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Subtypes of Toddlers with Autism Spectrum Disorders: Implications for Early and Future Diagnosis

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SUBTYPES OF TODDLERS WITH AUTISM SPECTRUM DISORDERS:

IMPLICATIONS FOR EARLY AND FUTURE DIAGNOSIS

by

LISA D. WIGGINS

Under the Direction of Diana L. Robins, Ph.D.

ABSTRACT

Autism spectrum disorders (ASDs) are a group of disorders that affect social, communication, and behavioral development. Identification of clinically distinct subtypes of ASDs, especially in the developmental period when delays or deficits are first recognized (i.e., in the first few years of life), can lend clues to etiology and trajectory and enhance current knowledge on early manifestations of the disorders. Moreover, identification of clinically distinct subtypes of ASDs may inform early identification efforts. Past research suggests that social relations, verbal abilities, nonverbal abilities, and the presence of certain stereotyped interests and behaviors (SIB) may be important factors in delineating subtypes of ASDs in toddlers. Yet there is no published study that examines empirically derived subtypes in a sample of such young children. Therefore, the purpose of this study was to determine whether clinically distinct subtypes can be derived from a sample of toddlers who fail an autism screen and are subsequently diagnosed

with developmental concerns, including an ASD. Results found that subtypes delineated by

social-communicative maturity were found in both of the aforementioned samples of children.

Furthermore, the ASD only sample was also distinguished by rate and intensity of certain types

of SIB. Implications for autism theory, early identification, and early intervention are discussed.

INDEX WORDS: Autism, Toddlers, Subtypes, Diagnosis

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LIST OF ABBREVIATIONS

ADI-R	Autism Diagnostic Interview-Revised
ADOS	Autism Diagnostic Observation Schedule
ASDs	Autism Spectrum Disorders
CARS	Childhood Autism Rating Scale
DD	Developmental delay
MSEL	Mullen Scales of Early Learning
VABS	Vineland Adaptive Behavior Scale
SIB	Stereotyped interests and behaviors

CHAPTER 1: INTRODUCTION

Children with autism spectrum disorders (ASDs) comprise a heterogeneous group that shows diverse levels of social, communication, behavioral, and intellectual development. Consequently, attempts to discover common features of ASDs essential for subtype classification have faced many challenges. Current diagnostic schemes typically recognize three distinct diagnoses within the class of ASDs: a) Autistic Disorder, b) Asperger's Disorder, and c) Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS; American Psychiatric Association, 1994). Children with Autistic Disorder are defined by qualitative impairments in social interaction, qualitative impairments in communication, stereotyped interests and behaviors (SIB), and developmental delays or deficits prior to three years of age; approximately 80% of these children have comorbid intellectual impairment (Gillberg & Billstedt, 2000). Conversely, children with Asperger's Disorder are defined by qualitative impairments in social interaction and SIB, but do not demonstrate delays in language, intellectual, or adaptive development. Children with PDD-NOS include a diverse group that shows qualitative impairments in social interaction and impairment in communication and/or SIB but does not meet full diagnostic criteria for other spectrum conditions (e.g., symptoms can present in two, rather than three domains, fewer than six symptoms may be present, or symptom onset can occur after three years of age). However, some researchers have questioned whether these diagnostic categories describe clinically distinct subtypes of ASDs which can delineate etiology, trajectory, and treatment options for the child (Fein, Stevens, Dunn, Waterhouse, Allen, Rapin et al., 1999). Identification of clinically distinct subtypes of ASDs in the developmental period when delays or deficits are first recognized (i.e., in the toddler years) can lend further clues to etiology and trajectory and enhance current knowledge on early manifestations of the disorders.

Expanding knowledge of early manifestations of ASDs will naturally improve diagnostic practices used to identify children at the onset of symptom presentation. Identification of children with ASDs soon after the onset of symptom presentation leads to early intervention efforts associated with improved developmental outcomes (see Rogers, 1998, for a review). For instance, gains in verbal and non-verbal communication, intelligence test scores, and peer interaction are often associated with early intervention efforts (Dawson & Osterling, 1997; Lovaas, 1987; McEachin, Smith, & Lovaas, 1993; Ozonoff & Cathcart, 1998; Rogers & Lewis, 1989; Sheinkopf & Siegel, 1998). Therefore, it is important that gold standard diagnostic instruments are sensitive to detecting ASDs in young children. Nonetheless, numerous studies have indicated that some of the most common diagnostic instruments are not sensitive at detecting ASDs in young children; further research is needed to identify subtypes of ASDs in young children and distinguish which subtypes are often misclassified by gold standard diagnostic instruments.

Behavioral Profiles of Young Children with ASDs

Similar to older children and adults with ASDs, qualitative impairments in social interaction are the strongest predictors of a subsequent diagnosis of an ASD in young children. Yet qualitative impairments in social interaction manifest quite differently in younger versus older cohorts. Research suggests that failure to orient to name and voice and failure to orient to faces are two of the most effective predictors of ASDs in children younger than four years of age (Baranek, 1999; Dawson, Toth, Abbott, Osterling, Munson, Estes, & Liaw, 2004; Lord, 1995; Osterling & Dawson, 1994). In fact, failure to look at others and failure to orient to name has been found to distinguish infants with ASDs from infants with intellectual disability and typical development as young as 12 months of age (Osterling, Dawson, & Munson, 2002). Deficits in

joint attention are also strong predictors of ASDs in young children (Baron-Cohen, Allen, & Gillberg, 1992; Baron-Cohen, Baird, Swettenham, Nightengale, Morgan, Drew et al., 1996; Dawson et al., 2004; Lord, 1995; Osterling and Dawson, 1994; Robins, Fein, Barton, & Green, 2001) and can discriminate children with ASDs from children with other developmental delays (DD) and children with typical development as early as 14 months of age (Sullivan, Finelli, Marvin, Garrett-Mayer, Bauman, & Landa, 2007). Lack of interest in other children is another social deficit that often discriminates children with ASDs from children with DD and children with typical development (Baron-Cohen, Allen, & Gillberg, 1992; Lord, 1995; Robins et al., 2001).

Aside from the myriad of social deficits found in young children with ASDs, impairments in communication and SIB are also implicated. In fact, although not specific to ASDs, delayed language acquisition is often cited as causing initial parental concern in the first or second year of life (DiGiacomo & Fombonne, 1998; Howlin & Asgharian, 1999). However, impaired conversational skills and stereotyped language, which are currently listed as diagnostic criteria for ASDs, are not applicable to very young children with ASDs (Stone, Lee, & Ashford, 1999). Furthermore, SIB, including a preoccupation with a restricted pattern of interests, insistence on specific and nonfunctional routines, stereotyped and repetitive motor mannerisms, and a preoccupation with parts of objects, are characteristic of older children and adults diagnosed with ASDs, but occur less often in younger cohorts (Adrien, Lenoir, & Martineau, 1993; Baranek, 1999; Stone, Lee, & Ashford, 1999; Stone, Hoffman, Lewis, & Ousley, 1994).

Some researchers have proposed a 2-factor model of SIB comprised of "lower-order" sensorimotor behaviors and "higher-order" cognitive rigidity (Carcani-Rathwell, Rabe-Hasketh, and Santosh, 2006; Moore & Goodson, 2003, Szatmari, Georgiades, Bryson, Zwaigenbaum,

Roberts, Mahoney et al., 2006). However, these factors have rarely been studied in young

children with ASDs. In one report, Moore and Goodson (2003) found that parents of toddlers

with ASDs reported more impairment in lower order behaviors, such as hand mannerisms,

repetitive objects use, and unusual sensory interests, than higher order behaviors, such as

compulsions and rituals and resistance to change. These results were further supported by

Richler and colleagues (2007) who studied SIB in toddlers with ASDs, toddlers with other DDs,

and toddlers with typical development. Results found a 2-factor model of SIB in toddlers: a

lower-order repetitive sensorimotor factor and a higher-order insistence on sameness factor.

Parents of toddlers with ASDs reported more lower-order repetitive sensorimotor behaviors in

their children, such as hand mannerisms, repetitive objects use, and unusual sensory interests,

than parents of children with DD or typical development, although lower-order behaviors were

commonly reported for children with DD. Higher-order behaviors, such as compulsions and

rituals and resistance to change, did not distinguish study groups. These results have not been

replicated using a child observation instrument as the dependent variable rather than a parent

report instrument.

It is not surprising that unusual sensory interests, which are part of the aforementioned

lower-order stereotyped behaviors, consistently distinguished young children with ASDs in past

research. Although not a part of standard diagnostic criteria, atypical sensory response is

included in screening and assessment measures commonly used to identify symptoms of ASDs

in young children (Lord, Rutter, DiLavore, & Risi, 1999; Lord, Rutter, & Le Couteur, 1994;

Robins, Fein, Barton, & Green, 2001) and the ability of sensory items to distinguish young

children with ASDs has yielded promising results. For instance, Dahlgren and Gillberg (1989)

found that unusual reactions to sound was one of the best discriminators between children with

ASDs, children with intellectual impairment, and children who were typically developing. Rogers, Hepburn, and Wehner (2003) found that young children with ASDs differed from those with other DD in tactile sensitivity, auditory sensitivity, and taste/smell sensitivity as measured by the Short Sensory Profile (Dunn, 1999); these findings were replicated by Wiggins and colleagues (2007). Furthermore, Wiggins and colleagues (2007) found that most (82%) children with ASDs showed definite differences from typical sensory response whereas most (61%) children with DD showed typical sensory performance. None of the children with an ASD in this analysis showed typical sensory performance. Based on these findings, the authors argue that sensory abnormalities are distinguishing symptoms of ASDs that should be considered in diagnostic algorithms for very young children.

