic disorder, suggests environmental factors play an important role in the development, and possibly the severity, of these disorders. Just as there were several investigations concerning the genetic causes of the disorder, there have been several inquiries as well as theories concerning the nongenetic causes. At one point, it was hypothesized that the measles-mumps-rubella (MMR) vaccine contributed to the onset of autism (Dawson & Faja, 2008; Muhle, Trentacoste, & Rapin, 2004). Research examining this relationship has revealed no association between autism and the MMR vaccine (Madsen et al., 2002; Taylor et al., 2002).

An environmental cause of autism has been argued to be intrauterine or postnatal exposure to mercury (Gupta, 2004; Muhle, Trentacoste, & Rapin, 2004). This hypothesis was rooted in the association between neurobehavioral complications and intrauterine exposure to high doses of methyl mercury. For example, a mother could introduce dangerous levels of mercury to her developing child through seafood contamination. In relation to postnatal exposure, it was hypothesized that a preservative containing ethyl mercury, thimerosal, that was added to many vaccines was a possible environmental risk factor (Dawson & Faja, 2008). However, a review by Ball, Ball, and Pratt (2001) examining the use of thimerosal in childhood vaccines suggested exposure to the preservative when administered a vaccine was not harmful. Furthermore, mercury poisoning can result in photophobia, dysarthria, seizures, and ataxia, and these symptoms are not seen in individuals with autism. Thus, not only is there a lack of
evidence to support a relationship exists between autism and mercury poisoning, there is evidence disputing any association between the two. Perinatal factors in relation to autism, aside from intrauterine mercury exposure, will be discussed later in this literature review.

Differential diagnosis for autistic disorder includes examining the other PDD subtypes (Asperger’s disorder, childhood disintegrative disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Rett’s disorder) childhood onset of schizophrenia, selective mutism, language disorders, mental retardation, stereotypic movement disorder, and ADHD (APA, 2000). In relation to schizophrenia, when Bleuler (1911) coined the term autism it was meant to describe a state of extreme social withdrawal in schizophrenia (as cited in Gupta, 2004). In a childhood onset of schizophrenia, the disorder usually appears after years of normal, or near normal, development (APA, 2000). An individual with autistic disorder could receive a schizophrenia diagnosis if he/she develops the characteristic features of it with active-phase symptoms of prominent delusions or hallucinations lasting for at least one month (APA, 2000).

As previously mentioned, an individual with autistic disorder may present with symptoms of overactivity and inattention that are characteristic of ADHD, but this diagnosis is not given if the individual meets the criteria for the autistic disorder diagnosis. Many of the symptoms associated with autistic disorder are not associated with ADHD, including impairment in communication and social interaction as well as the restricted patterns of behavior. Stereotypic movement disorder involves repetitive, seemingly driven, and nonfunctional motor behavior that markedly interferes with normal activities or results in self-inflicted bodily injury that requires medical treatment (APA, 2000). Motor stereotypies are typical in autistic disorder; therefore, if a child meets the criteria for an autistic disorder and displays motor stereotypies, then a diagnosis of stereotypic movement disorder would not be given.
An individual with mental retardation, particularly those who fall within the severe or profound range, may warrant an additional diagnosis of autistic disorder. If the individual has qualitative impairments in social and communicative skills as well as specific behaviors characteristic of autistic disorder, then an additional diagnosis may be given (APA, 2000). Selective mutism is a disorder involving a persistent failure to speak in certain social situations where speaking is expected, while speaking in other situations (APA, 2000). The communication deficits typically present in autistic disorder are different from this; the impairment is not context specific as it is in selective mutism. Additionally, a child with selective mutism does not have the severe impairment in social interaction and the restricted patterns of behavior, interests, and activities characteristic of autistic disorder (APA, 2000). Language impairment is a diagnostic feature in both expressive language disorder and mixed receptive-expressive language disorder. However, this impairment is not associated with the presence of impairment in social interaction and restricted, repetitive, and stereotyped patterns of behavior characteristic of autistic disorder (APA, 2000).

As noted above, autistic disorder must be differentiated from the other PDDs. Another disorder under the PDD umbrella is Rett’s disorder. One of the rarer disorders, Rett’s involves the development of several specific deficits following a period of normal functioning after birth (APA, 2000). That is, individuals have normal perinatal development with age-appropriate psychomotor functioning through the first five months of life. Additionally, the head circumference of the infant was normal at birth. After the period of normal development, between five and 48 months of age, the head growth decelerates. This is accompanied by a loss of previously acquired purposeful hand skills as well as the development of characteristic stereotyped hand movements such as hand wringing. Another diagnostic feature of Rett’s
disorder is problems with coordination of gait or trunk movements. The child’s social engagement will decrease early in the course of the disorder. However, social interaction often develops later on. There is also severe impairment in both expressive and receptive language skills.

Rett’s disorder is unique from the other PDD subtypes because it is the only one of these disorders to be directly linked to a particular genetic defect (Muhle, Trentacoste, & Rapin, 2004). Autistic disorder differs from Rett’s disorder in a number of ways, including the characteristic sex ratio and pattern of deficits. Autistic disorder occurs more frequently in males than females, whereas Rett’s disorder has been diagnosed only in females (APA, 2000). The characteristic pattern of head growth deceleration, loss of previously acquired purposeful hand skills, and the appearance of poorly coordinated gait or trunk movements seen in Rett’s disorder are not present in autistic disorder.

Like Rett’s disorder, childhood disintegrative disorder is characterized by a period of normal development followed by marked regression in functioning. However, children with this disorder, by definition, must have age-appropriate development for at least the first two years of life (APA, 2000). This includes all areas of functioning such as social interaction, verbal and nonverbal communication, play, motor skills, and adaptive behaviors. After these two years of normal development, and prior to 10 years of age, the child has a significant loss of previously acquired skills in at least two areas of functioning. Specifically, the abnormalities of functioning must be characterized by two of the following: qualitative impairment in social interaction, qualitative impairment in communication, or appearance of restricted, repetitive, and stereotyped patterns of behavior, interests, and activities (APA, 2000).
Childhood disintegrative disorder differs from Rett’s disorder in its characteristic sex ratio. That is, it appears to be more common in males and as previously mentioned Rett’s disorder has only been diagnosed in females (APA, 2000). Additionally, the two disorders differ in onset and patterns of deficits. Childhood disintegrative disorder also differs from autistic disorder. This disorder has a distinctive pattern of normal development for at least two years followed by severe regression in multiple areas of functioning. Developmental abnormalities are typically noted with the first year of life for autistic disorder (APA, 2000).

Pervasive developmental disorder not otherwise specified (PDD-NOS) is an appropriate diagnosis when a child has severe and pervasive impairment in the development of reciprocal social interaction associated with impairment in either communication skills (verbal or nonverbal) or with the presence of stereotyped behavior, interests, and activities (APA, 2000). However, the individual must not meet the criteria for another pervasive developmental disorder in order to be given the PDD-NOS label. The PDD-NOS category includes atypical autism. Atypical autism refers to a presentation that does not meet the diagnostic criteria for autistic disorder due to one or all of the following reasons: atypical symptomatology, late age at onset, or subthreshold symptomatology (APA, 2000).

Asperger’s disorder, also referred to as Asperger’s syndrome, entails impairment in social interaction; there are no cognitive deficits or significant delay in language development (Carlson, 2005). Additionally, there is development of restricted and repetitive patterns of behavior, activities, and interests (APA, 2000). The history of this disorder dates back to 1944, when the Viennese pediatrician Hans Asperger described a set of behavioral features for a condition he called autistic psychopathy (Gupta, 2004; Wilkerson, 1992). Asperger noted difficulties with social integration, peculiarities in the content and delivery of speech, and oddity in eye gaze

Males are approximately five times more likely to be diagnosed with Asperger’s disorder than females (APA, 2000). Data concerning the prevalence of this disorder is lacking. There have been limited epidemiological studies providing such data. As discussed in relation to the prevalence of autistic disorder, studies often use the ASD category. This makes it difficult to estimate the incidence of Asperger’s disorder. A review of four studies yielded a range of prevalence rates from 26 to 48 cases per 10,000 individuals (Gillberg & Coleman, 2000). However, all of these studies were conducted in Nordic countries and diagnosed individuals based on the Gillberg (1991, as cited in Gillberg & Coleman, 2000) definition, which differs from the criteria set forth by the DSM-IV-TR. Therefore, conclusions regarding the prevalence of Asperger’s disorder, particularly in the United States, cannot be drawn.

