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Symptom profiles and rates of diagnosis in autistic and other atypically developing infants and toddlers

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SYMPTOM PROFILES AND RATES OF DIAGNOSIS IN AUTISTIC AND OTHER
ATYPICALLY DEVELOPING INFANTS AND TODDLERS

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Dedication

I dedicate the completion of this doctoral degree to:

my wife Jenny, the unwavering voice of love and support without who I would

never have had the strength to continue down this path. You enable me to be a

better man.

my parents, Mary Ann and Robert, for fostering an environment of intellectual

curiosity and always teaching me to shoot for the stars. You have

provided uncompromising devotion and encouragement since day one.

my big brother Doug, my first hero in life who taught me that with sheer

willpower and determination anything is possible. I always looked up to

you, and I still do.

Tino LoVullo, my other big brother, who helped me to weather some

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Abstract

Although there are many assessment scales that aid in the diagnosis of Autism Spectrum Disorders (ASD), very few instruments are designed specifically to identify the condition in the population of infants and toddlers. The primary purpose of this study is to systematically examine the differences between scores on the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT)-Part 1 in a sample of at risk atypically developing children. Participants are children enrolled in Louisiana's EarlySteps Program, which provides support services (e.g., speech therapy, occupational therapy, physical therapy, behavior psychology) to infants/toddlers and their families from birth to 36 months of age. All children enrolled in EarlySteps have a medical condition that is likely to result in a developmental delay/atypical development (e.g., premature birth, seizure disorders, Down Syndrome), or are currently diagnosed with developmental delays. Using one-way analysis of variance (ANOVA) and multivariate analysis of variance (MANOVA), three groups (ASD alone, seizure disorder and ASD, and premature and ASD) were compared on BISCUIT-Part 1 total and subscale scores. Implications of these results and directions for future research are discussed.

Introduction

Autism Spectrum Disorders (ASD) are a group of neurodevelopmental conditions characterized by impairments in social functioning, communication deficits, and repetitive or restricted interests or behaviors (American Psychological Association [APA], 2000; Eikeseth, 2009; Matson & Boisjoli, 2007; Matson & Neal, 2009; Matson, Boisjoli, & Wilkins, 2007; Matson, Nebel-Schwalm, & Matson, 2007). Autistic disorder (AD), pervasive developmental disorder-not otherwise specified (PDD-NOS), and Asperger's disorder (AS) are typically thought to represent this spectrum of conditions due to their overlapping diagnostic criteria, as well as, range in the severity of symptoms.

One area that has created a high degree of interest in research is the early detection and diagnosis of ASD (Lord & Luyster, 2006; Matson, Wilkins, & Gonzalez, 2008). Many researchers believe this area to be a hot topic due to the push for early intervention services for children as young as 18 months of age (Ben-Itzchak, Lahat, Burgin, & Zachor, 2008; Matson & Smith, 2008). At present, no biological or genetic testing has been developed to assess ASD (Theoharides, Doyle, Francis, Conti, & Kalogeromitros, 2008). As such, the diagnostic assessment of ASD utilizes pencil and paper measures based on observations of the behavioral definitions of the condition. One such instrument, the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT) is an assessment battery designed to assess symptoms of autism, comorbid psychopathology, and problem behaviors in children under the age of three (Matson, Boisjoli, & Wilkins, 2007).

The BISCUIT has been shown to have excellent psychometric properties (Matson et al., 2009); however, thus far all studies conducted with the BISCUIT compare and contrast samples of children with autism and PDD-NOS to a heterogeneous group of atypically developing

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children (Davis et al., in press; Davis et al., 2010; Matson, Dempsey, & Fodstad, 2009; Matson, Fodstad, & Dempsey, 2009). The group of atypically developing children has commonly been defined in these studies as children whose development of communication, social, motor, and adaptive skills deviate significantly from average children. This group has been used in early BISCUIT studies as a control group (Davis et al., in press; Davis et al., 2010; Matson, Dempsey, & Fodstad, 2009; Matson, Fodstad, & Dempsey, 2009). The current study sought to divide the group of atypically developing children into separate groups of component, homogeneous medical diagnoses in an effort to ascertain the effects these conditions have on BISCUIT scores. All children in this study are enrolled in the EarlySteps program, an early intervention program in the state of Louisiana that provides services to children from birth to three years of age. These children have medical conditions likely to result in a developmental delay/atypical development (e.g., premature birth, seizure disorders, Down Syndrome), or are currently diagnosed with developmental delays.

The primary aim of this study was to examine the impact of the presence of these medical variables on the total and subscale scores of the BISCUIT. Since many of the medical conditions (e.g., premature birth, seizure disorders, Down Syndrome) are commonly found in children, the impact of these variables may be of considerable interest to researchers and clinicians performing early screening and diagnosis of ASD. A secondary goal was examining the number of children in each diagnostic group (e.g., autism, PDD-NOS, premature birth, seizure disorders, Down Syndrome) that exceed the cut-off for having a probable ASD as assessed by the BISCUIT. These data may serve to inform researchers and clinicians regarding the severity of ASD and expected symptom profile for these various medical conditions.

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This document will begin with an overview of the history and development of the diagnoses contained within the category of ASD under investigation in this study. The literature review is comprised mainly of information relevant to ASD since the primary diagnostic groups and assessment instruments used in the study pertain to ASD. The bulk of the review will contain content reflecting the two most prominent ASDs that can be diagnosed in early childhood, autism and PDD-NOS. Information regarding Aspergers Syndrome, Childhood Disintegrative Disorder, and Rett's Syndrome apply to older children or those with clear genetic conditions. As such, these disorders will not be reviewed in the present paper. Next, a discussion of various assessment instruments used to diagnose ASD will be conducted. Later, information about the three medical conditions under investigation (premature birth, seizure disorders/epilepsy, and Down syndrome) will be reported. Lastly, the rationale, methodology, and hypothesized results for the purposed study will be introduced.

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History of Autism Spectrum Disorders

The initial definition of autism stemmed from observations made by Dr. Leo Kanner (Kanner, 1943). Kanner's study contained information on 11 children in his practice that displayed similar patterns of behavior, including: atypical language development and use, social skills deficits and excesses, and insistence on sameness (routines) in their environment. An additional common characteristic linking these children was their apparent ignoring of the world at large, which Kanner referred to as "extreme autistic aloneness" (p. 242). While many changes in diagnostic criteria have occurred, the basic definition of autism has remained constant since the time of Kanner.

Initial reports of language by the parents of the 11 children were similar to those observed by Kanner himself. The children that would go on to receive a label of autistic disorder developed language according to normal milestones, and began memorizing and repeating nursery rhymes, poems, and songs at a very young age (e.g. 2 to 3 years). Despite this normal early language acquisition, once the children approached school age they did not begin asking or answering questions as most children their age did. Kanner hypothesized that the language of these children was being used for a function other than communication (Kanner, 1943). To support this hypothesis, Kanner reported that in addition to delayed speech, the children's language was characterized as literal and inflexible. The children's use of language was also irrelevant at times, with repetition of phrases they had previously heard, however in socially inappropriate ways. Kanner also observed that personal pronouns (e.g., I, you) were also used incorrectly. In addition to the other noted anomalies in language, the children's speech consisted of "quoting," (i.e. echoing,) something previously heard. The children also produced nonfunctional sounds in a repetitive manner. While Kanner noted that most of the children

developed these odd speech patterns, a few of the children in his initial paper failed to acquire verbal communication beyond a few words. Kanner labeled this latter group as mute (Kanner, 1943).

Reports of social skills difficulties were spread throughout Kanner's original account of autism (Kanner, 1943). Parent reports of infancy and early childhood comprised several references to their children's lack of interest in their social environment. Parents described their children as being self-sufficient, largely oblivious to their surroundings, hypnotized, and happiest when left alone. Kanner noted in his 1943 manuscript that upon entering a room, the children often paid no attention to the people in the room and instead went directly to objects. When forced to interact with other people, these children often exhibited behavioral challenges such as tantrums. Kanner stated that the little social interaction that was elicited from the children lacked consistent eye contact and reciprocity. The problem areas of social interaction and language have been consistently highlighted in the literature as key elements of the diagnosis of autism (Sevin et al., 1995).

Lastly, Kanner made detailed mention of the children's insistence on sameness. Most of the children displayed a limited amount of spontaneous activity. Typically, the children played with toys in the same manner. Blocks were often arranged by color or size, and beads were routinely strung in the same order. When these patterns/rituals were interrupted, or routines were changed, some of the children became uncomfortable, anxious, or angry (Kanner, 1943). Additionally, Kanner noted that many of the original 11 children became bothered at the sight of objects/patterns that were either incomplete or broken. Kanner also noted a large degree of anxiety about everyday stimuli in these children. For example, riding a tricycle horrified one child, while mechanical objects frightened another (e.g., mother's eggbeater, frightened another).