Yet the influence of chronological and mental age on the presence of SIB must also be taken into account. For instance, Lord and colleagues (2006) point out that young children with ASDs with higher verbal IQs tend to have fewer SIB. These results were further expanded by Bishop and colleagues (2006) who found that lower-order SIB are associated with lower nonverbal cognitive abilities and higher-order SIB are associated with higher nonverbal cognitive abilities. Osterling, Dawson, & Munson (2002) also implicated cognitive abilities in the presence of lower-order stereotyped behaviors: infants with ASDs in their sample could not be distinguished from infants with intellectual disability based on the presence of repetitive motor mannerisms. Furthermore, Militerni and colleagues (2002) found that autistic children aged 2-4 years displayed more repetitive motor and sensory behaviors than autistic children aged 7-11 years; children with higher IQ scores were less likely to show repetitive motor mannerisms and were more likely to show complex motor and verbal sequences (such as constructional play activity).

Studies that explore the developmental trajectory of young children with ASDs also can inform subtype distinctions. For instance, if the same factors that define the symptom set of toddlers with ASDs also predict prognosis, then these factors could be considered critical components of the early manifestations of the disorders. If not, the relationship between factors that define symptom sets in young children and variables that predict prognosis would warrant further investigation.

The Developmental Trajectory of Young Children with ASDs

Little is known about the developmental trajectory of ASDs for children diagnosed in early childhood. However, several research groups gathering longitudinal data recently have begun to publish preliminary results on the developmental course of ASDs from early childhood to early adulthood (Charman, Taylor, Drew, Cockerill, Brown, & Baird, 2005; Lord, Risi, DiLavore, Shulman, thrum, & Pickles, 2006; McGovern & Sigman, 2005). McGovern and Sigman (2005) followed 48 children diagnosed with an ASD between two and five years of age. These children were re-assessed at two time points: a) when they were 12-13 years of age and b) when they were 19-20 years of age. Results found that 98% of children diagnosed with autism in early childhood retained their diagnosis in middle childhood and 96% of children diagnosed with autism in early childhood retained their diagnosis as young adults. Even still, analyses of domain algorithm scores for the Autism Diagnostic Interview-Revised (ADI-R) found that social skills, non-verbal communication, verbal communication, and SIB improved with age. Moreover, adaptive skills and emotional responsiveness also improved with age. Improvements in autism symptoms, adaptive behavior, and emotional response were highly dependent on intellectual functioning: children with an ASD with an $IQ \geq 70$ showed larger improvements in all areas than children with an ASD with an $IQ < 70$.

Charman and colleagues (2005) gathered data on 29 toddlers diagnosed with autism; these children were re-assessed at three years of age and at seven years of age. One of the primary outcome measures at age seven asked about the child's development between the fourth and fifth birthday, which was used as a time point in data analyses. Therefore, data analyses included four time points: a) two years, b) three years, c) between four and five years, and d) seven years. Similar to McGovern and Sigman (2005), Charman and colleagues (2005) found a high degree of diagnostic stability from early childhood to middle childhood for children diagnosed with autism. Also like McGovern and Sigman (2005), autistic symptomatology for children in this sample seemed to improve with age. Specifically, social deficits remained stable from 2-3 years but showed significant improvement between four and five years, nonverbal communication skills steadily improved at each time point, and SIB increased at three years of age then declined between four and five years of age. Additionally, 7-year-old children with less severe symptoms were distinguished from their counterparts by higher non-verbal IQ scores and more language ability at two years of age. These findings are significant for several reasons. First, results reflect a degree of independence in trajectories of symptom severity across the different diagnostic domains of ASD. Secondly, results implicate non-verbal IQ and language ability as important predictors of symptom severity in school-aged children. Both of these findings are important for screening and diagnostic efforts and for attempts to classify or subgroup young children with ASDs.

In a recent study, Lord and colleagues (2006) studied stability of an ASD diagnosis from two to nine years of age and factors that predict later diagnosis. One hundred ninety-two children were evaluated for possible autism at two years of age; 80.4% of these children were re-evaluated when they were nine years of age. At both time points (i.e., two and nine years of age)

children received a standardized measure of intellectual functioning, the Autism Diagnostic

Observation Schedule (ADOS), and the ADI-R. Results found 76% agreement over time for

autism versus non-autism diagnoses, and 90% agreement for ASD versus non-ASD diagnoses.

The most reliable predictor of stable diagnosis was clinical judgment. Furthermore, SIB, as

measured by clinical observation and parent report, was one of the best predictors of a diagnosis

of an ASD at nine years of age. These interests and behaviors were not divided into lower-order

behaviors and higher-order behaviors for the purpose of these analyses. The authors note that

low verbal IQ was also associated with an increased probability of an ASD diagnosis at nine

years of age. Moreover, children with high verbal IQs showed little or no SIB and were more

likely to move from a diagnosis of autism to PDD-NOS or PDD-NOS to non-spectrum. These

results suggest that little to no SIB combined with a high verbal IQ may be a subtype of ASDs in

toddlers. However, this hypothesis has never been systematically examined and we do not know

whether children with this profile perform differently than children with other profiles on gold

standard diagnostic instruments.

Taken together, these studies suggest that the diagnosis of ASDs, and autism in

particular, is relatively stable from two years of age and symptoms of ASDs seem to improve

with age. More specifically, improvement in ASD symptoms is more pronounced for children

with higher verbal and nonverbal cognitive abilities and fewer SIB. As Lord and colleagues

(2006) point out, children with higher verbal IQs tend to have fewer SIB; possibly reflecting a

distinct subtype of ASDs in toddlers. Also, as mentioned previously, Bishop and colleagues

(2006) suggested that lower-order SIB are associated with lower nonverbal cognitive abilities

and higher-order SIB are associated with higher nonverbal cognitive abilities. Therefore,

subtypes of ASDs in young children may be differentiated by children with lower verbal and

nonverbal cognitive abilities and more lower-order stereotyped behaviors and children with higher verbal and nonverbal cognitive abilities and more higher-order stereotyped behaviors.

Diagnosing Young Children with ASDs

If the above hypothesis is true, that young children with ASDs may be differentiated by verbal abilities, nonverbal cognitive abilities, and SIB, then performance on gold standard diagnostic instruments may be affected by these same variables. But first, the general diagnosis of ASDs in young children should be considered. It is now well established that the diagnosis of ASDs should involve both parent interviews and clinician observations of the child (Charman & Baird, 2002; Committee on Children with Disabilities, 2001; Filipek, Accardo, Ashwal, Baranek, Cook, Dawson et al., 2000). Moreover, the diagnosis of ASDs should not be based on the results of a single diagnostic instrument. Rather, the diagnosis of ASDs should be based on a multi-disciplinary, comprehensive evaluation that includes measures of intellectual, adaptive, social, communication, and behavioral functioning as well as indicators of comorbid medical, developmental, and psychiatric conditions (Filipek et al., 2000). Gold standard ASD diagnostic algorithms identify characteristics that distinguish young children with ASDs from young children with other DDs or young children with typical development. For instance, items that most distinguished pre-verbal children with ASDs from pre-verbal children without ASDs on the ADOS were unusual eye contact, lack of showing, unusual quality of social overtures, and minimal direction of facial expressions (Lord, Rutter, DiLavore, & Risi, 1999). Items that most distinguished 3-5 year old children with ASDs from 3-5 year old children with language impairment or intellectual disability on the ADI-R were does not offer comfort, does not show and direct attention, unusual quality of social overtures, and lack of interest in other children (Lord, Rutter, & LeCouter, 1994).

Although there are many diagnostic instruments used to assess children with ASDs, some of the most commonly used and researched are the ADOS, ADI-R, and Childhood Autism Rating Scale (CARS). Due to the common use and study of these instruments, as well as their ability to detect young children with ASDs, the ADOS, ADI-R, and CARS have become known as three gold standard instruments for the assessment and diagnosis of ASDs. Therefore, discussion of performance on diagnostic instruments among young children with ASDs will be limited to these three instruments. A detailed description of each of these instruments, including scoring, reliability, and validity, can be found in the methods section of this report. However, brief descriptions of each instrument will be provided here to provide clarity for subsequent discussion.

The *ADOS* (Lord, Rutter, DiLavore, & Risi, 1999) is a standardized instrument in which the researcher observes the child and tries to elicit social interaction and communication using structured play activities. The examiner implements the module that best corresponds to the child's expressive language level in order to prevent language aptitude from impeding accurate diagnosis. Most toddlers receive Module 1, designed for children who are not regularly using phrase speech, or Module 2, designed for children who are using flexible three-word phrases. Both Module 1 and Module 2 of the ADOS contain scores in four domains: a) social, b) communication, c) SIB, and d) play. Only scores on the social and communication domains are considered for ASD classification.