There is limited data examining solely the etiology of Asperger’s syndrome. There have not been the major family or twin studies like those for autistic disorder. Many studies investigate it in relation to a spectrum disorder (i.e. ASD). That is, the studies use samples consisting of individuals with any of the following diagnoses: Asperger’s disorder, autistic disorder, or PDD-NOS. However, there does appear to be a genetic link. This is suggested by the increased frequency of Asperger’s disorder among family members who have the disorder (APA, 2000). In fact, the findings of several clinical studies implicate a genetic cause, with 30% to 60% of cases having a close relative with the disorder or something very similar (Gillberg & Coleman, 2000).

Diagnostically, Asperger’s disorder presents with severe and persistent impairment in social interaction as well as restricted and repetitive patterns of behavior, interests, and activities
Although there is no significant delay or deviance in language acquisition, more subtle aspects of social communication, such as reciprocity, may be affected. Individuals with Asperger’s disorder do not have any significant delays in cognitive functioning during the first three years of life. Age-appropriate development in this area is demonstrated by normal curiosity of their environment or the acquisition of adaptive skills (other than social interaction) and learning skills (APA, 2000). In order to receive a diagnosis of Asperger’s disorder, the disturbances in social interaction and restricted, repetitive behaviors, interests, and activities must cause clinically significant impairment in social, occupational, or other important areas of functioning.

According to the DSM-IV-TR diagnostic criteria for Asperger’s disorder, the restricted, repetitive, and stereotyped patterns of behavior, interests, and activities can present as one or more different manifestations (APA, 2000). One possible, and typical, manifestation involves an encompassing preoccupation with one or more stereotyped and restricted patterns of interest. It is abnormal either in intensity or focus. Often this preoccupation is with a circumscribed topic or interest, about which the individual amasses a great deal of knowledge. Furthermore, these interests and/or activities are pursued with immense intensity usually to the exclusion of other activities. Another possible manifestation is inflexible adherence to specific, nonfunctional routines or rituals. There may be stereotyped and repetitive motor mannerisms present. Persistent preoccupation with parts of objects is another possible manifestation.

The qualitative impairment in social interaction also has several possible clinical manifestations (APA, 2000). One such manifestation is marked impairment in the use of multiple nonverbal behaviors to regulate social interaction, which includes facial expression and eye contact. There may be a failure to develop peer relationships (such as friendships) appropriate for
the individual’s developmental level. Another possibility is a lack of social or emotional reciprocity (such as empathy; Gillberg & Coleman, 2000). The last clinical manifestation is a lack of spontaneous seeking to share enjoyment, interests, or achievements with others.

There are speech-language problems that are highly characteristic of Asperger’s disorder. These problems include flat prosody, pedantic speech, semantic-pragmatic problems, and conversational comprehension difficulties (Gillberg & Coleman, 2000). One of the diagnostic criterion for the disorder dictates “there is no clinically significant general delay in language” (APA, 2000). This criterion pertains to developmental milestones, such as use of single words or communicative phrases by specific ages, not to communication style. Therefore, an individual with Asperger’s disorder could have communication difficulties and unusual language usage. In fact, one may demonstrate a preoccupation with certain topics during a conversation. Additionally, there may be failure to appreciate and utilize conventional rules of conversation as well as failure to appreciate nonverbal cues (APA, 2000).

Unlike autistic disorder, mental retardation is rarely observed in Asperger’s disorder (only approximately 5% of cases), and when it is, it is mild in severity (APA, 2000; Gillberg & Coleman, 2000). Differences in ipsative cognitive functioning may be observed in individuals with Asperger’s disorder. That is, they often demonstrate strengths in areas of verbal ability, such as vocabulary, while having weaknesses in nonverbal areas (APA, 2000). Motor clumsiness and awkwardness may be observed in individuals with this disorder; however, these motor difficulties tend to be mild in nature (APA, 2000). Many individuals who later receive an Asperger’s diagnosis were previously diagnosed with ADHD, which may be due to the symptoms of over activity and inattention frequently seen in this population (APA, 2000).
There are some similarities in the differential diagnoses between Asperger’s disorder and autistic disorder. Like autistic disorder, Asperger’s disorder must be distinguished from other PDDs, childhood schizophrenia, selective mutism, and language disorders. Asperger’s disorder must also be distinguished from schizoid personality disorder and anxiety disorders. Childhood schizophrenia typically appears after years of normal development. Features characteristic of this disorder include hallucinations, delusions, and disorganized speech (APA, 2000). It is possible for an individual with Asperger’s disorder to receive a secondary diagnosis of schizophrenia if those features are present. Although the relationship between Asperger’s disorder and schizoid personality disorder is unclear, it appears that Asperger’s disorder has an earlier onset and the social difficulties characteristic of it are more severe (APA, 2000).

Unlike Asperger’s disorder, a child with selective mutism usually displays appropriate communication skills in some contexts. Additionally, severe social impairment and restricted patterns of behavior associated with Asperger’s disorder are not present in selective mutism. There is language impairment present in both expressive language disorder and mixed receptive-expressive language disorder. However, there is no associated social impairment and restricted, repetitive, and stereotyped patterns as there is with Asperger’s disorder. Some individuals may present with restricted and repetitive behaviors, which is suggestive of obsessive-compulsive disorder (OCD; APA, 2000). However, the preoccupations and interests in Asperger’s disorder are a source of some pleasure or comfort whereas the obsessions and compulsions characteristic of OCD are a source of anxiety. Additionally, the pervasive social impairment characteristic of Asperger’s disorder is not typically present in OCD. Some individuals with Asperger’s disorder may experience heightened and debilitating anxiety in social settings (APA, 2000). This disorder can be differentiated from anxiety disorders, such as social phobia, based on the presence of
social development impairments and repetitive, restricted behaviors, interests, or activities.

All of the PDDs (autistic disorder, Asperger’s disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), Rett’s disorder, and childhood disintegrative disorder) are characterized by problems in social interaction, but there are distinguishing differences between them. Rett’s disorder is diagnosed in females, while the other PDDs, including Asperger’s disorder, occur more frequently in males. Rett’s disorder also differs from Asperger’s disorder in course; that is, there is head growth deceleration, loss of previously acquired purposeful hand skills, and poor coordination in gait or trunk movements. Furthermore, Rett’s disorder is associated with gross impairments in language and communication as well as marked degrees of mental retardation. Diagnostic criteria for Asperger’s disorder dictates that there are no significant cognitive or language delays present. Marked impairments in cognitive ability and language are also present in childhood disintegrative disorder, another PDD. Childhood disintegrative disorder also differs from Asperger’s disorder in its pattern of developmental regression.

As previously indicated, Asperger’s disorder must be distinguished from autistic disorder. Interestingly, it is believed that Asperger’s is linked genetically and clinically to autism (Cederlund & Gillberg, 2004). For instance, some family case studies have shown an overlap of autism and Asperger’s disorder in families (Gillberg & Coleman, 2000). Perhaps this is why many consider autistic disorder and Asperger’s disorder to be on the same spectrum, which has led to the popularity of the ASD label in the literature. However, there are several critical characteristics that differentiate these two disorders. There are significant abnormalities in social interaction, language, and play in autistic disorder while early cognitive and language functioning is not significantly delayed in Asperger’s disorder (APA, 2000). Furthermore,
individuals with Asperger’s disorder tend to be significantly higher functioning in verbal ability than those with autistic disorder (Gillberg & Coleman, 2000).

Another difference pertains to the manifestation of the restricted, repetitive, and stereotyped behavior, activities, and interests. In autistic disorder, this is often characterized by the presence of motor mannerisms, preoccupation with parts of objects, rituals, and marked distress regarding change. In Asperger’s disorder, on the other hand, these are primarily observed in the all-encompassing pursuit of a circumscribed interest that involves a topic to which the individual devotes inordinate amounts of time gaining relevant knowledge (APA, 2000). Interestingly, some of the same medical conditions associated with autistic disorder, such as FXS, TCS, and neurofibromatosis, may be observed in individuals with Asperger’s disorder, but at a lower frequency (Gillberg & Coleman, 2000). For instance, the incidence of epilepsy in individuals with Asperger’s disorder is marginally more common than in the general population (no more than a few percent of the group) whereas up to 25% of those with autistic disorder have it (Gillberg & Coleman, 2000; APA, 2000). In general, there are fewer comorbid conditions associated with Asperger’s disorder than there are with autistic disorder (Dawson, Glasson, Dixon, & Bower, 2009).

