2014

Premature Birth as a Factor in Autism Spectrum Disorder

Rachel Lichtenstein Goldin
Louisiana State University and Agricultural and Mechanical College, rgoldi3@lsu.edu

Recommended Citation

PREMATURE BIRTH AS A FACTOR IN AUTISM SPECTRUM DISORDER

A Thesis

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Master of Arts

in

The Department of Psychology

by
Rachel Lichtenstein Goldin
B.A., Clark University, 2010
May 2015

TABLE OF CONTENTS

ABSTRACT

Autism Spectrum Disorder (ASD) is characterized by pervasive delays in socialization, communication, and repetitive behaviors and restricted interests. While there is a growing body of evidence on the etiology of ASD, there are a limited number of studies examining factors which may impact the differentiation of ASD compared to other developmental disabilities. Additionally, few studies have examined factors which may predict level of ASD symptom severity. The primary aim of this study was to investigate whether premature birth occurs more commonly in infants and toddlers (17-37 months) with ASD than those with atypical development. A secondary aim of this study was to investigate whether length of gestation predicts scores on the *Baby and Infant Screen for Children with aUtIsm Traits* (*BISCUIT*), *Part 1*, a measure of overall impairment, in participants with ASD. Participants were separated into two groups (i.e., ASD, atypical development), and compared on the basis of parent/caregiver reported incidence of premature birth and average weeks of gestation. Additional analyses included within group comparisons for the ASD diagnostic group by separating individuals who were born prematurely and full term and analyzing their total scores on the *BISCUIT-Part 1* were. Differences in overall level of functioning were assessed. Results of the current study indicate that infants and toddlers with atypical development are more likely to be born prematurely; however, average weeks of gestation did not significantly differ between the groups. Follow up analyses of participants with ASD revealed that premature birth was not a predictor of level of severity. Implications of these findings are discussed.

INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by pervasive deficits in the areas of socialization, communication, and repetitive behaviors and restricted interests. As the name of the disorder insinuates, presentation of the disorder and level of severity of symptoms varies considerably within the population (Ben-Itzchak & Zachor, 2007). In recent years, a significant amount of attention has been directed towards ASD, specifically, early detection of the disorder (Evans et al., 2001; Lord & Luyster, 2006; Matson, Wilkins, & Gonzalez, 2008; Werner, Dawson, Osterling, & Dinno, 2000, Wetherby et al., 2004). Much of this research has underscored the importance of early identification; but, little research has been designed to investigate why the disorder has such a diverse manifestation in symptom presentations and level of severity. The aim of this study was twofold. First, to determine whether premature birth more commonly occurs in those with ASD compared to individuals with atypical development. Second, to examine whether premature birth acts as a factor impacting autism severity in infants and toddlers.

Severity of ASD is important to assess so as to best inform treatment planning, and treatment implementation. The type, frequency and intensity of treatment a child receives is determined by how impaired a child is, and where their greatest deficits lie. Instruments such as the *Baby and Infant Screen for Children with aUtIsm Traits* (*BISCUIT*) have been developed to aid in this task. The *BISCUIT* is designed to screen for ASDs among infants and toddlers 17 to 37 months of age to determine ASD symptom severity (Matson, Wilkins, Sevin et al., 2008). For the current study Part-1 of the *BISCUIT* and number of weeks of gestation reported by parents/caregivers were used to examine incidence of premature birth, and whether symptom severity scores can be predicted by premature birth.

It is hypothesized the incidence of premature birth will not differ between infant and toddlers with a diagnosis of ASD compared to those deemed atypically developing. It is expected that infants and toddlers with ASD born prematurely, before 37 weeks of gestation, will have greater scores on the *BISCUIT-Part 1* compared to infants and toddlers with ASD carried full term. The history of ASDs and a description of the disorder, along with current research on the effects of prematurity on development are outlined below. Details of the current study and discussion of the findings are presented. The aim of this study is to expand knowledge on the relationship between premature birth and ASD.

AUTISM SPECTRUM DISORDERS

History

Autism. Swiss psychiatrist, Eugene Bleuler (1913), first coined the term "autism" in his paper "Autistic Thinking." Bleuler used the term autism to describe a trait of schizophrenia. The term "autistic thinking" was used to refer to when one gets lost in a fairy tale state of thinking resulting in a distorted view of reality. Autistic thinking, according to Bleuler, is illogical. Realistic or logical thinking represents instances in the outer world and their associations; when one's actions result in expected fixed results. If thinking deviates from or contradicts these established associations, it becomes autistic thinking. Bleuler stated that as long as the schizophrenic is collected in his thinking, and still aware of its contradictions, he is still logical. Once a person with schizophrenia becomes immersed in autistic thinking, he reaches a point where he no longer looks for justifications in the outer world and instead creates his own justifications; he believes fantasy is reality (Bleuler, 1913).

Bleuler's initial use of the word autism suggested withdrawal from reality and relationships. Leo Kanner (1943) used the term autism in his paper "Autistic Disturbance of Affective Contact," but instead to describe an inability to form relationships, rather than simply withdrawing from them. Kanner's work was influential and laid the foundation for research in ASD. In his paper, Kanner provides a detailed account of 11 children, between the ages of 2 and 8, with similar symptoms. The symptoms noted by Kanner include deficits in socialization, effective communication, stereotyped movements (e.g., spinning, arranging objects, moving hands and fingers in the air), repetitive actions and rituals, excellent rote memory, and lack of spontaneous activity. Kanner hypothesized that these symptoms collectively characterized one condition that he termed "early infantile autism" (Kanner, 1944, 1954). Prior to this, children with the symptom presentation described by Kanner, would have been viewed as feebleminded

or presenting with childhood schizophrenia. The distinction between early infantile autism and childhood schizophrenia made by Kanner allowed early infantile autism to be recognized as an independent disorder.

Children with autism, according to Kanner, are unable to relate to others and relate themselves to situations in an ordinary way. Reports by parents illustrated a child who was "happiest when left alone," "self-sufficient," and "perfectly oblivious to everything about him" (Kanner, 1943, p. 242). Kanner's description of autism suggested these features were present from birth. Kanner noted, "there is from the start an extreme autistic aloneness that, whenever possible, disregards, ignores, shuts out anything that comes to the child from the outside" (Kanner, 1943, p. 242). Therefore, these children as presented by Kanner, did not exhibit the withdrawal Bleuler described in schizophrenia. The lack of withdrawal occurring after the onset of the disorder was the defining feature which distinguished autism from childhood schizophrenia.

Kanner (1943) noted a few core features of early infantile autism, one of which was a delay in language acquisition. Eight of the 11 children Kanner followed acquired the ability to speak and three did not. The eight that were able to speak, however, were unable to convey meaning in their language. Their language consisted of repetitive words and phrases, and the children failed to put words together. Kanner suggested that these impairments in language contributed to the course of the disorder, as their language could not be used in a manner to communicate meaningful messages.

A second core feature of the children identified by Kanner (1943) was an insistence on sameness. Inconsistencies in daily routine, such as variations in the wording a requests or sequences of events, caused great distress. For instance, one child would not leave his bed after

a nap without hearing specific utterances from his mother. If his mother did not comply, he would scream until his mother said everything he wanted to hear. The child could not get out of his bed unless a specific sequence of events occurred. Moreover, Kanner noted that children with autism preferred objects that did not change in appearance or position. Objects with these characteristics do not threaten or impede on the child's aloneness. Kanner suggested that the extreme preoccupation with sameness contributes to the restricted range of interests and activities observed in these children.

Expanding on Kanner's work, Michael Rutter (1978) contributed to the establishment of autism as a separate disorder by highlighting the distinction between autism and schizophrenia. He argued that unlike individuals with schizophrenia, autism was a stable and always present disorder, where those with schizophrenia experienced period of relapse and remission. Likewise, delusions and hallucinations seen in schizophrenia were not present in children with autism. Children with schizophrenia initially developed social relationships, then withdrew from them, while children with autism never formed social relationships, thus, there was never a point where they withdrew. Rutter also noted a different age of onset for the disorders. Autism was present at infancy, whereas schizophrenia developed during early adolescence. Further, autism had a higher prevalence in males, while schizophrenia had an equal prevalence in females and males. Finally, Rutter noted that intellectual disabilities (ID) commonly co-occurred with autism and not schizophrenia (Rutter, 1978; Rutter & Bartak, 1971). Rutter's work was fundamental in distinguishing autism as an independent disorder. The distinction was crucial as it aided clinicians in correctly diagnosing the disorder and opening the door for more focused research on the population with autism (Matson & Minshawi, 2006).

In 1978, Rutter went on to provide a more comprehensive definition of autism (Matson & Minshawi, 2006; Volkmar & Klin, 2005). Rutter's definition was comprised of four criteria; onset prior to 30 months of age, impairment in social development, delay in language development, and insistence on sameness. An important component of the definition which set it apart from previous definitions was its qualifiers. Intellectual functioning had to be taken into account when evaluating each child in regards to their social deficits, language delays, and ritualized behavior. Further, Rutter stressed that medical and neurological measures had to be used to help rule-out other disorders when diagnosing.

Asperger's syndrome. Though Kanner is often the individual credited with first identifying autism as a unique disorder, he was not the first identified the disorder. In 1944, Hans Asperger, a graduate student in Austria, published a thesis entitled "Autistic psychopathy in childhood." Asperger's thesis described a disorder that was remarkably similar to Kanner's description of autism. In his thesis, Asperger used the term autism to describe an atypical personality he observed in the four children. He derived the name autism from the withdrawal from relationships Bleuler described in individuals with schizophrenia (Asperger, 1944). Common symptoms detailed by Asperger included appropriate cognitive development, limitations in social relationships, impairments in nonverbal communication, odd social behaviors or special interests, emotionally isolated, and lack of affection (Asperger, 1944). Asperger's findings did not receive as much recognition as Kanner's because his thesis was written in German and was not translated into English until 1991 by Uta Frith. Once translated into English, the symptoms outlined by Asperger were incorporated into the *Diagnostic Statistical Manual- IV* (*DSM-IV*) as Asperger's syndrome (AS; APA, 1994).

As recognition of Asperger's work spread, researchers began investigating similarities and differences between the population he described, and the population described by Kanner. Asperger considered the two populations different as he believed his syndrome to be a stable personality trait and Kanner's to be a psychotic process (Wing, 1981). Though the disorders had differences, most agreed that the disorders were more alike than unalike, and the main difference was severity in impairments (Van Krevelen, 1971; Wing, 1981; Wolf & Barlow, 1979). Rutter (1978) suggested that the population described by Asperger's had a milder form of autism.

Wing (1981) discussed more specific differences between the two disorders noting that young children with autism appeared "aloof and indifferent," while children with AS were "passive or make inappropriate one-sided approaches." Additionally, children with autism, he pointed out, were "mute or have delayed and abnormal speech," whereas children with AS had a good vocabulary and well developed grammar. Children with AS were atypical in that their speech was inappropriate in social situations and they struggled with "understanding complex meaning." Additionally, children with AS often used gestures improperly when accompanying speech whereas children with autism generally did not use gestures when speaking. Stereotyped and repetitive rituals are the main symptom of autism yet are absent in children with AS. Children with AS commonly have restricted or obsessive fascinations about which they accumulate numerous facts. Children with autism had abnormal sensory sensitivities which children with AS do not present with. Wing (1981) noted that the abnormal sensory sensitivities in children with autism were typically only seen in those who also had cognitive impairments. Those who were older and had typical intellectual function did not normally display that feature. Wing purported that in both disorders nonverbal communication was impaired and that "monotonous or peculiar vocal intonation" was common.

Taking Wing's observations into account, Van Krevelen (1971) believed that these differences made the disorders two distinct disorders; however, others have argued that the differences were not dissimilar enough to justify separate disorders (Bosch, 1962; Wing, 1981). Both disorders are characterized by impairments in language, social interactions and imaginative activities (Wing, 1981). Onset and degree of severity may vary, but as Wing asserted "there are similarities in the eventual chronic defect states that either may produce." Research continues today on the relationship between the two disorders. Until recently, both disorders were considered to be ASDs. Now, the term Asperger's has been dropped from the *Diagnostic and Statistical Manual* (*DSM*). Changes in diagnostic criteria for ASDs have changed over time. The reason for elimination of the term AS, is discussed in more depth below.

Diagnosis

The *Diagnostic and Statistical Manual, First Edition* (*DSM-I*; American Psychiatric Association [APA], 1952) was published in 1952 by the APA. It was created with the purpose of helping physicians classify the many disorders they were observing as a result of the events of World War II (Shorter, 1997). *DSM-I* allowed for the more accurate and uniform diagnose of psychological disorders by creating a systematic system for classification. The first revision of the *DSM-I* occurred in 1968 with the release of the second edition by the APA (APA, 1968). In 1980 more significant changes were made with the release of the third edition, *Diagnostic and Statistical Manual, Third Edition* (*DSM-III*; APA, 1980). The third edition introduced included clearer diagnostic criteria, a multiaxial structure, and diagnostic descriptions without influence of specific etiological theories (Matson & Minshawi, 2007; Volkmar & Klin, 2005). Additionally, the *DSM-III* was the first to base diagnostic criteria on evidenced based empirical research (Volkmar & Klin, 2005)

ASDs were first recognized as distinct disorders from schizophrenia in *DSM-III*. As mentioned above, Rutter was a crucial figure in establishing the disorders as distinct. Rutter and Bartak (1971) identified differences between the two disorders, ASD and schizophrenia, on the basis of gender distribution, level of intellectual functioning, age of symptom onset, and family history of psychotic disorders. The new umbrella category, Pervasive Developmental Disorders (PDDs), was used to house Infantile Autism, Childhood Onset Pervasive Developmental Disorder (COPDD), and Atypical Pervasive Developmental Disorder (APDD). This new category encompassed disorders that were life-long, varying in degree of symptomatology, and multifactorial. New criteria for Infantile Autism included the presence of symptoms before 30 months of age (Rutter & Bartak, 1971); serious lack of social response, gross language deficit, bizarre features of speech, and absence of thought disorder (Waterhouse, 1992).

Modifications of the PDDs were made in the 1987 revised version of *DSM-III*. Frist, the name Infantile Autism was changed to Autistic Disorder (AD). Second, COPDD and APDD were retired and replaced with Pervasive Developmental Disorder- Not Otherwise Specified (PDD-NOS). Third, the criterion which required presentation of symptoms before the age of 30 month for AD was removed. Fourth, a more comprehensive developmental set of criteria for AD was included. Lastly, considerations were made about joint diagnosis of AD with schizophrenia, and differential diagnosis (Waterhouse, 1992). In addition to providing clearer and more in depth diagnostic criteria of PDDs, in the 1990's the *DSM-III-R*, was translated into over 20 languages, providing worldwide recognition and attention to ASDs (APA, 1987).

In 1994, the *Diagnostic and Statistical Manual, Fourth Edition* (*DSM-IV*; APA 1994*)* was published. The revision reflected advances made since the publication of *DSM-III-R*. The *DSM-IV* provided even further detail about disorders including course of disorder, family

patterns, presence of disorder, differential diagnosis, and demographics details. Additional refinements were made to the category of PDDs. The term ASD was introduced. This change was made to emphasize that these diagnoses comprised n a spectrum of disorders and differ in severity. Moreover, AS, Childhood Disintegrative Disorder, and Rett's Disorder were added to the category. Detailed criteria were outlined for each disorder with the exception of PDD-NOS (APA, 1994). The purpose of PDD-NOS was to capture those with ASD who did not fit a more specific diagnosis. The large number of diagnoses under the PDD umbrella was attributed to the many diverse clinical features and varying degrees of severity diagnosed (Szatmari, 1992). The *DSM-IV* was revised slightly in 2000 with the publication of the *DSM-IV-TR* (APA, 2000). *DSM-IV-TR* retained most of the information from the *DSM-IV*, however; it shifted to person centered language. For example, "autistic individuals" was changed to "individuals with autism."

To receive a diagnosis of ASD according to the criteria of *DSM-IV-TR*, a child had to meet a certain number of criteria in the social impairments domain, communication deficits domain, and the repetitive/restricted behaviors domain. The number of criteria a child met in each domain, along with age of onset, determined whether a child received a diagnosis of AD, AS or PDD-NOS. For example, to receive as diagnosis of AD, a minimum of six criteria had to be met, and abnormal function had to be present before the age of 3. In order to receive a diagnosis of AS, AD had to first be ruled out, and three criteria had to be met. Those who failed to meet criteria for AD or AS, but still warranted to diagnosis of ASD, would receive a diagnosis of PDD-NOS (Mandy, Charman, Gilmour, & Skuse, 2011).

Most recently, in May 2013, the *Diagnostic and Statistical Manual, Fifth Edition (DSM-5*; APA, 2013*)* was introduced. The *DSM-5* is organized according to developmental

chronology, that is, disorders that present early in life appear before disorders that present later in life. Within broad categories, disorders that are typically present in childhood are listed first. The category title PDD was retired and replaced with ASD. Major changes were made to the ASD category. Most notably, AS, PDD-NOS, Rett's Disorder, and Childhood Disintegrative Disorder were removed. This first change was made because of concerns raised about the ambiguity of the division between the ASD subcategories, and a lack of consistency with assignment of diagnoses. Additionally, concerns were raised with regard to an overlap between high functioning autism and AS, as well as an overlap between PDD-NOS and AS. Members of the *DSM-5* committee believed that these disorders were all part of the same underlying condition, only differing on level of severity and one single spectrum better exemplifies the symptoms, course, and treatment of the disorder, hence, the use of the term ASD rather than PDD. Therefore, in the *DSM-5*, only one term remains, ASD.

Criteria for diagnosis of an ASD were also modified in the *DSM-5*. The original triad of symptomatology was condensed into a dyad; social and communication deficits, and restricted and repetitive patterns of behavior, interests, or activities. In *DSM-5*, to receive a diagnosis of ASD, a child must meet all three criteria in the social communication and social interaction domain (e.g., nonverbal communication, peer relationships, and social reciprocity). In addition, a child must meet two of the four criteria in the restricted and repetitive patterns of behavior, interests, or activities domain (e.g., stereotyped or repetitive movements, insistence on sameness, restricted or fixated interests, hyper- or hyporeactivity to sensory input). In the new domains, the criteria and number of criteria required make it more difficult to receive an ASD diagnosis then it was in *DSM-IV-TR* (APA, 2013; McPartland, Reichow & Volkmar, 2012; Metilla et al., 2011). The rationale for collapsing the social and communication domains into one domain was that

deficits in communication are ultimately related to social deficits and are captured by a single set of symptoms. Rationale for modifying the number of symptoms required for the restricted and repetitive patterns of behavior, interests, or activities domain was to improve specificity (APA, 2013; Frazier et al., 2012; Wing, Gould & Gillberg, 2011). Another change in the *DSM-5* included a change in age of onset, from beginning prior to 3 years of age (*DSM-IV-TR)* to symptoms beginning "in early childhood" (APA, 2013).