The *ADI-R* (Lord, Rutter, & Le Couteur, 1994) is a semi-structured, parent interview used to classify children with a mental age of $\geq$ 24 months as having autism or no autism; the ADI-R does not classify children with other ASDs. The ADI-R gathers comprehensive information about the child from a parent in three domains of development: social,

communication, and SIB. Autism classification is determined by scores on all three domains plus a domain that measures developmental delays by three years of age. It is important to note that although the ADI-R is only appropriate for children with a mental age of $\geq$ 24 months, it is often used with caution in clinical and research practice with very young children because of lack of other appropriate measures.

The *CARS* (Schopler, Reichler, & Renner, 1988) is a standardized observation instrument used to diagnose ASDs in children two years and older; parent report can also be considered when determining item scores. The CARS rates children suspected of having an ASD on 15 items, including body use, object use, adaptation to change, sensory response, verbal communication, nonverbal communication, intellectual response, and general clinical impressions. The final diagnostic algorithm represents a sum of item scores and classifies the child as having severe autism, mild-moderate autism, or no autism indicated.

Previous research, excluding initial validation studies, is inconclusive on whether the ADOS, ADI-R, and CARS have adequate sensitivity and specificity when used with toddlers with ASDs. Some studies suggest that the sensitivity and specificity of the ADOS and ADI-R (using clinical judgment as the gold standard) are poor to moderate when used alone, but improve significantly when used together; this is especially true for the broader category of ASDs rather than the diagnosis of just autism. For instance, Risi and colleagues (2006) studied performance on the ADOS and ADI-R among 270 children less than 36 months of age. Of these 270 children, 162 had a diagnosis of autism, 65 had a diagnosis of PDD-NOS, and 43 were typically developing. Results found that, when used alone, sensitivity and specificity for autism classification was .83 and .72 for the ADI-R and .98 and .59 for the ADOS; sensitivity and specificity was .81 and .87 when the ADI-R and ADOS were used together. However, for

classification of ASDs, the sensitivity and specificity was .86 and .63 for the ADI-R and .97 and .67 for the ADOS; sensitivity and specificity was .83 and .79 when the ADI-R and ADOS were used together. It is important to note that, for the purposes of these analyses, ASD classification on the ADI-R was defined as meeting social and communication criteria, meeting social criteria and within two points of communication criteria, meeting communication criteria and within two points of social criteria, or scoring within one point of both social and communication criteria. Therefore, SIB were not considered for an ADI-R classification of ASD, suggesting that SIB are not as relevant for an ADI-R classification of autism among higher-functioning children.

Other studies have failed to replicate the sensitivity and specificity estimates for the ADI-R reported by Risi and colleagues. For example, Ventola and colleagues (2006) studied 45 children who failed an autism screen and subsequently received a clinical evaluation that consisted of the ADOS, ADI-R, and CARS. Twenty-seven children were eventually diagnosed with autism, nine were diagnosed with PDD-NOS, and nine did not meet criteria for any ASD; this sample was different from the Risi and colleagues sample described above since children with nonASD delays were included in the former and not the latter. Results showed that the sensitivity and specificity for a diagnosis of autism or ASD was .97 and .67 for the ADOS, .53 and .67 for the ADI-R, and .89 and 1.00 for the CARS. When only the diagnosis of autism was considered (i.e., children with PDD-NOS were included in the group without autism), the sensitivity and specificity was .90 and .67 for the ADOS, .56 and .66 for the ADI-R, and .96 and .67 for the CARS. These results were replicated by Wiggins and Robins (2008) who studied 142 children who failed an autism screen and then received a similar clinical evaluation. Results of this analysis showed that sensitivity and specificity was .96 and .65 for the ADOS, .71 and .93 for the CARS, and.33 and .94 for the ADI-R. Sensitivity of the ADI-R only improved to .44

when only children diagnosed with autism were considered. However, when the ADI-R

behavioral domain was excluded from analyses, sensitivity improved to .79 for all children in the

ASD category. Taken together, these latter two studies suggest that out of the ADOS, ADI-R,

and CARS, the CARS has the highest sensitivity and specificity and, when SIB are not

considered, the ADI-R detects more children with broadly defined ASDs.

Identifying Subtypes of Young Children with ASDs

Previous literature on the profile of young children with ASDs, the trajectory of young

children with ASDs, and performance of young children with ASDs on diagnostic instruments

suggests that social relations, verbal abilities, nonverbal abilities, and presence of SIB may be

important factors that define early subtypes. However, there are very little data that identifies

characteristics that distinguish subgroups of young children with ASDs within the autism

spectrum. Instead, previous analyses on ASD subtypes have traditionally used older children

and adults with ASDs who present with distinctly different symptom sets. Therefore, it is

especially important to perform subtype analyses on young children with ASDs to identify

profile characteristics that can inform diagnostic practices and delineate the potential etiology,

trajectory, and treatment options for each child. For instance, subgroup membership may affect

performance of common diagnostic instruments, demanding consideration of clinical

manifestations of ASDs in diagnostic algorithms for young children. Etiologic risk factors can

be studied to determine whether certain risk factors increase the likelihood of membership in a

particular subgroup. Finally, the influence of subgroup membership on developmental

trajectories and response to treatment will lend further clues to early expressions of ASDs and

how to improve symptoms associated with the disorders.

Research on subtypes of ASD in older children and adults provide an initial framework for identifying subtypes of ASD in younger cohorts. It is important to note that the results of much of this research may not be relevant to younger cohorts, given different symptom profiles between younger and older cohorts. However, the methodology associated with this body of literature is relevant to devising studies on subtype analyses in young children. Therefore, a thorough review of ASD subtype analyses is warranted.

Clinical Consensus and Field Trial Studies

The literature on subtype analyses in ASDs can generally be divided into clinical consensus and field trial studies and empirical analyses. Original clinical classification of autism was described by Leo Kanner in 1943 and subsequently modified by Michael Rutter in 1978. Specifically, Kanner asserted that autism was a congenital condition that involved impairments in social interaction and SIB. Rutter's (1978) definition built upon Kanner's taxonomy and later research. Thus, Rutter described autism as a condition with early onset characterized by social and communication impairments not strictly due to intellectual impairment. In 1980, ASDs, or Pervasive Developmental Disorders, were included as a "new" class of disorders in the Diagnostic and Statistical Manual of Mental Disorders-Third Edition (DSM-III, American Psychiatric Association, 1980); diagnostic criteria were modified and expanded in subsequent editions (American Psychiatric Association, 1987, 1994). Current clinical consensus is standardized not only by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, American Psychiatric Association, 1994), but also by the current version of the International Classification of Disease (ICD-10, World Health Organization, 1990). The overarching purpose of both of these classification systems is to enhance communication among

clinicians and researchers so that clinical decisions and research findings are reliable and valid and treatments are carefully selected (Volkmar, 1998).

The ICD-10 defines ASDs as belonging to the broad category of Pervasive Developmental Disorders (PDDs). ASDs/PDDs are further categorized into Autistic Disorder, Atypical Autism, Rett's Syndrome, Childhood Disintegrative Disorder (CDD), Overactive Disorder associated with Intellectual disability and Stereotyped Hand Movements, Asperger's Syndrome, and other PDDs. Specifically, children with Autistic Disorder are defined by qualitative impairments in social interaction, qualitative impairments in communication, SIB, and developmental delays or deficits prior to three years of age. Atypical Autism differs from Autistic Disorder in either age of onset or failure to fulfill full diagnostic criteria; this subtype often occurs in profoundly retarded individuals or persons with severely impaired receptive language. The etiology of Rett's syndrome has been identified as a genetic mutation which subsequently causes language regression, motor regression, deceleration in the rate of head growth, and hand stereotypies (Van Acker, Loncola, Van Acker, 2005). CDD is also defined by a loss of skills after three years of age; due to the low incidence of CDD (Fombonne, 2002), many exclude this diagnosis when referring to the broad category of ASDs/PDDs. An Overactive Disorder associated with Intellectual disability and Stereotyped Hand Movements is an ill-defined disorder used to describe individuals with moderate to severe intellectual disability who exhibit problems with hyperactivity and inattention and frequently show stereotyped behaviors. Children with Asperger's Disorder are defined by qualitative impairments in social interaction and SIB, but do not demonstrate delays in language, intellectual, or adaptive development. Other PDDs is a residual diagnostic category used for disorders that fit the general description of ASDs/PDDs but lack of adequate information to meet diagnostic criteria for other

ASD/PDD conditions; this is commensurate with the DSM-IV terminology of "Not Otherwise Specified" (NOS).