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Kanner viewed the combination of language and social deficits, coupled with an insistence on sameness, stereotyped patterns of behavior, echolalia and obsessive behavior, as a disorder that differed from previously documented childhood conditions. At that time, the most closely linked problem area was considered to be childhood schizophrenia; however, Kanner hypothesized that autism was an entirely separate syndrome (Kanner, 1943). Kanner conceded that the combination of echolalia, stereotypy, obsessiveness, and "extreme autistic aloneness" (i.e. focus on self) overlapped with some of the basic characteristics of schizophrenia. However, Kanner believed that the age of onset differentiated the two disorders. Childhood schizophrenia, Kanner noted, typically began after at least two years of seemingly typical development, whereas the children he described exhibited social withdrawal throughout early development. Kanner noted a distinction when he observed that schizophrenia had a low incidence in the families of children with autism as opposed to the high incidence of schizophrenia in the families of children with childhood schizophrenia (Kanner, 1943). In addition, Kanner believed that the children's good rote memory, intelligent parents, and lack of physical deformity were evidence that children with autism were of average, if not above average intelligence, providing further differentiation from what he considered to be more severe forms of psychopathology (Kanner, 1943). Kanner concluded his paper by stating that children with autism were born with an innate inability to develop normal affective contact with other people. This statement led to a long and widely held belief that autism was a form of emotional reactivity.

In 1956, Kanner and Eisenberg further refined the definition of autism. Eisenberg and Kanner (1956) reduced the features of autism to two categories of behavior: 1) extreme aloneness and 2) insistence on sameness. It should be noted that this definition of autism lacked the emphasis on language abnormalities present in Kanner's (1943) original manuscript.

Drawing back to the differentiation Kanner proposed in his initial writings between autism and schizophrenia, Eisenberg and Kanner (1956) included in their new definition of autism an age of onset, stating that autism occurred prior to the age of two.

Kanner is still quoted when talking about the origins of autism and the features that define the condition. While his core description remains today, some refinements in the diagnostic definition have occurred. The following section explores the development of the diagnosis of autism after Kanner's initial account.

Descriptions of Autism Post Kanner

Eisenberg and Kanner provided a streamlined set of symptoms and characteristics for autism (Eisenberg & Kanner, 1956). A plethora of researchers and clinicians have since written on the topic, in an attempt to further refine the definition. The efforts of Creak and Rutter are particularly noteworthy and will be addressed in this section.

More than 20 years after Kanner's original description of infantile autism, Creak (1961) developed a set of criteria for the identification of early childhood psychosis. Creak presented nine characteristics that could be readily observed in children. Creak's nine points were: 1) gross and continuing impairment of emotional relationships, described as aloofness and difficulty playing with peers; 2) age inappropriate lack of awareness of personal identity, including abnormal body posturing, self-injury and personal pronoun confusion in expressive language; 3) pathological preoccupation with certain objects or their characteristics, without regard for the function of the item; 4) resistance to environmental change and effort to maintain or restore sameness; 5) abnormal perceptual experience, marked by excessive or unpredictable response to sensory stimuli, such as insensitivity to pain and temperature; 6) acute or excessive anxiety, usually triggered by changes in the environment; 7) loss of speech or failure to acquire or

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develop language and the occurrence of echolalia or pronoun reversal (using "you" instead of "I" when referring to oneself); 8) distorted pattern of motility, including abnormal gait, unusual body posturing, rocking or spinning; and, 9) history of serious retardation, although some intellectual functions may be normal or exceptional.

While many of his characteristics overlapped with Kanner's, Creak, like other researchers of the era, believed that these behaviors were actually a form of childhood schizophrenia. It should be noted that Creak failed to further operationalize his criteria or indicate how these behavior patterns were related to childhood onset schizophrenia. As a result, Creak's nine features were incorporated into many subsequent descriptions of autism and commonly used autism assessment instruments. For example, the Childhood Autism Rating Scale (CARS; Schopler, Reichler, DeVellis, & Daly, 1980) includes items related to strict adherence to routines and abnormal use of the senses. Additionally, the *DSM*-IV criteria for autism, which will be discussed at length later in this document, incorporated many of Creak's (1963) nine points.

Rutter and Associates' Definition of Autism

Another influential researcher in the early development of the categorization "autism" was Sir Michael Rutter at the University of London. In 1968, focusing on the efforts of Kanner and Creak, Rutter sought to further clarify the definition/classification of autism. Rutter believed that an important step in defining a new disorder was determining whether or not the condition significantly differs from established disorders. As Kanner (1943) pointed out in his original account of autism, an overlap existed between the characteristics of autism and schizophrenia. Additionally, it was valuable to ascertain whether autism was a variant of intellectual disability (ID) or a separate syndrome. Rutter (1968) argued that autism could, in fact, be differentiated from both schizophrenia and ID.

Rutter's 1968 paper thoroughly examined and provided information regarding the differentiation between autism and schizophrenia. In 1911, Bleuler originally used the term "autism" to describe the active withdrawal from social relations into a rich fantasy life (delusions) seen in individuals with schizophrenia (Bleuler, 1950). Rutter felt that this "unfortunate choice of name" (p.139) led to much of the confusion between the two conditions (Rutter, 1978a). Using the current research available at the time, Rutter discerned a number of differences between autism and schizophrenia. First, he cited the higher male-to-female ratio in autism over schizophrenia (Rutter, 1978a). In addition, Rutter speculated, incorrectly, that a higher proportion of children with autism came from parents with high socioeconomic status and above average intelligence (Rutter, 1978a). It was later found that persons of high socioeconomic standing had more resources and were more likely to seek, and pay for services. Rutter also noted that persons with autism lacked evidence of delusions or hallucinations and had relatively poor intellectual functioning overall. Finally, Rutter noted that autism had a stable course as compared to the potential for improvement and relapse in schizophrenia (Rutter, 1978a). Rutter deemed the lack of compelling evidence for an association between the two disorders to mean that autism was a distinct condition, not merely a variant of schizophrenia.

While Kanner had speculated that children with autism had normal intellectual functioning, Rutter called attention to the fact that there was no empirical evidence to support Kanner's claim (Rutter, 1968). Rutter noted that the intellectual functioning of children with autism typically fell at a level below average. Prior to this point, researchers had generally assumed that the features of autism interfered with the ability to perform, thus differentiating autism from ID. However, later research supported Rutter's assertion of lower intellectual functioning.

In 1967, Rutter and Lockyer concluded that half of the children with autism in their sample obtained intellectual quotients (IQ) scores below average on standardized intelligence tests. The IQ scores obtained for that sample were found to be both stable and good predictors of intellectual functioning later in life (Lockyer & Rutter, 1969). Rutter was quick to point out that despite intellectual functioning in the below average range, autism should not be considered another form of ID (Rutter, 1968). He supported his argument by highlighting the fact that not all children with autism had concurrent ID and that the intellectual functioning of one third to one quarter of children with autism in his sample was within the normal range (Rutter & Lockyer, 1967). Finally, Rutter postulated that the low intellectual functioning found in some children with autism may be more a product of language deficits than global intellectual deficits (Rutter, 1968).

In 1978, Rutter stated that autism was a distinct syndrome because the behaviors observed occurred with uniformity across all subjects and were specific to autism. As such, autism could be differentiated from other developmental disorders. Due to the high rates of comorbidity between autism and ID, Rutter believed any definition of autism should incorporate intellectual functioning and developmental level. Thus, Rutter advised that developmental level was essential to understanding the diagnosis of autism (Rutter, 1978). Rutter believed that autism could not be diagnosed solely on the presence of social and language impairments. Rutter (1978) gave the example of a 4-year-old child with a mental age of six months. According to Rutter, autism could only be diagnosed in this hypothetical child if the social and language deficits exhibited were abnormal for the child's mental age and showed the clinical features specific to autism (p.144).

Rutter divided the features of autism into three broad groups. These categories of behaviors were, 1) impaired social relations, 2) delayed and/or abnormal language development, and 3) insistence on sameness (Rutter, 1978b). The social deficits noted by Rutter included lack of attachment and bonding during infancy, failure to anticipate being picked up or held and failure to seek comfort from parents. Lack of eye contact was also considered a prominent feature of the social deficits seen in autism. Rutter noted that the quality of eye contact was important in persons with autism. Based on his research, Rutter stated that children with autism did not use eye gaze in the same fashion as typically developing children or avoid eye contact the same way highly anxious/shy children might (Rutter, 1978b).