A difference between the two disorders also lies in their respective developmental course. That is, in general, the prognosis for Asperger’s disorder appears significantly better than in autistic disorder (APA, 2000). Many adults with Asperger’s disorder are capable of gainful employment and personal self-sufficiency. On the other hand, only a small percentage of adults with autistic disorder go on to live and work independently; partial independence is possible in about one-third of cases. Given these distinguishing features and course, one might conclude there could be a difference in etiology between the two disorders. This study seeks to investigate
whether or not this difference exists by analyzing the perinatal factors related to each disorder in comparison to a group of normal counterparts.

**Perinatal Factors and Pervasive Developmental Disorders**

A number of studies have offered evidence that perinatal events are related to later functioning, including developmental delays, neurologic deficits, and emotional dysfunction. Research has shown that perinatal complications are associated with several childhood disorders, including Pervasive Developmental Disorders (PDDs; Dean & Davis, 2007). Investigations concerning perinatal development and PDDs have focused on several factors, including teratogen exposure, infections, and delivery complications. Overall, the results have been inconsistent; however, it should be noted that there is considerable variation among these studies, including methodology, sample size, variable selection, statistical analyses, data quality, and the use of control groups (Glasson et al., 2004; Nelson, 1991). Regardless, research has well established that perinatal factors are more prevalent in children with developmental issues, including autism. Burd, Severhud, Kerneshian, and Klug (1999) succinctly describe the potential importance of perinatal factors in relation to autism. They state,

> If prenatal or perinatal risk factors that are in a causal chain influencing either the severity of or the risk of developing autism could be identified, this data could have important implications in prevention and treatment. These risk factors and the temporal unfolding of risk would both be appropriate to target as starting points to initiate interventions that may decrease both the severity and prevalence of the disorder (p. 441).

The majority of studies examining perinatal complications as risk factors for autism focus on significant differences between individuals who have a diagnosis and those who are typically
developing. Such studies include Rodier and Hyman (1998) who examined teratogens and autism. They showed a relationship between the disorder and intrauterine exposure thalidomide. A similar study found a link between autism and intrauterine exposure to valproic acid (Christianson, Chesler, & Kromberg, 1994). Additionally, this type of research has suggested a link between congenital rubella infection and autism (Chess, Fernandez, & Korn, 1978). It should be noted that due to the great reduction of rubella in western countries due to immunization, very few individuals in the recent autistic population had a congenital rubella infection (Muhle, Trentacoste, & Rupin, 2004).

Burd et al. (1999) also compared a group of individuals who were diagnosed with autism and a control group to investigate perinatal risk factors. They conducted univariate analyses in order to identify significant differences in perinatal development. They found a link between autism and birth weight. Additionally, this study indicated other relevant perinatal factors, including paternal age, delayed prenatal care, and terminations of previous pregnancies. Additionally, they developed a prediction model for autism based on perinatal factors, but did not indicate the accuracy of the model.

Wilkerson, Volpe, Dean, and Titus (2002) took a different approach when investigating the connection between perinatal factors and autism. They used the MPS to gather perinatal history. Then they used a multivariate approach to compare individuals with autism to typical peers. The results of a predictive discriminant analysis indicated that differences on perinatal variables alone were able to correctly identify 65% of the children as either typical or autistic. The most significant broad predicative factors for being classified in the autistic group were intrauterine stress, gestational age at birth, and maternal morphology. When examining factors in an item-by-item fashion, the authors found low birth weight, abnormal presentation at delivery,
use of prescription medications during pregnancy, and viral infections were the better predictors of autism.

Another approach used to investigate the role of perinatal factors in autism is analyzing the results of multiple previously conducted studies. One literature review suggested that environmental stress during gestation might play a significant role in the etiology of autism (Kinney, Munir, Crowley, & Miller, 2008). According to the review by Gillberg and Coleman (2000), herpes simplex viral encephalitis occurring during the neonatal period has been linked to autism; these children could have been infected during gestation, delivery through an infected birth canal, or in the immediate postnatal period. Congenital cytomegalovirus infection has also been implicated in the occurrence of autism, but many of these cases also involved concomitant neurologic disorders.

A comprehensive meta-analysis of studies exploring prenatal factors and the risk of autism indicated few factors have been examined in multiple well-conducted studies (Gardener et al., 2009). Although maternal medication use has been implicated, limited studies have investigated specific types of medications. The results of the meta-analysis found advanced maternal and paternal age, maternal bleeding during the pregnancy, gestational diabetes, psychiatric medication use, being first born, and birth abroad had the strongest evidence for an association with autism. Additionally, the results provided strong evidence against certain factors having a role in autism. Those factors were previous fetal loss, maternal pre-ecamplsia, proteinuria, hypertension, and swelling.

There are very few studies investigating a link between Asperger’s disorder and perinatal factors. One such study was a Swedish investigation of 100 males diagnosed with Asperger’s disorder (Cederlund & Gillberg, 2004). The diagnostic group was compared with general
population data. Specifically, they qualitatively compared differences. For instance, they found that 10% of the mothers for the diagnostic group had bleeding during the second or third trimester, which was approximately twice the incidence rate for normal pregnancies. Additionally, Twenty-two of the 99 children (about 22%) in the study had hyperbilirubinemia, which generally occurs only in about 10% of all newborn infants. Overall, 58 of the 100 participants had one or more remarks in their records indicating a serious problem occurred during the perinatal period (Gillberg & Cederlund, 2005).

There have been numerous studies utilizing heterogeneous diagnostic samples to investigate the relationship between perinatal factors and autism. Particularly, the majority of these studies utilized participants with any of the three diagnoses (i.e. autistic disorder, Asperger’s disorder, pervasive developmental disorder not otherwise specified) included under the ASD label in the diagnostic group (e.g., Bilder, Pinborough-Zimmerman, Miller, & McMahon, 2009; Herbert, 2010; Kolevzon, Gross, & Reichenberg, 2007). Among studies utilizing a heterogeneous diagnostic ASD group there are differences in methodology.

Kolevzon et al. (2007) conducted a literature review. They found that both parental characteristics and obstetric conditions appeared to increase the risk of an ASD. The relevant parental characteristics included advanced paternal age and advanced maternal age. Obstetric risk factors for ASD fell into two categories: (1) birth weight and gestational age, and (2) intrapartum hypoxia and fetal hypoxia.

Another investigation involved a longitudinal study with infants in the neonatal intensive care unit (NICU; Gardner et al., 2008 as cited in Yirmiya & Charman, 2010). The findings revealed a 2-fold risk of ASD in this sample. The characteristics of those children who were later diagnosed with ASD included being born at lower gestational age and birth weight than the
matched comparison group (NICU babies without a later diagnosis of ASD). There were also early behavioral differences in the infants. Those with an ASD showed higher incidences of visual asymmetry, increased hypertonicity in arms, and better head extension compared to their counterparts.

Badawi et al. (2006) also conducted a longitudinal study. They followed newborns with encephalopathy and a group of randomly selected term controls. Neurobehavioral and cognitive follow-ups were conducted when the subjects were 3 years old and 5 years old. The data from each group were compared. Children who had encephalopathy as a newborn were 5.9 times more likely to be later diagnosed with an ASD than their normal counterparts.

Similarly, Durkin et al. (2008) chose to investigate a specific risk factor. They focused on the association of advanced maternal and paternal age with ASD. Examining the link retrospectively, the authors compared the parental data of children diagnosed with an ASD and a control group. The results suggested that both advanced maternal and paternal age were independently associated with ASD. Advanced maternal age was identified as a risk factor for having a child with an ASD in another study (Croen, Grether, & Selvin, 2002). The focus was maternal characteristics as risk factors for ASD, which were examined retrospectively. Data from children diagnosed with an ASD and controls were used in multivariate models that produced risk estimates. The results indicated women over the age of 35 were shown to be at a significantly higher risk of having a child with an ASD. Increased risk was also associated with the child being male, plurality, and the mother being black.

Another retrospective comparison of children diagnosed with an ASD and their control counterparts examined if a family history of psychiatric disorders was a risk factor for ASD (Daniels et al., 2008). Odd ratios indicated parents of children with autism were more likely to
have been hospitalized for a mental disorder compared to the parents of the control subjects. Specifically, schizophrenia occurred more frequently in the parents of children with ASD compared with the control parents. The mothers of children with ASD were more likely to have depression or a personality disorder than the control mothers. Mann et al. (2010) also conducted a retrospective investigation. They too generated odds ratios from data of children diagnosed with ASD and control subjects. The results suggested maternal preeclampsia was associated with greater odds of being diagnosed with an ASD. After controlling for birth weight, the relationship was slightly reduced but still significant.