Along with modifying existing criteria, *DSM-5* includes a table where severity of ASD can be ranked on one of three levels, representing level of support needed. A description is provided for each level with the type of support required regarding the two psychopathological domains; social communication, and restricted, repetitive behaviors. Level 1, "requiring support" captures children who are able to speak in full sentences and engage in communication, but are still unable to foster relationships. Without support, those in Level 1 will show noticeable impairments in social communication. In addition, these children are characterized as being inflexible, and struggle with organization and planning, which hinders independence.

Level 2, "requiring substantial support" captures children who have evident deficits in both verbal and nonverbal communication that persist even with support. Social interactions are limited and typically are restricted to special interests. Furthermore, inflexibility of behaviors, difficulty with change, and restricted and repetitive behaviors occur frequently enough to be obvious to observers. Lastly, those who have severe deficits in both verbal and nonverbal communication, restricted initiation, and response to social communication which cause immense impairment, fall under Level 3, "requiring very substantial support." Children classified as Level 3 experience significant distress with change, and their inflexibility and restricted/repetitive behaviors cause extreme impairments with overall functioning. Levels of

12

severity can be rated separately such that a child can be assigned different levels of support for social communication and restricted/repetitive behaviors.

Additionally, the fifth edition of the manual provides guidelines for clinicians on how to properly record diagnoses. If the ASD is associated with another disorder, or a medical or genetic condition, clinicians should write "autism spectrum disorder associated with" and list additional disorders or conditions. Following the primary diagnoses, level of severity should be recorded, whether or not there is an accompanying intellectual disability, and whether language impairment exists with clarification of the level of verbal functioning. The manual refers to this additional information as "specifiers." The goal of the specifiers is to aid in describing current symptomatology. It is noted that severity of the specifiers may vary over time as it is common that symptoms of ASD vary and manifest over time.

Collapsing the subtypes of PDD into a single category of ASD has been controversial and has elicited much dispute throughout the field. A main point of discontent has been the impact the change will have on prevalence of the disorder. The stricter criteria requirements will likely slow the apparent increase in prevalence of the disorder, and may cause many who initially met criteria to lose their designation. Recent studies have indicated that 30 to 45% of those currently with a diagnosis of ASD may no longer meet under the *DSM-5*. Individuals with a diagnosis of PDD-NOS are influenced the most by the new criteria requirements (Matson, Belva, Horovitz, & Bamburg, 2012; Matson, Kozlowski, Hattier, Horovitz, & Sipes, 2012; McPartland, Reichow, & Volkmar, 2012; Worley & Matson, 2012). Before the publication of *DSM-5*, concerns were raised that those who would no longer met criteria would lose important services and eligibility. To address these concerns, provisions were made with the publication of the *DSM-5* that those with existing services would be able to retain their services, despite no longer meeting criteria for

a diagnosis of ASD. Other impacts of the major change remain to be seen as the full transition to *DSM-5* is still underway.

Prevalence

The prevalence of ASD has increased rapidly in recent years (Center for Disease Control and Prevention [CDC], 2012). There is considerable disagreement with regard to the underlying cause of this precipitous increase. Originally rates of ASD were estimated to be 5 per 10,000 (Charman, 2008; Inglese & Elder, 2009a). In the 1980, estimated rates surged from 30 per 10,000 to 60 per 10,000 (Fombonne, 2003, 2005). To investigate the increase in prevalence, the CDC established the Autism and Developmental Disorders Monitoring Network (ADDM). Most recent data from ADDM estimate rates of ASD at 1 in 110 children (CDC, 2010).

Numerous explanations have been proposed to explicate the rise in prevalence. One explanation has attributed the increase in prevalence to a broader definition of ASD (Fombonne, 2003). The original definition of autism described by Kanner (1943) captured a narrower set of individuals than the current definition of ASD (Wing & Gould, 1979). Another explanation credited the increase to greater awareness of the disorder among the general public and professional (Fombonne, 2003; Matson & Kozlowski, 2011, Steyn & Le Couteur, 2003). Thus, clinicians are much more likely to give a diagnosis of ASD now than they would have 30 years ago (Fombonne, 2009). A third explanation suggests that a contributing factor is the recent recognition that ASD can be comorbid with other conditions (Wing & Potter, 2009). This acknowledgment contriubtes to higher rates because children cannot be denied diagnosis of ASD because they also are affected by another disorder. Collectively, these explanations do not support the claims that autism is now an "epidemic." Increased rates can be accredited to the combined effect of all these factors (Howlin, 2006).

Before the publication of the *DSM-5*, the most commonly occurring of the ASDs was PDD-NOS. PDD-NOS occurred at a rate of 37.1 per 10,000 people (Fombonne, 2009). AD had the next highest prevalence rate of 13 to 10 per 10,000, followed by AS having a prevalence rate of 9.5 per 10,000 children (Howlin, 2006). Childhood Disintegrative Disorder and Rett's Disorder occurred least frequently, estimated at of 0.6 per 10,000 people. Prevalence rates using the new *DSM-5* criteria are not yet available.

The ratio of males to females with an ASD is estimated to be approximately 4 to 1. In higher functioning individuals, those who held a diagnosis of AS before the new *DSM-5* criteria were instated, were estimated to be 10 to 1 ratio of males to females (Howlin, 2006). Some have suggested higher rates of ASD in Hispanics and children in higher socio-economic subgroups (SES;Dyches, Wilder, Sudweeks, Obiakor, & Algozzine, 2004; Liptak et al., 2008); however, little support has corroborated these findings (Bertoglio & Hendren, 2009; Nicholas, 2008). Therefore, most experts believe that ASD occurs at similar rates regardless of ethnicity or SES.

Core Features

Socialization. Socialization impairments are considered to be the main deficits in ASD (Rutter, 1968; Sevin, Knight, & Braud, 2007). In Kanner's (1943) paper, he described the children he observed as having an "inability to relate themselves in the ordinary way to people and situations from the beginning of life" (p. 242). Kanner's original observations have been corroborated by many researchers, and agreement is present in the field that socialization impairments are the central feature of ASD (Sevin et al., 2007; Volkmar, Cohen, Bregman, Hooks, & Stevenson, 1989; Walters, Barrett, & Feinstein, 1990). Deficits in socialization are highly impairing, as they inhibit children with ASD from interacting with others and engaging

with their environment (Travis & Sigman, 1998). A variety of socialization impairments are observed in children with ASD, however, some features are common throughout the population.

Distinguishing features of socialization deficits in children with ASD include lack of social and emotional reciprocity (Dawson & Murias, 2010), preference of playing alone (Eveloff, 1960; Rutter & Barak, 1971), failure to imitate others (Charman et al., 1997; Smith & Bryson, 1994), inappropriate eye contact, absence of socially appropriate facial expressions and gestures, and inability to share interests with others or relate to others' interests (APA, 2000). Many of these deficits can be observed early in life (Charman et al., 1997). One theoretical approach to autism is the "theory of mind." This theory attributes the inability to socialize to a lack of inter-subjectivity. Individuals with ASD in unable to appreciate another's perspective or put themselves in that individuals place. Consequently, the individual with ASD struggles in understanding feelings, beliefs, intentions and thoughts of others (Baron-Cohen, 1991). This theory, however, has not received overwhelming support. Researchers have shown that high functioning individuals with ASD are often able to accurately perform tasks that require theory of mind skills, but still have socialization impairments (Robertson et al., 1999; Volkmar & Pauls, 2003).

Communication. Deficits in communication skills are also considered a central feature of ASD (Noens & Van Berckelaer-Onnes, 2005; Rutter, 1968; Rutter & Bartak, 1971). Around 33-50% of children with ASD never gain functional speech (Noens & Van Berckelaer-Onnes, 2005). Those who do develop functional speech often do not use their speech to socialize with others or in a functional manner (Folstein, 1999). Consequently, impairments in communication are found to be the first cause of concern for parents (DeGiacomo & Fombonne, 1998; Howlin & Moore, 1997).

Abnormalities in speech, such as abnormal quality of voice, inflection and stress patterns, characterize the speech of children with ASD. Children with ASD also evince impairments in nonverbal communication. Examples of nonverbal communication include eye-to-eye gaze, pointing, and facial expressions (Noens & Van Berckelaer-Onnes, 2005). Compared to children with other developmental delays, children with autism use fewer nonverbal communication techniques (Stone, Ousley, Yoder, Hogan, & Hepburn, 1997). Communication impairments, along with impairments in socialization, prove to be an immense hindrance for children with ASD in the formation of relationships with others.

Along with deficits in expressive language, children with ASD also exhibit difficulties in receptive language (Luyster, Kadlec, Carter, & Tager-Flusberg, 2008; Noens & Van Berckelaer-Onnes, 2005). Children with ASD often fail to respond to their name or show preferences towards words such as "mommy" (Charman, Drew, Baird, & Baird, 2003). This behavior is thought to be a result of unawareness rather than ignorance (Eveloff, 1960).

In *DSM-5*, to meet criteria for the social communication and social interaction domain, which encompasses both core features of ASD, socialization and communication, a child must meet all three criteria in the domain. The first criterion, deficits in social-emotional reciprocity, describes an inability to participate in and initiate back and forth conversation, and a failure to share interests or emotions, and respond to interest or emotions of others. The second criterion, deficits in nonverbal communicative behaviors used for social interactions, describes abnormal eye contact and body language, and deficits in, or lack thereof the combined use of verbal and nonverbal communication. The last criterion, deficits in developing, maintaining, and understanding relationships, is characterized by difficulties in making friends, or total lack of

interest in peers, and problems adjusting behavior in accordance with changes in environment (APA, 2013).

Repetitive Behaviors and Restricted Interests. The final core feature of ASD is repetitive behaviors and restricted interests, also known as "stereotypy." Stereotypic behaviors include unusual movements (e.g., tapping, hand flapping, body rocking, pacing), and repeated and unusual vocalizations (Goldman et al., 2009; Lanovaz & Sladeczek, 2011). These behaviors are not usually harmful but may interfere in the development of social relationships and new skills (Lang et al., 2009; Matson et al., 2006; Morrison & Rosales-Ruis 1997; Wolery, Kirk, & Gast, 1985), and may delay normal development (Matson & Dempsey 2008a; Matson, Hamilton et al., 1997; Matson, Kieley et al., 1997). Considerable variation occurs among the presentation of these symptoms in children with ASD. Types of interests and preoccupations, and the intensity of the behaviors can differ immensely.

Rutter (1978) initially outlined these behaviors in five categories; abiding by strict rules of play lacking in imagination, strong attachment to specific objects or toys, odd preoccupations, obsessive rituals, and resistance to change. The first, abiding by strict rules of play lacking in imagination, described behaviors such as lining up toys rather than playing with them functionally or as they are intended to be played. The second, strong attachment to specific objects or toys is characterized by strong preference for only certain toys. In addition to a strong preference for certain objects, children with ASD sometimes exhibit their preferred object to people, as was observed by Kanner (Kanner, 1944, 1954). The third, odd preoccupations, described very specific preoccupations, such as spinning the wheels of a car rather than playing with the entire toy. The fourth, obsessive rituals (e.g., counting, tapping), often develops as a result of preoccupations. The final behavior, resistance to change, referred to an insistence on

sameness. If change occurs or something is disturbed, children with ASD often become very upset and distressed.

The behaviors outlined by Rutter are still considered valid but have been modified and refined over time. As of most recent, the *DSM-5* includes four subtypes for the restricted, repetitive patterns of behaviors, interest, or activities domain. A child must meet at least two of the following criteria in this category to be considered for diagnosis of ASD. The first, stereotyped or repetitive motor movements, is characterized by actions such as lining up toys, echolalia, and hand flapping. The second, insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior, describes rigid patterns of behavior, need for stable routine, and distress or frustration caused by small changes. The third, highly restricted, fixated interests that are abnormal in intensity or focus, considers preoccupations with objects, perseverative interests, and strong attachments to object. The fourth, hyper- or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment, characterizes abnormal sensory sensitivities to pain, temperature, sounds, light, smells or textures among other things. Behaviors may include excessive touch of objects or extreme fascination in movement (APA, 2013). The fourth criterion is the main change in the criteria of restricted, repetitive patterns of behaviors, interest or activities from *DSM-IV-TR* to *DSM-5*.

Assessment

Historically, the development of a standardized and uniform method of diagnosing ASD has been a struggle. Recently, significant improvement has been made with diagnostic measures, but conflict still exists over the best method of diagnosis. Current diagnostic approaches aim at differentiating individuals with ASD from individuals with other developmental disorder, ID,

and sensory deficits (Howlin, 2006). Additionally, researchers have evinced that accurate assessment should begin with a detailed account of developmental history, which gathers information on the development of communication, social skills, odd or abnormal behaviors or interests, and repetitive behaviors (Howlin, 2006).

Bernard Rimland developed the first diagnostic instruments to assess for ASD, termed the *Diagnostic Forms E-1* and *E-2* (Rimland, 1964, 1971). Form *E-1* was comprised of 67 questions for children up to age 7 (Rimland, 1964). After examining the completed forms, Rimland found that most changes in behavior were occurring around age 5. Thus, Rimland created a revised form, *Form E-2,* for assessment from birth to age 5. *Form E-2* is composed of 80 questions, which assessed social interactions, speech and motor abilities, illness development, intelligence, and reaction to sensory stimuli (Rimland, 1971). The forms were intended to distinguish ASD from other disorders (Rutter, 1978).

Short comings of many of the early questionnaires included an inability to assess higher functioning individuals, more emphasis on parental report rather than expert observation, single setting observations, and quality of behaviors (Rutter & Schopler, 1988). To avoids these short comings, a variety diagnostic measures are recommended to create the most accurate and reliable assessment (Matson & Goldin, 2014). Recommended diagnostic measures include the *Autism Behavior Checklist* (*ABC*), *Childhood Autism Rating Scale* (*CARS*), *Autism Diagnostic Interview – Revised* (*ADI-R*), *Autism Diagnostic Observation Schedule* (*ADOS*) and, the *Autism Spectrum Disorders-Diagnostic for Children* (*ASD-DC*).

The *ABC* (Krug, Arick, & Almond, 1980a, 1980b) was developed to aid in distinguishing ASD from other disorders characterized by abnormal behaviors. The *ABC* consists of 57 items that gather information on symptoms that can be observed; sensory, relating, body and object

use, language, social, and self-help skills (Krug et al., 1980b). The measure is informant rated

and items are in a yes/no format. Items are assigned a score from 1 to 4. Scores are then

summed to create a total score. Higher scores indicate greater impairment; scores below 53 are

in the unlikely autism range, scores within the range 53-67 are in the questionable autism range,

and scores of 67 or higher are in the probable autism range (Sevin, Knight, & Braud, 2007;

Volkmar et al., 1988). Originally inter-rater reliability, criterion validity, and concurrent validity

for the measure were reported to be high (Krug et al., 1980b). However, more recent research is

not consistent with these findings, suggesting that reliability and validity are lower (Sevin,

Matson, Coe, Fee, & Sevin, 1991; Volkmar et al., 1988). Thus, it has been suggested that the

ABC be used as a screening tool rather than a diagnostic instrument (Volkmar et al., 1988).

The *CARS* (Schopler, Reichler, DeVellis, & Daly, 1980) was developed to better assess

ASD in very young children, an ability that was lacking in other instruments existing at the time

(Schopler et al., 1980). The measure is comprised of 15 scales; impairment in human

relationships, imitation, inappropriate affect, bizarre use of body movement and persistence of

stereotypes, peculiarities in relating to nonhuman objects, resistance to environmental change,

peculiarities of visual responsiveness, peculiarities of auditory responsiveness, near receptor

responsiveness, anxiety reaction, verbal communication, nonverbal communication, activity

level, intellectual functioning, and general impressions. Items are rated on a scale of 1 to 4,

ranging from normal to severely abnormal. The *CARS* is more widely used than the *ABC*, and

has been shown to have high reliability with an inter-rater reliability of .71, an internal

consistency of .94, and a test-retest reliability of .88 (Schopler et al.,1980). Additional strengths

of the measure are that it is brief and easy to administer. The *CARS* has also been translated into

several languages. The *CARS,* however, was developed before the publication of the *DSM-IV-*

TR and *DSM-5*, therefore, it does not weigh social deficits as the most pervasive impairment of ASD (Lord & Risi, 1998). Despite this limitation, the measure is still well regarded (Inglese & Elder, 2009b).

The *ADI-R* (Lord, Rutter, & Couteur, 1994) is a semi-structured interview tool designed to aid in the diagnosis of ASD. The revised version of the *Autism Diagnostic Interview* (*ADI*) was created to fix weakness of the *ADI*. The *ADI-R* is designed to be used beyond solely research purposes, assess children as young as 3 years, and contains more autism-specific questions. The measure consists of five sections; opening questions, communication, social development and play, repetitive and restricted behaviors, and general behavior problems. Scoring of the *ADI-R* is based upon the *DSM-IV-TR* and *ICD-10* diagnostic criteria. Inter-rater reliability of the *ADI-R* is high, ranging from .62 to .89 (Lord, Rutter, & Couteur, 1994). Some weaknesses include a lengthy administration time, approximately 2 hours; findings are based solely on parent report, and extensive training necessary to administer the measure.

To correct for some of the weaknesses of the *ADI-R*, the *ADOS* (Lord et al., 2000) was developed to administer in conjunction with the *ADI-R*. The *ADOS* is an interactive tool used with children suspected of having ASD, and is comprised of domains that evaluate communication, social skills, and play. A limitation of the *ADOS* is that it over identifies those without or poor expressive language, thus the *Autism Diagnostic Observation Schedule – Generic* (*ADOS-G*) was developed to address the issue. The *ADOS-G* contains four modules; each module is designed to assess individuals with differing levels of expressive language. A module is chosen before administration depending on the child's expressive language capacities. Administration of the measure takes about 30 minutes and includes the same domains as the *ADOS*, but with the addition of a domain that evaluates imaginative object use. Items are rated

on a three-point scale from no evidence of abnormality related to autism to definite evidence. Scores are then calculated to conclude the presence of ASD. The measure has good inter-rater reliability, ranging from .65 to .78 (Lord et al., 2000). A short coming of the *ADOS-G* is its inability to address development over time. As the measure is, it can only provide a measurement of current functioning. Further, the *ADOS-G* is not designed to evaluate restricted and repetitive behaviors which are a core symptom of ASD, and like the *ADI-R*, extensive training is required for administration (Lord et al., 2000).