Rutter's second category of behavior was abnormal language use. Based on available research at the time, Rutter concluded that children with autism failed to show early prelanguage skills such as waving and social imitation. While many children with autism fail to develop useful speech, those that do, exhibit a number of abnormalities such as echolalia (i.e. repeating words or phrases), rare use of gestures (e.g. lack of pointing), and pronoun reversal (e.g. referring to self in third person). Based on Rutter's definition, speech did not seem to be used as a means of social communication for children with autism. For example, a child with autism may request an item without making eye contact, using polite phrases or appropriate vocal inflection, and without appropriate affect.

The final category of behaviors proposed by Rutter was insistence on sameness. Children with autism often exhibit rigid, inflexible patterns of play. Often times, a child with autism may become attached to an object, although the object's function may be irrelevant. For example, a toy car may be carried around constantly but never played with. Additionally, Rutter noted that routines may be rigidly adhered to, with a marked resistance to modify either routine or the

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appearance of the environment. Rutter also reported that children with autism might develop symptoms similar to obsessions that can take different forms. For example, a child with autism may insist on turning a light switch on and off repeatedly.

While Rutter was able to develop categories of behavior specific to autism, he was unsure whether to include an age of onset in the diagnostic criteria. He cited research pertaining to the differences in etiology, symptomology, and prognosis that exist between disorders with early versus late onset. While many of the disintegrative conditions that begin in late childhood and early adolescence share characteristics with autism, many of the behaviors differ significantly. As a result, Rutter agreed with Kanner on the importance of differentiating autism from the later onset disorders (Rutter, 1978b). Without empirical data to guide the decision, Rutter felt that it was important to have a cutoff before the age of 3 because some of the "disintegrative psychoses" (p.145) began around that age. Thus, in the absence of further data at that time, Rutter adopted the 30-month cutoff recommended by both Eisenberg and Kanner (1956) and The World Health Organization (WHO, 1948).

Rutter's work proved to be influential in developing and refining the definition of autism and its systematic use through the inclusion of his criteria in the Diagnostic and Statistical Manual of Mental Disorders (*DSM*). The following sections contain information reflecting the current *DSM* classification for autism and its related disorders.

Current Definitions of ASD

Autistic Disorder

The current *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision (DSM-IV-TR)* (American Psychiatric Association (APA), 2000) definition of autism emphasizes that the essential features are impaired development of social interaction, communication, and restricted range of interest and activities. The first criterion of the diagnosis is social skills deficits. An individual must exhibit impaired social interaction manifested by at least two of the following behaviors: marked impairment in the use of several nonverbal forms of communication (such as eye contact, facial expression and gaze), failure to establish developmentally appropriate peer relations, lack of spontaneous seeking of shared interests with others, or lack of social or emotional reciprocity (APA, 2000).

The second criterion, qualitative impairment in communication, is endorsed if the individual manifests at least one of the following behaviors: lack of or delay in the development of speech, inability or impairment in initiating or sustaining conversation, stereotyped or repetitive use of language, or lack of imaginative or imitative play. The third criterion, restricted, repetitive, and stereotyped patterns of behavior is endorsed when at least one of the following behaviors is exhibited: preoccupation with one or more stereotyped patterns of interest, inflexible adherence to specific, nonfunctional routines, stereotyped and repetitive motor behaviors, or preoccupation with parts of objects (APA, 2000). In addition to these criteria, the onset of abnormal function must be prior to age three. Finally, the authors of the *DSM-IV-TR* caution that the clinician or researcher should determine whether the symptoms are better accounted for by either Rett's Disorder or Childhood Disintegrative Disorder. By including specific rule out

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diagnoses, the *DSM-IV-TR* forces clinicians, in theory, to give appropriate consideration to other disorders that share similar symptoms.

Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS)

The concept of a separate diagnostic subcategory for individuals who do not meet the criteria for a specific disorder yet evince similar characteristics is seen throughout the *DSM*. Examples include Anxiety Disorder NOS, Cognitive Disorder NOS, Mood Disorder NOS, and Psychotic Disorder NOS (APA, 2000). The same is true within the category of ASD, with the inclusion of PDD-NOS.

The diagnosis of PDD-NOS pertains to children with severe and pervasive impairment in social interaction, deficits in nonverbal communication and/or stereotyped behaviors and interests who do not meet the criteria for a specific PDD (i.e. Autism, AS, Rett's Disorder, CDD), Schizophrenia, Avoidant Personality Disorder or Schizotypal Personality Disorder (APA, 2000). Also included in the category of PDD-NOS is "atypical autism". The term "atypical autism" can be used to refer to children who fail to meet criteria for a diagnosis of autism due to a later age of onset, subthreshold symptomology and/or atypical symptomology (APA, 2000). Largely in clinical practice, the category of PDD-NOS is used as a catch-all for children whose symptom patterns do not meet the criteria for a specific ASD, yet are significantly different than the symptomatology characteristic of autism or another developmental disorder.

Intellectual Disability (ID)

ID, or mental retardation as it is known in the *DSM-IV-TR*, is a condition appearing prior to adulthood characterized by impaired cognitive functioning and adaptive skills. In the *DSM*, a diagnosis of ID is made by meeting three criteria: 1) below average intellectual functioning; 2) significant limitations in adaptive skills; and 3) onset before age 18 (APA, 2000). Determination of significantly impaired cognitive functioning is made through the use of one of many standardized, individually administered intelligence tests (i.e., Standford-Binet, Wechsler Intelligence Scales; APA, 2000). To qualify as having below average intellectual functioning, an individual must have an Intelligence Quotient (IQ) at 70 or below, two standard deviations below the mean.

The second criterion, limitations in adaptive functioning, reflects the inability of an individual to cope with life demands typical of someone of their age, background, and community surroundings (APA, 2000). To meet criteria for impairments in adaptive functioning, limitations in two or more of the following areas must be present: communication, self-care, home living, social/interpersonal skills, use of community resources, self-direction, functional academic skills, work, leisure, health, and safety (APA, 2000). The Vineland Adaptive Behavior Scales (VABS), among other instruments, have been designed to assess the adaptive skills profiles of individuals from birth through adulthood (Sparrow, Balla, & Cicchetti, 1984).

Onset before age 18 is the final criterion for a diagnosis of ID. *DSM-IV-TR* (APA, 2000) states that the age of onset depends on the etiology and level of intellectual impairment. This typically translates that more severe ID tends to be recognized earlier in life than milder levels of ID. In addition, specific genetic syndromes typically result in a diagnosis of intellectual disability

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as early as birth (Greenspan, 1999). One example of these genetic conditions is Fragile X Syndrome.

The *DSM* categorizes four levels of ID that reflect the level of intellectual impairment: 1) Mild ID (IQ 50-55 to 70), 2) Moderate ID (IQ 35-40 to 50-55), 3) Severe ID (IQ 20-25 to 35-40), and 4) Profound ID (IQ below 20-25). According to various reports, Mild ID accounts for approximately 85% of all persons with ID (APA, 2000; Greenspan, 1999). These individuals typically develop a wide range of communication and social skills and are often not easily distinguished from non-disabled individuals. The second level of impairment, Moderate ID, accounts for approximately 10% of all cases of ID. These individuals typically acquire communication skills during childhood. With moderate supervision, they profit from vocational training and attend to their own personal care (APA, 2000). The third level of impairment, Severe ID, accounts for approximately 3% to 4% of all persons with ID. Often these people lack verbal communication in early childhood; however, they may learn to communicate and gain simple self-help skills during later years. Persons with severe ID usually require supervision in most settings (APA, 2000). The most severe level of impairment is Profound ID. Individuals with Profound ID account for only about 1% of all persons with ID. Individuals diagnosed with Profound ID typically have considerable impairment in communication, self-help skills, and sensorimotor functioning (APA, 2000).

Communication Disorders

Communication disorders are a class of conditions that present with difficulty in understanding and/or producing verbal language. Several studies examined differences in children with autism and developmental communication disorders. Many of these studies suggest tenable differences (Bishop & Norbury, 2002, Rutter, 1978c). Bishop and Norbury

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(2002) found that children with specific language impairments tended to be sociable children and did not evince the stereotypic repetitive behaviors seen in autism. Though the differences between ASD and communication disorders are not always clearly defined and may lie on a continuum of impairments, the distinction between these disorders should be based on the whole picture of the child, not based on specific symptoms. Bishop and Norbury (2002) contend that if the three hallmark criteria of impairments are present, a diagnosis of ASD is most likely warranted. At the opposite end of the language spectrum, if odd/idiosyncratic language is present without any impairments in social interaction, a diagnosis of ASD would not be justifiable (Bishop & Norbury, 2002).