Despite the number of studies utilizing a mixed sample of various PDD subtypes, few have investigated differences among the disorders within the spectrum. There were only two studies using an ASD sample that compared perinatal factors among the various diagnoses (Dawson, Glasson, Dixon, & Bower, 2009; Glasson et al., 2004). Glasson et al. (2004) conducted a retrospective comparison of individuals diagnosed with an ASD and control subjects. Analyzes included Chi-square tests, odds ratios, and t tests. The results indicated that children who had autistic disorder had the greatest number of complications. Those in the PDD-NOS group had similar types of complications as those in the autistic disorder group. However, fewer variables were statistically significant. Children in the Asperger’s group had the fewest obstetric differences from the control group. Interestingly, compared to those with autistic disorder, children with Asperger’s disorder were more likely to have had a vacuum or forceps delivery. The results of this study also included a prediction model for ASD that included birth order, maternal age, threatened abortion, fetal distress, and elective cesarean section.

Using the same data as Glasson et al. (2004), Dawson, Glasson, Dixon, and Bower (2009) investigated birth defects in relation to ASDs. They found an overall significantly higher
number of birth defects in the ASD group than the control group. Specifically, the results indicated congenital anomalies of the ear, face, and neck were over 11 times more likely in children with an ASD. Additionally, children with an ASD were 4.3 times more likely to have nervous system disorders and 1.9 times more likely to have urogenital defects. Interestingly, when the diagnostic groups were compared, cases with autism and PDD-NOS had similar proportions of birth defects, but those with Asperger’s disorder had fewer defects. This study also utilized the siblings of individuals with an ASD. The odds of having a birth defect increased 50% for individuals with an ASD when compared to their unaffected siblings. The odds of an unaffected sibling having a birth defect were 20% higher than that of controls.

If these two disorders are truly on the same spectrum, then one may conclude based on these research findings (i.e. Dawson, Glasson, Dixon, & Bower, 2009; Glasson et al., 2004) that perinatal factors might be related to the severity of autism. However, with so little data available on the etiology of Asperger’s disorder, including perinatal information, it is difficult to draw a firm conclusion. Additional data comparing the perinatal factors related to autistic disorder and those related to Asperger’s disorder might help determine if such environmental factors contribute to both disorders as well as if there is a significant difference between the two.
CHAPTER THREE

Methods

This chapter offers specific information concerning the methodology of the present study. First, a description of the participants is presented. Second, information about the selected instrumentation, including the Maternal Perinatal Scale (MPS), is provided. Third, the data collection process, including sampling procedures, is described. Fourth, the statistical analyses employed are presented.

The present investigation evaluated the ability of the Maternal Perinatal Scale (MPS; Dean & Gray, 1985) to differentiate individuals in the autistic disorder group from those in the Asperger’s disorder group, and a non-clinical group, based on a reported history of perinatal complications. More specifically, the primary purpose of this study was to determine if perinatal data would provide accurate predictions of group membership for children diagnosed with either autistic disorder or Asperger’s disorder. A secondary goal of the research was to determine if there are significant differences in the number of reported complications among the three groups. To that end, children with autistic disorder, children with Asperger’s disorder, and children with no history of psychiatric or neurologic conditions were compared.

Prior to data collection, approval to conduct the study was obtained from the Institutional Review Board (IRB) at Ball State University. The IRB requires a thorough description of the study, including the manner in which the data were to be collected, in order to determine the potential risks for those who participate in the study. In this investigation, the participants did not receive experimental treatment. Rather, the biological parents of children of interest to the researcher completed an electronic version of the MPS and a background questionnaire. Approval to conduct this investigation was granted by the IRB in fall 2011.
Participants

The sample consisted of 37 typically developing children, 21 children previously diagnosed with autistic disorder, and 15 children previously diagnosed with Asperger’s disorder, yielding a total sample size of 73. The children included in the study ranged in age from 3 years old to 17 years, which was one of the criteria to be included in the study. The demographic information for the children included in this study is available in Table 1.

Table 1

Child Demographics

<table>
<thead>
<tr>
<th></th>
<th>Autistic Group</th>
<th>Asperger’s Group</th>
<th>Non-clinical Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Male Children</td>
<td>16</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Number of Female Children</td>
<td>5</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td>Age Range of Children</td>
<td>3.25 years-17.58 years</td>
<td>6.75 years-17.75 years</td>
<td>3.17 years-17.92 years</td>
</tr>
<tr>
<td>Average Age of Children</td>
<td>8.3 years</td>
<td>12.76 years</td>
<td>10.11 years</td>
</tr>
</tbody>
</table>

As indicated in Table 2, the children previously diagnosed with autistic disorder had a mean age of 8.3 years (8 years, 4 months). The children previously diagnosed with Asperger’s disorder had a mean age of 12.76 (12 years, 9 months). The children in the non-clinical, or control, group had a mean age of 10.11 years (10 years, 1 month). The male to female ration for the children in the autistic group was 3:1, which is consistent with the population estimate of 4:1 (Volkmar et al., 2004). Research indicates that males are five times more likely to be diagnosed with Asperger’s disorder than females (APA, 2000), which is consistent with the ratio for this sample. For the non-clinical group, the ratio was approximately 1:1. However, one child’s gender was not reported, so that child was excluded from the gender frequency count.
The demographic information for the biological parents who participated in the study is available in Table 2.

Table 2

*Parent Demographics*

<table>
<thead>
<tr>
<th></th>
<th>Autistic Group</th>
<th>Asperger’s Group</th>
<th>Non-clinic Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Male Parents</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Number of Female Parents</td>
<td>20</td>
<td>15</td>
<td>37</td>
</tr>
<tr>
<td>Age Range of Parents</td>
<td>28 years-54 years</td>
<td>33 years-58 years</td>
<td>25 years-52 years</td>
</tr>
<tr>
<td>Average Age of Parents</td>
<td>37.89 years</td>
<td>42.8 years</td>
<td>40.51 years</td>
</tr>
</tbody>
</table>

As indicated in Table 3, the majority of parents who participated in the study were female. The parents of children who had been diagnosed with autistic disorder had a mean age of 37.89 years (37 years, 11 months). The parents of the children in the Asperger’s group had a mean age of 42.8 years (42 years, 10 months). The parents of the children in the non-clinical group had a mean age of 40.51 years (40 years, 6 months). For annual household income, 43.2% of parents of children in the autistic group fell within the $50,000-$99,999 range. The reported annual household income for 53.3% of the Asperger’s group was in the $50,000-$99,999 range. The annual household income for 43.2% of the non-clinical group fell within the $50,000-$99,000 range.

In terms of race, all of the parents for the children in the autistic group selected Caucasian. All of the parents in the Asperger’s group identified as Caucasian with the exception of one parent who selected Asian/Pacific Islander. All of the parents of the typically developing children identified as Caucasian with the exception of one who selected African-American. The parents also reported their educational history. All of the parents for the autistic group indicated
having at least some college education. The majority (86.7%) of parents for the Asperger’s group indicated they had at least some college. All the parents for the non-clinical group reported having at least some college education.

Because prior research has shown that advanced maternal age (35 years or older) at the time of birth is a risk factor for having a child diagnosed with ASD (Croen, Grether, & Selvin, 2002; Durkin et al., 2008; Glasson et al., 2004), mother’s age at the time of birth was collected. The age at birth for the mothers in the autistic group ranged from 20 to over 40. Six of the 21 mothers were 35 years old or older. The age of the mothers at the time of birth for the children in the Asperger’s group ranged from 20 to over 40. Five of the 15 mothers were 35 years old or older. The age of the mothers at the time of birth for the children in the non-clinical group ranged from 15 to over 40. Thirteen of the 37 mothers were 35 years old or older.

Instrumentation

The dependent variable measure for this investigation was the Maternal Perinatal Scale (MPS; Dean & Gray, 1985), a standardized self-report measure that systematically assesses perinatal complications (Gray, Dean, & Rattan, 1987). The scale is intended to identify factors that place a child at risk of developmental deviations or neurological abnormality (Strom, 1991), including a broad range of both biological and environmental factors. It contains 47 multiple-choice items written at a fourth grade reading level (Wilkerson, 1992). The items describe events during an infant’s gestation, birth, and first month of life as well as the mother’s medical history. Items on the measure were constructed based on established risk factors that occur during the perinatal period (Gray, Dean, & Rattan, 1987). The MPS has been used to investigate perinatal events in relation to several developmental outcomes, including emotional/behavior disorders (Batchelor, Dean, Gray, & Wenck, 1991), school achievement (Gray et al., 1992), mental
retardation (Gray, Dean, Strom, Wheeler, & Brockley, 1987), sensory processing difficulties (2009), and infantile autism (Wilkerson, Volpe, Dean, & Titus, 2002). In the present study, biological mothers were administered an electronic version of the MPS.