The DSM-IV subclassifies PDDs into five subgroups instead of the seven subgroups identified by ICD-10. These subgroups include Autistic Disorder, Asperger's Syndrome, PDD-NOS, Rett's Syndrome, and CDD; subgroups were derived after a field trial for ASDs in DSM-IV (Volkmar, Klin, Siegel, & Szatmari, 1994). The field trial included 125 clinicians from 21 sites worldwide who evaluated nearly 1000 subjects with ASDs and other developmental disabilities. After the evaluation, the clinician provided a best estimate clinical diagnosis (independent of any classification system) as well as an ASD diagnosis using DSM-III, DSM-III-R, and ICD-10 criteria. Results found that best estimate clinical diagnoses were most closely related to DSM-III and ICD-10 criteria. Adding age of onset before three years of age reduced the false positive rate of DSM-III-R diagnoses. However, after careful consideration, the field trial group decided to modify DSM-III and DSM-III-R criteria so the newly proposed DSM-IV criteria more closely resembled ICD-10 criteria. Increased compatibility with ICD-10 not only increased the sensitivity and specificity of the DSM-IV taxonomy, but also simplified the diagnostic decision process in countries using different diagnostic systems. Additional analyses suggest that DSM-IV criteria are reliable and valid when differentiating children with ASDs from children without ASDs and when identifying Autistic Disorder and Asperger's Disorder; DSM-IV is less reliable and accurate when differentiating Autistic Disorder from PDD-NOS (Mahoney, Szatsmari, & MacLean, 1998). Therefore, future research is needed to determine whether diagnostic categories put forth by the ICD-10 and DSM-IV describe homogeneous subgroups of ASDs that can, in fact, validate clinical decisions and research findings and inform treatment planning.

Empirical Analyses

One of the earliest attempts to classify children with ASDs other than clinical consensus and field trial studies was a study conducted by Wing and Gould in 1979. In this study, individuals with autism were classified according to sociability as aloof, passive, and active-but-odd. Socially aloof persons were most severely impaired, rejected social contact, and were indifferent to others. Persons described as passive rarely initiated social contact but readily accepted social approaches made by others. Finally, those described as active-but-odd made social approaches, but these approaches seemed to serve a restricted or repetitive preoccupation. These subtypes have been validated in studies conducted in more recent years (Borden & Ollendick, 1994; Volkmar, Cohen, Bregman, Hooks, & Stevenson, 1989). For instance, Borden and Ollendick (1994) classified 53 children diagnosed with ASDs according to the social subtypes described by Wing and Gould (1979). Raters agreed on assignment in 72% of the cases, yielding a kappa value of .56 or fair agreement. Reliability for assignment to the passive subtype was poor (.38), in contrast to good agreement for aloof (.62) and active-but-odd (.60) assignments; very few children were classified as passive ($n = 9$). Persons classified as aloof and active-but-odd were clinically distinct from one another in terms of social interaction, language/communication, SIB, adaptive functioning, and intellectual functioning. Specifically, the aloof group was rated as more deviant across measures than the active-but-odd group. The authors concluded that findings could be used to develop individualized treatment plans for persons with ASDs and to promote research on more homogeneous samples of persons with ASDs.

Other studies have used data generated techniques to classify persons with ASDs instead of clinical judgment. Many of these data generated techniques utilized a statistical method called

cluster analysis to classify individuals with ASDs into clinically distinct groups; a summary of cluster analytic studies examining subtypes of ASDs can be found in Table 1. Cluster analysis relies on the partitioning of data into distinct clusters so data characteristics within a cluster share some common trait. For instance, a nonverbal IQ below 70 points may define one cluster whereas a nonverbal IQ above 70 points may define another cluster. Cluster analysis, like diagnostic systems, is used to describe relatively homogeneous subgroups of ASDs to validate clinical decisions and research findings, inform treatment planning, and provide clues to etiology. It is important to note that many cluster analytic studies on subtypes of ASDs have taken a broader developmental perspective than the earlier work conducted by Wing and Gould (1979). For instance, whereas Wing and Gould were strictly interested in social subtypes, most cluster analytic studies typical define subtypes based on a wide variety of data, including social, communication, and behavioral functioning and developmental histories. Furthermore, Wing and Gould used ratings on an individual interview item (i.e., quality of social response) to define subgroups rather using cluster analysis. Therefore, a comparison between cluster analytic studies and the work by Wing and Gould will not be presented.

One example of a cluster analytic study that utilized behavioral data and developmental histories was a study conducted by Siegel and colleagues in 1986. In this study, 46 persons with autistic disorder who were 4-20 years of age were classified according to results of a developmental history questionnaire, parent report of current behaviors, and behaviors coded from a videotaped diagnostic evaluation. Results found four clinically distinct groups defined by classic autism, severe intellectual disability, schizotypal personality traits, and anxious/negativistic behaviors. Cluster I was classically autistic; these individuals had moderate intellectual disability, limited social relatedness, unusual preoccupations, no functional language,

and atypical prosody. Cluster II had severe intellectual disability and was nonverbal, socially

unresponsive, and had high rates of motor stereotypies. The individuals described as schizotypal

in cluster III had tangential speech, unusual play, and bizarre ideations. Cluster IV were the

most anxious and negativistic; individuals in cluster IV avoided social interaction and

communication and displayed hyperactivity. In addition to the aforementioned clusters, Siegel

and colleagues (1986) found that the developmental history varied for individuals depending on

cluster membership. For instance, cluster I was characterized by complications in delivery

(especially head injuries), cluster II was characterized by congenital abnormalities and delayed

developmental milestones, cluster III was characterized by maternal history of miscarriage, and

cluster IV was characterized by prenatal difficulties (e.g., infection, toxemia, and use of

medications during pregnancy).

A 4-cluster solution was also found by Eaves and colleagues (1994). Specifically, four

clusters were found for children with ASDs who were 3-12 years of age: typical autism, low

functioning autism, high functioning autism (i.e., Asperger's Disorder or persons with

schizotypal traits), and hard-to-diagnose autism (Eaves, Ho, & Eaves, 1994). The typical autism

cluster showed a mean verbal IQ of 60, a mean performance IQ of 70, social isolation, abnormal

nonverbal communication, conversational deficits, motor stereotypies, and sensory

preoccupations. Individuals in the low functioning autism cluster had severe intellectual

disability and were primarily nonverbal and unaware of others; low functioning persons also

showed high rates of motor stereotypies, sensory preoccupations, and self-injurious behaviors.

In contrast, individuals in the high-functioning autism cluster were social and highly verbal, but

showed odd use of language, conversational deficits, and difficulties with peer interaction.

Individuals with hard-to-diagnose autism had mild to moderate intellectual disability and a

family history of learning disability. Similar to Eaves and colleagues (1994), Sevin and

colleagues (1995) found a 4-cluster solution for persons with ASDs who were 2-22 years of age:

a low functioning cluster, moderate cluster, mild cluster, and high functioning cluster.

Descriptions of the low functioning cluster and high functioning cluster were comparable across

the Eaves (1994) and Sevin (1995) reports. Sevin's cluster of moderate autism was similar to

Eaves's cluster of typical autism in that both groups showed at least moderate social and

language impairments and high rates motor stereotypies and sensory preoccupations. However,

parallels between Sevin's cluster of mild autism and Eaves's cluster of hard-to-diagnose autism

were less evident. For instance, Eaves's hard-to-diagnose autism was split between children who

showed social and nonverbal language impairments and children who did not show social and

nonverbal language impairments; very few children showed motor stereotypies whereas a large

majority had sensory preoccupations. In contrast, children in Sevin's mild autism group showed

moderate social and language impairments and mild rates of SIB and sensory abnormalities; this

group did not differ from Sevin's moderate autism group in degree of social and language

impairments but did differ from his moderate autism group in degree of motor stereotypies and

sensory abnormalities (i.e., the mild autism group had fewer motor stereotypies and sensory

abnormalities).

　　　　Many of the aforementioned studies have been criticized for not systematically

measuring intellectual functioning and for including individuals with a broad array of

chronological and developmental ages. As mentioned previously, narrowing the subtype or

cluster focus to young children may yield useful information for early screening and diagnostic

efforts associated with improved developmental outcomes. To address these concerns, Fein and

colleagues (1999) performed a cluster analysis on 633 preschool children with delayed or deviant

communication. Participants were later divided into three study groups: a) ASD, b)

Developmental Language Disorder (DLD), and c) non-ASD with low cognitive functioning

(low-IQ = nonverbal IQ lower than 80). All children were initially evaluated between 36 and 60

months of age (DLD) or between 36 and 84 months of age (ASD and low-IQ). The initial

evaluation included cognitive, behavioral, and psychiatric measures, including the Wing (1985)

Autistic Disorders Checklist in Children. Cluster analysis confirmed the existence of two

clinically distinct subgroups of ASD in the preschool population (a cluster of non-ASD children

was also found). Both ASD clusters contained children with impairments in eye contact, social

play, and the use of language for communication. However, Cluster I was also defined by higher

intellectual functioning and children who offered inappropriate help in times of distress, showed

naïve or bizarre imitation, interpreted language literally, had one-sided conversations, and had

preoccupations with special interests or topics. On the other hand, Cluster II was defined by

lower intellectual functioning and failure to perceive others' distress, showed a complete lack of

imitation, failed to understand simple commands, were mute, and had a higher frequency of

stereotyped movements and sensory preoccupations. The primary variable that distinguished

high- and low-functioning clusters was nonverbal IQ above or below 65 points.