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Prevalence of ASD

An issue that has received increasing attention over the past few years is the prevalence of ASD. Researchers agree that the number of people diagnosed with ASD has increased since the time of Kanner. At present, there is a large debate in the literature as to what accounts for this increase. Kanner spoke to the rarity of ASD when he reported that out of the 20,000 emotionally disturbed children he had assessed in his 30 years of practice, he had only seen approximately 150 children with ASD. The issue of rarity and causality was first addressed in an epidemiological study of ASD conducted in the 1966 (Lotter, 1966). Lotter investigated the rates of autism and childhood schizophrenia among children 8 through 10 years old. Lotter found a rate of 2.1/10,000 for autism, as well as, an additional 2.4/10,000 children presented with many of the symptoms of autism but not enough for a formal diagnosis.

Recent Studies

In 1999, Eric Fombonne published a review of 23 epidemiological studies which were conducted across 12 countries, as well as, rural and urban settings. The samples of the studies ranged from 5,120 to 899,750 children, with the median sample size of 73,301 participants. Fombonne (1999) found that overall prevalence rates ranged from 0.7/10,000 to 21.1/10,000, with a median rate of 5.2/10,000. Fombonne (1999) also reported that studies with smaller sample size tended to report larger prevalence rates. Additionally, Fombonne looked at the difference in prevalence rate when studies were divided by time around the median publication year, 1988. The median prevalence rate for the 12 studies prior to 1988 was 4.3/10,000, whereas the median prevalence rate for the 11 studies conducted after 1988 was 7.2/10,000. Fombonne (1999) stated that this comparison indicates an increased prevalence of ASD in the latter decade,

most likely due to the more accurate diagnosis of the disorder and the broader diagnostic conceptualization of autism in *DSM* as opposed to Kanner's original account.

Role of Diagnostic Substitution

In another recent study, Croen, Grether, Hoogstrate and Selvin (2002) examined the prevalence of ASD in the state of California. Croen and colleagues used a sample of all children born from 1987 to 1994 enrolled with the California Department of Developmental Services. The authors identified 5,991 children with a diagnosis of "full syndrome ASD" based on the state's Department of Developmental Services definition of ASD. Diagnoses were provided by a number of disciplines including psychology, neurology, psychiatry, and pediatrics. The authors noted that the diagnoses were typically based on *DSM* criteria (e.g., either *DSM-III-R* or *DSM-IV* depending on the time the child was diagnosed).

Croen et al. (2002) also attempted to assess the impact of diagnostic substitution on the prevalence of ASD by comparing the prevalence of ASD with the prevalence of ID from unknown etiology. Diagnostic substitution is the idea that when one diagnosis becomes more popular, clinicians begin to make the new diagnosis in place of a previous diagnosis. In this case, Croen et al. (2002) were looking to see whether the rate of ID was declining at the same time the rate of ASD was increasing. If this were the case, it could provide support for the argument that clinicians were beginning to diagnose ASD instead of ID in more children.

Croen and colleagues (2002) reported that the overall prevalence of ASD among children born between 1987 and 1994 in California was 11.0/10,000. When birth year cohorts were compared, rates ranged from 5.8/10,000 in 1987 to 14.9/10,000 in 1994, a difference that was statistically significant. This pattern of increase was seen across gender, ethnicity, maternal age and maternal education (Croen et al., 2002). The authors found a 17.6% increase in the rate of

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ASD for the 1987-1990 birth cohorts, followed by a marked increase in prevalence for the 1990-1992 cohorts and then a leveling off for the 1993 and 1994 birth cohorts (Croen et al., 2002).

Sixty-two percent of the children with ASD did not have a diagnosis of ID on their records, and the prevalence of children with ASD but no ID increased from 3.1/10,000 in 1987 to 9.9/10,000 in 1994. Of additional interest, the age at which the children entered the government's service delivery system decreased with each successive birth year (Croen et al., 2002). This earlier entry into services may be the result of either earlier detection of ASD or governmental attempts to increase the public's awareness of available services for children with disabilities.

Most recently, a study published in *Pediatrics* found a parent-reported autism prevalence rate of one in every 91 American children, including one in 58 boys (Kogan, Blumberg, Schieve, Boyle, Perrin, et al., 2009). The most recent ASD prevalence estimate reported by the Centers for Disease Control (CDC) in 2007 was approximately one in 150 (including one in 94 boys). Again this indicates that the rates of ASD are on the rise and present a significant issue to children and families in America.

Prevalence of Autism Associated With Other Pediatric Conditions

Research has demonstrated that many disorders have a well established association with ASD such as fragile X syndrome (Bailey et al., 1999) and tuberous sclerosis (Gillberg, Gillberg, & Ahlsen, 1994; Hunt & Shepard, 1993). While these relationships are well documented in the literature, the amount of research examining autism symptomotology in other commonly occurring conditions is lacking. A goal of this study was to examine the severity of ASD symptoms in a population of infants and toddlers with atypical development. Atypical development is defined as exhibiting behaviors that fall outside of the normal, or expected, range of development. These behaviors emerge in a way or at a pace that is different from other same-aged children. Although not all children reach each milestone at the same time, there is an expected time-frame for reaching these developmental markers.

The children recruited in this study fell into this category of atypical development (for more information, see the Participants section). At present, there are three conditions that are commonly prevalent in the subset of children with ASD: premature birth, seizure disorders/epilepsy, and Down syndrome. These conditions were chosen for inclusion in this study due to their high comorbidity with ASD and the lack of literature on the affect the presence of these diagnoses have on the severity of ASD presentation. What follows is a brief overview for each of these conditions, as well as, the state of the current literature on these disorders in the context of ASD. While other conditions such as ID occur at high rates among children diagnosed with an ASD, it is not included for investigation in this study due to the untenable nature of intelligence scores in the population under investigation (e.g., infants and toddlers). The review of literature will begin with findings related to premature birth, followed by a discussion of seizures, and lastly studies reflecting Down Syndrome.

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Prematurity

In general, to be classified as a premature birth, delivery occurs at less than 37 weeks gestational age (Goldenberg, Culhane, Iams, & Romero, 2008). In the United States, the preterm delivery rate is 12–13% of live births; whereas in Europe and other developed countries, reported rates are generally 5–9% (Slattery & Morrison, 2002; Goldenberg, Culhane, Iams, & Romero, 2008). Although most preterm babies survive, they are at increased risk of neurodevelopmental impairments (Goldenberg, Culhane, Iams, & Romero, 2008).

At present, researchers have consistently identified prematurity and low birth weight as important perinatal risk factors for the development of ASD (Bilder et al., 2009; Larsson et al., 2005; Maimburg & Vaeth, 2006; Schendel & Bhasin, 2008; Wier et al., 2006). A recent large sample size study of adults born at very low gestational age compared with term-born adults described a significant increased risk for ASD, with a relative risk of 7.3 among those born at 28 to 30 weeks gestation, increasing to nearly 10 in those born at 23 to 27 weeks gestational age (Moster, Lie, & Markestad, 2008). These data suggest that the incidence of ASD among survivors of preterm birth is inversely related to gestational age.

Seizure Disorders/Epilepsy

According to Fisher and colleagues (2005) a seizure disorder is described as recurrent, transient symptoms of abnormal excessive or synchronous neuronal activity in the brain. Often, the seizures are accompanied by thrashing movements or a brief loss of awareness (Fisher et al., 2005). Seizures can also manifest as an alteration in mental state, tonic or clonic movements, convulsions, and various other psychic symptoms. Seizures are classified in terms of their origin within the brain as follows: 1) partial, previously known as focal, or 2) generalized. Partial

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seizures only involve a localized part of the brain, whereas generalized seizures involve the whole of both hemispheres (Fisher et al., 2005).

The current available prevalence studies on the presence of seizures in persons with ASD are scarce. Studies that examine this topic are hindered by the use of small sample sizes. Rossi and colleagues (2000) reported on 60 inpatients from 12 to 29 years of age with autism. The authors demonstrated that 38.3% of their ASD group exhibited seizure activity. Rossi et al. (2000) also states that the rates of seizure activity found in their study are much higher than what is reported in the general psychiatric literature (e.g., 7%). Similar findings were also reported by Danielsson, Gillberg, Billstedt, Gillberg, and Olsson (2005) and Saemundson, Ludvigsson, Hilmarsdottir, and Rafusson (2007). Gabis, Pomeroy, and Andriola (2005) and Oslejskova and colleagues (2008) report a co-occurrence of seizures/epilepsy and ASD at 40%.

Down Syndrome

Trisomy 21, also known as, Down syndrome is a genetic condition characterized by having three copies of human chromosome 21. It is one of the most commonly diagnosed genetic conditions. In 2006, the Centers for Disease Control and Prevention estimated the rate as one per 733 live births in the United States (5,429 new cases per year) (CDC, 2006). Down syndrome is associated with several physical and neurological abnormalities. These abnormalities can vary from person to person and may include: ID, decelerated growth, flat hypoplastic face with short nose, prominent epicanthic skin folds, small low-set ears with prominent antihelix, fissured and thickened tongue, laxness of joint ligaments, pelvic dysplasia, broad hands and feet, stubby fingers, transverse palmar crease, lenticular opacities, and heart disease (Cronk et al., 1988; Roberts, Price, & Malkin, 2007; Roizen & Patterson, 2003; Rubin et al., 1998).