The MPS has been shown to be both reliable and valid (Gray, Dean, & Rattan, 1985; Gray, Dean, Rattan, & Bechtel, 1987). Previous research has shown that information parents report on the MPS is consistent with perinatal information available in their child’s medical records; correlation coefficients ranged from .42 to 1.00 with 91% of the coefficients exceeding an $r$ of .90 (Gray, Dean, Rattan, & Bechtel, 1988). This means parents are able to accurately report perinatal information when using the MPS. Gray, Dean, and Rattan (1987) look at the test-retest reliability of the MPS. When parents completed the MPS on two separate occasions, there was significant agreement between the two administrations, ranging from .85 to 1.00. Thus, research has provided evidence that the MPS is a structured, reliable measure that provides information comparable to that found in medical records.

A scoring system developed by Trammell (2012) established response values for each item on the MPS. These values were calculated from CDC data for a large number of developmental conditions taken together and validated against a sample of individuals with and without developmental and cognitive deficits. Response values are added together to produce the Maternal Subscale score, the Labor/Neonatal Subscale score, and the Overall score. The specific scale items, scoring system values, and cutoff scores for each scale for making at-risk determinations are available in the Appendix.

Data Collection

All of the subjects’ information was collected from their biological parents. Each parent completed an online survey at an undisclosed location of her/his choosing. The survey was
posted on http://www.surveygizmo.com. Participants were not required to be members of the website to complete the survey. The survey included informed consent as well as all the items from the MPS and demographic questions. The online format allowed for anonymity. All the parents who participated were eligible for a prize drawing as an incentive to complete the online survey. There were four $50 gift cards for Target available as the prize. Four separate parents received one of these gift cards. The recipients of the gift cards were selected randomly. Winners were contacted via an email address they provided at the end of the survey.

A child was considered typically developing if he/she had no history of a neurologic or psychological diagnosis. The parents of these children were recruited through one method. This method consisted of sending an advertisement via electronic mail to employees at Ball State University. All of these participants were volunteers. The parents for the children diagnosed with either autistic disorder or Asperger’s disorder were recruited through flyers posted at clinics that provide treatment services to children as well as newsletters and mailing lists for organizations related to these diagnoses. Based on parent report, a qualified professional, such as a pediatrician, psychologist, psychiatrist, neurologist, or neuropsychologist, diagnosed all of the children in these two groups.

Data Analysis

Three of the research questions for this study involved examining the number of reported perinatal complications. The first research question examined the relationship between the number of perinatal complications experienced and a diagnosis of autistic disorder. The second research question examined the relationship between the number of perinatal complications experienced and a diagnosis of Asperger’s disorder. The third research question pertained to whether or not a difference exists in the number reported perinatal complications between
Asperger’s disorder and autistic disorder. In order to answer these research questions, a univariate analysis of variance (ANOVA) was conducted to compare all three groups in terms of number of reported perinatal complications. Before conducting the ANOVA, the total number of perinatal complications reported was calculated for each child in each group. Calculating the total number of perinatal complications for each individual involved adding up the number of complications.

There was also a fourth research question. Could a later diagnosis of autistic disorder or Asperger’s disorder be predicted based solely on perinatal development? A Classification and Regression Tree (CART) analysis was conducted in order to answer that question. The perinatal data used for the CART analysis were the responses to 18 items from the MPS, which corresponds to the items utilized in the scoring system. Each of the 18 items was a variable in the analysis. The goal of the CART was to create a prediction model that accurately classified the children according to their group membership based on data from the MPS. In general, a CART is used to construct a prediction model. It uses a series of if-then rules to classify data (Goel et al., 2009). Data are partitioned one variable at a time into nodes (Loh, 2011). This process continues until the procedure can no longer decrease heterogeneity with further divisions. The process results in terminal nodes, which are the final predictions for the individuals. Prediction error is measured in terms of misclassification.

For example, you could conduct a CART to predict whether or not someone had a head injury based on scores from a measure of intelligence. In this case, the CART would explore all the possible scores in order to best split the subjects into two different groups: head injury and non-head injury. The CART will make multiple splits until the groups are as homogeneous as possible in terms of head injury history. The first score the CART selects could be an 80 on
processing speed. Thus, if someone has a processing speed standard score of 80 or lower then he/she goes into a specific node, or group. If someone has a processing speed score higher than 80, then he/she goes into a different node. Next, the CART could determine to split the subjects in the 80 or lower processing speed node based on a memory score of 75. Those with both a processing speed of 80 or lower and a memory score of 75 or lower would be in one node and those with both a processing speed of 80 or lower and a memory score higher than 75 would be in another node.

The CART in the example made two divisions, which resulted in three terminal nodes. That means that additional splits would not significantly improve group prediction. The three terminal nodes are (1) processing speed higher than 80, (2) processing speed of 80 or lower and a memory score of 75 or lower, and (3) processing speed of 80 or lower and memory score higher than 75. Each terminal node represents a classification prediction. The classification is based on whichever group has the most subjects in that node. For example, if the first node had 80% non-head injury subjects, the prediction would be that anyone who has a processing speed higher than 80 has not had a head injury. That would mean 20% of the subjects in that node were misclassified. That is, the model predicted the wrong group membership for those subjects. In addition to providing a misclassification rate for each terminal node, a CART provides an overall misclassification rate. That rate indicates how accurately, in general, the CART predicted group membership of the subjects.
CHAPTER FOUR

Results

This study examined the relationship between perinatal factors and a diagnosis of autistic disorder or Asperger’s disorder. Perinatal factors were measured by the Maternal Perinatal Scale (MPS; Dean & Gray, 1985). There were multiple research questions this study examined. The first question was whether or not there was a relationship between the number of compromising obstetrical events and a later diagnosis of autistic disorder. The second question was whether or not there was a relationship between the number of perinatal complications and a later diagnosis of Asperger’s disorder. The third question was whether or not there was a significant difference in the number of reported perinatal complications between individuals diagnosed with autistic disorder and those diagnosed with Asperger’s disorder. The fourth, and final, question was whether or not a later diagnosis of autistic disorder or Asperger’s disorder could be predicted based solely on perinatal development.

Research Questions One, Two, and Three

In order to determine if any significant differences existed between the groups, all three groups were compared in term of total number of perinatal complications reported. This included all of the risk factors measured by the MPS. The calculation involved a simple count of all the complications endorsed for each child. A univariate analysis (ANOVA) was then conducted, which compared the mean number of complications for the groups. In addition to conducting an ANOVA, the three assumptions for ANOVA were analyzed. The assumption of normality was met based on a normal Q-Q plot for each diagnostic group. The assumption of independence of subjects was also met given the data collection procedures. Levene’s test of homogeneity of variance was not significant, $F(2,70) = 1.005, p = .371$, indicating that assumption was also met.
The results of the ANOVA indicated the groups were significantly different, $F(2,70) = 7.993$, $p = .001$. A pairwise comparison, Tukey’s HSD test, revealed the autistic group and the control group were significantly different. Specifically, it indicated the autistic group had a higher mean number of risk factors, $p = .001$. A pairwise comparison of the Asperger’s group and the control group indicated they were not significantly different, $p = .062$. A pairwise comparison of the Asperger’s group and the autistic group indicated they were not significantly different, $p = .569$. The mean number of complications for each group are listed in Table 3.

Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Number of Complications</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autistic Disorder</td>
<td>9.05</td>
<td>2.33</td>
</tr>
<tr>
<td>Asperger’s Disorder</td>
<td>8.20</td>
<td>1.78</td>
</tr>
<tr>
<td>Control</td>
<td>6.86</td>
<td>2.38</td>
</tr>
</tbody>
</table>

Research Question Four: Could Perinatal Data Predict Diagnosis?

A Classification and Regression Tree (CART) analysis was conducted to examine whether perinatal complications (i.e., items on the MPS) would accurately predict diagnostic group membership (no diagnosis, autistic disorder, or Asperger’s disorder). The perinatal data utilized in the CART analysis were 18 items from the MPS, which corresponds to the items used in the scoring system. The original tree resulted in 11 terminal nodes with a residual mean deviance of 1.842 and a misclassification error rate of 38%. This means that based on the variables included, 38% of the individuals were mislabeled in terms of group membership. The misclassification rate for the control group was 18.92%, the rate for the autistic group was 42.9%, and the rate for the Asperger’s group was 80%. The CART model used seven of the 18 variables included. These variables were previous pregnancies, amount of bleeding, gestational
age, length of labor, maternal weight gain, mother’s age at child’s birth, and inducement of labor.