The significance of the Fein et al. (1999) study is that fewer subgroups of children with

ASD were found when the cluster focus was narrowed to a preschool population. This finding

suggests that the course of ASDs becomes more heterogeneous as children age and that distinct

variables can be identified that predict cluster membership in young children. However, the

relationship of preschool cluster membership to future prognosis was still uncertain. Therefore,

Stevens and colleagues (2000) expanded upon Fein's report with a longitudinal examination of

subgroups of children with ASDs by cluster analysis. Using the same database as Fein and

colleagues (1999), Stevens et al. (2000) replicated a 2-cluster solution when the preschool children were school-aged; these two clusters were labeled high-functioning ASD and a low-functioning ASD. Almost all (98%) of the low-functioning children in preschool remained low-functioning when school-aged; a small proportion (2%) of the low functioning children in preschool were labeled high-functioning when school aged. Conversely, fewer than half (38%) of the high-functioning children in preschool remained high-functioning when school-aged; more than half (62%) of the high-functioning children in preschool became low-functioning by school age. More specifically, some high-functioning preschool children showed improvements in social, communication, and adaptive functioning whereas others worsened in these areas. Furthermore, similar to the Fein et al. (1999) findings in preschoolers, the most important predictor of school-aged cluster membership was nonverbal IQ.

Although recent cluster analyses have shed light on the differing nature of ASDs in preschool versus adult populations, many questions still remain. For instance, in the one study that examined cluster solutions in a preschool population (Fein et al., 1999), the mean age of the sample was almost five years. Although five years is close to the age when most children with ASDs are diagnosed (Wiggins, Baio, & Rice, 2006), parents often express concerns about their child's development in the first few years of life (De Giacomo & Fombonne, 1998). Yet there are no published studies on subtypes of ASDs in children younger than five years of age. As previously mentioned, identifying homogeneous, clinically distinct subgroups of children with ASDs in the first few years of life will support early identification and early diagnostic efforts. Identification of such subgroups may also facilitate treatment planning if subgroup membership is associated with differential response to treatment.

Furthermore, several limitations of published reports deserve consideration when applied to younger cohorts. First, differences in sample characteristics, variables studied, and numbers of clusters found confuses the literature and complicates interpretation of findings (Table 1). For instance, studies that utilized a sample of children diagnosed with Autistic Disorder cannot be applied to the broad range of ASD phenotypes found in young children. Second, many studies used unstandardized or unpublished measures designed solely for the purpose of cluster analysis (Eaves, Ho, & Eaves, 1994; Fein et al., 1999; Prior et al., 1998; Siegel et al. 1986; Stevens et al., 2000) or measures that are not routinely used in clinical or research practice. Third, there are no published studies that examine subgroup differences in characteristics that define the early symptom profile of children with ASDs and the developmental trajectory of children with ASDs, particularly verbal abilities, nonverbal cognitive abilities, and SIB in the first few years of life. Consequently, there is no published report that examines how subgroup membership for very young children with ASDs affects performance on common diagnostic measures. Again, examining the influence of subgroup membership on common diagnostic measures will help inform early diagnostic efforts associated with improved developmental outcomes.

Purpose of Study, Research Questions, and Hypotheses

Given the limitations of past research and lack of information on subgroups of young children with ASDs, the purpose of the current study was to examine empirically derived subgroups of children with ASDs in the first few years of life. In order to address many of the aforementioned limitations, as well as maintain a comprehensive scope, research questions addressed: a) empirically derived subgroups of children who fail an autism screen in the toddler years and are subsequently diagnosed with developmental concerns, b) empirically derived

Table 1

Published Cluster Analyses on Persons with ASDs

Primary Author	Year Published	Sample Size and Age	Sample Diagnoses[1]	Primary Independent Variables	Clusters Identified	Cluster Descriptions
Siegel	1986	N = 46 4-20 years, *M* = 10.7 years	AD	Developmental history questionnaire, parent report of current behavior, behaviors coded from a videotaped diagnostic evaluation	4	1. Classic autism 2. Severe intellectual disability 3. Schizotypal personality traits 4. Anxious/negativistic behaviors
Eaves	1994	N = 166 3-12 years, *M* = 7.1 years	AD, ASD, ASP, AT, HFA	Behaviors coded retrospectively from hospital charts	4	1. Typically autistic 2. Low-functioning autism 3. High-functioning autism 4. Hard-to-diagnose autism
Sevin	1995	N = 34 2-22 years, *M* = 7.7 years	AD, ASD	Childhood Autism Rating Scale, Autism Behavior Checklist, Ritvo-Freeman Real Life Rating Scale, Vineland Adaptive Behavior Scales	4	1. Severe autism 2. Moderate autism 3. Mild autism 4. High-functioning autism
Prior	1998	N = 135 3-21 years, *M* = 10.22 years	AD, ASD, HFA (only high functioning children included)	Autistic Disorders Checklist, Peabody Picture Vocabulary Test	3	1. Autism 2. ASD 3. Mild ASD
Fein	1999	N = 194 3-7 years, *M* = 4.9 for ASD	ASD, Developmental Language Disorder, low-IQ	Autistic Disorders Checklist, Peabody Picture Vocabulary Test, Vineland Adaptive Behavior Scales	2	1. Low-functioning autism 2. High-functioning autism
Stevens	2000	N = 138 7-9 years, *M* = 8.6 years	ASD	Autistic Disorders Checklist, Peabody Picture Vocabulary Test, Vineland Adaptive Behavior Scales	2	1. Low-functioning autism 2. High-functioning autism

[1]AD = Autistic Disorder, including infantile autism and residual state autism; ASD = Autism Spectrum Disorder or Pervasive Developmental Disorder; ASP = Asperger's syndrome; AT = autistic tendencies; HFA = high functioning autism

subgroups of children who fail an autism screen and are subsequently diagnosed with an ASD in the toddler years, c) characteristics that define clinically distinct subgroups, d) how ASD subgroup membership forecasts performance on common diagnostic instruments, and e) how ASD subgroup membership predicts diagnosis two years later. The standardized instrument chosen for cluster analysis was the CARS (Appendix A), which is a standardized clinical rating scale completed by a trained observer. Individual items from the CARS were chosen as cluster variables because the CARS is associated with the highest rates of sensitivity and specificity and the highest agreement with clinical judgment when used in toddler evaluations (Ventola et al., 2006; Wiggins & Robins, 2008). It is important to note that these conclusions were drawn from samples that overlap with the proposed sample for this research. However, given that clinical judgment is considered the gold standard in ASD assessment (Lord, 1995) and the CARS has the highest agreement with clinical judgment in this sample of children, the CARS was deemed the most appropriate cluster instrument for the proposed analyses.

Another reason the CARS was deemed the most appropriate cluster instrument is that it includes 15 items that encompass variables implicated in previous research as important in delineating the early symptom profile of ASDs, the trajectory of ASDs, and performance on diagnostic instruments. Specifically, the CARS includes several items assessing social and emotional response (e.g., relating to people), one item assessing verbal communication, one item assessing nonverbal communication, one item assessing intellectual response, and several items assessing SIB; including one item assessing a high-order behavior (i.e., resistance to change) and three items assessing lower-order behaviors (i.e., body use, object use, and sensory response). Moreover, CARS items are rated on a 7-point scale, which provides a broader range of scores than other diagnostic instruments, such as the ADI-R and ADOS, which are rated on a 3-point

scale for the diagnostic algorithm. Therefore, the CARS provides a broader range of scores than other diagnostic instruments.

Items from other diagnostic, cognitive, or adaptive measures were not used as cluster variables since these items were used to validate the cluster solution and were used as dependent variables in subsequent analyses. Furthermore, CARS items are expected to provide the most accurate cluster solution since this instrument has the highest rates of sensitivity and specificity, the highest agreement with clinical judgment, contains specific items of interest, and provides a broader item scoring range than other instruments used in toddler evaluations.

To determine the feasibility of this project and make hypotheses regarding subtype characteristics, a preliminary cluster analysis was performed for children who failed an autism screen and were subsequently diagnosed with an ASD. The cluster analysis found three distinct subgroups of toddlers with ASDs; one cluster with 95 children, one cluster with 47 children, and one cluster with 44 children. No further analyses other than descriptive statistics of the ASD sample were conducted. Based on the past research outlined in this document, it is hypothesized that these three ASD subgroups will be distinguished by social relations, verbal ability, nonverbal ability, and SIB. Specifically, the three ASD subgroups are expected to include one group with higher social, language, and intellectual functioning and fewer lower-order SIB, one group with lower social, language, and intellectual functioning and more lower-order SIB, and one group with lower social, language, and intellectual functioning and fewer SIB. Although lower functioning is expected to be associated with atypical object use, atypical body use, and atypical sensory response, higher functioning is not expected to be associated with resistance to change in a toddler population with ASDs. This latter hypothesis was based on past research that suggests higher-order SIB are rarely endorsed in very young children with ASDs and do not

distinguish children with ASDs from other DDs (Moore & Goodson, 2003; Richler, Bishop, & Lord, 2007; Stone, Lee, & Ashford, 1999), suggesting that a 2-factor model of SIB may not emerge until after the toddler years.

These results are expected to persist for children with ASDs when validation techniques are employed to further characterize subgroups using intellectual, adaptive, and additional ASD diagnostic measures. Furthermore, it is expected that children with ASD with higher social, language, and intellectual functioning and fewer lower-order SIB will more likely be missed by common diagnostic instruments, resulting in reduced sensitivity for this particular subgroup. It is also expected that children with ASD with higher social, language, and intellectual functioning and fewer lower-order SIB will be more likely to receive a diagnosis of PDD-NOS or a nonASD disorder, compared to an Autistic Disorder diagnosis at four years of age.