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Currently, literature linking autism and Down Syndrome is limited. Large population-based studies of Down syndrome have reported autistic disorder in 1% to 2%, which was based on medical record reviews for psychiatric disorders (Reilly, 2009). Rates of 3.3% to 11.0% have been reported in smaller clinical or convenience samples evaluated using clinical diagnostic criteria for autistic disorder (Reilly, 2009). Two population-based studies have screened children with Down syndrome for ASD. Kent and colleagues (1999) found ASD in 12.1% of 33 children who completed testing. They estimated population prevalence of ASD and autistic disorder to be 7% and 1.7%, respectively. Another study conducted by Lowenthal and associates (2007) reported ASD in 15.6% of children with Down syndrome.

Assessment of ASD in Infants and Toddlers

With the literature about the various ASDs on the rise, many seek to develop and refine screeners and diagnostic tools to assess the core symptoms of ASD. This section focuses on measures specific to ASD that assist in screening for symptoms and for diagnostic decision making. Measures included in this section are rating scales, parent reports, and structured interviews designed for use in the population of infants and toddlers. Assessment measures and screeners that focus on older age groups/populations or are observational in nature are beyond the scope of this paper and will not be reported.

Checklist for Autism in Toddlers (CHAT)

The primary purpose of the CHAT is to serve as an autism screener. The CHAT was created to assess children at 18 months of age who exhibit deficits in joint attention and pretend play (Baron-Cohen, et al., 2000). A positive result on the CHAT may indicate a risk for a diagnosis of ASD later in the child's life. The CHAT is designed to be used in conjunction with a comprehensive diagnostic evaluation. The measure takes approximately 5-10 minutes to administer and is given to the primary caregiver of the child by primary health care workers or clinicians. The CHAT is comprised of two sections: 1) key questions related to joint attention and pretend play, and 2) observational items. Five items from section one are key items and the remainder are used to assist the clinician in differentiating autism from other general developmental delays (Baron-Cohen, et al., 2000). A failure on all of the five key items in section one indicates a high probability risk for autism; however, Baron-Cohen et al. (2000) state that children can be at "medium" risk for autism if they fail both items containing content reflecting a deficit in proto-declarative pointing. Section two is comprised of observational items that are directly filled out by a clinician or healthcare professional. The authors make a

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recommendation to administer the CHAT twice in order to determine if the failed items remain failed for both administrations (Baron-Cohen, et al., 2000).

The predictive validity of the CHAT was demonstrated by assessing 91, 18 month old toddlers (Baron-Cohen, et al., 2000). In this study, 4 of the 91 children failed all five key item questions. These four children were all reassessed at 34 months of age and diagnosed with autism (Baron-Cohen, et al., 2000). In addition, 16,235 children, 18 month olds were assessed with the CHAT with 38 failing the key items. At a one month follow-up, 12 of these 38 again failed all five items. A reassessment at 42 months revealed that 10 of the 12 who failed all five keys items on both administrations of the CHAT had a diagnosis of ASD (Baron-Cohen, et al., 2000). Thus, support for the temporal stability and predictive validity of the measure was demonstrated. The sensitivity of the *CHAT* was found to be 18%, specificity was 100%, PPP was 75%, and NPP was 99.7% (for autism). However, for all ASDs, the sensitivity was 21.3%, specificity was 99.9% and PPV 58.8% (Baron-Cohen, et al., 2000).

Modified Checklist for Autism in Toddlers (M-CHAT)

In 2001, an update to the CHAT was published that featured significant modifications. The M-CHAT is a 23 item, parent report measure that is used as a screener during pediatric visits. The measure relies solely on parental reports of skills and behaviors exhibited by their child to help with the identification of early signs of autism. Early signs of autism were defined by the authors as symptoms of ASD occurring at the approximate age of 24 months (Robins, Fein, Barton, & Green, 2001). Item content for the M-CHAT was broadened to identify an expanded number of symptoms of ASD. M-CHAT items were derived from the original CHAT item pool in addition to findings from home videos, clinical experience, instruments used for older children, and hypotheses from the available literature on ASD at the time (Robins, Fein,

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Barton, & Green, 2001). Respondents are asked to answer each question "Yes" or "No" based on how their child typically functions.

Robins et al. (2001) presented the psychometric properties of the M-CHAT. Of the 26 items on the scale, six items were found to best discriminate between those children with and without an ASD (i.e., critical items). Internal reliability was .85 for the entire scale and .83 for critical items. A discriminant function analysis classified 33 of 38 toddlers correctly as having an ASD and 1188 of 1196 without an ASD. Based on this data, the sensitivity and specificity were calculated as .87 and .99, respectively. In addition, Positive Predictive Power was found to be .8 with the Negative Predictive Power being .99. In order to have a positive screen on the M-CHAT, a child must fail three or more total items or two or more critical items. Using this algorithm, the sensitivity of the measure increased from the abovementioned value, ranging from .87-.97. The authors note that the M-CHAT was designed as a screener to be used in primary healthcare settings. As such, additional measures must be given to corroborate the diagnosis of ASD.

Childhood Autism Rating Scale (CARS)

The CARS is a behavior rating scale comprised of 15 items: relating to people, imitation, emotional response, body use, object use, adaptation to change, visual response, listening response, taste, smell, and touch response and use, fear or nervousness, verbal communication, nonverbal communication, activity level, level and consistency of intellectual response, and general impressions (Schopler et al., 1980). Each item on this scale can be scored: 1 (within normal limits for a child that age), 2 (mildly abnormal), 3 (moderately abnormal), or 4 (severely abnormal) and are all item scores are summed to yield a total score (Schopler et al., 1980). Midpoints between these values can be used when the respondent believes that the behaviors fall

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between two of the aforementioned values. Respondents are asked to score items by comparing the child's behavior to that of a typically developing child. The total CARS scores can fall into the three classifications: 1) non autistic range (below 30), 2) mild to moderate autistic range (score between 30 and 36.5), and 3) moderate to severe autistic range (score between 37 and 60).

Thus far, the psychometric studies for the CARS have yielded promising results. Initial psychometric properties of the CARS were determined using 537 children enrolled in the TEACCH program over a 10-year period (Schopler et al., 1980). Fifty-one percent of the children studied scored above the cutoff score of 30. Internal consistency of the CARS has been described as high, with a coefficient alpha of .94 (Schopler et al., 1988), indicating the degree to which all of the 15-scale scores constituted a single construct rather than several individual behaviors. Interrater reliability was established using two raters for 280 cases. The average reliability of .71 indicated good overall agreement between raters (Schopler et al., 1988). Twelve-month test-retest data was also collected. Criterion-related validity was determined by comparing CARS diagnoses to diagnoses made independently by child psychologists and psychiatrists. Diagnoses correlated at $r = .80$, which indicated that the CARS diagnosis was in agreement with clinical judgments (Schopler et al., 1988). The CARS has also been shown to have 100% predictive accuracy when distinguishing between groups of autistic and mentally retarded children, which was superior to the ABC and Diagnostic Checklist (Teal & Wiebe, 1986).

The validity of the CARS under different settings has also been researched (Schopler et al., 1988). CARS scores of 41 children taken through parent interview were compared to scores derived from direct observation. Schopler et al. (1988) found that mean scores under the two conditions were not significantly different and the correlation of $r = .83$ further indicated good

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agreement. In addition, diagnoses based on parent interview and direct observation agreed in 90% of the cases. The authors suggested that valid CARS ratings and diagnoses could be achieved through parent interview (Schopler et al., 1988).

Autism Diagnostic Interview (ADI)

The ADI is a standardized structured interview designed to be administered to a primary caregiver, for those individuals ages five through early adulthood, who also have a mental age of at least two years (Le Couteur et al., 1989). The ADI focuses on the three core deficits found in ASD (e.g., social interaction, communication and language, repetitive behaviors and restricted interests) as well as the age of symptom onset (Le Couteur et al., 1989). This measure assesses a child's behavior related to the abovementioned areas during the first 5 years of life, and during the 12-month time period prior to the ADI administration. Each item of the ADI contains the following: an initial probe, codes with instructions regarding the detail of information required, and supplemental probes. The interviewer must obtain details of the behaviors specific to each item. As such, interviewers must be highly trained and familiar with the symptoms of ASD. Each item in this measure can be scored as a 0 (behavior was not present), 1 (behavior was exhibited, but not severe or frequent enough to warrant a rating of 2), 2 (abnormality is present), 3 (abnormality is present and more severe than a 2), or 7 (some abnormality is present, but not as specified in the coding instructions). The ADI takes approximately 2 to 3 hours to complete.