An illustration of the tree is in Figure

Figure 1. Original Classification Tree

The original tree was pruned, which means the number of terminal nodes was reduced. This was done in order to avoid over-fitting the data. Since the sample is small, there is a risk of making splits that are meaningful for the sample but would be arbitrary in the population. The first step for pruning the tree involved generating a deviance plot, which is presented in Figure 2. The deviance plot along with misclassification error rate statistics indicated seven terminal nodes was a good balance of parsimony, prediction error, and deviance.
Next, the original tree was pruned to seven terminal nodes. This pruned tree had a misclassification error rate of 42% and a residual mean deviance of 1.859. However, it did not have a terminal node for Asperger’s, which meant it no longer predicted an Asperger’s diagnosis for any children. In an effort to maintain the ability to predict an Asperger’s diagnosis as well as the balance of parsimony and deviance, the original tree was pruned to eight nodes instead of seven. The resulting tree was able to predict an Asperger’s diagnosis with minimal costs to parsimony. Therefore, eight terminal nodes were retained for the pruned tree.

*Figure 2.* Deviance of classification trees by the number of terminal nodes in the model.
The pruned tree had a residual mean deviance of 1.853 and an overall misclassification error rate of 40%, indicating the group membership of 60% of the 73 children was accurately predicted. The misclassification rate for each group was calculated. The results indicated the rate for the control group was 16.2%, the rate for the autistic group was 52.4%, and the rate for the Asperger’s group was 80%. These results indicated the model accurately predicted approximately 84% of the control children, 48% of children with autistic disorder, and 20% of children with Asperger’s. The majority of children with Asperger’s were classified as non-clinical, and approximately half of the children with autistic disorder were classified as non-clinical. The composition of each terminal node in the pruned tree is illustrated in Table 4.

Table 4

<table>
<thead>
<tr>
<th>Terminal Node</th>
<th>Total Number of Subjects</th>
<th>Percent of Subjects with Autistic Disorder</th>
<th>Percent of Subjects with Asperger’s</th>
<th>Percent of Subjects from Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td>7</td>
<td>57.1%</td>
<td>14.3%</td>
<td>28.6%</td>
</tr>
<tr>
<td>Two</td>
<td>12</td>
<td>8.3%</td>
<td>16.7%</td>
<td>75.0%</td>
</tr>
<tr>
<td>Three</td>
<td>6</td>
<td>0.0%</td>
<td>33.3%</td>
<td>66.7%</td>
</tr>
<tr>
<td>Four</td>
<td>12</td>
<td>8.3%</td>
<td>33.3%</td>
<td>58.3%</td>
</tr>
<tr>
<td>Five</td>
<td>5</td>
<td>20.0%</td>
<td>60.0%</td>
<td>20.0%</td>
</tr>
<tr>
<td>Six</td>
<td>15</td>
<td>40.0%</td>
<td>0.0%</td>
<td>60.0%</td>
</tr>
<tr>
<td>Seven</td>
<td>6</td>
<td>33.3%</td>
<td>33.3%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Eight</td>
<td>10</td>
<td>60.0%</td>
<td>10.0%</td>
<td>30.0%</td>
</tr>
</tbody>
</table>

All of the variables from the original tree were used with the exception of inducement. An illustration of the pruned tree is in Figure 3.
Figure 3. Final classification tree with eight terminal nodes.

The pruned tree serves as a prediction model for autistic disorder and Asperger’s disorder. The first predictive factor in the model is maternal weight gain. If the mother gained less than 16 pounds, then the child goes into the autistic disorder group. This is not the only predictive factor of autistic disorder. According to the decision tree, if the mother gained more than 16 pounds, gestation lasted between 37 weeks and 41 weeks, the number of previous pregnancies was one to three, no bleeding during the pregnancy, and the mother was less than 35 years old, then the child falls into the autistic group. The decision tree also provides a prediction model for Asperger’s disorder. First, the mother had to gain 16 pounds or more, then the length of gestation was between 37 weeks and 41 weeks, the number of previous pregnancies was none or more than 3, and labor lasted longer than 16 hours.
The first predictor in the pruned tree model is maternal weight gain. Based on the scoring system (Trammell, 2012), a higher score for this item means the mother gained less than 16 pounds total. The tree was modified to be more user-friendly. The scoring system is complex, so the modification included changing the labels for each decision from an MPS item name and score to descriptive information. This way, the user will not have to consult the scoring table to make a decision for each factor. The modified tree is illustrated in Figure 4.
Figure 4. Prediction model formatted for ease of use.
CHAPTER FIVE

Discussion

This study sought to further the research on perinatal complications as risk factors of autism. Specifically, it focused on autistic disorder and Asperger’s disorder. These groups were selected after a review of the research literature. Some of the previous studies concerning autism focused on one particular diagnostic group, such as autistic disorder or Asperger’s disorder (e.g. Cederlund & Gillberg, 2004; Kinney, Munir, Crowley, & Miller, 2008). Other studies utilized a heterogeneous sample made up of individuals diagnosed with autistic disorder, Asperger’s, and/or Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS; e.g. Yirmiya & Charman, 2010; Kolevzon, Gross, & Reichenberg, 2007; Reichenberg et al., 2006). Few studies have examined whether autistic disorder and Asperger’s disorder differed in terms of perinatal development. One study by Dawson et al. (2009) did compare these groups and found a difference in the number of birth defects. This study investigated a difference in the number of perinatal complications between these two groups.

Numerous studies have utilized a control group when investigating perinatal complications and autism (e.g., Dawson et. al., 2009; Glasson et al., 2004; Larsson et al., 2005; Wilkerson et al., 2002). This study also utilized a control group in order to provide a baseline of perinatal complications in the general population. Previous procedures for collecting perinatal data typically involved a review of medical records. Some studies used an informal parent interview. Wilkerson et al. (2002) took a different approach and employed the Maternal Perinatal Scale (MPS; Dean & Gray, 1985). The MPS is a structured and reliable measure of perinatal complications (Gray et al., 1988; Gray, Dean, & Rattan 1987). This study also utilized the MPS.
Specifically, the perinatal complications utilized in this investigation are all complications that are measured by the MPS.

This investigation had a few questions it sought to answer. The first question examined the association between the number of complications and a diagnosis of autistic disorder. This question was investigated by comparing children diagnosed with autistic disorder with typically developing counterparts on the total number of perinatal complications. To that end, an analysis of variance was conducted, which compared all three groups. The findings of that analysis indicated there was a significant difference between children with autistic disorder and typically developing children. Children who had been diagnosed with autistic disorder had a higher number of complications compared to those in the control group. This result was not surprising because it is consistent with previous findings. Indeed, Larsson et al. (2005) found a higher number of perinatal complications among individuals with autistic disorder compared to a normal cohort. These findings suggest there is a link between the number of perinatal complications and a later diagnosis of autistic disorder. However, further research is necessary to substantiate this finding as well as investigate the nature of this relationship.

The second research question also involved examining the total number of perinatal complications. This comparison was between children diagnosed with Asperger’s disorder and children in the control group. The results of the previously mentioned analysis of variance indicated there was not a significant difference between the two groups. This means children who are later diagnosed with Asperger’s disorder had a similar number of perinatal complications as children who have no neurologic or psychological diagnoses. Previous research has shown an association between an Asperger’s diagnosis and specific perinatal complications (Cederlund & Gillberg, 2004; Gillberg & Cederlund, 2005). Although an association between the
number of perinatal complications and a diagnosis of Asperger’s disorder has not been investigated, previous studies indicated some individuals diagnosed with Asperger’s did not have any perinatal complications (Gillberg & Cederlund, 2005). The results of this study suggest such an association does not exist. Thus, it is possible the type of perinatal complications is more indicative of an Asperger’s diagnosis than the number of perinatal complications. More systematic research in this area would elucidate the relationship between perinatal complications and Asperger’s disorder.