Another highly regarded measure for children, the *ASD-DC* (Matson, Gonzalez, Wilkins, & Rivet, 2008), was designed to differentiate between autism, AS, and PDD-NOS, as was previously defined by the *DSM-IV-TR*. The *ASD-DC* is an informant based measure and is comprised of 40 items. Each item is rated as either "0"=not a problem or impairment, "1"= mild problem or impairment or "2"= severe problem of impairment. All items are summed to produce a total score. Administration is intended to take 10 minutes. An adult version of the measure, *Autism Spectrum Disorders-Diagnostic for Adults* (*ASD-DA*), also exists. The *ASD-DC* has good inter-rater reliability and test-retest reliability of .67 and .77, respectively, and excellent internal consistency of .99 (Matson, Gonzalez, Wilkins, & Rivet, 2008). Favorable features of the measure are its short administration time, and its additional batteries designed to measure comorbid psychopathology and problems behaviors in both children and adolescents aged 3 to 16 years. One weakness is that it relies solely on informant reporting.

Early Detection and Intervention

The importance of early detection of ASD is undisputed. Early detection and intervention can result in better long-term outcomes (Corsello, 2005; Fenske, Zalenski, Krantz, & McClannahan, 1985; Manning-Courtney et al., 2003; Matson, 2007; Smith, 1999). ASD is

most commonly diagnosed around age 3 years, though some ASD symptomatology is present in infancy (Charman, 2008). In a recent study, parents of children with autism reported first becoming concerned with their child's development at 23.4 months old. Despite initial concerns, most parents did not seek a professional consultation until 4 month later. From the time the parents first noticed symptoms to the time their child was official diagnosed averaged 32 months (Chakrabarti, 2009). Delay in diagnosis may be a result of many factors such as lack of knowledge of typical child development, parental denial, and overlap of symptomatology with other disorders or other developmental delays which may be incorrectly credited with causing the presenting symptoms (DeGiacomo & Fombonne, 1998).

Identifying autism at an early age poses difficulties for the research community. The dearth of reliable data starting at infancy makes it necessary to rely on retrospective rather than prospective data from birth through the early months until diagnosis. Despite these difficulties, some attention has been paid to studying early detection (Elsabbagh & Johnson, 2007; Martinez-Pedraza & Carter, 2009). Benefits of using the available, albeit imperfect, early detection data include improved outcomes, decreased parental and family stress, earlier intervention and implementation of services and support, and earlier comprehensive evaluation to examine possible comorbid disorders (Dawson & Osterling, 1997; Matson, Wilkins, & Gonzalez, 2008). Additionally, the data suggest that children who received early intervention perform better on standardized intelligence tests (Ben-Itzchak & Zachor, 2007; Harris et al., 1991) and show better adaptive skills, social skills, and communication skills (Manning-Courtney et al., 2003; Martinez-Pedraza & Cater, 2009; Matson, 2007). Children who benefited the most from early intervention began receiving interventions between 24-48 months of age (Roger, 1996).

The most empirically supported treatment for ASD is Applied Behavioral Analysis (ABA; Campbell, 2003; Matson, 2009; Matson et al., 2011; Neidert, Dozier, Iwata, & Hafen, 2010). Through ABA, behaviors are modified using established learning principles (Baer, Wolf & Risley, 1968). ABA teaches new skills and shapes behavior through modeling, chaining, repetitive practice, and reinforcement (Leach, 2010; Martinez-Pedraza & Carter, 2009; Weis, Fiske, & Ferraioli, 2008).

Along with early detection and intervention, continual re-evaluation of children with ASD is imperative. Symptoms of ASD, as well as severity of symptoms, may change through development (Matson & Goldin, 2014). Continual evaluation makes it more likely that appropriate and effective treatment will be provided.

Etiology

Numerous theories have been proposed to explain the etiology of ASD. Originally, ASD was thought to be a result of bad parenting. It was believed that mothers who lacked warmth and provided insufficient emotional support caused autism in their children (Bettelheim, 1967). These mothers were referred to as "refrigerator mothers." This notion, however, is no longer thought to be valid. As the prevalence of ASD rose, alternate etiologies, such as environmental factors, have been favored.

Vaccines, particularly the Measles Mumps Rubella (MMR) vaccine, received most of the attention with regard to the increased prevalence of ASD largely due to the work of Andrew Wakefield et al. (1998). Wakefield suggested that autism was due to gastrointestinal disturbances caused by the MMR vaccine. Due to wide spread media attention of Wakefield's work, the study had a huge impact on parents (Charman, 2008). In reaction, many parents to choose not to vaccinate their children (Evans et al., 2001). In the UK, there was a 12% drop in

the administration of the MMR vaccine, and the occurrence of measles increased 24-fold over

the decade following the publication of Wakefield's article (Thomas, 2010). However,

Wakefield's findings were not replicated by other researcher groups. These studies found no

evidence for a causal link between the MMR vaccine and autism (Honda, Shimzu, & Rutter,

2005; Smeeth et al., 2004). In 2010, Wakefield's research was ruled fraudulent by UK General

Medical Council. At this time there is no scientific research supported the claim that vaccines

caused autism. Wakefield was found guilty of unethical manipulation of evidence and having

other undisclosed conflicts of interest (Burns, 2010). Though environmental factors continue to

be of interest in the field of ASD, the trend of research is shifting focus.

A more empirically supported cause for ASD is genetics. Currently, genetics are thought

to be the primary cause of ASD, with heritability estates of more than 90% (Freitag, 2007;

Zafeiriou, 2013). There is an increased risk of ASD in siblings of children with ASD (Cassel et

al., 2007). Additionally, family studies have shown higher rates of autism symptomatology in

first degree relatives (Freitag, 2007).

In some cases, brain anomalies have been identified in individuals with ASD and a causal

relationship has been postulated (Joshi et al., 2012). Techniques used to study this potential

relationship include functional magnetic imaging (fMRI), magnetic resonance spectroscopy

(MRS), and diffusion tensor imaging (DTI). In children with ASD there are some data to

suggest dysregulation in glutamatergic activity (Gruber et al., 2012; Joshi et al., 2012;

McDougle, 2002), and increased white matter volume causing disturbances in connectivity

(Minshew & Williams, 2007).

Parental age, prenatal environment, birth order, and in vitro fertilization, among many

other variables, have been proposed as possible causes of ASD. Most of these studies are very

recent and do not as yet have enough empirical support to draw firm conclusions about potential

relationships. What these studies suggest is that the etiology of ASD is multi-factorial and/or

multiple factors must be present to cause ASD. For this reason, and the significant increase in

prevalence, much current research is focused on identifying factors that may lead to the

development of the disorder.

SEVERITY OF SPECTRUM

As the name of the disorder insinuates, ASD is characterized by a varying degree of severity (Ben-Itzchak &Zachor, 2007). Degree of severity can differ in regard to overall presentation of the disorder, and between the core symptoms of the disorder (e.g., socialization/nonverbal communication, repetitive behaviors/restricted interest, and communication). Explanations for why children have more severe or milder presentations, also known as higher or lower functioning, is unknown. However, there is a plethora of research on the characteristics of those who are lower functioning versus who are higher functioning. Determining level of severity and whether it predicts deficits in the core symptoms of ASD is crucial in improving long-term outcomes because of its influence on time of initiating interventions and treatment regimens (Corsello, 2005; Fenske, Zalenski, Krantz, & McClannahan, 1985; Goldin, Matson, Beighley, & Jang, 2013; Hattier & Matson, 2012; Manning-Courtney et al., 2003; Matson, 2007; Smith, 1999). Determining level of severity is important for considering the type, frequency and intensity of intervention (Goldin, Matson, Beighley, & Jang, 2013; Liss et al., 2011; Matson & Boisjoli, 2009). Discussed below are the levels of severity frequently observed, and the overall implications of severity on symptom presentation.

Socialization

Deficits is social skills include failure to make eye contact, lack of joint attention, absence of pretend play, and disinterest in playing with peers or making friends (Howlin, 1986; Rutter, 1978, Volkmar, Carter, Grossman, & Klin, 1997). The degree of how impaired a child with ASD is in each of these areas varies; however, regardless of the level of functioning, all children with ASD possess socialization impairments (Volkmar, 1987). Lower functioning

children generally show a total lack of initiating or engaging in social relationships (APA, 2013). Typically these children show a complete disinterest in their peers, preferring to play alone (Howling, 1986). However, not all children with ASD are uninterested in developing social relationships. Higher functioning children with ASD may desire social interaction, but struggle because they lack an understanding of socially appropriate behaviors (Wilkins & Matson, 2007). Greater deficits in communication contribute to greater deficits in social skills, due to an inability to successfully communicate (Newborg, 2005). Without social skills, it makes creating and maintaining social relations with adults and peers extremely difficult (Matson, Fodstad, Hess, & Neal, 2009; Matson & Wilkins, 2007; Matson, Wilkins, & Gonzalez, 2008).

Engagement in repetitive behaviors also impacts socialization. Repetitive behaviors can cause children with ASD to standout from their typically developing peers and restricted interests can make it difficult for typically developing peers to relate to children with ASD. It has been reported that individuals who engage in stereotypies exhibit worse social skills than those without stereotypic behavior (Bishop et al., 2004; Matson, Smiroldo & Bamburg, 1998; Piven, Palmer, Jacobi, Childress, & Arndt, 1997). Consequently, level of impairment in both communication, and repetitive behaviors and restricted interests, can impact the ability of children with ASD to form relationships (Hattier & Matson, 2012). Additional research is needed to better understand how the core features of ASD interact as a result of level of impairment.

Communication

Considerable variation in level of impairment of communication skills is commonly observed in children with ASD (Charman, Drew, Baird, & Baird, 2003; Liselotte, Hedvall, Fernell, Gillberg, & Norrelgen, 2012; Wetherby et al., 2004). Researchers have suggested that

children who are lower functioning present with greater semantic impairments than children who are higher functioning (Charman et al., 2005; Luyster, Qui, Lopez, & Lord, 2007; Horovitz & Matson, 2010). However, some researcher have shown that the degree to which severity of ASD affects communication is small (Goldin, Matson, Beighley, & Jang, 2013; Hattier & Matson, 2012; Liselotte, Hedvall, Fernell, Gillberg, & Norrelgen, 2012). Rationale for this finding may rest upon the fact that communication impairments in a core feature of ASD and pervasive through the entire population (Rutter, 1968; Rutter & Bartak, 1971).

The influence of ASD on verbal communication compared to nonverbal communication has been assessed. The data suggest that severity of ASD better predicts nonverbal communication than verbal communication (Liselotte, Hedvall, Fernell, Gillberg, & Norrelgen, 2012; Luyster, Qui, Lopez, & Lord, 2007). This finding might be attributed to the skills required for nonverbal communication, such as imitation, social play, gestures, and make believe play. These actions make up some of the main problems characterizing children with ASD (Gillberg, Nordin, & Ehlers, 1996). Hence, nonverbal communication may be more strongly effected by severity of ASD than verbal communication.

Repetitive Behaviors and Restricted Interests

Severity of ASD symptoms is positively correlated with more stereotypic behaviors and greater levels of the behaviors (Bodfish et al., 2000; Matson & Dempsey, 2008a; Matson, Wilkins, Macken & Rojahn, 2008). Research indicates that children with severe ASD, compared to those with moderate or mild ASD, are more likely to engage in repeated and unusual body movements, repeated and unusual vocalizations, and unusual play with objects (Matson, Wilkins, Macken & Rojahn, 2008). Though the degree and frequency varies depending on severity, the

type of stereotypies not tend to vary (Matson & Dempsey, 2008b). There is a paucity of research

on why these differences occur.

The severity of repetitive behaviors and restricted interests influence the other core

features of ASD. More severe repetitive behaviors and restricted interests can make it harder for

children to communicate and form relationships with their peers. Repetitive behaviors can

appear odd to typically developing peers making them less likely to engage in play, and

restricted interests make it hard for typically developing peers to relate (Matson, Taras, Sevin,

Love & Fridley, 1990). More severe repetitive behaviors and restricted interests negatively

impact communication and social skills making the overall presentation of ASD appear more

severe.

Predictors of Severity

Currently, making early predictions of symptom severity and developmental course is

very difficult. The importance of acquiring this knowledge is beginning to gain recognition,

though at this time, few studies have examined factors that may contribute to severity (Kuhl,

2005; Wallace, Anderson, & Dubrow, 2008). Wallace, Anderson, and Dubrow (2008) explored

associations between obstetric and parental psychiatric variables that could impact the severity of

ASD symptoms. The authors investigated prenatal, perinatal, and neonatal characteristics in

relation to scores on the *ADI-R* and *ADOS*.   With regard to obstetric conditions, the authors

found that hypertension, preeclampsia, albuminuria and generalized edema were significantly

associated with increased severity of ASD symptoms. With regard to psychiatric variables,

parental depression was significantly related to increased severity of repetitive behaviors.

However, it could not be definitively determined whether parental depression caused more

severe repetitive behaviors, or if more severe repetitive behaviors caused parental depression.

Additionally, the authors found that parental anxiety was significantly associated with increased scores on the social/communication domain of the *ADOS*. Whether paternal anxiety caused or was a result of more severe social/communication impairments could likewise not be determined (Wallace, Anderson, & Dubrow, 2008). Despite these short comings, the authors suggested that there is some connection between these variables and level of severity. Therefore, it is important that research continues in this area to better understand the relationship of obstetric variables and ASD.

Another area that is beginning to receive attention is the interaction of symptoms in predicting severity. Sipes, Matson, and Horovitz (2011) investigated how poor motor skills affected social interaction. The authors found that poor gross and fine motor skills were significantly associated to greater social impairments. Motor impairments can make it harder for children to carry out social tasks, thus interfering with the development of social relationships (Sipes, Matson, & Horovitz). Severe impairments in motor skills could possibly be used as a predictor of level of severe deficits in social skills. Findings of this sort are extremely important in planning treatment approaches.

Research of this type is still in the early stages but has the potential to have a great impact on the field. Determining factors that may predict severity of ASD symptoms can improve methods and approaches of identifying those who would benefit from early risk screening for ASD. Additionally, increased knowledge in this area can better inform the development of treatment plans, specifically areas that should be targeted for intervention and the intensity and frequency of treatment based on level of severity.

PREMATURE BIRTH

Premature birth is defined as delivery that occurs at fewer than 37 weeks of gestation (Goldenberg, Culhane, Iams, & Romero, 2008). Factors thought to cause preterm labor include infection or inflammation, uteroplacental ischaemia, uterine overdistension, stress, immunologically mediated processes, maternal age, substance use, socioeconomic status, and level of education (Goldenberg et al., 2008; Romero et al., 2006). That being said, preterm labor is most likely caused by combination of many gene/pathway-environmental interactions (Green et al., 2005; Iams, 1998; Merikangas & Risch, 2003; Villar et al., 2004).

Premature birth affects about 1 in 8 births in the US every year (Green et al., 2005). Of all of those born premature in the US, 5% are born at fewer than 28 weeks (extreme prematurity), 15% are born at 28 to 31 weeks (severe prematurity), 20% are born at 32 to 33 weeks (moderate prematurity), and 60-70% are born at 34 to 36 weeks (near term; Goldenberg et al., 2008). Rates of those born between 36 and 33 weeks of gestation have risen over the previous two decades whereas those born 32 weeks or fewer have stayed relatively stable. These time trends have been attributed to an increased incidence of women 35 years and older having children and the use of infertility treatments. Many infertility treatments result in multiple births (Reynolds, Schieve, Martin, Jeng, & Macaluso, 2003; Russell, Petrini, Damus, Mattison, & Schwarz, 2003; Wright, Schieve, Reynolds, Jeng, & Kissin, 2004).

Premature birth generally occurs in one of three ways: 1) induced labor or caesarean section; 2) spontaneous preterm labor with intact membranes; 3) spontaneous preterm premature rupture of the membranes. Induced birth accounts for 30-35% of premature births, spontaneous preterm labor accounts for 40-45% of premature births, and preterm premature rupture of membranes results in 25-30% of premature births (Goldenberg et al., 2008).

Gestational Development

Age of viability, 22-26 weeks of gestation, is the first point when a baby can potentially survive, though assistance is required. Of premature births, the highest rate of survival occurs during the third trimester, 25-38 weeks of gestation (Berk, 2009). Fetal development, especially of the brain, continues throughout the third trimester. A fourfold increase in cortical volume occurs between 24 and 30 weeks of gestation as a result of neuronal and axonal growth, myelination, synaptogenesis, and focused apoptosis (Kerstjens, Winter, Bocca-Tjeertes, Bos, & Eijneveld, 2012). These developments correspond to a rapid increase of brain connectivity (Kerstjens et al., 2012; Volpe, 2009).

Increasing numbers of convolutions and grooves develop to expand the surface area of the cerebral cortex, which prior to 24 weeks, is predominantly smooth (Berk, 2009; Lan et al., 2000). Between 27 and 29 weeks of gestation, sulcus formation occurs primarily in the occipital lobe and around the central fissure. The occipital lobe is the visual processing center of the brain where the visual cortex is located, and the central fissure separates the parietal lobe from the frontal lobe, and the primary motor cortex from the primary somatosensory cortex (Smith & Kosslyn, 2007). By 36 weeks of gestation, sulcus formation is comparable to that of an adult (Lan et al., 2000).

Development of the subplate zone reaches its greatest maturity between 27 and 30 weeks of gestation. Most cortical synapses and "waiting" afferent axons are located in the subplate zone. Therefore, the subplate zone is crucial in facilitating cortical connects in the cerebral cortex. From 28 weeks of gestation onward, the extracellural matrix, which provides structural and biochemical support to nearby cells, slowly disappears from the sublpate zone giving rise to changes in the appearance of the cerebral cortex. Injury to subplate neurons can result in motor

and cognitive deficits. Hypoxia, deprivation of oxygen, is one way the subplate neurons may be injured (Radoš, Judaš, & Kostović, 2006).