CHAPTER 2: METHODS

Participants

The original sample consisted of 300 toddlers who failed an autism screen; 186 toddlers were subsequently diagnosed with an ASD, 102 toddlers were subsequently diagnosed with other DD, and 12 toddlers were subsequently found to have typical development. Since the focus of these analyses were on toddlers who failed an autism screen and were subsequently found to have developmental concerns, the 12 toddlers with typical development were dropped from the study, leaving a final sample of 288 toddlers. All children were identified from a two-site ongoing screening study at the University of Connecticut and Georgia State University; children were diagnosed with an ASD between 13-37 months of age based on the results of a comprehensive clinical evaluation (see subsequent sections for details on how children were identified and diagnosed). Children were diagnosed based on DSM-IV definitions of Autistic

Disorder, PDD-NOS, Asperger's Disorder, and other clinical diagnoses such as intellectual disability and language delay. Again, 12 children who were found to be typically developing were excluded from analyses so characteristics that distinguish children with ASDs from children with other DD could be explored.

Participant Recruitment

Participants were identified from an ongoing screening study at the University of Connecticut and Georgia State University. Specifically, children were identified because they failed an autism screen administered during a routine well-baby visit at the child's pediatrician's office or a visit to the state-wide early intervention program. Details on the development of the autism screen and the recruitment process for the dataset used in this study are outlined in the following sections.

Development of the Modified Checklist for Autism in Toddlers

Participants were identified for inclusion in this study because they failed the Modified Checklist for Autism in Toddlers (M-CHAT); failure of the M-CHAT indicates risk for ASDs. The M-CHAT was initially developed by Robins and colleagues (Robins, Fein, & Barton, 2001) in an attempt to create a relatively brief ASD screen that could be completed by parents of very young children. The authors hoped to develop a sensitive and specific screen that would detect ASDs in the earliest developmental stages to prevent delayed diagnosis and failure to implement specialized interventions as soon as possible. Furthermore, the authors hoped to develop a screen that could be used in general pediatric practice, rather than secondary or tertiary clinics, since general pediatric care is often the only developmental care children receive before they are school-aged. Due to the demands of busy pediatric offices, it was also important that the screen to be brief and relatively easy to administer and score.

Until the development of the M-CHAT, there was not a brief parental screen appropriate for very young children that could be administered in general pediatric settings. Therefore, the authors chose to modify an existing screening instrument that had promising psychometric properties in very young children. The instrument chosen for modification was the Checklist for Autism in Toddlers (CHAT; Baron-Cohen, Allen, Gillberg, 1992). The CHAT was developed and validated in Great Britain in order to identify children with an ASD by 18-months of age. Items were derived to test the hypothesis that children who do not display joint attention and pretend play by 18-months are at an increased risk for developing ASDs (Baron-Cohen, Allen, Gillberg, 1992). The final 14 CHAT items include nine items answered by parents and five additional behaviors observed by a healthcare professional. The nine items asked of parents were (a) does your child enjoy being swung, bounced on your knee, etc?, (b) does your child take an interest in other children?, (c) does your child like climbing on things, such as up stairs?, (d) does your child enjoy playing peek-a-boo/hide-and-seek?, (e) does your child ever PRETEND, for example, to make a cup of tea using a toy cup and teapot, or pretend other things?, (f) does your child ever use his/her index finger to point, to ASK for something?, (g) does your child ever use his/her index finger to point, to indicate INTEREST in something?, (h) can your child play properly with small toys (e.g., cars or bricks) without just mouthing, fiddling, or dropping them?, and (i) does your child ever bring things over to you (parent), to SHOW you something? The five additional items asked of healthcare providers were (a) during the appointment, has the child made eye contact with you?, (b) get the child's attention then point to something interesting across the room and say "Oh look! There's a (name of toy)!" Watch the child's face. Does the child look across to see what you're pointing at?, (c) get the child's attention, then give child a miniature tot cup and teapot and say "Can you make a cup of tea?" Does the child pretend to

pour out tea, drink it, etc.?, (d) say to the child "Where's the light?" or "Show me the light." Does the child POINT with his/her index finger to show you the light?, and (e) Can the child build a tower of bricks [i.e., blocks]? If so, how many?

The authors of the CHAT initially hypothesized that five key items that assessed protodeclarative pointing, gaze monitoring, and pretend play would distinguish children with ASDs from other at-risk or typically developing children. To test their hypothesis, they administered the CHAT to 50 randomly selected, typically developing children and 41 siblings of children with ASDs at 18-months of age. Four children in the ASD sibling sample failed two or more of five key items; all four of these children were diagnosed with Autistic Disorder 12 months later. None of the other 37 children in the ASD sibling sample failed more than one key item; these children did not receive a clinical diagnosis of Autistic Disorder at the 12-month follow-up. Furthermore, all of the typically developing children passed all key items. These results indicated that the CHAT was useful in differentiating children with ASDs at 18-months of age and that protodeclarative pointing, gaze monitoring, and pretend play distinguish children with ASDs from other children (Baron-Cohen, Allen, Gillberg, 1992). A follow-up study published four years later extended these findings and showed that, of 16,000 children screened, 83.3% of those who failed items on all three key behaviors received a diagnosis of Autistic Disorder; none of the children who failed items that assessed protodeclarative pointing alone, or protodeclarative pointing and pretend play, received an autism diagnosis (although 68.2% of this latter group received diagnoses of DD without autism, Baron-Cohen et al., 1996).

When developing the M-CHAT, the authors retained the nine parent-report items from the CHAT. Additional M-CHAT items were generated from an extensive review of the literature and clinical opinion on behaviors thought to exist in very young children with ASDs. All items

were constructed in a simple yes/no response format. Preliminary analyses of the first 600

participants led to further refinement of the M-CHAT and determination of cut-off criteria. The

final instrument included 23 items (listed in Appendix B); the ASD cut-off score was initially

defined as failure of two of eight critical items derived from discriminant function analyses

(DFA) of the first 600 participants or failure of any three items.

Initial validation of the M-CHAT was conducted on 1,293 children who received the

screen at the 18- or 24-month well baby visit (n = 1,122) or received the M-CHAT at the onset of

an early intervention evaluation (n = 171). If the child failed the M-CHAT at initial screen, a

follow-up interview (see Appendix C for an example interview item) was conducted to verify

responses on the paper-and-pencil form and elicit examples of the behavior in question. If

results of the follow-up interview still indicated risk for ASDs, the family was invited to receive

a free, comprehensive clinical evaluation. Of the 1,293 children screened, 1,161 did not require

additional follow-up (i.e., these children passed the M-CHAT at initial screen); 74 children failed

the M-CHAT but passed the follow-up interview and did not receive a clinical evaluation. Fifty-

eight children who failed the M-CHAT and subsequent follow-up interview were evaluated

clinically. Of these 58 children, 39 were determined to have an ASD and 19 were determined

not to have an ASD. Chi-square analyses found that all items, except those that assessed

enjoyment when being swung or bounced on the knee and ability to walk, distinguished children

with ASDs from children without ASDs. DFA identified six, instead of eight, critical items,

which involved joint attention (protodeclarative pointing, following a point, and bringing objects

to show a parent), social relatedness (interest in other children and imitation), and

communication (responding to name). Sensitivity and specificity of the M-CHAT, based on the

DFA classification, was .87 and .99, respectively. More recent validation analyses have found

that the M-CHAT has a positive predictive value of .57-.74 when combined with the follow-up interview in a similar sample of children (Kleinman et al., 2008; Robins, 2008)

Recruitment using the Modified Checklist for Autism in Toddlers

Participant recruitment for the dataset chosen for this study involved administration of the M-CHAT in pediatric and early intervention practices in Connecticut and parts of Massachusetts, Rhode Island, and New York (UConn) and metropolitan Atlanta, Georgia (GSU). The M-CHAT was administered during 18- and 24-month well child visits or early intervention provider visits. Specifically, providers were sent M-CHAT screens along with an informed consent form. The receptionist or office nurse gave the M-CHAT packet to parents of eligible children (i.e., any child seen for an 18 or 24 month well child visit). If parents agreed to be in the study and signed the informed consent form, they were asked to complete the M-CHAT in the waiting room or while waiting for the pediatrician in the examination room. In some pediatric sites, a research assistant or staff member of the practice helped the parent complete the form. The pediatrician may have reviewed the M-CHAT before seeing the child, but review of the M-CHAT by the pediatrician was not a necessary component of the study. At the end of the week, or when numerous M-CHAT forms had been completed, the receptionist or office nurse returned completed M-CHAT forms to the UConn or GSU site.

UConn and GSU study staff scored M-CHAT forms and entered data into a research database. If M-CHAT results indicated risk for ASDs (as described in the section above), a member of the study team called the family to administer the follow-up interview (see Appendix C for example interview item). As stated previously, the follow-up interview clarifies responses on the paper-and-pencil form and elicits examples of target behaviors. For instance, if the family indicated on the M-CHAT that the child does not take an interest in other children, the

interviewer would ask if the child is still not taking an interest in other children. If the answer were "yes", the interviewer would then ask how the child responds to the presence of another child on the playground or in the supermarket. If the respondent gave examples of or affirmed that the child smiled or looked at other children more than half of the time, the item would be scored as a pass. If the respondent said the child only showed aggressive behavior when in the presence of another child, the item would be scored as a fail. If risk for ASDs was still indicated after the follow-up interview, the family was invited for a free, comprehensive clinical evaluation. All families who received a comprehensive toddler evaluation were invited back for a follow-up evaluation around the child's fourth birthday.