The third research question examined whether there was a difference in the total number of perinatal complications between the diagnostic groups. That is, perinatal data from children diagnosed with autistic disorder was compared to perinatal data from children diagnosed with Asperger’s disorder. The results indicated there was not a significant difference in the total number of perinatal complications between the two groups. Although few investigations have compared these groups, Glasson et al. (2004) found a qualitative difference between those with autistic disorder and those with Asperger’s disorder. Those with autistic disorder had a greater number of complications. Thus, it is somewhat surprising there was not a significant difference in the number of perinatal complications between the two. However, some experts believe the two are not unique conditions (APA, 2013). Indeed, the fifth edition of the Diagnostic and Statistical Manual (DSM-V; APA, 2013) does not distinguish between the two. It utilizes a spectrum approach with specific indicators of severity and certain symptoms. Additionally, genetic studies have not been able to identify unique genes for each condition and some of the symptoms overlap (APA, 2000; Bailey et al., 1995; Bonora et al., 2006; Gillberg & Coleman, 2000). Overall, it may be better to investigate perinatal complications in relation to specific symptoms as opposed to diagnosis. Such investigations would be beneficial because they could
provide predictors of maladaptive behaviors, which would then contribute to early identification and treatment.

The fourth research question examined if an individual’s diagnosis of autistic disorder or Asperger’s disorder could be predicted based solely on perinatal data. A previous study was able to predict if an individual had a diagnosis of autism or not with 65% accuracy using perinatal data only (Wilkerson et al., 2002). In order to predict diagnosis of the participants in the current study, a Classification and Regression Tree (CART) analysis was conducted. The CART was used in an attempt to create a prediction model that would correctly identify an individual as having autistic disorder, Asperger’s disorder, or no history of diagnosis based on his/her perinatal history. The results indicated the prediction model misclassified 40% of participants. This means almost half of the subjects were believed to belong to the wrong diagnostic group. However, predicting group membership with 60% accuracy is consistent with the previous study that did so with 65% accuracy (Wilkerson et al., 2002). Overall, perinatal complications do provide some information in terms of risk of a later autistic disorder or Asperger’s diagnosis, but the utility of this information is limited due to the likelihood of a false classification.

The results of the CART analysis were used to create a prediction model. The prediction model utilized six of the 18 items on the Trammell (2012) scoring system, indicating they were the best predictors of diagnosis. These six factors were previous pregnancies, amount of bleeding, gestational age, length of labor, maternal weight gain, and mother’s age at the time of the child’s birth. Previous findings have shown the predictive value of advanced maternal age (Gardener et al., 2009; Reichenberg et al., 2006; Burd et al., 1999), maternal weight gain (Institute of Medicine, 1996), and gestational age of the child at birth (Trachtenberg & Goleman,
1998a; Trachtenbarg & Goleman, 1998b) for later negative outcomes. Consequently, it is not surprising that the prediction model utilized those three factors.

The prediction model contained two terminal nodes classified as having individuals with autistic disorder. As previously indicated, this provided two different sets of parameters. The prediction model misclassified 11 of the 21 individuals (52%) who were diagnosed with autistic disorder. This suggests a later diagnosis of autistic disorder can be predicted with 48% accuracy when only considering an individual’s perinatal history. However, one of the sets of parameters in the model used to predict this diagnosis did not have any perinatal complications tied to it. Thus, perinatal data in isolation is not a good predictor of a later autistic disorder diagnosis.

The prediction model contained only one terminal node classified as having individuals with Asperger’s disorder. This particular node had only five total individuals. Three of those 5 individuals actually had a diagnosis of Asperger’s disorder. Thus, 12 of the 15 total subjects with Asperger’s disorder were misclassified. That is, 80% were incorrectly labeled. Interestingly, 10 of the 15 individuals (67%) in this group were classified as no diagnosis. These findings suggest Asperger’s disorder cannot be accurately predicted from perinatal data alone. By and large, the CART model was better at correctly identifying individuals with no diagnosis. Only six of the 37 individuals (16%) in the no diagnosis group were misclassified. This is not surprising given the lower number of individuals in each of the diagnostic groups compared to the number of those without a diagnosis.

Overall, answering the research questions provided interesting results. When looking at the association between perinatal complications and a later diagnosis of autistic disorder, the results indicated the number of perinatal complications, experienced by individuals diagnosed with autistic disorder was significantly higher than those of a normal cohort. The comparison
between individuals diagnosed with Asperger’s disorder and the control group yielded different results. There was not a significant difference in the number of complications reported for those with Asperger’s disorder and those with no diagnosis. Additionally, the number of perinatal complications for those in the Asperger’s group was not significantly different from those diagnosed with autistic disorder. These comparisons suggest that the higher the number of perinatal complications experienced, the higher a child’s risk for later being diagnosed with autistic disorder. On the other hand, this study does not provide evidence that the number of perinatal complications affects the risk of later being diagnosed with Asperger’s disorder.

However, this study investigated more than the presence of complications. It sought to predict a future diagnosis of autistic disorder or Asperger’s disorder using perinatal complications. More specifically, predicting a diagnosis using the estimated risk of complications experienced. Every complication had an associated risk based on the weight of each perinatal factor endorsed. Because the weights are assigned based on how harmful a particular factor is to future development, they help determine the utility of perinatal complications as predictors. This type of information is more useful for clinicians. The purpose of a perinatal measure is to provide pertinent information that will allow clinicians to determine if a child is at-risk. This will then help individuals be diagnosed earlier, and as a result, have better outcomes from early treatment.

The prediction model, as established by the results of the CART analysis, did differentiate between autistic disorder and Asperger’s disorder. There was some overlap in the predictive factors related to each diagnosis, but the model indicated unique sets of perinatal risk factors. Unfortunately, the prediction model was only 60% accurate. Not to mention, one of the unique sets of perinatal predictors for autistic disorder was not tied to any known risk factors.
Thus, the findings from this study do not support predicting Asperger’s disorder or autistic disorder based solely on perinatal history. However, perinatal complications can still have utility to clinicians. They are still risk factors, which in conjunction with other relevant risk factors, such as family history, could mean a child is diagnosed at an early age.

**Limitations and Future Directions**

It is difficult to draw firm conclusions on the results of this study due to some limitations. One limitation of this study is the sample. Due to the selected recruiting methodology, the parents who completed the MPS are primarily from upper socioeconomic groups as evidenced by the household incomes and higher level of education obtained. This may have a confounding effect on the data since mothers in these groups may have received better prenatal care and fewer perinatal complications when compared to mothers from lower socioeconomic groups. Not to mention, there was a limited number of minorities represented. Thus, this sample does not accurately represent the population, and as such, is limited in generalizability.

Another limitation of the sample was the size. Small numbers for each group means a lack of power. When there is insufficient statistical power and the null hypothesis is not rejected, one might question whether the phenomenon truly does not exist (Cashen & Geiger, 2004). Therefore, it could be possible there are modest differences in perinatal development between the groups, but the power was too low for such differences to be detected. It is also possible no such differences exist but due to insufficient power it cannot be concretely determined. Future researchers should work to get a large, representative sample. Although getting such a sample would be difficult, it would certainly help the results be more definitive and generalizable.

Another limitation is the measure used in the study. The MPS has been shown to be a structured, reliable measure of perinatal complications (Gray, Dean, Rattan, & Bechtel, 1988;
Gray, Dean, and Rattan 1987). However, the validation studies for the scale were conducted over 30 years ago. Not to mention, the items on the scale may be out of date. For instance, cesarean deliveries were used less frequently in the past. The rate of cesarean delivery was 54% in 2006, which is an increase of almost 20% from the rate in 1996 (Martin et al., 2009). Thus, cesarean delivery may no longer be a good predictor of later developmental deviation.

Another issue with using the MPS is that its newly developed scoring system has not been well researched (Trammell, 2012). While it provides weights to account for differences in the amount of risk a particular perinatal factor has, it only addresses a limited number of potential threats to a developing fetus. For instance, the scoring system does not take into account known risk factors for later developmental deviation such as maternal drug use, prenatal exposure to toxins, and viral infections (Milberger et al., 1997; Chelune & Edwards, 1981). Another concern is that the Trammell (2012) scoring system did not include the maternal health risk factors. Thus, those items are simply added up. That means each item is given equal weighting, which may not be an accurate reflection of the impact each risk factor truly has. Future research should focus on establishing or re-establishing a measure of perinatal development that includes factors recently identified/confirmed by research to put an individual at risk for negative outcomes. Additionally, that measure should provide meaningful information in a simple fashion, such as a scoring system, so as to be useful for clinicians.

Another limitation was the design of the study. Perinatal information was collected retroactively. The ideal design would be longitudinal. This would allow for a direct relationship between perinatal development and specific later developmental outcomes. The lengthy time and expense needed to conduct such a study were not within the scope of this project. Future research should take a longitudinal approach to establishing the association of perinatal complications
with later outcomes, including autism. Such information would assist clinicians in identifying individuals at risk early and providing early treatment.