As the brain is developing rapidly through the third trimester, premature birth can disrupt brain development (Kapellou, 2006). During typical development, the surface area of the brain develops faster than the volume of the brain. This phenomenon occurs most dramatically in late fetal development. Premature birth disrupts this pattern of growth and can result in developmental delays. Premature babies have been found to have less cortical surface and cortical gray matter compared to babies born full term (Ajayi-Obe, Saeed, Cowan, Rutherford, & Edwards, 2000; Inder, Warfield, Wang, Hüppi, & Volpe, 2005).

Kapellou and colleagues (2006) used MRI to examine the cortical surface area and cerebral volume of 119 infants born prematurely. Median gestational age of the participants was 27 weeks (range 22-29 weeks). Sixty-three of the participants underwent follow up neurodevelopmental assessment at about 2 years of age (range 19.5-28.9 months). In these participants, the relationship between gestational age at birth and neurodevelopmental outcomes was also examined. Results indicated that the pattern of brain development was sensitive to environmental effects. In late fetal development, the cortical area grows faster than the cortical volume; however, in infants born preterm, reduced cortical growth was observed. Kapellou and colleagues (2006) postulated that the reduced growth of cortical area may be a result of reduced connectivity rather than a reduced number of cortical neurons (Ajayi-Obe, Saeed, Cowan, Rutherford, & Edwards, 2000). Premature birth may disrupt association fibers and synaptic development which play a role in cortical growth, especially during later fetal development. Therefore, the fewer the weeks of gestation, the greater the disruption. Additionally, the rate of brain growth has been related to risk of development delays later. That is, the slower the rate of

surface area growth to volume, the more likely developmental delays will be present (Kapellou et al., 2006; MacKay, Smith, Dobbie, & Pell, 2010).

Prematurity and Developmental Delays

Premature birth is a risk factor for psychiatric disorders, ASD, and general developmental delays including cognitive deficits, social difficulties, and speech and language deficits (Able & Allin, 2005; Hack et al., 2009; Hwang, Weng, Cho, & Tsai, 2013; Indredavik et al., 2004; Kerstjens, Winter, Bocca-Tjeertes, Bos, & Eijneveld, 2012; MacKay, Smith, Dobbie, & Pell, 2010; Moore, Johnson, Hennessy, & Marlow, 2012; Veen et al., 1991). As gestational age decreases below 36 weeks, likelihood of developmental delays increase exponentially (Kerstjens, Winter, Bocca-Tjeertes, Bos, & Eijneveld, 2012).

Goldenberg and colleagues (2002) found that as much as half of all pediatric neurodevelopmental problems can be ascribed to premature birth. Birth before 32 weeks of gestation is correlated with greater incidence and severity of developmental problems (Green et al., 2005). Some neurodevelopmental impairments include cerebral palsy, ID, sensory impairments, and developmental lags (Saigal & Doyle, 2008). Additionally, minor neuromotor dysfunction and poor coordination are common in infants born prematurely along with deficits in other cognitive areas such as attention, visual processing, academic progress, and executive functioning (Anderson & Doyle, 2004; Goyen, Lui, & Woods, 1998; Hadders-Algra, 2002). Rates of attention deficits/hyperactivity disorder (ADHD) are significantly higher in those born before 28 weeks of gestation (Foulder-Hughes & Cooke, 2003; Saigal & Doyle, 2008). Aylward (2005) reported that preterm infants appear more shy and withdrawn, and exhibit more traits of social maladaptation.

In a study of 2,517 Dutch children 4 years of age, researchers found that the risk of developmental delays increased steadily as gestation age decreased from 25 to 36 weeks, assessed by abnormal scores on a validated developmental screening instrument. Areas of development affected included fine motor functioning, gross motor functioning, communication, problem-solving, and personal-social functioning. The researchers concluded their findings may be a result of the rapid growth of the brain during the third trimester of pregnancy (Kerstjens et al., 2012).

Matson, Hess, Sipes, and Horovitz (2010) found that children with developmental delays born prematurely experienced significant delays in attaining their development milestones. However, compared to children with Down syndrome or Global Developmental Delay, children born prematurely did not present with as great delays (Matson, Hess, Sipes, & Horovitz, 2010). The authors indicated that a limitation of this study was their inability to account for weeks of gestation. Combining all children born prematurely may have limited the ability to determine temporal relationships between length of gestation and development delays, as other researchers have reported (Hwang, Weng, Cho, & Tsai, 2013). Future research in this area would benefit from examining those who were born "more" or "less" premature, separately (Matson et al., 2010).

Prematurity and ASD

Though ASD has a well-established strong genetic component, some research has indicated that not all cases may be a result of genetic factors (Abel et al., 2013; State & Levitt, 2011). This notion has lead researchers to begin to explore more closely rates fetal development as a potential contributing factor to the development of ASD (Abel et al., 2013). One focus of this research has been on premature birth; indicating premature birth as a significant risk factor

for ASD (Abel et al., 2013; Dodds et al., 2011; Hack et al., 2009; Hultman, Sparén, & Cnattingius, 2002; Hwang, Weng, Cho, & Tsai, 2013; Indredavik et al., 2004; Larsson et al., 2005). In a study of 219 extremely preterm children (<26 weeks gestation), researchers found an 8% prevalence of ASD at 11 years of age, compared to a 1% prevalence rate in the general population (Johnson et al., 2010). Furthermore, two studies of hundreds of preterm children showed that the risk of ASD in very preterm children was about twice that of their full term peers (Buchmayer et al., 2009; Schendel & Bhasin, 2008). Another study that examined children born early preterm (<28 weeks of gestation), later preterm (28-36 weeks of gestation), and full term (> 37 weeks of gestation), and reported similar findings. They suggested that the prevalence of ASD was 2-4 times higher in preterm children than in children born full term (Hwang, Weng, Cho, & Tsai, 2013). Lastly, a study of children in India found that premature birth of fewer than 37 weeks was significantly related to ASD with odds ratio of 2.11 (Mamidala et al., 2013). Taken together, these data suggest a strong association between premature birth and likelihood of developing of ASD. This research adds to evidence emerging that the pathophysiology of ASD begins prenatally (Movsas & Paneth, 2012).

A study by Abel et al (2013) looked at ID in relation to prematurity and risk of ASD. The authors found that premature birth was a strong factor for development of ASD, especially with comorbid ID (Abel et al., 2013). Children with ASD and comorbid ID tended to be overall lower functioning. Thus, Abel et al (2013) findings suggest that those born prematurely with ASD are at higher risk of developing more severe symptomology because of the increased likelihood of having comorbid ID (Baird et al., 2006; Klin et al., 2007; Sparrow, Balla, & Cicchetti, 1984). However more evidence is needed to support this hypothesis.

In a study by Movsas and Paneth (2012), the mothers of participants with ASD (range 4-21 years of age) born preterm, full term, or post term were asked to report on their child's development. The researchers reported that infants who were born at <34 week of gestation tended to have overall more severe symptoms in social cognition, social communication, and autistic mannerisms than infants born later in gestation. In the participants born at 34-36 weeks of gestation, differences in autism symptomatology compared to those born full term were negligible. The researchers purported that their findings may reflect greater attention paid to development by mothers of premature children. The findings were based on maternal reports which required mothers to recall the development of their child 4-21 years after their birth (Movsas & Paneth, 2012). Despite the limitations, these findings highlight a relationship between level of severity and premature birth. Further investigation of this relationship is warranted as it may provide a basis on which to institute therapy at an earlier age than now occurs that in term could potentially result in a better long term prognosis for the children.

PURPOSE

Though a significant amount of research has been published examining ASD symptomology in infants and toddlers, little is understood on why differences in symptom severity exist across the population (Ben-Itzchak &Zachor, 2007; Goldman et al., 2009; Noens & Van Berckelaer-Onnes, 2005; Sevin, Knight, & Braud, 2007). Acquiring knowledge about factors that may contribute to the severity of ASD symptoms is critical. Such factors can inform early risk assessments, evaluations, and treatment, consequently improving the quality of life for individuals with ASD and their families (Corsello, 2005; Dawson & Osterling, 1997; Elsabbagh & Johnson, 2007; Fenske, Zalenski, Krantz, & McClannahan, 1985; Manning-Courtney et al., 2003; Martinez-Pedraza & Carter, 2009; Matson, 2007; Matson, Wilkins, & Gonzalez, 2008; Smith, 1999).

Premature birth has been suggested as a possible risk factor for ASD (Abel et al., 2013; Dodds et al., 2011; Hack et al., 2009; Hultman, Sparén, & Cnattingius, 2002; Hwang, Weng, Cho, & Tsai, 2013; Indredavik et al., 2004; Larsson et al., 2005). The relationship between premature birth and ASD severity, however, has not been well documented. As premature birth is a significant risk factor for many developmental delays and psychiatric disorders, investigating the developmental outcomes of those with ASD born prematurely is imperative and may provide some insight into why such variation in symptom severity exists (Able & Allin, 2005; Hack et al., 2009; Hwang, Weng, Cho, & Tsai, 2013; Indredavik et al., 2004; Kerstjens et al., 2012; MacKay, Smith, Dobbie, & Pell, 2010; Moore, Johnson, Hennessy, & Marlow, 2012; Veen et al., 1991).

The current paper serves to extend knowledge on incidence of premature birth and its association with severity of ASD in infants and toddlers. To assess symptom severity, the

BISCUIT-Part 1 was administered to the parents/caregivers of infants and toddlers between the ages of 17 and 37 months. Premature birth and weeks of gestation were determined from parent/caregiver report on the demographics section of the *BISCUIT*. The purpose of this study was to investigate rate of premature birth compared to atypically developing peers, and the ASD symptom profile of infants and toddlers born premature versus infants and toddlers born full term. This research is important for enhancing our knowledge of the epidemiology of premature birth in this population and the effects of premature birth on ASD symptomology. Findings from this study may aid in enhancing treatment planning that could result in a better prognosis for individuals born prematurely with ASD. Additionally, the findings may provide parents and caregivers with a better idea of the course of development their child may experience.

Hypothesis 1

It was first hypothesized that premature birth would not be more prevalent in infants and toddlers with ASD compared to those with atypical development. This was based on literature indicating increased risk of both ASD and atypical development in those born prematurely (Abel et al., 2013; Johnson et al., 2010; Kerstjens et al., 2012; Wong, Huertas-Ceballos, Cowan, & Modi, 2014). Additionally, it was hypothesized that no difference in average weeks of gestation would be found between participant with ASD and participants with atypical development born prematurely.

Hypothesis 2

Second, after reviewing existing literature on premature birth and ASD symptom presentation, it was predicted that infants and toddlers born prematurely would exhibit more severe ASD symptomatology than infants and toddlers born full term. This predication is based on findings that children born full term present with less ASD symptomatology (Movsas &

41

Paneth, 2012). Additionally, because more general developmental delays are common in those born prematurely, it is hypothesized that additional developmental delays might exacerbate symptoms of ASD (Kerstjens, De Winter, Bocca-Tjeertes, Bos, & Reijneveld, 2012).

Participants

The sample consists of 1655 infants and toddlers ranging from 17 to 37 months of age (*M* = 25.78, *SD* = 4.84). Participants were recruited through the EarlySteps program funded by the State of Louisiana. EarlySteps is Louisiana's Early Intervention System housed under the Individuals with Disabilities Education Act, Part C. Infants and toddlers from birth to 36 months of age qualify for services if they have developmental delays or a medical condition likely to result in a developmental delay. Participants with ASD in this study had a diagnosis of ASD according to the *DSM-5* criteria or were classified as atypically developing. Diagnoses of ASD were made by a licensed doctoral level clinical psychologist with over 30 years of experience. During the provision of diagnoses, the psychologist was blind to *BISCUIT* scores. The diagnosis relied upon scores attained on the *Modified Checklist for Autism in Toddlers* (*M-CHAT;* Robins, Fein, Barton, & Green, 2001), *DSM-5* criteria algorithm for ASD, and the developmental profiles from the *Battelle Developmental Inventory, Second Edition* (*BDI-2*; Alfonso, Rentz, & Suehee, 2010; Matson, Boisjoli, Hess, & Wilkins, 2010). Several (n=203) participants were also given a second diagnosis serving to establish inter-rater reliability by another doctoral level psychologist with a percent agreement of 98.97 (Matson, Boisjoli, Hess, & Wilkins, 2010). Atypical development was determined by developmental quotient score on the *BDI-2* and total score on the *BISCUIT-Part 1*. Participants were considered as developing atypically if their *BDI-2* developmental quotient score fell below 70, signifying significant developmental delays and if their total *BISCUIT-Part 1* score fell below 17, signifying little to no ASD symptomatology.

Participants within the ASD group ranged from 17-37 months of age (*M* = 26.21; *SD* = 4.58). With regard to gender and race/ethnicity, 76.1% of the participants were male and 23.9%

were female, of which 48.5% were Caucasian, 41.7% were African American, 2.6% were Hispanic, and 7.2 % were of other or unspecified ethnicity. In regards to the atypically developing group, participants ranged from 17-37 months of age ($M = 25.25$; $SD = 5.1$). Within this group, 70.3% were male and 29.7% were female, of which 45.4% were Caucasian, 44.5% were African American, 4.3% were Hispanic, and 5.8 % were of other or unspecified ethnicity.

Preliminary analysis was conducted to ensure that the groups did not differ significantly on demographic variables (i.e., age, gender or ethnicity; Matson, Rivet, Fodstad, Dempsey & Boisjoli, 2009). The results of a one-way between-subjects analysis of variance (ANOVA) revealed no significant differences between groups in terms of age. Chi-square analyses indicated that the groups did not differ significantly with regard to gender or race/ethnicity. Demographic information is presented within Table 1.

Table 1
Demographic Information (N = 1655)

Demographic Characteristics	**Diagnostic Group**	
	ASD (*n* = 738)	Atypical (*n* = 916)
Age (in months)		
Mean (SD)	26.21 (4.58)	25.25 (5.1)
Range	17-36	17-36
Gender %		
Male	76.1%	70.3%
Female	23.9%	29.7%
Race/Ethnicity %		
Caucasian	48.5%	45.4%
African-American	41.7%	44.5%
Hispanic	2.6%	4.3%
Other/Unspecified	7.2%	5.8%

Measures

       Baby and Infant Screen for Children with aUtIsm Traits-Part 1. The *Baby and Infant Screen for Children with aUtIsm Traits* (*BISCUIT*) is a measure designed to aid in early detection of ASD in children 17 to 37 months of age (Matson, Boisjoli, & Wilkins, 2007). The measure is comprised of three parts assessing ASD symptomatology, comorbid psychopathology, and challenging behaviors. Part 1 of the *BISCUIT* contains 62 items rated by the parent or caregiver of the child. Informants are instructed to rate their child in comparison to same-aged peers on a Likert scale ranging from 0 to 2. A score of 0 corresponds to "not different; no impairment," 1 corresponds to "somewhat different; mild impairment," and 2 corresponds to "very different; severe impairment" from same-aged peers. Factor analysis of the items revealed three distinct factors: socialization/nonverbal communication, repetitive behaviors/restricted interest, and communication (the full list of items can be found in the Appendix; Matson, Boisjoli, Hess, & Wilkins, 2010). Total scores below 17 are classified as "no autism/atypical development". Total scores between 18 and 34 are classified as "possible ASD/PDD-NOS" and total scores of 35 or higher are classified as "probable ASD/PDD-NOS" (Horovitz & Matson, 2014; Matson et al., 2009a). All factors will be examined in this study, in addition to total score as a measure of ASD symptom severity. Additionally, the *BISCUIT* includes a section to collect data for age, race, gender, birth weight, diagnoses, and current medication.

       The *BISCUIT-Part 1* has an excellent internal reliability ($r = .97$) and has been found to have an overall correct classification rate of .89 (Matson et al., 2009b). Further, the measure has been shown to have good convergent validity with the *M-CHAT* and the Personal-Social domain of the *BDI-2* (Matson, Wilkins, & Fodstad, 2011). Internal consistency of all factors was also

found to be excellent. The socialization/nonverbal communication factor has an internal consistency of $\alpha = 0.93$. This factor is consists of 24 items. Examples of items include "ability to make and keep friends," "development of social relationships," "plays appropriately with others," and "motivated to please others." Measures of repetitive behaviors/restricted interest factor has an internal consistency of $\alpha = 0.90$ and is made up of 23 items. Examples of items include "abnormal fascination with the movement of spinning objects," "interest in a highly restricted set of activities," "becomes upset if there is a change in routine," and "engages in repetitive motor movements for no reason." Finally, the communication factor has an internal consistency of $\alpha = 0.87$ and includes seven items. Examples of items include "use of language to communicate," "communication skills," "language development," and "communicates effectively" (the full list of all factor items can be found in the Appendix; (Matson, Boisjoli, Hess, & Wilkins, 2010).

Procedure

Measures were administered to parents or caregivers by an individual whose licensure or certification met the provider requirements of the EarlySteps program. Providers come from a variety of disciplines, including psychology, speech-language pathology, social work, occupational therapy, and physical therapy (Matson et al., 2009a). Extensive training is given to all providers prior to administering the *BISCUIT-Part 1* to participants to ensure standardized administration. Additionally, all providers receive education on ASDs and training on other screening measures used. The full EarlySteps screening process includes the administration of the *BISCUIT-Part 1* and the *BDI-2* among other measures; assessment also includes direct observation. Information on birth was gathered as part of the demographic information collected at the beginning of the *BISCUIT*. If premature birth was indicated, then weeks of gestation was

recorded. Parents and legal guardians of the participants serve as informants on all measures and

provided informed consent for participation. This present study was approved by the Louisiana

State University Institutional Review Board and Louisiana's Office for Citizens with

Developmental Disabilities.

Statistical Procedures

Appropriate group sizes for the study were determined *a priori* by using GPOWER , a

power analysis computer program (Erdfelder, Faul, & Buchner, 1996). Settings used for

GPOWER were those which are well established and accepted within the research field; a power

of .80, alpha of .05 and effect size (f 2) of .02 (Cohen, 2008; Hinkle, Wiersma & Jurs, 2003).

The power analysis determined group sizes of 310 participants, which the current sample

exceeded.

To address the first research question, a chi-square analysis was conducted to compare

that rate of reported premature birth between diagnostic groups (i.e., ASD and atypically

developing). Participants were considered premature if they gestated for fewer than 37 weeks,

which is considered the entire length of a normal pregnancy (Hwang, Weng, Cho, & Tsai, 2013;

Karlber & Albertsson-Wikland, 1995). Next, an independent-samples *t*-test was conducted on

just those reported to be born prematurely to determine whether the two groups differed

significantly with respect to number of weeks of gestation. Group membership served as the

independent variable (IV) and weeks of gestation served as the dependent variable (DV).