During ADI development, a scoring algorithm was created based off ICD-10 (WHO, 1992) diagnostic criteria (Le Couteur et al., 1989). As such, not all items comprising the ADI are loaded into the algorithm (i.e., only 14 items from the social interaction area, 12 from the language/communication area, and 6 from the restricted interests and repetitive behavior factor into the algorithm). Deficits related to one of the abovementioned areas need to be present prior

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to age 36 months, with at least a score of 10, 8, and 4, on the socialization, verbal communication, and restricted and repetitive interests domains respectively.

Psychometric properties of the ADI were reported by Le Couteur et al. (1989). Internal consistency statistics were computed for all items within each of the three core ASD deficit content areas. For items comprising the social interaction content area, K = .66-.97. For items comprising the communication/language, restricted interests/repetitive behaviors, and age of onset content areas, K = .64 - .87, .55 -. 92, and .76 - .90, respectively. In addition, Intraclass Correlation Coefficients were above .93 for the socialization, communication, and restricted interests/repetitive behaviors content areas.

Diagnostic validity was assessed by comparing the children in the autism group with those in the ID group in each of the three ADI categories. The ADI was able to differentiate between autism and ID across all items in the three areas except for one (unusual attachment to objects). In addition, all 16 children in the autism group met the ADI's algorithm requirements for a diagnosis of autism, as opposed to none of the children in the ID group (Le Couteur et al., 1989).

Autism Diagnostic Interview-Revised (ADI-R)

The ADI-R is a semi-structured interview administered to a parent or guardian by a trained interviewer (Lord, Rutter, & Le Couteur, 1994). This scale is a modified version of the ADI, assessing symptoms of autism prior to five years of age. Some items from the ADI were retained while new items were added to allow for better differentiation between those with autism and those with ID (Lord, Rutter, & Le Couteur, 1994). Items that are asked during the interview focus on observable and reportable behaviors and rely on the interviewer's judgment for coding. The coding for the ADI-R is consistent with the coding procedures for the ADI. Items

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relating to typical development or deficits in these skills are coded for abnormality during the ages of 4 to 5. There are a total of 93 items which span four content areas: 1 (impairments in social interaction), 2 (impairments in communication, either verbal or nonverbal), 3 (restricted and repetitive interests or behaviors), or 4 (age of onset by 36 months of age). Of the 93 items, a total of 37 are included in the diagnostic algorithm, which aligns with the *DSM-IV* (APA, 1994) and ICD-10 (WHO, 1992). In order to meet criteria for autistic disorder an individual must meet or exceed cutoff scores across all 4 domains. Cutoffs for the content areas are as follows: social impairment = 10, restricted and repetitive interests or behaviors = 3 and age of onset = 1. For the communication content area, there are separate cutoffs for verbal and nonverbal participants, which are 8 and 7 respectively.

Using the abovementioned cutoffs, sensitivity and specificity exceeded .90. Initial psychometric analyses by Lord et al. (1994) indicated that the K_W = .64 - .89 for social interaction, .69 - .89 for communication, and .63 - .86 for restricted and repetitive behaviors. Furthermore, inter-rater and test retest reliability were good (K_W ranging from .62 to .89). In addition, social, restricted and repetitive behaviors, and communication content areas of the ADI-R had internal consistencies of α = .95 (social), .69 (restricted and repetitive behaviors), and .84 (communication). Psychometric studies conducted by independent researchers have yielded lower reliability estimates for the ADI-R (Lecavalier et al., 2006). More recently, Charman et al., (2005) showed that the ADI-R at age 2 did not accurately predict a diagnosis of autism at age 7, but assessment with the ADI-R at age 3 did. Also, the utility of the ADI-R total algorithm for distinguishing between autism and other developmental disabilities has been tested with sensitivity estimates ranging from .86 to 1.00 and specificity estimates ranging from .75 to .96 (Lord et al., 1997).

Concluding Comments on Assessment of ASD

As the reader will note, there is a wide variety of scales one could use in the assessment of ASD. While these scales have years of psychometric research behind them, many flaws are apparent. Some of the measures are aimed to be administered in a primary care setting (e.g., CHAT and M-CHAT). Other instruments require a high degree of training and time to administer (e.g., ADI and ADI-R). A newer assessment scale specific to examining the symptoms of ASD in a population of at risk infants and toddlers has been developed to address many of these documented shortcomings. This scale and its psychometric properties will be presented in the *Measures* section of this paper.

Purpose and Rationale

The purpose of the present study was to examine the differences between scores on the BISCUIT Part 1 for children diagnosed with ASD and co-occurring medical conditions such as seizure disorders or premature birth. The primary goal of the study was to examine whether the presence of various medical conditions have an effect on BISCUIT scores in an attempt to identify any possible symptom differences between these groups. As presented in preceding sections of this paper, it is highly likely that clinicians and assessors will be asked to evaluate a heterogeneous group of children suspected of having ASD. Many of these conditions co-occur at high rates alongside ASD and are likely to be the cause of atypical development or developmental delays. Some of these conditions include prematurity and seizure disorders/epilepsy. Given the importance of early identification and the limited number of instruments that accurately assess ASD in infants and toddlers, it is necessary to establish whether the presence of commonly occurring medical conditions result in different scores on the BISCUIT. This paper serves as an investigative study that may have important implications for the assessments of at risk infants and toddlers. The information obtained may be useful to researchers and clinicians who aim to further clarify the diagnostic issues in ASD.

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Method

Participants

Data used in this study came from a database originally created to quantify the psychometric properties of the BISUIT. The participants in this study were infants and toddlers enrolled in Louisiana's EarlySteps Program. EarlySteps is Louisiana's Early Intervention System under the Individuals with Disabilities Education Act, Part C, which provides services to infants and toddlers and their families from birth to 36 months. Children qualify if they have a medical condition likely to result in a developmental delay, or have developmental delays. No participant was excluded based on age, gender, or ethnicity.

Originally, it was proposed to place participants in the following groups: autism only, PDD-NOS only, premature and autism, seizure disorder/epilepsy and autism, and Down Syndrome and autism. An a priori power analysis was conducted in order to determine the sample size required for the original proposed design using the statistical program, G*Power 3 (Faul, Erdfelder, Lang, & Buchner, 2007). For the power analyses, the alpha level was set at .05 with a power of .80. Additionally, a medium effect size was used for this study as this has been determined to be the largest effect size appropriate for studies in the behavioral sciences (Cohen, 1988).

Using the criteria listed above, the total sample size needed to determine significant differences for the omnibus analysis of variance (ANOVA) using BISCUIT-Part 1 total score was 200 children. For the follow-up multivariate analysis of variance (MANOVA) testing specific BISCUIT-Part 1 subscales, a sample size of 150 participants was required. Taken together, a minimum of 200 participants was necessary to complete data analysis on the initial proposed design. This meant that a minimum of 20 participants were needed in each group so

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that it would be possible to conduct the aforementioned statistical analyses. In the most recent iteration of the aforementioned BISCUIT database, a total of 2279 children were available to be included in the study. Only six children were identified as having Down Syndrome with a co-occurring ASD (n=3 with Autistic Disorder, n=3 with PDD-NOS). As such, the originally proposed group design did not meet the minimum sample size criteria set forth by the power analysis and thus would have lacked significant statistical power. Due to this development, an alternative method of data analysis was conducted and will be described below.

Participants were placed into one of three groups: ASD alone (which included children with either autism or PDD-NOS), premature and ASD, and seizure disorder and ASD. Children with ASD and Down Syndrome were removed from consideration due to lack of sample size. The autism and PDD-NOS groups were collapsed across all conditions as the principle hypothesis under investigation is whether or not the presence of medical diagnoses effect the range and severity of ASD symptoms. Again, an a priori power analysis was conducted in order to determine the sample size required for these new groups using G*Power 3. The alpha and power levels were the same as the original proposal, .05 and .80 respectively. In addition, a medium effect size was used to complete the analysis.

Employing these values, the total sample size needed to determine significant differences for the omnibus ANOVA using BISCUIT-Part 1 total score was 159 children. For the follow-up MANOVA testing specific BISCUIT-Part 1 subscales, a sample size of 48 participants is required. Taken together, a minimum of 159 participants was necessary to complete data analysis on the new grouping design. This translates into 53 participants per group.