Primary Measures

The *Modified Checklist for Autism in Toddlers* (Robins et al., 1999, 2001) has been described previously (see section on development of the M-CHAT) and will not be reviewed in extensive detail here. Briefly, the M-CHAT is a short parent-report checklist designed to detect risk for ASDs in very young children. Failure of the instrument is defined as any three of 23 items failed, or any two of six critical items failed. Critical items were identified by empirical methods using discriminant function analyses (Robins et al., 2001), and include: (a) does not point to show interest, (b) does not follow a point, (c) does not bring objects to show a parent, (d) is not interested in other children, (e) does not imitate, and (f) does not respond to name. Estimated sensitivity and specificity of the M-CHAT, based on the DFA classification, was .87 and .99, respectively.

The *Autism Diagnostic Interview-Revised* (Lord, Rutter, & Le Couteur, 1994) is a semi-structured, parent interview used to classify children with a mental age of ≥ 24 months as autism or no autism; the ADI-R does not classify children with other ASDs. The ADI-R gathers

comprehensive information about the child from a parent in three domains of development: social, communication, and SIB. The ADI-R interview contains approximately 93 scores, 42 of which are included in a final diagnostic algorithm based on the Diagnostic and Statistical Manual of Mental Disorders-4th Edition (DSM-IV; American Psychiatric Association, 1994). The final diagnostic algorithm is further divided into four areas: social (16 items), communication (13 items), SIB (8 items), and developmental delays less than three years of age (5 items). Examples of diagnostic items in each domain are interest in other children (social), pointing to express interest (communication), unusual preoccupations (SIB), and emergence of first single words after 24 months (developmental delays less than three years of age). Individual items are scored as 0, 1, or 2 on the diagnostic algorithm. Autism classification, subsequently referred to as the ADI-R total score, is determined by scores on all four sub-domains: a score of 10 or higher on the social domains, a score of 7 or 8 or higher on the communication domain (depending on whether the child is nonverbal or verbal), a score of 3 or higher on the SIB domain, and a score of 1 or higher indicating developmental delays less than three years of age must be obtained for autism classification. Inter-rater reliability for ADI-R algorithm items scored on children 36-59 months of age were between .64 and .89 (Lord, Rutter, & Le Couteur, 1994). Discriminant validity was measured in a sample of children 39-59 months of age with autism ($n = 25$) and language impairment or intellectual disability ($n = 25$); all ADI-R algorithm items significantly distinguished children with autism from children with intellectual or language impairment (Lord, Rutter, & Le Couteur, 1994).

It is important to note that although the ADI-R is only appropriate for children with a mental age of ≥ 24 months, it is often used in clinical and research practice with very young children because of lack of other appropriate measures. Specifically, there is not another parent

interview that gathers comprehensive diagnostic information on very young children and can distinguish those with autism from those without autism. In response to this dilemma, the authors of the ADI-R have created a revised version of the interview that is more appropriate for toddler samples, the ADI-R Toddler Version (ADI-R-TV). The ADI-R-TV is currently being field tested and was used in a portion of the current sample. The primary differences between the ADI-R-TV and the ADI-R are that the ADI-R-TV contains questions only appropriate for toddlers and not appropriate for older children, and that non-algorithm items that are not appropriate for young children were eliminated. For instance, the ADI-R-TV contains several questions on toilet training; the ADI-R-TV does not contain questions on advanced conversational skills. Despite these differences, the diagnostic algorithm for the ADI-R-TV is an exact replica of the diagnostic algorithm of the ADI-R. Furthermore, criteria for scoring and determining autism classification are the same. Therefore, the ADI-R-TV will subsequently be called the ADI-R throughout this report.

The *Autism Diagnostic Observation Schedule* (Lord et al., 1999) is a standardized instrument in which the researcher observes the child and tries to elicit social interaction and communication using structured play activities. The examiner implements the module that best corresponds to the child's expressive language level in order to prevent language aptitude from impeding accurate diagnosis. Most children in this study were administered Module 1, designed for children who are not regularly using phrase speech. Module 1 of the ADOS contains 29 scores, 17 of which are included in a final diagnostic algorithm. The final diagnostic algorithm is further divided into four domains: social (7 items), communication (5 items), SIB (3 items), and play (2 items). Examples of items in each domain are unusual eye contact (social), frequency of vocalizations directed toward others (communication), unusual sensory interests

(SIB), and functional play with objects (play). Individual items are scored as 0, 1, or 2 on the diagnostic algorithm. ASD diagnosis, subsequently referred to as the ADOS total score, is determined by scores on the social and communication domains: a score of 2 or higher on the communication domain, a score of 4 or higher on the social domain, and a score of 7 or higher on the communication and social interaction combined score must be obtained for ASD classification. The mean inter-rater reliability for Module 1 items is 92% and reliability for ASD classification is 100%. Validity has been measured with sensitivity and specificity values of 97% and 94% for autism versus ASD and 100% and 79% for children diagnosed with ASD versus children who are typically developing (Lord et al., 2000).

The *Childhood Autism Rating Scale* (Schopler, Reichler, & Renner, 1988) is a standardized observation instrument used to diagnose ASDs in children two years and older; parent report can also be considered when determining item scores. The CARS rates children suspected of having an ASD on 15 items, including relating to people, imitation, emotional response, body use, object use, adaptation to change, visual response, listening response, sensory response, fear or nervousness, verbal communication, nonverbal communication, activity level, intellectual response, and general clinical impressions. Individual items are scored on a 7-point Likert scale rated from one to four in half-point increments. The final diagnostic algorithm represents a sum of item scores and classifies the child as having severe autism (37-60 points), mild-moderate autism (30-36 points), or no autism indicated (15-29 points). Reliability estimates for the CARS are as follows: internal consistency is .94, inter-rater reliability is .71, and test-retest reliability is .88. Criterion-related validity was established by correlating total CARS scores and general clinical rating of autism severity obtained during the same diagnostic session. The resulting correlation was .84. In a recent study conducted by Wiggins and Robins

(2008), diagnostic agreement between the CARS and clinical judgment was better than diagnostic agreement between the ADI-R and ADOS and clinical judgment.

The *Mullen Scales of Early Learning* (MSEL, Mullen, 1995) is a standardized measure of cognition appropriate for children from birth to 68 months of age. The examiner presents a series of tasks created to measure five cognitive domains: (a) gross motor, (b) fine motor, (c) expressive language, (d) receptive language, and (e) visual reception. Examples of tasks appropriate for a 24-month old child for each domain are running swiftly (gross motor), turning pages in a book (fine motor), labeling pictures (expressive language), recognizing body parts (receptive language), and matching objects (visual reception). Raw scores can be converted to t-scores, percentile ranks, and age equivalents. An early learning composite, created from all domains except gross motor, is also provided. Reliability estimates for the MSEL are as follows: internal consistency estimates for MSEL domains for 0-2 year-old children range from .63-.83, internal consistency for the early learning composite is .87, inter-rater reliabilities for 0-6 year-old children range from .91-.97, and test-retest reliabilities range from .71-.96. Concurrent validity was supported with high correlations between the MSEL Early Learning Composite and Bayley Mental Development Index (r = .70), the MSEL gross motor scale and Bayley psychomotor development scale (r = .76), the MSEL fine motor scale and the Peabody fine motor scale (r = .65-.82), the MSEL receptive language scale and Preschool Language Assessment (PLA) auditory comprehension scale (r = .85), the MSEL expressive language scale and the PLA verbal ability scale (r = .80).

The *Vineland Adaptive Behavior Scales* (VABS, Sparrow, Balla, & Cichetti, 1984) is a semi-structured parent interview that assesses personal and social sufficiency in individuals from birth to 18 years. Specifically, the VABS assesses four domains of adaptive behavior:

communication, daily living skills, socialization, and motor abilities; these four domains are further divided into subdomains. Examples of questions appropriate for a 24-month old child for each domain are whether the child names at least three objects (communication), demonstrates caution around hot objects (daily living), plays simple interaction games (socialization), and walks across the room (gross motor). Raw scores can be converted to standard scores, percentile ranks, and age equivalents. An adaptive behavior composite, created from all domains, is also provided. Internal consistency estimates for parents of 0-5 year-old children are .89-.93 for VABS domains and .97 for the adaptive behavior composite. Inter-rater reliabilities for parents of 0-6 year-old children are .61-.82 for VABS domains and .80 for the adaptive behavior composite. Test-retest reliabilities for parents of 0-2 year-old children are .86-.95 for VABS domains and .96 for the adaptive behavior composite. Confirmatory factor analyses for 3-6 year-old children confirmed a four factor structure consisting of communication, daily living, socialization, and motor domains. Additional analyses on children with ASDs found significantly lower adaptive behavior composites for an ASD clinical group versus a non-clinical reference group; the lowest subdomain scores for the ASD group were in interpersonal relationships, play and leisure time, and expressive communication.