Finally, a second independent samples *t*-test was conducted exclusively on participants

with ASD. Participants in this analysis were divided into two groups; those born full term (FT; *n*

= 884) and those born prematurely (PRE; 45). To address the unequal samples sizes, the select

random cases function in SPSS was used. In situations with unequal samples sizes, Field (2009)

47

suggests generating similar sample sizes to ensure robustness of statistical tests. Therefore, a

random sample of 60 participants in the FT group was selected by utilizing the select random

cases function in SPSS. Two additional independent random samples of 60 participants from the

FT group were run for comparison to add confidence in the statistical findings. Group

membership served as the IV and total scores on the *BISCUIT-Part 1* served as the DV, as a

measure of ASD severity with higher scores reflecting greater impairments. Preliminary analysis

was again conducted to ensure the groups did not differ significantly for demographic variables.

All statistical analyses will be carried out using SPSS 21.0.

The first sample examined consisted of 916 participants with ASD and 739 atypically developing participants. A chi-square test for association was conducted between diagnosis and likelihood of being born premature. Result indicated that there was a significant association between diagnosis and premature birth, X^2 (1) = 9.34, $p < .002$. This seems to represent the fact that based on the odds ratio, the odds of a child being born premature was 1.83 times higher if they had a diagnosis of atypical development. More specifically, of the 739 atypically developing participants, 64 (8.7%) were born prematurely; whereas, of the 916 participants with ASD, 45 (4.9%) were born prematurely (Table 2).

Table 2
Rates of Premature Birth

	Premature	**Full Term**	**Total**
	$n = 109$	**$n = 1546$**	**N = 1655**
ASD	45	871	739
Atypical	64	675	916

Note: SD = Standard Deviation, ASD = Autism Spectrum Disorder

Expanding on the pervious analysis, an independent-samples t-test was run to determine if there were differences in average number of weeks of gestation between premature participants in the ASD group and the atypically developing group. Prior to analysis, the data was screened for missing information and violation of assumptions. There were no outliers in the data, as assessed by inspection of a boxplot for values greater than 1.5 box-lengths from the edge of the box. *BISCUIT-Part 1* score was normally distributed, as assessed by Shapiro-Wilk's test ($p > .05$), and there was homogeneity of variances, as assessed by Levene's test for equality of variances ($p = .491$). As shown in Figure 1, on average, no significant difference was found between the ASD group ($M = 30.62$, $SD = 3.99$) and the atypical group ($M = 29.14$, $SD = 4.29$) in regard to number of weeks of gestation $t(1) = 1.83$, $p > .05$ (Table 3).

Table 3

Weeks of Gestation Means for ASD and Atypically Developing Participants

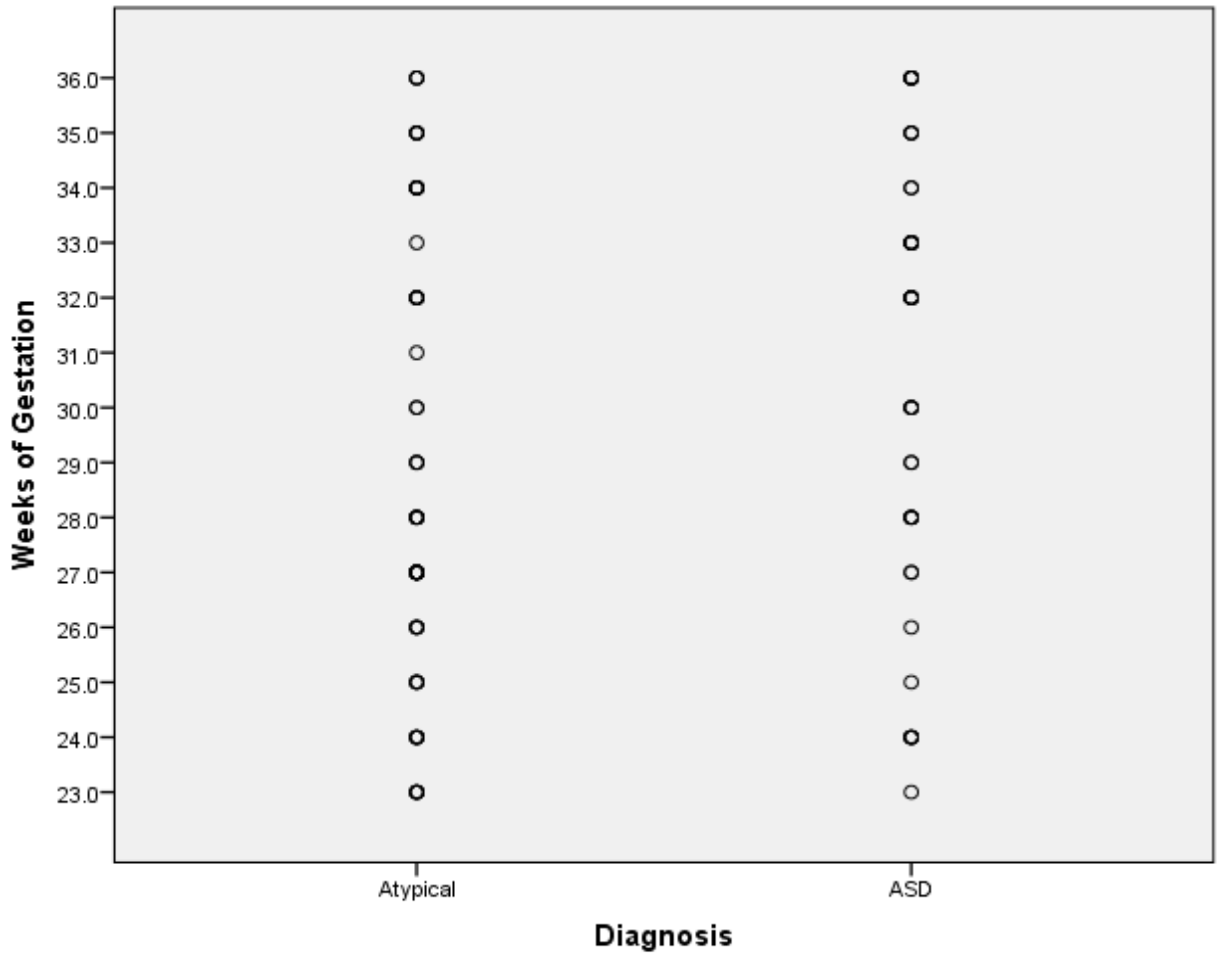|	Diagnosis		*t*	*df*
	ASD M (SD)	Atypical M (SD)		
Weeks of Gestation	30.62 (3.99)	29.14 (4.29)	1.83	1

Figure 1. Weeks of Gestation Means for ASD and Atypically Developing Participants

There were 45 participants in the PRE group and 60 participants in the FT group. As previously mentioned, the 60 participants in the FT group were randomly selected from a larger sample of 884 participants. An independent samples *t*-test was run to determine if there was a

difference in ASD symptom severity between those in the PRE group and the FT group. Prior to

analysis, the data was screened for missing information and violation of assumptions. There

were no outliers in the data, as assessed by inspection of a boxplot. Engagement scores for each

level of gender were normally distributed, as assessed by Shapiro-Wilk's test ($p > .05$), and there

was homogeneity of variances, as assessed by Levene's test for equality of variances ($p = .639$).

The results of the independent samples t-test established that the total *BISCUIT* score was

higher for the PRE group ($M = 55.20$, $SD = 22.98$) than the FT group ($M = 53.62$, $SD = 21.71$);

however a statistically significant difference was not found in mean *BISCUIT* score between the

PRE group and the FT group, $M = 1.58$, 95%, CI[-7.12, 10.29], $t(103) = .361$, $p > .05$, $d = .102$

(Table 4). Figure 2 illustrates the insignificant findings. The analysis was repeated two

additional times using novel random samples from the FT group; all three samples converged on

the same conclusion.

Table 4
BISCUIT Part-1 Means for Premature and Full Term Participants

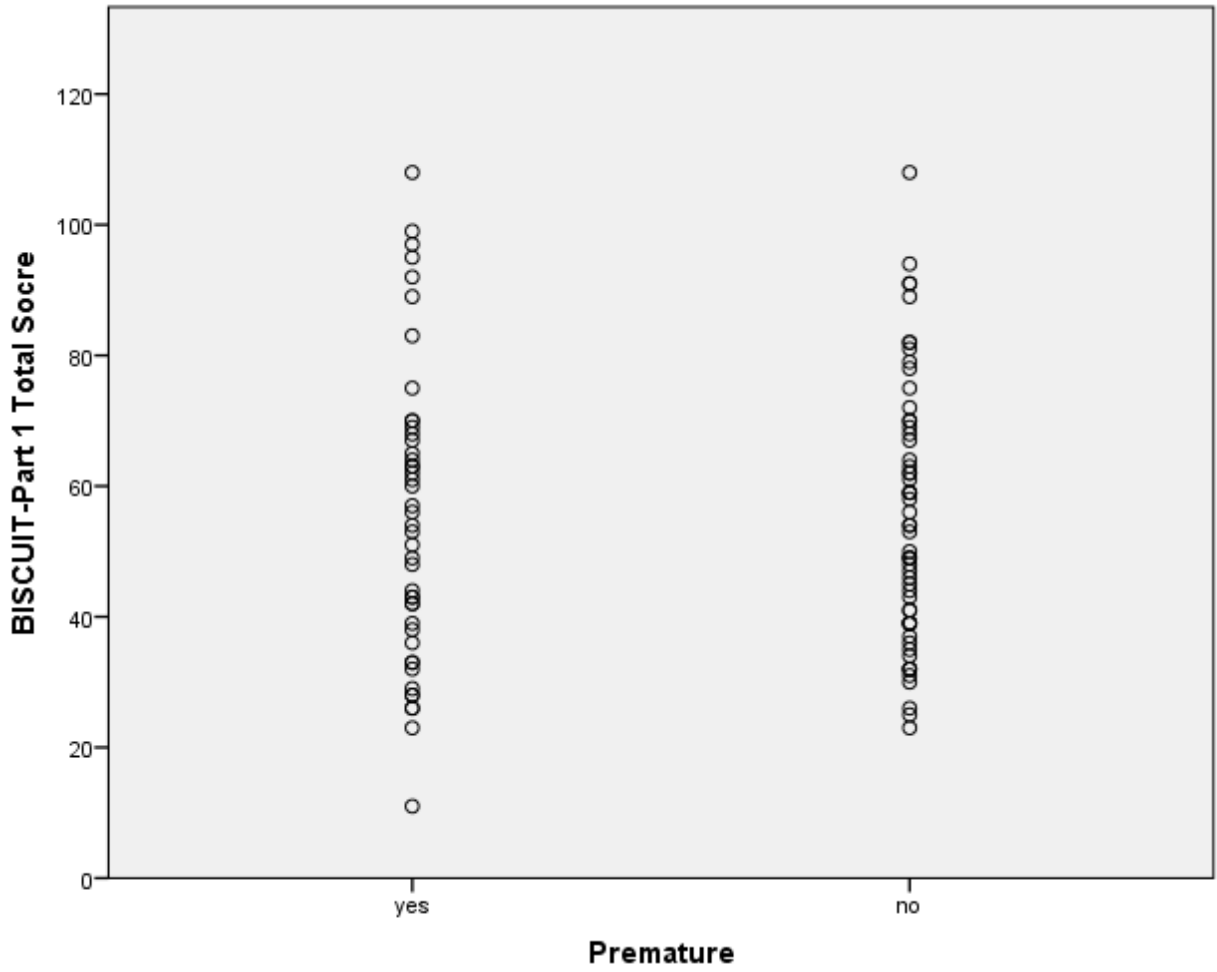|	Group		*t*	*df*
	PRE **M (SD)**	**FT** **M (SD)**		
BISCUIT Part-1 Total Score	55.2 (22.98)	53.62 (21.71)	.361	103

Figure 2. Overall Level of Severity Means for PRE and FT participants

DISCUSSION

Premature birth is a risk factor for cognitive deficits, ASD, developmental delays, and various psychopathologies (Able & Allin, 2005; Hack et al., 2009; Hwang, Weng, Cho, & Tsai, 2013; Indredavik et al., 2004; Kerstjens et al., 2012; MacKay, Smith, Dobbie, & Pell, 2010; Moore, Johnson, Hennessy, & Marlow, 2012; Veen et al., 1991). Researchers have repeatedly reported that fewer weeks of gestation disrupts brain development, likely contributing to abnormalities in brain functioning (Ajayi-Obe, Saeed, Cowan, Rutherford, & Edwards, 2000; Kapellou et al., 2006). As toddlers, those born prematurely tend to need more support services compared to peers born full term once they reach school age (Foulder-Hughes & Cooke, 2003; MacKay, Smith, Dobbie, & Pell, 2010). Although the effect of premature birth on development has received considerable attention, few studies have examined outcome differences in those with developmental disorders born prematurely.

Given that researchers overwhelmingly agree that early identification of ASD and atypical development can occur by 3 years of age (Baghdadli, Picot, Pascal, Pry, & Aussillou, 2003; Charman, 2008), and that early intervention can result in improved long-term outcomes (Corsello, 2005; Fenske, Zalenski, Krantz, & McClannahan, 1985; Manning-Courtney et al., 2003; Matson, 2007; Smith, 1999), differences in the impact of premature birth on development disorders is crucial. Types of screening measures used, early intervention procedures administered, and long-term care programs are disorder specific. ASD specifically differs from other developmental disorders in how it presents and manifests over the life-span. Thus, the current study sought to examine the incidence of premature birth and average weeks of gestation in those with ASD compared to those with atypical development. Further, the effect of

premature birth on severity of ASD was examined in relation to individuals with ASD born full term.

Hypothesis 1

Results from the current study indicated that premature birth occurred significantly more in those with atypical development than those with ASD. A participant with atypical development was 1.83 times more likely to be born prematurely. Atypical development was characterized by significant developmental delays in a variety of domains (e.g., personal/social, adaptive, motor, communication, and cognitive development) and low rates of ASD symptomatology. The diversity of the developmental delays characterizing the atypical group may add to this finding. Greater incidence of ID, sensory impairments, minor neuromotor dysfunction, poor coordination, attention, visual processing impairments, poor academic progress, executive functioning impairments, and developmental lags are common in those born prematurely (Anderson & Doyle, 2004; Goyen, Lui, & Woods, 1998; Hadders-Algra, 2002; Saigal & Doyle, 2008). While the atypical group captures many of these developmental disorders, ASD is a singular disorder. Therefore, the diverse make-up of the atypical group may explain the increased rate of prematurity, as deficits and impairments due to premature birth can present in a variety of areas.

Focusing on the atypical group by dividing it into smaller categories such as general developmental delays, language disorders, motor coordination disorders would be beneficial in expanding the recent findings. Dividing the atypical group into specific disorders would provide additional information on the rates of premature birth in each disorder and how they compare to rates in ASD. The findings may reveal whether premature birth is a greater risk factor for one type of disorder over another. An additional step would be to look into average weeks of

gestation of each specific disorder to determine if there is any trend in weeks of gestation and observed impairments and deficits.

In our study, despite differences in the incidence of premature birth, no difference was found between the groups in regard to average weeks of gestation. Interestingly, Goldenberg and colleagues (2008) found that in the United States, 60-70% of babies delivered prematurely are born between 34-36 weeks. In the current study, the largest percentage of participants, 36.7% (n = 40, range 27-23), were born at 27 weeks or fewer. Given the general consensus among researchers that fewer weeks of gestation increases the likelihood of developmental disabilities (Goldenberg, 2002; Green et al., 2005; Kapellou et al., 2006), this finding is revealing.

For comparison purposes, in the current sample, the percentages of participants born in each category of premature birth is as follows; Extreme prematurity (fewer than 28 weeks of gestation, n = 40) 36.7%, severe prematurity (28-31 weeks, n = 24) 22%, moderate prematurity (32-33 weeks, n = 20) 18.3%, near term (34-36 weeks, n = 25) 22.9%. These percentages differ from Goldenberg and colleagues' sample as follows; 5% born at extreme prematurity, 15% born at severe prematurity, 20% born at moderate prematurity, and 60-70% born at near term (Goldenberg, Culhane, Iams, & Romero, 2008). The most striking differences occur between the extremely prematurity group and the near term group. The greatest percentage of participants in the present study where born extremely premature whereas most individuals in the general population were born near term. This finding may be attributed to the relationship between fewer weeks of gestation and increased risk of atypical development (Hwang, Weng, Cho, & Tsai, 2013; Kapellou et al., 2006; Kerstjens, Winter, Bocca-Tjeertes, Bos, & Eijneveld, 2012). As our sample only examines those with ASD and atypical development, based on the literature it should be expected that the average weeks of gestation be lower. Therefore, this finding

supports prior work suggesting that fewer weeks of gestation results in greater risk of ASD, and a variety of developmental delays (Anderson & Doyle, 2004; Goyen, Lui, & Woods, 1998; Hadders-Algra, 2002; Matson, Hess, Sipes, & Horovitz, 2010; Saigal & Doyle, 2008).

Disruption in neurodevelopment might also provide an explanation for these results. Fewer weeks of gestation are associated with a greater degree of brain disruption (Kapellou et al., 2006). Fewer weeks of gestation is associated with an increase in need for special education services for children born preterm (Foulder-Hughes & Cooke, 2003; Green et al., 2005; MacKay, Smith, Dobbie, & Pell, 2010). As our study sample is made up of participants enrolled in EarlySteps, these participants are already seeking services due to developmental concerns. The data support the hypothesis that greater brain disruption is linked to greater need for support services.

A discrepancy between the study sample and those reported by Goldenberg and colleagues (2008) lies in the percent of individuals born in each stage of prematurity. For the general population, percent of individuals born increased as weeks of gestation increased. Replication of this finding was not found in the current sample. The largest percent of participants was found in the extreme prematurity group with the severe, moderate, and near term prematurity groups differing minimally in incidence rates. This difference is likely attributable to the source of study participants in the current study. A further investigation of the demographics of participants in each stage of prematurity may be revealing.