For this study, diagnoses for the participants were made by a licensed doctoral level psychologist who has over 30 years of experience in the field of developmental disabilities. This

person was blind to BISCUIT scores (see below for description of measures). Using clinical judgment, diagnoses were made based on the *DSM-IV-TR* criteria for autism and for PDD-NOS (American Psychiatric Association [APA], 2000), M-CHAT scores, and developmental profile scores from the Battelle Developmental Inventory-2nd Edition (BDI-2; Newborg, 2005). Similar methodology used to arrive at a Pervasive Developmental Disorder diagnosis has been described in the literature (e.g., Fombonne et al., 2004).

At this time of this writing, a total of 2279 children were evaluated for possible inclusion in the study. Of the 2279 children, 673 children were classified as having an ASD (autism or PDD-NOS). In an effort to obtain the most pure representations of each group, children were eliminated if there was a presence of other genetic/medical conditions including Klinefelter Syndrome, Fragile X Syndrome, or Down Syndrome. Of the 673 children with ASD, 19 were eliminated for having the aforementioned medical diagnoses. The remaining 654 children were assigned to groups as follows: ASD alone (n=608), seizure and ASD (n=26), and premature and ASD (n=20). Due to restrictions on between groups data analyses with unequal sample sizes, a random selection of the 608 children with ASD was conducted to limit the number of children in the group to 30. This step was taken to ensure the orthogonal nature of the design (e.g., tests of main effects and interactions are independent). Tabachnick and Fidell (2007) states that a problem arises in univariate and multivariate designs that have unequal sample sizes. It would be unclear if the marginal means used in the computation of the test statistic (ANOVA or MANOVA) would be due to the mean of the means or the marginal mean of the scores (Tabachnick & Fidell, 2007). As such, it is recommended that researchers take care to ensure relatively equal sample sizes. In light of this information, it was decided to randomly select cases from the larger ASD group until a sample size of 30 was obtained.

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Measures

Baby and Infant Screen for Children with aUtisIc Traits-Part1 (BISCUIT-Part1)

The BISCUIT-Part1 is a 62 item informant-based measure that was designed to assess symptoms of AD and PDD-NOS in infants and toddlers ages 17 to 37 months (Matson, Boisjoli, Wilkins, 2007). Items comprising the BISCUIT-Part1 were obtained from a review of research literature, the *DSM-IV-TR* (APA, 2000), the ICD-10 (WHO, 1992), and a clinical psychologist with expertise with this population. Items are read to the parent or caregiver aloud and they are instructed to rate each item by comparing the child to other children his/her age with the following ratings: 0 (not different; no impairment), 1 (somewhat different; mild impairment), or 2 (very different; severe impairment). An exploratory factor analysis of the items yielded a three factor solution; socialization/nonverbal communication, repetitive behavior/restricted interests, and communication (Matson, Boisjoli, Hess, & Wilkins, in press). The internal consistency of these factors was .93, .91, and .82, respectively. The BISCUIT-Part1 had an internal consistency coefficient of .97 (Matson, Wilkins, et al., 2009). Cutoff scores were determined to differentiate between Autistic Disorder, PDD-NOS, and no ASD (n = 1007; Matson et al. in press). A score of 17 had the best trade-off between sensitivity and specificity and was chosen as the cutoff for nonASD and probable ASD/PDD-NOS. A score of 39 was selected to differentiate between autism and PDD-NOS. Overall, the sensitivity and specificity of the BISCUIT-Part1 was found to be 93.4% and 86.6%, respectively, with an overall correct classification of 88.8%.

In addition, psychometric analyses were conducted to examine the convergent and divergent validity (with the M-CHAT, Charman et al; Robins et al., 2001 and the Battelle Developmental Inventory-Second Edition (*BDI-2*; Newborg, 2005). The BISCUIT-Part1 converged with the M-CHAT (*r* = .80) and with the person-social domain of the BDI-2 (*r* = -

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.50). Divergence between the BISCUIT-Part1 and the adaptive domain from the *BDI-2* was demonstrated (r = -.19) (Matson, Wilkins, & Fodstad, in press).

Demographic Form

In addition to the administration of the BISCUIT-Part 1, parents of the participants were asked to complete a demographic form. This form contained information including: age, ethnicity, as well as, the presence of medical diagnoses. The presence of medical diagnoses (premature and seizure disorder/epilepsy) were used for group assignment.

Procedures

Prior to initiation of the study, Institutional Review Board (IRB) approval was obtained from Louisiana State University and Louisiana's Office for Citizens with Developmental Disabilities (OCDD), the organization that oversees the EarlySteps program. A one-on-one parent assessment and child observations were conducted by qualified personnel certified to conduct assessments and provide services for the State of Louisiana's EarlySteps program. The assessors were certified or licensed in disciplines such as occupational therapy, physical therapy, social work, speech-language pathology, or psychology. The degrees held ranged from bachelor to doctoral level. All of the administrators attended a full day workshop, which included specific information on ASD, scale development, and test administration issues specific to the measures used for this study. The BISCUIT-Part 1 and demographic form were given as part of a larger battery of assessments, which included measures of physical and social development. Test administration for each child took place in his/her home or daycare setting where the assessors interviewed the child's primary caregiver according to the instructions of each test. Only parents who agreed to their child's participation in the study gave informed consent and their data was included in the analysis.

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Analyses

A one-way ANOVA was conducted using diagnostic group (ASD alone, seizure disorder and ASD, and premature and ASD) as the independent variable and total score on the BISCUIT-Part 1 as the dependent variable. In addition, a MANOVA was conducted with diagnostic group (ASD alone, seizure disorder and ASD, and premature and ASD) serving as the independent variable and BISCUIT-Part 1 subscale scores (socialization/nonverbal communication, repetitive behavior/restricted interests, and communication) as the dependent variable. Finally, an item-analysis using a logistic regression was completed in order to determine which specific items differed across diagnostic group (ASD alone, seizure disorder and ASD, and premature and ASD).

Hypothesized Results

Based on existing literature, several predictions can be made regarding the outcome of this study. First, it was hypothesized that children assigned to the various medical condition groups (seizure disorder and ASD; and premature and ASD) would differ significantly on the total scores for the BISCUIT-Part 1 compared to the ASD alone control group. Further, it was postulated that children in these medical groups would differ significantly from the ASD alone group on the BISCUIT-Part 1 subscale scores. Finally, it was hypothesized that specific patterns of responding will emerge between the various groups (e.g., specific BISCUIT-Part 1 items would be differentially endorsed across groups). These hypotheses are based on the research outlined previously indicating that a higher percentage of individuals with ASD and a co-occurring diagnosis of seizure activity and premature birth demonstrate more severe symptoms of ASD.

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Results

All data analyses were conducted using SPSS 16.0. Prior to the completion of analyses, data were examined for missing values, outliers, and consistency with the assumptions of analysis of variance (ANOVA) and multivariate analysis of variance (MANOVA). The pattern of missing data was analyzed using the MVA (Missing Values Analysis) function. Data were assessed to determine if missingness on certain variables was specifically related to other variables. MVA determined that 5.9% of all items across all participants were missing. Separate variance t-tests showed no systematic relationship between missing BISCUIT item values for all combinations of binary pairings of BISCUIT item scores ($p < .05$). While there are no firm guidelines for how much missing data can be tolerated for a sample of a given size, Tabachnick and Fidell (2007) provide a loose rule of approximately 5% missing data being acceptable. Due to the MVA function indicating that missing data did not occur on a systematic basis, it was decided that no participant would be removed based on missing values alone. In an effort to estimate the missing values, mean substitution was used. This process occurred by means being calculated from the available data and used to replace missing values prior to completing the investigative data analysis. In the absence of other diagnostic information (e.g., direct observations conducted by this writer), the mean for each item is the best guess about the value of a variable. This method was chosen due to its conservative nature (e.g., the mean for the entire distribution of scores does not change and the researcher is not required to guess at missing values). The remainder of data screening procedures were completed by analyzing each BISCUIT item score, total score, and subscale score separately across groups (ASD alone, seizure and ASD, and premature and ASD). No univariate or multivariate outliers were discovered using this process.

Demographic variables were analyzed to ensure that the groups under investigation did not differ significantly. First, the mean ages of the participants were analyzed using one-way analysis of variance (ANOVA) to make certain that there are no significant differences between groups on mean age. Then, the prevalence of all other demographic variables (e.g., gender, ethnicity) were analyzed via Chi-square analysis to ensure that there are no significant differences between groups. Table 1 presents the results of this demographic variable analysis. No significant differences were found with respect to age. Chi-square analysis determined that children in the premature and ASD group differed significantly in terms of gender breakdown as compared to both the ASD alone and seizure and ASD groups. This could be accounted for by the relatively smaller sample size of the premature and ASD group as compared to the two other groups. No differences were noted with respect to ethnicity across all three groups using the chi-square analysis.