Despite the limitations, this study did find a significant link between autistic disorder and the number of perinatal complications experienced. Future research should further investigate this link, particularly the nature of it. The results of the current study indicated perinatal complications alone do not accurately predict a future diagnosis of autistic disorder or Asperger’s disorder. However, the goal for better understanding the etiology of these conditions is that they can be identified early and therefore treated early. Perinatal complications are risk factors, and in combination with other relevant risk factors, could facilitate early identification. More importantly, perinatal complications have the potential to predict which symptoms will develop, and that would facilitate early, targeted treatment. Therefore, future research should focus on the relationship between perinatal complications and specific symptoms.
References


The development of autism: Perspectives from theory and research (pp. 39-60).

Mahwah, NJ: Lawrence Erlbaum Associates.
Appendix

Perinatal Factors Assessed by the MPS (Dean, Gray, & Anderson, 1996)

Factors Prior to Pregnancy
- Mother’s weight
- Mother’s height
- Father’s height
- Number of prior births
- Mother’s age at time of birth
- History of gynecological surgery
- History of previous problem pregnancy

Factors During Pregnancy
- Vaginal Bleeding
- Amount of maternal psychosocial stress
- Weight Gain
- First consulted physician
- Pregnancy Planning
- Medication & vitamin use during pregnancy
- Mean number of cigarettes during pregnancy
- Mean number of alcohol during pregnancy
- Edema

Maternal Disorders
- Maternal medical conditions

Labor and Delivery
- Anesthesia employed during delivery
- Length of labor
- Induced labor
- Forceps use
- Multiple pregnancy
- Presentation of infant during delivery
- Time from water break to labor
- Child’s color at birth

Birth Weight and Gestational Age
- Child’s birth weight
- Months to term

Social-Cultural Factors
- Mother’s race
- Father’s race
- Family’s socioeconomic status
## Maternal Perinatal Scale Scoring System Scores for Responses

<table>
<thead>
<tr>
<th>MPS Item</th>
<th>Response</th>
<th>Beta Weight</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Previous Children</td>
<td>None</td>
<td>-.043</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>Referent</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>-.177</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>5 or more</td>
<td>-.233</td>
<td>2.3</td>
</tr>
<tr>
<td>Prenatal Care Obtained</td>
<td>1st Trimester</td>
<td>Referent</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>2nd Trimester</td>
<td>-.421</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>3rd Trimester</td>
<td>-.784</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>-.269</td>
<td>2.6</td>
</tr>
<tr>
<td>Maternal Weight Gain</td>
<td>Less than 16 pounds</td>
<td>-.319</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>16-35 pounds</td>
<td>Referent</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>36-40 pounds</td>
<td>-.005</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>41-45 pounds</td>
<td>-.011</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>46 or more pounds</td>
<td>-.030</td>
<td>0.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Present prepregnancy</td>
<td>.581</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td>Present during pregnancy</td>
<td>.550</td>
<td>5.5</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>Referent</td>
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</tr>
<tr>
<td>Bleeding</td>
<td>Present</td>
<td>-.066</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>Excessive</td>
<td>-.529</td>
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<td>Referent</td>
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<tr>
<td>Eclampsia</td>
<td>Present</td>
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<td></td>
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<tr>
<td>Rh Sensitivity</td>
<td>Present</td>
<td>.074</td>
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<tr>
<td></td>
<td>Absent</td>
<td>Referent</td>
<td>0.0</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td>1 drink per week</td>
<td>-.031</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>2 drinks per week</td>
<td>-.265</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>3 drinks per week</td>
<td>-.186</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>4 drinks per week</td>
<td>-.018</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>5 or more drinks per week</td>
<td>-.319</td>
<td>3.2</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td>1-5 cigarettes per day</td>
<td>-.018</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>6-10 cigarettes per day</td>
<td>.000</td>
<td>0.0</td>
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<tr>
<td></td>
<td>11-20 cigarettes per day</td>
<td>-.121</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>21-40 cigarettes per day</td>
<td>.439</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>40+ cigarettes per day</td>
<td>3.506</td>
<td>35.1</td>
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<tr>
<td>Gestation</td>
<td>Less than 20 weeks</td>
<td>-3.110</td>
<td>31.1</td>
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<tr>
<td></td>
<td>20-27 weeks</td>
<td>-1.538</td>
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<td>28-31 weeks</td>
<td>-.621</td>
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<td></td>
<td>32-33 weeks</td>
<td>-.688</td>
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<td></td>
<td>34-36 weeks</td>
<td>-.503</td>
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<td></td>
<td>37-41 weeks</td>
<td>Referent</td>
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<td></td>
<td>42 weeks</td>
<td>-.065</td>
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<tr>
<td>Labor</td>
<td>Precipitous labor (&lt; 3 hrs)</td>
<td>-.129</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>Referent</td>
<td>0.0</td>
<td></td>
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<tr>
<td>-------------------------</td>
<td>----------</td>
<td>-----</td>
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<tr>
<td>3-16 hours</td>
<td>-0.584</td>
<td>5.8</td>
<td></td>
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<tr>
<td>Prolonged labor (&gt;16hrs)</td>
<td>0.0</td>
<td>0.0</td>
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<table>
<thead>
<tr>
<th>Plurality</th>
<th>Referent</th>
<th>0.0</th>
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<tbody>
<tr>
<td>Singleton</td>
<td>-0.342</td>
<td>3.4</td>
</tr>
<tr>
<td>Twin</td>
<td>-0.679</td>
<td>7.0</td>
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<tr>
<td>Triplet</td>
<td>-0.438</td>
<td>4.4</td>
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<tr>
<td>Quadruplet</td>
<td>-1.349</td>
<td>13.5</td>
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<tr>
<td>Quintuplet+</td>
<td>0.0</td>
<td>0.0</td>
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<table>
<thead>
<tr>
<th>Labor Induced</th>
<th>Referent</th>
<th>0.0</th>
</tr>
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<tbody>
<tr>
<td>Present</td>
<td>-0.171</td>
<td>1.7</td>
</tr>
<tr>
<td>Absent</td>
<td>0.0</td>
<td>0.0</td>
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<table>
<thead>
<tr>
<th>Presentation</th>
<th>Referent</th>
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<tbody>
<tr>
<td>Breech</td>
<td>-0.131</td>
<td>1.3</td>
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<tr>
<td>Cephalic</td>
<td>0.0</td>
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<table>
<thead>
<tr>
<th>Forceps Use</th>
<th>Referent</th>
<th>0.0</th>
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<tbody>
<tr>
<td>Present</td>
<td>-0.248</td>
<td>2.5</td>
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<tr>
<td>Absent</td>
<td>0.0</td>
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<table>
<thead>
<tr>
<th>Birthweight</th>
<th>Referent</th>
<th>0.0</th>
</tr>
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<tbody>
<tr>
<td>Less than 499 grams</td>
<td>-6.757</td>
<td>67.6</td>
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<tr>
<td>500-999 grams</td>
<td>-3.868</td>
<td>38.7</td>
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<tr>
<td>1000-1499 grams</td>
<td>-2.778</td>
<td>27.8</td>
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<tr>
<td>1500-1999 grams</td>
<td>-2.164</td>
<td>21.6</td>
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<tr>
<td>2000-2499 grams</td>
<td>-1.258</td>
<td>12.6</td>
</tr>
<tr>
<td>2500-3999 grams</td>
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<td>0.0</td>
</tr>
<tr>
<td>4000-4499 grams</td>
<td>-0.208</td>
<td>0.8</td>
</tr>
<tr>
<td>4500-4999 grams</td>
<td>-0.628</td>
<td>6.3</td>
</tr>
<tr>
<td>5000-8165 grams</td>
<td>-1.365</td>
<td>13.6</td>
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<table>
<thead>
<tr>
<th>Maternal Age</th>
<th>Referent</th>
<th>0.0</th>
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<tbody>
<tr>
<td>Less than 15 years</td>
<td>0.46</td>
<td>0.5</td>
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<tr>
<td>15-19 years</td>
<td>0.01</td>
<td>0.0</td>
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<tr>
<td>20-34 years</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>35-39</td>
<td>1.164</td>
<td>1.6</td>
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<tr>
<td>More than 40 years</td>
<td>-1.698</td>
<td>17.0</td>
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**Maternal Perinatal Scale Cutoff Scores**

<table>
<thead>
<tr>
<th>MPS Scales</th>
<th>80% Cutoff Score</th>
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<tbody>
<tr>
<td>Overall</td>
<td>10.50</td>
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<tr>
<td>Maternal Subscale</td>
<td>5.21</td>
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<tr>
<td>Labor/Neonatal Subscale</td>
<td>6.70</td>
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