Hypothesis 2

Level of ASD severity was compared between participants with ASD born prematurely and those born full term. Results did not support the second hypothesis that infants and toddlers born prematurely would present with more severe ASD symptomology. This is somewhat

unexpected given prior data indicating that more severe impairments are often observed in those born prematurely (Abel et al., 2013; Baird et al., 2006; Klin et al., 2007; Sparrow, Balla, & Cicchetti, 1984).

Limitations of the current study may contribute to this discrepancy. The current sample size for those born prematurely was relatively small, with only 46 participants. With a larger sample it is possible that a significantly greater degree of severity would have been observed. The mean *BISCUIT-Part 1* score for the PRE group was 55.2, compared to 53.6 for the FT group. The PRE group had a slightly higher average *BISCUIT-Part 1* score, indicating a greater degree of severity, but not significantly more than the FT group. Future research on this topic would benefit from examining a larger PRE group for the following reasons. First, as mentioned above, greater differences in severity scores may be observed between the PRE group and the FT group, or the study findings may be replicated. Second, with a larger PRE group, stages of prematurity could be examined in regard to overall severity. Due to the small sample size, level of severity in regard to weeks of gestation on a continuum could not be measured.

Studying severity scores in relation to degree of prematurity may highlight differences that are not apparent when all those born prematurely are analyzed together. If results suggest that fewer weeks of gestation within those born prematurely is highly predictive of more severe ASD, researchers can focus on what is occurring in-utero that may have been disrupted or altered due to premature birth. As suggested by Abel and colleagues (2013) clinicians and service providers may be able to provide improved assessment and earlier treatment planning to individuals with ASD at increased risk for severe symptoms with this knowledge. Early intervention may be implemented with greater intensity or greater specificity in those born extremely premature if it is known they are at higher risk for severe impairments. Families of

individuals with ASD would also benefit from this type of knowledge as they may be able to better prepare for the possible course of their child's ASD. As ASD is a spectrum manifesting itself differently in each individual, no steadfast rules can be asserted, but if a child is a higher risk for severe symptoms of the disorder, being informed of this risk can only help the family and providers.

A third reason to replicate this study with a larger sample would be to examine if weeks of gestation impacts severity scores differently within the core features of ASD; socialization, communication, and repetitive behaviors and restricted interests. It has been reported that there is considerable variability in level of impairment among persons with ASD (Bodfish et al., 2000; Charman, Drew, Baird, & Baird, 2003; Liselotte, Hedvall, Fernell, Gillberg, & Norrelgen, 2012; Matson & Dempsey, 2008a; Matson, Wilkins, Macken & Rojahn, 2008; Wetherby et al., 2004; Volkmar, 1987); however, little is known with regard to what may cause or predict this variation. To my knowledge, no research to date investigated degree of prematurity in relation to severity level of the individual core features of ASD. Implications of this type of research again could better inform treatment planning and longer term outcomes.

Conclusion

Taken together, these findings do not support premature birth as a predictor of ASD or a more severe presentation of the disorder, but the results do support prior observations that the more premature an infant, the more likely they are to have atypical development (Foulder-Hughes & Cooke, 2003; Goldenberg, 2002; Green et al., 2005). As the survival rate of premature infants' increases with technological advances, attention must be paid to the developmental outcomes of this population (Behrman & Butler, 2007; Foulder-Hughes & Cooke, 2003; Goldenberg, 2002; Green et al., 2005). Screening children born prematurely early for

developmental delays or ASD will help identify those who may need early intervention. Early

intensive implementation of intervention has been suggested to lead to better prognosis (Matson,

Wilkins, & Gonzalez, 2008). Therefore, as we know that premature birth is a risk factor for ASD

and developmental delays, and that early intensive intervention is beneficial, researchers must

continue to study the interaction between premature birth and development so that screening methods

and intervention methods can be further refined to best serve this population.

REFERENCES

Abel, K. M., & Allin, M. A. (2005). *Placental programming and neurodevelopmental outcomes, in Placenta and Neurodisability*. London: The MacKeith Press.

Abel, K .M, Dalman, C., Svensson, A. C., Susser, E., Dal, H., Idring, A., . . . Magnusson, C. (2013). Deviance in fetal growth and risk of autism spectrum disorder. *American Journal of Psychiatry, 170*, 391-398.

Ajayi-Obe, M., Saeed, N., Cowan, F. M., Rutherford, M. A., & Edwards, A. D. (2000). Reduced development of cerebral cortex in extremely preterm infants. *The Lancet, 356*(9236), 1162-1163.

Alfonso, V. C., Rentz, E. A., & Suehee, C. (2010). Review of the developmental inventory, second edition. *Journal of Early Childhood & Infant Psychology, 6*, 21-40.

American Academy for Pediatrics. (1986). Screening for developmental disabilities. *Pediatrics, 78*, 526–528.

American Psychiatric Association (1952). *Diagnostic and Statistical Manual of Mental Disorders* (1st ed.) Washington DC: American Psychiatric Association.

American Psychiatric Association (1968). *Diagnostic and Statistical Manual of Mental Disorders* (2nd ed.) Washington DC: American Psychiatric Association.

American Psychiatric Association (1980). *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed.). Washington, DC: Author.

American Psychiatric Association (1987). *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed. - Revised). Washington, DC: Author.

American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington, D.C.: Author.

American Psychiatric Association (2000). *Diagnostic and Statistical Manual of Mental Disorders-Text Revision, (4th ed., text rev.).* Washington, DC: Author.

American Psychiatric Association (2012). DSM-5. Retrieved August 8, 2013 from www.dsm5.org

American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders, (5th ed.).* Washington, DC: Author.

Anderson, P. J. & Doyle, L. W. (2004) Executive functioning in school-aged children who were born very preterm or with extremely low birth weight in the 1990s. *Pediatrics, 114*, 50–57.

Aylward, G. P. (2005). Neurodevelopmental outcomes of infants born prematurely. *Journal of Developmental and Behavioral Pediatrics, 26*, 427–40.

Baer, D. M., Wolf, M. M., & Risely, T. R. (1968). Some current dimensions of applied behavior analysis. *Journal of Applied Behavior Analysis, 1*, 91–97.

Baghdaldli, A., Picot, M. C., Pascal, C., Pry, R., & Aussilloux, C. (2003). Relationship between age of recognition of first disturbances and severity in young children with autism. *European Child and Adolescent Psychiatry, 12*, 122-127.

Baird, G., Simonoff, E., Pickles, A., Chandler, S., Loucas, T., Meldrum, D., & Charman, T. (2006). Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: The Special Needs and Autism Project (SNAP*). Lancet, 368*, 210–215.

Baron-Cohen, S. (1991). The development of a theory of mind in autism: deviance and delay? *Psychiatric Clinics of North America, 14,* 33-51.

Behrman, R. E., & Butler, A. S. (2007). Neurodevelopmental, health, and family outcomes for infants born preterm. In A. S. Butler & R. E. Butler, A. S., & Behrman, R. E. (Eds.). *Preterm Birth: Causes, Consequences, and Prevention*. Washington, DC: National Academies Press.

Ben-Itzchak, E., & Zachor, D. A. (2007). The effects of intellectual functioning and autism severity on outcome of early behavioral intervention for children with autism. *Research in Developmental Disabilities, 28,* 287–303.

Berk, L. E. (2009). *Child development.* (8th ed.). Boston, MA: Pearson Education, Inc.

Bertoglio, K. & Hendren, R. L. (2009). New developments in Autism. *Psychiatric Clinics of North America, 32,* 1–14.

Bettelheim, B. (1967). *The Empty Fortress*. New York, NY: The Free Press.

Bishop, D. V. M., Mayberry, M., Wong, D., Maley, A., Hill, W., & Hallmayer, J. (2004). Are phonological processing deficits part of the broad autism phenotype? *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics), 128*, 54–60.

Bodfish, J. W., Symons, F. J., Parker, D. E. & Lewis, M. H. (2000). Varieties of repetitive behavior in autism: comparisons to mental retardation. *Journal of Autism and Developmental Disorders, 30*(30), 237-243.

Bosch, G. (1962). *Infantile Autism* (trans. D. Jordan and I. Jordan). New York, NY. Springer-Verlag.

Buchmayer, S., Johansson, S., Johansson, A., Hultman, C. M., Sparen, P., & Cnattingius, S. (2009). Can association between preterm birth and autism be explained by maternal or neonatal morbidity? *Pediatrics, 124*, e817–e825.

Campbell, J. M. (2003). Efficacy of behavioral interventions for reducing problem behavior in persons with autism: a quantitative synthesis of single-subject research. *Research in Developmental Disabilities, 24*, 120-38.

Cassel, T. D., Messinger, D. S., Ibanez, L. V., Haltigan, J. D., Acosta, S. I., & Buchman, A. C. (2007). Early social and emotional communication in the infant siblings of children with Autism Spectrum Disorders: An examination of the broad phenotype. *Journal of Autism and Developmental Disorders, 37*, 122-132.

Centers for Disease Control and Prevention (2010). *Prevalence of Autism Spectrum Disorders (ASDs).* Retrieved August 22, 2010, from http://www.cdc.gov/ncbddd/autism/data.html.

Centers for Disease Control and Prevention (2008). *MMR vaccine does not cause autism.* Retrieved August 22, 2010, from http://www.immunize.org/catg.d/p4026.pdf.

Chakrabarti, S. (2009). Early identification of autism. *Indian Pediatrics, 46*, 412-414.

Charman, T. (2008). Autism Spectrum Disorders. *Psychiatry, 7,* 331 – 334.

Charman, T., Drew, A., Baird, C., & Baird, G. (2003b). Measuring early language development in preschool children with autism spectrum disorder using the MacArthur Communicative Development Inventory (Infant Form). *Journal of Child Language, 30*, 213-236.

Charman, T., Swettenham. J., Baron-Cohen, S., Cox, A., Baird, G., & Drew, A. (1997). Infants with autism: An investigation of empathy, pretend play, joint attention, and imitation. *Developmental Psychology, 33,* 781-789.

Charman, T., Taylor, E., Auriol, D., Cockerhill, H., Brown, J.-A., & Baird, G. (2005). Outcome at 7 years of children diagnosed with autism at age 2: Predictive validity of assessments conducted at age 2 and 3 years of age and pattern of symptom change over time. *Journal of Child Psychology and Psychiatry, 46*(5), 500–513.

Cohen, B. H. (2008). *Explaining Psychological Statistics*. Hoboken, NJ: John Wiley & Sons, Inc.

Corsello, C. M. (2005). Early Intervention in Autism. *Infants & Young Children, 18*, 74-85.

Dawson, G., & Murias, M. (2009). Autism. In L. R. (Ed.), Squire, *Encyclopedia of Neuroscience* (pp. 779 – 784). Oxford, England: Academic Press.

Dawson, G., & Sterling, L. (2008). Autism Spectrum Disorders. In M. M. Haith & J. B. Benson (Ed.), *Encyclopedia of Infant and Early Childhood Development* (pp. 137 – 143). Oxford, England: Academic Press.

Dawson, G., & Osterling, J. (1997). Early intervention in autism. *The effectiveness of early intervention*, 307-326.

DeGiacomo, A., & Fombonne, H. (1998). Parental recognition of developmental abnormalities in autism. *European Child and Adolescent Psychiatry, 7,* 131-136.

Dodds, L., Fell, D. B., Shea, S., Armson, B. A., Allen, A. C., & Bryson, S. (2011). The role of prenatal, obstetric and neonatal factors in the development of autism. *Journal of autism and developmental disorders, 41*(7), 891-902.

Dyches, T. T., Wilder, L. K., Sudweeks, R. R., Obiakor, F. E., & Algozzine, B. (2004). Multicultural issues in autism. *Journal of Autism and Developmental Disorders, 34*, 211-222.

Elsabbagh, M., & Johnson, M. H. (2007). Infancy and Autism: Progress, prospects, and challenges. *Progress in Brain Research, 164,* 355 – 383.

Erdfelder, E., Faul, F., & Buchner, A. (1996). GPOWER: A general power analysis program. *Behavior Research Methods, Instruments, & Computers*, *28*, 1-11.

Eveloff, H. H. (1960). The autistic child. *Archives of General Psychiatry, 3*, 66-81.

Evans, M., Stoddart, H., Condon, L., Freeman, E., Grizzell, M., & Mullen, R. (2001). Parent's perspectives on the MMR immunisation: A focus group study. *British Journal of General Practice, 51*, 904-910.

Fenske, E. C., Zalenski, S., Krantz, P. J. & McClannahan, L. E. (1985). Age at intervention and treatment outcome for autistic children in a comprehensive intervention program. *Analysis and Intervention in Developmental Disabilities, 5*, 49-58.

Field, A. (2009). *Discovering statistics using SPSS*. London: Sage Publications.

Fombonne, E. (2003). Epidemiological surveys of Autism and other Pervasive Developmental Disorders: An update. *Journal of Autism and Developmental Disorders, 33*, 365-382.

Fombonne, E. (2005). The changing epidemiology of autism. *Journal of Applied Research in Intellectual Disabilities, 18*, 281-294.

Fombonne, E. (2009). Epidemiology of Pervasive Developmental Disorders. *Pediatric Research, 65*(6), 591-598.

Frazier, T. W., Youngstrom, E, A., Speer, L., Embacher, R., Law, P., Constantino, J., . . . Eng, C. (2012). Validation of proposed DSM-5 criteria for autism spectrum disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *51*, 28-40.

Freitag, C. M. (2007). The genetics of autistic disorders and its clinical relevance: A review of the literature. *Molecular Psychiatry 12,* 2–22.

Gillberg, C., Nordin, V., & Ehlers, S. (1996). Early detection of autism. Diagnostic instruments for clinicians. *European Child and Adolescent Psychiatry, 5*, 67–74.

Goldenberg, R. L. (2002). The management of preterm labor. *Obstetrics and Gynecology, 100*, 1020-37.

Goldenberg, R. L., Culhane, J. F., Iams, J. D., & Romero, R. (2008). Epidemiology and causes of preterm birth. *Lancet, 371*, 75–84

Goldin, R. L., Matson, J. L., Beighley, J. S., & Jang, J. (2014). Autism spectrum disorder severity as a predictor of Battelle Developmental Inventory – Second Edition (BDI-2): Scores in toddlers. *Developmental Neurorehabilitation, 17*, 39-43.

Goldman, S., Wang, C., Salgado, M. W., Greene, P. E., Kim, M., & Rapin, I. (2009). Motor stereotypies in children with autism and other developmental disorders. *Developmental Medicine & Child Neurology, 51*, 30–38.

Goyen, T. A., Lui, K., & Woods, R. (1998). Visual-motor, visual-perceptual, and fine motor outcomes in very-low-birthweight children at 5 years. *Developmental Medicine and Child Neurology, 40*, 76–81.

Green, N. S., Damus, K., Simpson, J. L., Iams, J., Reece, E. A., Hobel, C. J., ... & Schwarz, R. H. (2005). Research agenda for preterm birth: recommendations from the March of Dimes. *American Journal of Obstetrics and Gynecology,193*(3), 626-635.

Gruber, O., Hasan, A., Scherk, H., Wobrock, T., Schneider-Axmann, T., Ekawardhani, S., ... Falkai, P. (2012). Association of the brain-derived neurotrophic factor val66met polymorphism with magnetic resonance spectroscopic markers in the human hippocampus: in vivo evidence for effects on the glutamate system. *European Archives of Psychiatry and Clinical Neuroscience, 262*, 23–31.

Hack, M., Taylor, H. G., Schluchter, M., Andreias, L., Drotar, D., & Klein, N. (2009). Behavioral outcomes of extremely low birth weight children at age 8 years. *Journal of Developmental and Behavioral Pediatrics, 30*, 122–130.

Hadders-Algra, M. (2002). Two distinct forms of minor neurological dysfunction: perspectives emerging from a review of data of the Groningen Perinatal Project. *Developmental Medicine & Child Neurology, 44*(8), 561-571.

Harris, S. L., Handleman, J. S., Gordon, R., Kristoff, B., & Fuentes, F. (1991). Changes in Cognitive and Language Functioning of Preschool Children with Autism. *Journal of Autism and Developmental Disorders, 21*, 281-290.

Hattier, M. A., & Matson, J. L. (2012). An examination of the relationship between communication and socialization deficits in children with autism and PDD-NOS. *Research in Autism Spectrum Disorders, 6*, 871-880.

Hinkle, D. E., Wiersma, W., & Jurs, S. G. (2003). *Applied statistics for the behavioral sciences*. Boston, MA: Houghton Mifflin Company.

Honda, H., Shimzu, Y., & Rutter, M. (2005). No effect of MMR withdrawal on the incidence of autism: a total population study. *Journal of Child Psychology & Psychiatry, 46*, 572-579.

Horovitz, M., & Matson, J. L. (2010). Communication deficits in babies and infants with autism and pervasive developmental disorder-not otherwise specified (PDD-NOS). *Developmental Neurorehabilitation, 13*, 390–398.

Horovitz, M. & Matson, J. L. (2014). The Baby and Infant Screen for Children with aUtIsm Traits- Part 1: Age-based scoring procedures. *Journal of Developmental and Physical Disabilities, 26*, 1-22.

Howlin, P. (1986). An overview of social behavior in autism. In E. Schopler & G. B. Mesibov (Eds.), *Social behavior in autism* (pp. 103-126). New York: Plenum Press.

Howlin, P. (2006). Autism spectrum disorder. *Psychiatry, 5*(9), 320-324.

Foulder-Hughes, L. A., & Cooke, R. W. I. (2003). Motor, cognitive, and behavioural disorders in children born very preterm. *Developmental Medicine & Child Neurology, 45*(02), 97-103.

Hultman, C. M., Sparén, P., & Cnattingius, S. (2002). Perinatal risk factors for infantile autism. *Epidemiology*, 13(4), 417-423.

Hwang, Y. S., Weng, S. F., Cho, C. Y., & Tsai, W. H. (2013). Higher prevalence of autism in Taiwanese children born prematurely: A nationwide population-based study. *Research in Developmental Disabilities, 34(*9), 2462-2468.

Inder, T. E., Warfield, S. K., Wang, H., Hüppi, P. S., & Volpe, J. J. (2005). Abnormal cerebral structure is present at term in premature infants. *Pediatrics, 115*(2), 286-294.

Indredavik, M. S., Vik, T., Heyerdahl, S., Kulseng, S., Fayers, P., & Brubakk, A. M. (2004). Psychiatric symptoms and disorders in adolescents with low birth weight. *Archives of Disease in Childhood, 89*, F445–F450.