Table 1 – Demographic Characteristics of Children in Analysis

	ASD Alone (N=30)	Seizure and ASD (N=26)	Premature and ASD (N=20)
Mean Age (months)	25.80	25.85	23.50
Age Minimum-Maximum (months)	15 - 35	18-34	12-33
Gender			
Male	21 (70.0%)	16 (61.5%)	11 (55.0%)
Female	9 (30.0%)	10 (38.5%)	9 (45.0%)
Ethnicity			
Causasian	16 (53.3%)	12 (46.2%)	10 (50.0%)
African American	12 (40.0%)	9 (34.6%)	9 (45.0%)
Hispanic	1 (3.3%)	3 (11.5%)	0 (0.0%)
Other	1 (3.3%)	2 (7.7%)	1 (5.0%)

An ANOVA was conducted to determine whether diagnostic groups (ASD alone, seizure and ASD, and premature and ASD) varied significantly with respect to their average total scores

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on the BISCUIT-Part 1. The ANOVA indicated that BISCUIT total scores were not significantly different between the three diagnostic groups ($F_{2,74} = 0.360$, $p > .05$). In addition, a MANOVA was conducted to evaluate whether the diagnostic groups (ASD alone, seizure and ASD, and premature and ASD) differed on the three subscale scores of the BISCUIT-Part 1. Wilks' Lambda did not reveal a significant effect for diagnostic group with respect to each BISCUIT-Part 1 subscale score ($F_{6,130} = 0.760$, $p > .05$). Mean BISCUIT total and subscale scores are presented in Tables 2 and 3.

Table 2 – Mean Group Differences for BISCUIT Total Scores

	ASD Alone (N=30)	Seizure and ASD (N=26)	Premature and ASD (N=20)
BISCUIT Total Score	44.93 (21.59)	44.42 (26.52)	39.60 (20.21)

* Standard Deviations presented in parentheses
**Higher values indicate more impairment

Table 3 – Mean Group Differences for BISCUIT Subscale Scores

BISCUIT Subscale	ASD Alone (N=30)	Seizure and ASD (N=26)	Premature and ASD (N=20)
Socialization/Nonverbal Communication	15.50 (8.95)	17.04 (10.37)	14.42 (9.38)
Repetitive Behavior/Restricted Interests	17.93 (12.38)	14.74 (10.00)	17.21 (12.14)
Communication	11.25 (2.53)	11.43 (3.29)	11.11 (3.05)

* Standard Deviations presented in parentheses
**Higher values indicate more impairment

While differences were not observed across diagnostic groups at the total or subscale score level, an item analysis was conducted to determine if any specific symptoms assessed on the BISCUIT-Part 1 could accurately predict diagnostic group membership. A multinomial regression was performed with all BISCUIT-Part 1 items serving as predictor variables, and the diagnostic group as the outcome variable. Mulitnomial regression was conducted using these

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items as the full model. The full model as compared to the constant only model was statistically

significant, X^2 (62, N = 74) = 149.81, *p<.05* indicating that the model increased the accuracy in

distinguishing between infants who have ASD alone versus those with a co-occurring seizure

disorder or premature birth. Multinomial regression yielded 6 items of the BISCUIT-Part 1 that

significantly contributed to the predictor model for diagnostic group membership. A summary of

the 6 significant BISCUIT items with mean item scores per diagnostic group are presented in

Table 4. In order to determine the strength of the association between

Table 4 - Item Analysis Results – Mean Item Scores

BISCUIT ITEM DESCRIPTION	ASD Alone (N=30)	Seizure and ASD (N=26)	Premature and ASD (N=20)
3) Age appropriate self-help adaptive skills	1.13 (.547)	1.58 (.643)	1.75 (.550)
7) Ability to recognize the emotions of others	.633 (.809)	1.15 (.732)	.650 (.875)
21) Able to understand subtle cues or gestures of others	.533 (.776)	1.12 (.816)	.350 (.671)
23) Body posture and/or gestures	.467 (.776)	1.04 (.916)	.450 (.759)
45) Make-believe or pretend play	1.07 (.842)	1.31 (.788)	.650 (.813)
61) Isolates self	.966 (.759)	.654 (.846)	.500 (.688)

* Standard Deviations presented in parentheses
**Higher values indicate more impairment

the predictor model and group membership, the Cox and Snell test statistic was computed,

yielding a value of 0.886, suggesting substantial predictor model strength. In inspecting the

distribution of scores for each item, varying patterns emerge between groups. For example,

across items 7, 21, 23, and 45 the seizure and ASD group evinced more impairment as compared

to the ASD alone and premature and ASD groups. Item 3 (age appropriate self-help and

adaptive skills) was more problematic for children in the premature and ASD group as compared

to the ASD only and seizure and ASD groups. Lastly, children with ASD alone scored high than

the other groups on item 61 (isolates self).

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Discussion

In this study, the degree to which having an additional medical diagnosis effects the symptom presentation of ASD in infants and toddlers was evaluated using ANOVA, MANOVA, and multinomial regression. The omnibus level predictions that the presence of a seizure disorder or premature birth status would have a significant effect on overall ASD symptomotology as measured by the BISCUIT-Part 1 was not supported. ANOVA and MANOVA failed to uncover significant differences between these groups on the BISCUIT-Part 1 as a whole and at the subscale level. One potential contributing factor to the lack of significant results is the possibility that the ASD diagnosis present across all three groups accounted for the majority of the variance in the symptom presentation. It is not a stretch to postulate that the children recruited into this study have similar symptom profiles mainly due to their presence on the autism spectrum as opposed to co-occurring general medical conditions.

For the regression analysis, six items on the BISCUIT-Part 1 were able to predict group membership at a level better than chance. The most common pattern contained within these items showed that children in the seizure disorder group typically experienced a higher level of symptom impairment as compared to children in the other two groups for four of the six identified items. However, the magnitude of the relationships on these items was not evaluated due to sample size concerns (see below).

While studies evaluating the autism symptoms of older children and adults have found significant differences in ASD symptoms as a function of the degree of prematurity and amount of seizure activity (Bilder et al., 2009; Larsson et al., 2005; Maimburg & Vaeth, 2006; Saemundson, Ludvigsson, Hilmarsdottir, & Rafusson, 2007; Schendel & Bhasin, 2008; Wier et al., 2006), this type of data was not available for the sample under investigation at the time of

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this study. It is possible that there is untapped within group variances (i.e., children with a low amount of seizure activity versus children with a high amount of seizure activity) that is not being measured by the current study. Future research in this area could look to conduct analyses in which both the presence of a medical condition and the degree severity of those conditions are evaluated with respect to ASD symptoms.

While discussing the implications of the findings, it is important to note some limitations of the current study. First, all of the participants in the study were obtained from an early intervention program designed to help children who have incurred some sort of developmental delay/disorder. It is possible that infants and toddlers with milder difficulties who would not have been identified to receive services through the EarlySteps program would have presented with different behavioral phenotypes for both co-occurring medical condition, as well as, ASD symptoms. Second, this study is a cross-sectional in nature. As such, it is unknown whether a co-occurring medical condition can lead to increased severity of ASD symptoms in the future. Additional prospective longitudinal research is needed to ascertain that information.

One looming limitation occurs at the level of statistical analysis present in the study. The amount of children available for inclusion in the study deviated from the sought after sample sizes derived from the a priori power analysis. This could have several far reaching effects into why the ANOVA and MANOVA did not yielded statistically significant results. All other considerations being equal, effects are more difficult to detect in smaller samples as opposed to larger samples. It is possible that with an increased sample size, the statistical power of the ANOVA and MANOVA would have been increased to an optimum level where differences between groups would be more likely to be detected. That being said, future studies could seek to replicate these findings with larger sample sizes of infants and toddlers.

Finally, determining the potential mechanism of action between various medical diagnoses and ASD symptom severity is in its infancy. It is highly possible that there are several unidentified variables that account for any observed or lack of observed differences between the medical groups. Further research should be conducted to evaluate additional potential mediating and moderating factors.

Despite the limitations presented above, the results of this investigation may shed light into the validity of the BISCUIT as a diagnostic measure. Taken together, the results indicate that the BISCUIT-Part 1 did not detect differences between groups of children with ASD alone versus children with ASD and a co-occurring medical condition. This finding is noteworthy as the BISCUIT is designed to be utilized for a population of children that have already been identified as having a developmental disability/delay. As such, the fact that the BISCUIT was not sensitive to other, potentially extraneous, medical conditions is important. It demonstrates that the BISCUIT continues to measure symptoms of ASD despite the presence of other conditions that are found at high rates in the population of at risk infants and toddlers. In essence, the BISCUIT displayed a high degree of validity in assessing autism spectrum symptomotology and is quickly solidifying itself as a robust and precise instrument for measuring these problems in children.

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Vita

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