Inglese, M. D., & Elder, J. H. (2009a). Caring for children with Autism Spectrum Disorder, part I: Prevalence, etiology, and core features. *Journal of Pediatric Nursing, 24,* 41 – 48.

Inglese, M. D., & Elder, J. H. (2009b). Caring for children with Autism Spectrum Disorder, part II: Screening, diagnosis, and management. *Journal of Pediatric Nursing, 24,* 49–59.

Johnson, S., Hollis, C., Kochhar, P., Hennessy, E., Wolke, D., & Marlow, N. (2010). Autism spectrum disorders in extremely preterm children. *Journal of Pediatrics, 156*, 525–531.

Joshi, G., Biederman, J., Goldin, L.R., Crowley, D., Furtak, S., Lukas, S., & Gönenç, A. (2013). Magnetic resonance spectroscopy study of the glutamatergic system in adolescent males with high-functioning autistic disorder: A pilot study at 4T. *European Archives of Psychiatry and Clinical Neuroscience, 263*, 379-384

Kapellou, O., Counsell, S. J., Kennea, N., Dyet, L., Saeed, N., Stark, J., ... & Edwards, A. D. (2006). Abnormal cortical development after premature birth shown by altered allometric scaling of brain growth. *PLoS Medicine, 3*(8), e265.

Karlberg, J., & Albertsson-Wikland, K. (1995). Growth in full term small-for-gestational-age infants: from birth to final height. *Pediatric Research, 38*(5), 733-739.

Kerstjens, J. M., De Winter, A. F., Bocca-Tjeertes, I. F., Bos, A. F., & Reijneveld, S. A. (2012). Risk of developmental delay increases exponentially as gestational age of preterm infants decreases: a cohort study at age 4 years. *Developmental Medicine & Child Neurology, 54*(12), 1096-1101.

Klin, A., Saulnier, C. A., Sparrow, S. S., Cicchetti, D. V., Volkmar, F. R., & Lord, C. (2007). Social and communication abilities and disabilities in higher functioning individuals with autism spectrum disorders: the Vineland and the ADOS. *Journal of Autism and Developmental Disorders, 37*, 748–59.

Kodric, J., Sustersic, B., & Paro-Panjan, D. (2010). Assessment of general movements and 2.5 year developmental outcomes: pilot results in a diverse preterm group. *European Journal of Paediatric Neurology, 14*(2), 131-137.

Krug, D. A., Arick, J. R., & Almond, P. J. (1980a). *Autism screening instrument for educational planning*. Portland, OR: ASIEP Education.

Krug, D. A., Arick, J. R., & Almond, P. J. (1980b). Behavior checklist for identifying severely handicapped individuals with high levels of autistic behavior. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 21,* 221–229.

Kuhl, P. K., Conboy, B. T., Padden, D., Nelson, T., & Pruitt, J. (2005). Early speech perception and later language development: Implications for the "critical period." *Language Learning and Development, 1*, 237-264.

Lan, L. M., Yamashita, Y., Tang, Y., Sugahara, T., Takahashi, M., Ohba, T., & Okamura, H. (2000). Normal Fetal Brain Development: MR Imaging with a Half-Fourier Rapid Acquisition with Relaxation Enhancement Sequence 1. *Radiology, 215*(1), 205-210.

Lang, R., O'Reilly, M., Sigafoos, J., Lancioni, G. E., Machalicek, W., Rispoli, M., & P., White. (2009). Enhancing the effectiveness of a play intervention by abolishing the reinforcing value of stereotypy: a pilot study. *Journal of Applied Behavior Analysis, 42*, 889–894.

Lanovaz, M. J., & Sladeczek, I. E. (2011). Vocal stereotypy in children with autism: structural characteristics, variability, and effects of auditory stimulation. *Research in Autism Spectrum Disorders, 5*, 1159–1168.

Larsson, H. J., Eaton, W. W., Madsen, K. M., Vestergaard, M., Olesen, A. V., Agerbo, E., . . . Mortensen, P. B. (2005). Risk factors for autism: perinatal factors, parental psychiatric history, and socioeconomic status. *American Journal of Epidemiology*, *161*(10), 916-925.

Liptak, G. S., Benzoni, L. B., Mruzek, D. W., Nolan, K. W., Thingvoll, M. A., Wade, C. M., & Fryer, G. E. (2008). Disparities in diagnosis and access to health services for children with autism: Data from the National Survey of Children's Health. *Journal of Developmental & Behavioral Pediatrics, 29*, 152-160.

Liselotte, K., Hedvall, A., Fernell, E., Gillberg, C., & Norrelgen, F. (2012). Language and communication skills in preschool children with autism spectrum disorders: Contribution of cognition, severity of autism symptoms, and adaptive functioning to the variability. *Research in Developmental Disabilities, 33*, 172-180.

Liss, M., Harel, B., Fein, D., Allen, D., Dunn, A., Dunn, M., . . . Rapin I. (2011). Predictors and correlates of adaptive functioning in children with developmental disorders. *Journal of Autism and Developmental Disorders, 31*, 219–230.

Lord, C., & Luyster, R. (2006). Early diagnosis of children with Autism Spectrum Disorders. *Clinical Neuroscience Research, 6,* 189 – 194.

Lord, C., & Risi, S. (1998). Frameworks and Methods in Diagnosing Autism Spectrum Disorders. *Mental Retardation and Developmental Disabilities Research Reviews 4*, 90-96.

Lord, C., Risi, S., Lambrecht, L., Cook, E.H., Leventhal, B.L., Pickles, A., & Rutter, M.J. (2000). Autism Diagnostic Observation Schedule-General (ADOS-G): A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders, 30,* 205–223.

Lord, C., Rutter, M., & Couteur, A. (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*, 659-685.

Luyster, R. J., Kadlec, M. B., Carter, A., & Tager-Flusberg, H. (2008). Language assessment and development in toddlers with autism spectrum disorders. *Journal of Autism and Developmental Disorders, 28*, 1426-1438.

Luyster, R., Qiu, S., Lopez, K., & Lord, C. (2007). Predicting outcomes of children referred for autism using the MacArthur-Bates Communicative Development Inventory. *Journal of Speech, Language, and Hearing Research, 50*, 667–681.

MacKay, D. F., Smith, G. S., Dobbie, R., & Pell, J. P. (2010). Gestational Age at Delivery and Special Educational Need: Retrospective Cohort Study of 407,503 Schoolchildren. *Plos Medicine, 7*(6), 1-10.

Mamidala, M. P., Polinedi, A., PTV, P. K., Rajesh, N., Vallamkonda, O. R., Udani, V., . . . Rajesh, V. (2013). Prenatal, perinatal and neonatal risk factors of Autism Spectrum Disorder: A comprehensive epidemiological assessment from India. *Research in Developmental Disabilities, 34*(9), 3004-3013.

Mandy, W., Charman, T., Gilmour, J., & Skuse, D. (2011). Toward specifying pervasive developmental disorder-not otherwise specified. *Autism Research, 4*(2), 121-131.

Manning-Courtney, P., Brown, J., Molloy, C. A., Reinhold, J., Murray, D., Sorensen-Burnworth, R.,…Kent, B. (2003). Diagnosis and treatment of Autism Spectrum Disorders. *Current Problems in Pediatric and Adolescent Health Care, 23,* 283 – 304.

Martinez-Pedraza, F. L., & Carter, A. S. (2009). Autism spectrum disorders in young children. *Child and Adolescent Psychiatric Clinics of North America, 18,* 645 – 663.

Matson, J. L. (2007). Determining treatment outcome in early intervention programs for autism spectrum disorders: A critical analysis of measurement issues in learning based interventions. *Research in Developmental Disabilities, 28,* 207 – 218.

Matson J. L. (2009). *Applied behavior analysis for children with autism spectrum disorders*. New York, NY: Springer.

Matson, J. L., Belva, B. C., Horovitz, M., & Bamburg, J. (2012). Comparing symptoms of autism spectrum disorders in a developmentally disabled adult population using the current *DSM-IV-TR* diagnostic criteria and the proposed *DSM-5* diagnostic criteria. *Journal of Developmental and Physical Disabilities, 24,* 403-414.

Matson, J. L., & Boisjol, J. A. (2009). The token economy for children with intellectual disabilities and autism: A review. *Research in Developmental Disabilities, 30*, 240-248.

Matson, J. L., Boisjoli, J. A., Hess, J., & Wilkins, J. (2010). Factor Structure and Diagnostic Fidelity of the Baby and Infant Screen for Children with aUtIsm Traits - Part 1 (BISCUIT Part - 1). *Psychiatry Research*, *13*, 72-79.

Matson, J. L., Boisjoli, J., & Wilkins, J. (2007). *Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT)*. Baton Rouge, LA: Disability Consultants, LLC.

Matson, J. L., & Dempsey, T. (2008a). Stereotypy in adults with autism spectrum disorders: relationship and diagnostic fidelity. *Journal of Developmental and Physical Disabilities, 20*, 155-165.

Matson, J. L. & Dempsey, T. (2008b). Autism spectrum disorders: pharmacotherapy for challenging behaviors. *Journal of Developmental and Physical Disabilities, 20,* 175-191.

Matson, J. L., Fodstad, J. C., Hess, J., & Neal, D. (2009). Social and communication behaviors in infants and toddlers with autism and pervasive developmental disorder not otherwise specified. *Developmental Neurorehabilitation, 12*, 152–157.

Matson, J. L., & Goldin, R. (in press). What is the future of assessment for autism spectrum disorders: Short and long term. *Research in Autism Spectrum Disorders*.

Matson, J. L., Gonzalez, M. L., Wilkins, J., & Rivet, T. T. (2008). Reliability of the Autism Spectrum Disorder-Diagnostic for Children (ASD-DC). *Research in Autism Spectrum Disorders, 2,* 533-545.

Matson, J. L., Hamilton, M., Duncan, D., Bamburg, J., Smiroldo, B., Anderson, S., . . . Kirkpatrick- Sanchez, S. (1997). Characteristics of stereotypic movement disorder and self-injurious behavior as assessed with the Diagnostic Assessment for the Severely Handicapped (DASH-II). *Research in Developmental Disabilities, 18*, 457–469.

Matson, J. L., Hess, J. A., Sipes, M., & Horovitz, M. (2010). Developmental profiles from the Battelle Developmental Inventory: A comparison of toddlers diagnosed with Down syndrome, global developmental delay, and premature birth. *Developmental Neurorehabilitation, 13,* 234-238.

Matson, J. L., Kiely, S. L., & Bamburg, J. W. (1997). The effects of stereotypies on adaptive skills as assessed with the DASH-II and the Vineland Adaptive Behavior Scale. *Research in Developmental Disabilities, 18*, 471–476.

Matson, J. L., & Kozlowski, A. M. (2011). The increasing prevalence of autism spectrum disorders. *Research in Autism Spectrum Disorders, 5*, 418-425.

Matson, J. L., Kozlowski, A. M., Hattier, M. A., Horovitz, M., & Sipes, M. (2012). DSM-IV vs DSM-5 diagnostic criteria for toddlers with autism. *Developmental Neurorehabilitation*, *15*(3), 185-190.

Matson, J. L., Mahan, S., Fodstad, J. C., Worley, J. A., Neal, D., & Sipes, M. (2011) Effects of symptoms of co-morbid psychopathology on challenging behaviours among infants and toddlers with Autistic Disorder and PDD-NOS as assessed with the Baby and Infant

Screen for Children with aUtIsm Traits (BISCUIT). *Developmental Neurorehabilitation, 14,* 129-139.

Matson, J. L., & Minshawi, N. F. (2006). *Early intervention for autism spectrum disorders: A critical analysis*. Oxford, England: Elsevier Science, Inc.

Matson, J. L., & Minshawi, N. F. (2007). Functional assessment of challenging behavior: Toward a strategy for applied settings. *Research in Developmental Disabilities, 28*, 353-361.

Matson, J. L., Minshawi, N. F., Gonzalez, M. L., & Mayville, S. B. (2006). The relationship of comorbid problem behaviors to social skills in persons with profound mental retardation. *Behavior Modification, 30*, 496–506.

Matson, J.L., Rivet, T.T., Fodstad, J.C., Dempsey, T., & Boisjoli, J.A. (2009). Examination of Adaptive Behavior Differences in Adults with Autism Spectrum Disorders and Intellectual Disability. *Research in Developmental Disabilities, 30,* 1317-1325.

Matson, J. L., Taras, M. E., Sevin, J. A., Love, S. R., & Fridley, D. (1990). Teaching self-help skills to autistic and mentally retarded children. *Research in Developmental Disabilities, 11*, 361-378.

Matson, J. L., & Wilkins, J. (2007). A critical review of assessment targets and methods for social skills excesses and deficits for children with autism spectrum disorders. *Research in Autism Spectrum Disorders, 1*, 28–37.

Matson, J. L., Wilkins, J., & Fodstad, J. C. (2011). The validity of the Baby and Infant Screen for Children with aUtIsm Traits: Part 1 (BISCUIT: Part1). *Journal of Autism and Developmental Disorders, 41*, 1139-1146.

Matson, J. L., Wilkins, J., & Gonzalez, M. (2008). Early identification and diagnosis in Autism Spectrum Disorders in young children and infants: How early is too early? *Research in Autism Spectrum Disorders, 2*, 75–84.

Matson, J. L., Wilkins, J., & Macken, J. (2008). The relationship of challenging behaviors to severity and symptoms of autism spectrum disorders. *Journal of Mental Health Research in Intellectual Disabilities, 2,* 29-44.

Matson, J. L., Wilkins, J., Sharp, B., Knight, K., Sevin, J. A., & Boisjoli, J. A. (2009a). Sensitivity and Specificity of the *Baby and Infant Screen for Children with aUtism Traits (BISCUIT)*: Validity and cut-off scores for autism and PDD-NOS in toddlers. *Research in Autism Spectrum Disorders, 3*, 924-30.

Matson, J. L., Wilkins, J., Sevin, J. A., Knight, C., Boisjoli, J. A., & Sharp, B. (2008). Reliability and item content of the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT): Parts 1–3. *Research in Autism Spectrum Disorders, 3*, 336-344.

Matson, J. L., Wilkins, J., Sevin, J. A., Knight, C., Boisjoli, J. A., & Sharp, B. (2009b). Reliability and item content of the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT): Parts 1–3. *Research in Autism Spectrum Disorders, 3*, 336-344.

Mattila, M., Kielinen, M., Linna, S., Jussila, K., Ebeling, H., Bloigu, R., . . . Moilanen I. (2011). Autism spectrum disorders according to DSM-IV-TR and comparison with DSM-5 draft criteria: An epidemiological study. *Journal of the American Academy of Child & Adolescent Psychiatry, 50*, 583-592.

McDougle, C. J. (2002). Current and emerging therapeutics of autistic disorder and related pervasive developmental disorders. In Davis, K. L., Charney, D., Coyle, J. T., & Nemeroff, C. (Eds.), *Psychopharmacology: The Fifth Generation of Progress.* Philadelphia, PA: Lippincott Williams & Wilkins.

McPartland, J. C., Reichow, B., & Volkmar FR. (2012). Sensitivity and specificity of proposed DSM-5 diagnostic criteria for autism spectrum disorder. *Journal of the American Academy of Child & Adolescent Psychiatry, 51*, 368-383.

Merikangas, K. R., & Risch, N. (2003). Genomic priorities and public health. *Science, 302*(5645), 599-601.

Minshew, N. J., & Williams, D. L. (2007). The new neurobiology of autism: cortex, connectivity, and neuronal organization. *Archives of Neurology, 64*(7), 945-50.

Moizeau, C. E. (2003.) The problem of preterm birth: effective primary prevention. *Primary Care Update for OB/GYNS, 10*(1), 33–39.

Moore, T., Johnson, S., Hennessy, E., & Marlow, N. (2012). Screening for autism in extremely preterm infants: problems in interpretation. *Developmental Medicine & Child Neurology, 54*(6), 514-520.

Morrison, K., & Rosales-Ruis, J. (1997). The effect of object preferences on task performance and stereotypy in a child with autism. *Research in Developmental Disabilities, 18*, 127–137.

Movsas, T. Z., & Paneth, N. (2012). The effect of gestational age on symptom severity of children with autism spectrum disorder. *Journal of Autism and Developmental Disorders, 42*, 2431-2438.

Neidert, P. L., Dozier, C. L., Iwata, B. A., & Hafen, M. (2010). Behavior Analysis in intellectual and developmental disabilities. *Psychological Services, 7*, 103-113.

Newborg, J. (2005*). Battelle developmental inventory (2nd ed.).* Itasca, IL: Riverside.

Nicholas, J. S., Charles, J. M., Carpenter, L. A., King, L. B., Jenner, W., & Spratt, E. G. (2008). Prevalence and characteristics of children with autism spectrum disorders. *Annals of Epidemiology, 18*, 130–136.

Noens, I., & Van Berckelaer-Onnes, I. A. (2005). Captured by details: sense-making, language and communication in autism. *Journal of Communication Disorders, 38*, 123-141.

Ozonoff, S., Iosif, A., Baguio, F., Cook, I. C., Hill, M. M., Hutman, T., … Young, G. S. (2010). A prospective study of the emergence of early behavioral signs of autism. *Journal of the American Academy of Child & Adolescent Psychiatry, 49,* 256 – 266.

Piven, J., Palmer, P., Jacobi, D., Childress, D., & Arndt, S. (1997). Broader autism phenotype: Evidence from a family history study of multiple-incidence autism families. *American Journal of Psychiatry, 154*, 185–190.

Radoš, M., Judaš, M., & Kostović, I. (2006). In vitro MRI of brain development. *European Journal of Radiology, 57*(2), 187-198.

Reynolds, M. A., Schieve, L. A., Martin, J. A., Jeng, G., & Macaluso, M. (2003). Trends in multiple births conceived using assisted reproductive technology, United States, 1997–2000. *Pediatrics, 111*, 1159-1162.

Rimland, B. (1964). *Infantile autism*. New York: Appleton-Century-Crofts.

Rimland, B. (1971). The Differentiation of Childhood Psychoses: An Analysis of Checklists for 2,218 Psychotic Children. *Journal of Autism and Childhood Schizophrenia, 1*, 161-174.

Robertson, J. M., Tanguay, P. E., L'ecuyer, S., Sims, A., Waltrip, C. (1999). Domains of social communication handicap in autism spectrum disorder. *Journal of the American Academy of Child & Adolescent Psychiatry, 38,* 738 – 745.

Robins, D. L., Fein, D., Barton, M. L., & Green, J. A. (2001). The Modified Checklist for Autism in Toddlers: An initial study investigating the early detection of autism and pervasive developmental disorders. *Journal of Autism & Developmental Disorders*, *31*(2), 131.

Rogers, S. J. (1996). Brief Report: Early Intervention in Autism. *Journal of Autism and Developmental Disorders, 26*, 243-246.

Romero, R., Espinoza, J., Kusanovic, J. P., Gotsch, F., Hassan, S., Erez, O., ... & Mazor, M. (2006). The preterm parturition syndrome. BJOG: *An International Journal of Obstetrics & Gynaecology, 113*(s3), 17-42.

Russell, R. B., Petrini, J. R., Damus, K., Mattison, D. R., & Schwarz, R. H. (2003). The changing epidemiology of multiple births in the United States. *Obstetrics and Gynecology,101*, 129-35.

Rutter, M. (1968). Concepts of autism: A review of research. *Journal of Child Psychology and Psychiatry, 9*, 1-25.

Rutter, M. (1978). Diagnosis and definition of childhood autism. *Journal of Autism and Childhood Schizophrenia, 8*, 139-161.

Rutter, M. (1979). Language, cognition and autism. In R. Katzman (Ed.), *Congenital and Acquired Cognitive Disorders*. New York: Raven.

Rutter, M. (1983). Cognitive deficits in pathogenesis of autism. *Journal of Child Psychology and Psychiatry, 24*, 513-31.

Rutter, M. (1985). Infantile autism and other pervasive developmental disorders. In M. Rutter & L. Hersov (Eds.), *Child and adolescent psychiatry: Modern approaches* (2nd ed., pp. 545-564). Oxford: Blackwell Scientific.

Rutter, M., & Bartak, L. (1971). Causes of infantile autism: Some considerations from recent research. *Journal of Autism and Childhood Schizophrenia, 1*, 20-32.

Saigal, S., & Doyle, L. W. (2008). An overview of mortality and sequelae of preterm birth from infancy to adulthood. *The Lancet, 371*(9608), 261-269.

Schendel, D., & Bhasin, T. K. (2008). Birth weight and gestational age characteristics of children with autism, including a comparison with other developmental disabilities. *Pediatrics, 121, 1155–1164.*

Schopler, E., Reichler, R., DeVellis, R., & Daly, K. (1980). Toward Objective Classification of Childhood Autism: Childhood Autism Rating Scale (CARS). *Journal of Autism and Developmental Disorders, 10*, 91-103.

Sevin, B. M., Knight, C. L., & Braud, S. A. (2007). Autism and pervasive developmental disorders. *International Review of Research in Mental Retardation, 34,* 163 – 196.

Sevin, J. A., Matson, J. L., Coe, D. A., Fee, V. E., & Sevin, B. M. (1991). A Comparison and Evaluation of Three Commonly Used Autism Scales. *Journal of Autism and Developmental Disorders, 21*, 417-432.

Shorter, E. (1997). *A history of psychiatry: From the era of the asylum to the age of Prozac*. NY: John Wiley & Sons, Inc.

Sipes, M., Matson, J. L., & Horovitz, M. (2011). Autism spectrum disorders and motor skills: The effect on socialization as measured by the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT). *Developmental Neurorehabilitation, 14*, 290-296.

Smeeth, L., Cook, C., Fombonne, E., Heavey, L., Rodrigues, L., Smith, P., & Hall, A.J. (2004). MMR vaccination and pervasive developmental disorders: a case-control study. *Lancet, 364*, 963-969.

Smith, T. (1999). Outcome of early intervention for children with autism. *Clinical Psychology: Science and Practice, 6*, 33-49.

Smith, I., & Bryson, S. (1994). Imitation and action in autism: A critical review. *Psychological Bulletin, 116*, 259-273.

Smith, E. E. & Kosslyn, S. M. (2007). *Cognitive Psychology: Mind and Brain*, 1st edition. Upper

Saddle River, NJ: Prentice Hall.

Sparrow, S., Balla, D., & Cicchetti, V. (1984). *Vineland adaptive behavior scales.* (Eds.), Circle Pines, MN: American Guidance Service.

State, M. & Levitt, P. (2011). The conundrums of understanding genetic risks for autism spectrum disorders. *Nature Neuroscience, 14*, 1499-1506.

Steyn, B., & Le Couteur, A. (2003). Understanding autism spectrum disorders. *Current Pediatrics, 13*, 274-278.

Stone, W. L., Ousley, O. Y., Yoder, P. J., Hogan, K. L., & Hepburn, S. L. (1997). Nonverbal Communication in Two- and Three-Year-Old Children with Autism. *Journal of Autism and Developmental Disorders, 27*, 677-696.

Szatmari, P. (1992). Epidemiology of attention-deficit hyperactivity disorder. In G. Weiss & M. Lewis (Eds.), *Child and adolescent psychiatric clinics in North America, Attention-deficit hyperactivity disorder* (pp. 361-371). Philadelphia: W. B. Saunders.

Thomas J. (2010) Paranoia strikes deep: MMR vaccine and autism. *Psychiatric Times, 27,* 1-6.

Travis, L., & Sigman, M. (1998). Social deficits and interpersonal relationships in autism. *Mental Retardation and Developmental Disabilities Research Reviews, 4*, 65-72.

Van Krevelin, D. A. (1971). Early infantile autism and autistic psychopathy. *Journal of Autism and Child Schizophrenia, 1*, 82-86.

Veen, S., Ens-Dokkum, M. H., Schreuder, A. M., Verloove-Vanhorick, S. P., Ruys, J. H., & Brand, R. (1991). Impairments, disabilities, and handicaps of very preterm and very-low birthweight infants at five years of age. *The Lancet, 338*(8758), 33-36.

Volkmar, F., Cicchetti, D. V., Dykens, E., Sparrow, S. S., Leckman, J., & Cohen, D. (1988). An evaluation of the autism behavior checklist. *Journal of Autism and Developmental Disorders, 18*, 81-97.

Volkmar, F., Cohen, D., Bregman, J., Hooks, M., & Stevenson, J. (1989). An examination of social typologies in autism. *Journal of the American Academy of Child and Adolescent Psychiatry, 28*, 82-86.

Volkmar, F. R., Carter, A., Grossman, J., & Klin, A. (1997). Social development in autism. In D. J. Cohen & F. R. Volkmar (Eds.), *Handbook of Autism and Pervasive Developmental Disorders 2nd Edition* (pp. 173-194). New York: John Wiley & Sons, Inc.

Volkmar, F. R., & Klin, A. (2005). Issue in the classification of autism and related conditions. In F. R. Volkmar, R. Paul, A. Klin & D. J. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders* (3rd ed., Vol. 1, pp. 5-41). Hoboken, NJ: John Wiley and Sons.

Volkmar, F. R., & Pauls, D. (2003). Autism. *The Lancet, 362,* 1133 – 1142.

Volpe, J. (2009). Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. *Lancet Neurology, 8*(1), 110-124.

Wakefield, A., Murch, S., Anthony, A., Linnell, J., Casson, D., Malik, M., . . . Walker-Smith, J.A. (1998). Ileal-lymphoid-nodular Hyperplasia, Non-specific Colitis, and Pervasive Developmental Disorder in Children. *Lancet, 351*, 637-641.

Wallace, A. E., Anderson, G. M., & Dubrow, R. (2008). Obstetric and parental psychiatric variables as potential predictors of autism severity. *Journal of Autism and Developmental Disorders, 38*, 1542-1554.

Walters, A., Barrett, R., & Feinstein, C. (1990). Social relatedness and autism: current research, issues, directions. *Research in Developmental Disabilities, 11*, 303-326.

Werner, E., Dawson, G., Osterling, J., & Dinno, N. (2000). Brief report: recognition of autism spectrum disorder before one year of age: A retrospective study based on home videotapes. *Journal of Autism and Developmental Disorders, 30*, 157-162.

Wetherby, A. M., Woods, J., Allen, L., Cleary, J., Dickinson, H., & Lord, C. (2004). Early indicators of autism spectrum disorders in the second year of life. *Journal of Autism and Developmental Disorders, 34*(5), 473–493.

Wilkins, J. & Matson, J.L. (2007). Social Skills. In J.L. Matson & L.M. Glidden (Eds.), *International Review of Research in Mental Retardation, Vol. 34.* Waltham, MA: Academic Press.

Wing, L. (1981). Asperger's syndrome: a clinical account. *Psychological Medicine, 11*(1), 115-129.

Wing, L., & Gould, J. (1979). Severe impairments of social interaction and associated abnormalities in children: epidemiology and classification. *Journal of Autism and Developmental Disorders, 9*(1), 11-29.

Wing, L., Gould, J., & Gillberg, C. (2011). Autism spectrum disorders in the DSM-V: Better or worse than the DSM-IV? *Research in Developmental Disabilities, 32*, 768-773.

Wing, L., & Potter, D. (2002). The epidemiology of autism spectrum disorders: Is the prevalence rising? *Mental Retardation and Developmental Disabilities Research Reviews, 8*, 151-161.

Wolf, S. & Barlow, A. (1979). Schizoid personality in childhood: A comparative study of schizoid, autistic and normal children. *Journal of Child Psychology and Psychiatry, 20*, 29-46.

Wolery, M., Kirk, M., & Gast, D. L. (1985). Stereotypic behavior as a reinforcer: Effects and side effects. *Journal of Autism and Developmental Disorders, 15*, 149–161.

Wong, H. S., Huertas-Ceballos, A., Cowan, F. M., & Modi, N. (2014). Evaluation of Early Childhood Social-Communication Difficulties in Children Born Preterm Using the Quantitative Checklist for Autism in Toddlers. *The Journal of Pediatrics, 164*(1), 26-33.

Worley, J. A., & Matson, J. L. (2012). Comparing symptoms of autism spectrum disorders using the current DSM-IV-TR diagnostic criteria and the proposed DSM-5 diagnostic criteria. *Research in Autism Spectrum Disorders, 6,* 965-970.

Zafeiriou, D. I., Ververi, A., Dafoulis, V., Kalyva, E., & Vargiami, E. (2013). Autism Spectrum Disorders: The Quest for Genetic Syndromes. *American Journal of Medical Genetics Part B, 162B*, 327–366.

APPENDIX A

Factor Loadings for the BISCUIT-Part 1

Item		Factor 1 Repetitive Behavior/ Restricted Interests	Factor 2 Socialization/ Nonverbal Communication	Factor 3 Communication
58.	Abnormal, repetitive motor movements involving entire body	.*		
41.	Use of facial expressions	*		
29.	Eye-to-eye gaze	*		
48.	Becomes upset if there is a change in routine	*		
42.	Abnormal fascination with the movement of spinning objects	*		
27.	Restricted interests and activities	*		
39.	Interest in a highly restricted set of activities	*		
26.	Display a range of socially appropriate facial expressions	*		
8.	Maintains eye contact	*		
43.	Curiosity with surroundings	*		

4.	Engages in repetitive motor movements for no reason	*
34.	Abnormal preoccupation with parts of an object or objects	*
61.	Isolates self	*
49.	Needs reassurance, especially if events don't go as planned	*
57.	Abnormal, repetitive hand or arm movements	*
55.	Limited number of interests	*
6.	Prefers food of a certain texture or smell	*
38.	Expects others to know their thoughts, experiences, and opinions without communicating them	*
33.	Sticking to odd routines or rituals that don't have a purpose of make a difference	*
11.	Reactions to normal, everyday sounds	*
13.	Reaction to normal, everyday lights	*
30.	Reaction to sounds and sights	*

44	Saying words or phrases repetitively	*	
7.	Ability to recognize the emotions of others		*
51.	Responds to others' distress		*
20.	Interest in another person's side of the conversation		*
46.	Understand of appropriate jokes, figures of speech, or sayings		*
18.	Ability to make and keep friends		*
47.	Gives subtle cues or gestures when communicating with others		*
21.	Able to understand the subtle cues or gestures of others		*
22.	Use of too few or too many social gestures		*
19.	Interest in participating in social games, sports, and activities		*
59.	Development of social relationships		*
23.	Body posture and/or gestures		*
28.	Motivated to please others		*

36.	Reads nonverbal cues of other people	*	
32.	Facial expressions corresponds to environmental events	*	
12.	Responds to others social cues	*	
14.	Peer relationships	*	
52.	Socializes with other children	*	
35.	Plays appropriately with others	*	
62.	Participation in games or other social activities	*	
45.	Make-believe or pretend play	*	
10.	Social interactions with others his/her age	*	
17.	Shares enjoyment, interests, or achievement with others	*	
2.	Intellectual abilities	*	
3.	Age appropriate self-help and adaptive skills	*	
9.	Use of language to communicate		*
1.	Communication skills		*
5.	Verbal communication		*

50.	Language development	*
16.	Use of language in conversations with others	*
24.	Communicates effectively	*
53.	Use of non-verbal communication	*

Note. Factor loadings of each item are indicated by an asterisk.

APPENDIX B

Bobby Jindal
GOVERNOR

Kathy Kliebert
SECRETARY

State of Louisiana
Department of Health and Hospitals

December 4, 2013

Dr. Johnny L. Matson
Department of Psychology
Louisiana State University
324 Audubon Hall
Baton Rouge, LA 70803

Via email: johnmatson@aol.com

Re: Autism in Early Childhood

Dear Dr. Matson:

Thank you for submitting the above-referenced proposal. We have taken into advisement information provided in the proposal package. We find that all areas of concerns were clarified and the project has been approved by Expedited Review.

The IRB approves the project for the purposes of investigating developmental patterns and differences in atypically developing children with and without autism spectrum disorders. If you should desire to conduct additional research using the data collected under this project, that proposal much be submitted separately to the IRB for review.

I am requesting that the Principal investigator report to the DHH IRB any emergent problems, serious adverse reactions, or changes to protocol that may affect the status of the investigation and that no such changes be instituted prior to DHH IRB review, except where necessary in order to eliminate immediate hazards. The investigator also agrees to periodic review of this project by the DHH IRB at intervals appropriate to the degree of risk to assure that the project is being conducted in compliance with the DHH IRB's understanding and recommendations.

If I can be of any further assistance to you, please feel free to contact me.

Sincerely,

Nell W. Allbritton, MPA
Director, Institutional Review Board
Department of Health and Hospitals
628 North 4th Street, Third Floor
Baton Rouge, Louisiana 70802
(225) 342-4169
nell.allbritton@la.gov

Bienville Building • 628 N. 4th Street • P.O. Box 629 • Baton Rouge, Louisiana 70821-0629
Phone #: 225/342-9509 • Fax #: 225/342-5568 • WWW.DHH.LA.GOV
"An Equal Opportunity Employer"

82

Application for Exemption from Institutional Oversight

LSU

Unless qualified as meeting the specific criteria for exemption from Institutional Review Board (IRB) oversight, ALL LSU research/ projects using living humans as subjects, or samples, or data obtained from humans, directly or indirectly, with or without their consent, must be approved or exempted in advance by the LSU IRB. This Form helps the PI determine if a project may be exempted, and is used to request an exemption.

– Applicant,Please fill out the application in its entirety and include the completed application as well as parts A-F, listed below, when submitting to the IRB. Once the application is completed, please submit two copies of the completed application to the IRB Office or to a member of the Human Subjects Screening Committee. Members of this committee can be found at http://research.lsu.edu/CompliancePoliciesProcedures/InstitutionalReviewBoard%28IRB%29/item24737.html

– A Complete Application Includes All of the Following:
   (A) Two copies of this completed form and two copies of parts B thru F.
   (B) A brief project description (adequate to evaluate risks to subjects and to explain your responses to Parts 1&2)
   (C) Copies of all instruments to be used.
      *If this proposal is part of a grant proposal, include a copy of the proposal and all recruitment material.
   (D) The consent form that you will use in the study (see part 3 for more information.)
   (E) Certificate of Completion of Human Subjects Protection Training for all personnel involved in the project, including students who are involved with testing or handling data, unless already on file with the IRB. Training link: (http://phrp.nihtraining.com/users/login.php)
   (F) IRB Security of Data Agreement: (http://research.lsu.edu/files/item26774.pdf)

1) Principal Investigator: Dr. Johnny L. Matson   **Rank:** Clinical Director

Dept: Clinical Psychology   **Ph:** (225) 578-8745   **E-mail:** johnmatson@aol.com

2) Co Investigator(s): please include department, rank, phone and e-mail for each
   *If student, please identify and name supervising professor in this space

IRB# E 8292 LSU Proposal #

☑ Complete Application

☑ Human Subjects Training

3) Project Title: Autism in Early Childhood

Study Exempted By:
Dr. Robert C. Mathews, Chairman
Institutional Review Board
Louisiana State University
203 B-1 David Boyd Hall
225-578-8692 | www.lsu.edu/irb
Exemption Expires: 4/30/2016

4) Proposal? (yes or no) no   **If Yes, LSU Proposal Number**

Also, if YES, either ○ This application **completely** matches the scope of work in the grant

OR ○ More IRB Applications will be filed later

5) Subject pool (e.g. Psychology students) | Young children assessed for developmental delay via EarlySteps

*Circle any **"vulnerable populations" to be used:** (children <18; the mentally impaired, pregnant women, the ages, other). Projects with incarcerated persons cannot be exempted.

6) PI Signature [signature]   **Date** 4-19-13   (no per signatures)

** I certify my responses are accurate and complete. If the project scope or design is later changes, I will resubmit for review. I will obtain written approval from the Authorized Representative of all non-LSU institutions in which the study is conducted. I also understand that it is my responsibility to maintain copies of all consent forms at LSU for three years after completion of the study. If I leave LSU before that time the consent forms should be preserved in the Departmental Office.

Screening Committee Action: Exempted ✓   Not Exempted ____   Category/Paragraph 4

Signed Consent Waived?: Yes / No

Reviewer Mathews   **Signature** Rob C Matth   **Date** 5/1/13

VITA

Rachel L. Goldin was born in Boston, Massachusetts, in 1988. She received her Bachelor of Arts degree in psychology from Clark University in 2010. Following completion of her degree, she was employed Massachusetts General Hospital, Boston, Massachusetts, as a research coordinator and assistant in the department of pediatric psychopharmacology. She subsequently enrolled in Louisiana State University's Clinical Psychology Doctoral Program in 2012. Her current clinical and research interests are the assessment and treatment of individuals with Autism Spectrum Disorders and other developmental disabilities, with a particular emphasis on factors influencing the course and presentation of the disorder.