It is important to note that 4% of the sample received the VABS-II (revised edition). The VABS-II is similar to the VABS in that it is a semi-structured parent interview that assesses personal and social sufficiency in four domains of adaptive behavior; these four domains are further divided into subdomains. However, the VABS-II offers updated norms based on the most recent census report, expanded age range (from birth to 90 years of age), updated item content, and revised interview format that lists items by subdomain. Furthermore, the VABS-II

offers developmental profiles for a variety of childhood disorders, including intellectual disability and ASDs.

Correlations between the VABS and VABS-II range from .65 to .91 for children 0-2 years of age. Specifically, correlations between the two measures are .65 for the communication domain, .75 for the daily living skills domain, .85 for the socialization domain, .91 for the motor skills domain, and .82 for the adaptive behavior composite.

Procedures Utilized for Research

Families of children who failed the M-CHAT, failed the follow-up interview, and agreed to participate in the study were scheduled for a free, comprehensive clinical evaluation. The clinical evaluation took place at the UConn clinic, GSU clinic, child's home, or early intervention provider's site. Two weeks prior to the scheduled evaluation, the family was mailed a history form to complete and return to UConn or GSU study personnel. The history form included questions concerning the pregnancy history of the mother and birth and early developmental history of the child. For instance, the mother was asked whether she was hospitalized or had toxemia, bleeding, fever, rash, diabetes, or other complications during pregnancy. The mother was also asked if a Cesarean section was performed, if labor was induced, if the child was considered premature, and if the child required oxygen immediately after birth.

Information elicited on early developmental history included information medical treatments (e.g., for otitis media, seizures, visual defects, and hyperactivity), attainment of developmental milestones (e.g., age when child first smiled at mother, crawled, used single words, and followed simple directions), descriptions of childhood behavior (e.g., whether the child appeared very quiet as a baby, had an unusual long attention span for a preferred activity,

and laughed or cried unexpectedly), and information on family history (e.g., date of birth for mother, father, and siblings and medical and psychiatric diagnoses for family members).

When the family arrived for the clinical evaluation, they were escorted into a child-friendly evaluation room that accommodated a research assistant, two clinicians, the parent, and the child. At the onset of the evaluation, study staff reviewed the informed consent form, asked written permission to videotape the evaluation, and gathered any missing information from the history form. Evaluations began after all questions were answered and all permissions were received.

Evaluations were completed by at least two clinicians: a licensed psychologist or developmental pediatrician who specializes in ASDs and a doctoral student working under her supervision. Evaluations consisted of both child and parent measures and included the ADI-R, ADOS, CARS, MSEL, and VABS. All clinicians had prior experience with the diagnostic measures before study administration. Furthermore, clinicians who administered the ADI-R and ADOS had established standard research reliability, which entails 90% algorithm reliability on three consecutive administrations of the ADI-R and 80% algorithm reliability on three consecutive administrations of the ADOS. It is important to note that scores from the ADOS and CARS were generated from a similar behavioral sample and the same clinician often administered both of these instruments. However, previous reliability exercises found that inter-rater reliability for the CARS differed on average of 2.8 out of 60 points for a subset of children included in this sample, suggesting that CARS was scored according to a standardized protocol and scoring scheme.

The MSEL, ADOS, and CARS were videotaped if videotape permission was received. The MSEL, ADOS, and CARS were administered to the child in one part of the room and the

VABS and ADI-R was administered to the parent in another part of the room. Although the child and parent worked in separate sides of the room, they were able to see and interact with each other throughout the evaluation. If the child had difficulty separating from the parent (or difficulty warming to examiners), the parent was asked to sit with the child at the evaluation table. Breaks were given to the child and parent as needed.

The evaluation took approximately 2.5 hours to complete. After the evaluation was complete, clinicians instantly scored the instruments and discussed evaluation results. Immediate feedback was provided to the family; questions and concerns were addressed by the licensed clinical psychologist or developmental pediatrician. The family was mailed a comprehensive evaluation report within one month of the clinical evaluation. The evaluation report described scores on each instrument and provided an overall developmental profile, relevant clinical diagnoses, and relevant treatment recommendations for the child. All families were invited back to the UConn or GSU clinic around the child's fourth birthday to repeat the evaluation process. The same instruments and procedures from the 2-year evaluation were used for follow-up.

Data Analyses

Data analyses addressed the following research questions: (a) Are there empirically derived subgroups of children who fail an autism screen and are subsequently diagnosed with developmental concerns in the toddler years?, (b) Are there empirically derived subgroups of children who fail an autism screen and are subsequently diagnosed with ASDs in the toddler years?, (c) What characteristics best define clinically distinct subgroups?, (d) How does ASD subgroup membership forecasts performance on common diagnostic instruments?, and (e) How does ASD subgroup membership predict diagnosis two years later?. Determining empirically

derived subgroups of toddlers via cluster analysis was the primary focus of the study since all other analyses were based on resultant clusters.

Cluster Analysis

Two hierarchical cluster analyses were performed to classify empirically derived subgroups of children who fail an autism screen in the toddler years. The first cluster analysis included children with any diagnosis indicating developmental delay; the second cluster analysis included children with an ASD only. Cluster analysis is a multivariate statistical procedure that classifies cases in a dataset that are similar to one another. Unlike factors analysis or other statistical methods, cluster analysis is typically used to classify cases rather than variables or items. Therefore, for the purpose of this study, cluster analysis was used to locate children with ASDs and DDs most similar to one another on CARS items and sort them into homogeneous groups. Hierarchical cluster analysis was preferred because it can be used with datasets of a few hundred individuals and is not sensitive to skewed data.

Cluster analysis is typically divided into six discrete steps: (a) obtaining the data matrix, (b) standardizing the data matrix, (c) computing the resemblance matrix, (d) executing the clustering method, (e) determining the number of clusters, and (f) validating the cluster solution. Each of these steps will be addressed, in turn, in the following sections.

Obtaining the data matrix.

Obtaining the data matrix is a relatively easy step in the cluster analysis process. Essentially, the data matrix consists of rows that represent cases and columns that represent cluster variables. For the purpose of this project, the data matrix was an SPSS data file that contained client identification numbers and scores for each CARS item.

Standardizing the data matrix.

Standardizing the data matrix is optional, but considered standard procedure for most clustering methods. Standardizing the data matrix converts original scores into z-scores, which is useful when cluster variables are measured on different scales. Converting original scores into z-scores is also useful for changing numerical values into dimensionless values and for creating measures of dispersion meaningful to the population studied. Therefore, standardization techniques were employed in this study.

Computing the resemblance matrix.

The resemblance matrix is a matrix that contains resemblance measures between each pair of cases. The resemblance measures are known as resemblance coefficients, and are calculated from a formula that represents the similarity or dissimilarity between cases. The most common resemblance coefficient used in cluster analysis is the squared Euclidean distance coefficient (Aldenderfer & Blashfield, 1984). The squared Euclidean distance coefficient measures the literal distance between two cases when represented in a multidimensional plane defined by cluster variables. Therefore, the Euclidean distance formula is the measure of the hypotenuse of a right triangle defined on the abovementioned plane. Since the Euclidean distance coefficient is essentially the Pythagorean Theorem, the quantitative formula is represented by: $c = (a^2 + b^2)^{1/2}$.

Executing the clustering method.

There are several clustering methods that can be employed to classify cases into homogeneous groups, including single linkage, complete linkage, average linkage, and Ward's method. Single linkage, complete linkage, and average linkage use the following procedure for merging cases into clusters: Once a squared Euclidean distance coefficient is calculated for each

pair of cases, the two cases with the lowest coefficient are merged into one cluster (e.g., the smaller the squared Euclidean distance coefficient the more similar the two cases). The resemblance matrix is then recalculated considering the merged pair as one case; this procedure is repeated until all cases have been defined into one overarching cluster group and (potentially) several subgroups. The difference between these three methods is that when adding cases into a cluster, single linkage considers the minimum distance between all other cases in that cluster, complete linkage considers the maximum distance between all other cases in that cluster, and average linkage considers the average distance between all other cases in that cluster (Romesburg, 1984).

Unlike other clustering methods, Ward's method bases the decision to merge clusters on pairs of cases that would result in the smallest increase in variance. Therefore, every possible merger must be considered before reaching a conclusion to merge cases. But before mergers are considered, the mean for each cluster must be determined. The mean for each cluster is a value that represents the average variable values for cases being considered in a particular cluster. After cluster means are determined, the difference between each case in a given cluster and the cluster mean are calculated and squared. The squared differences are then added, giving a sum of squares value for each cluster. Change in variance is determined by adding the sum of squares values for all clusters; cases that result in the least change in variance are merged together. Typically, Ward's method results in the most well-defined and homogeneous groups of cases. Furthermore, Ward's method has shown excellent recovery of known cluster structures (Aldenderfer & Blashfield, 1984). However, there are some limitations associated with Ward's method. For instance, Ward's method is described as a "space-dilating" method that causes clusters to recede on formation, thus producing distinct subgroups of relatively equal size.

Therefore, whereas other clustering methods may find one large subgroup, Ward's method may produce two subgroups using the same data. Also, cases are never unmerged in subsequent steps, meaning that the minimum variance at each step depends on clusters already formed.

Despite these limitations, Ward's method tends to produce well-defined, homogeneous subgroups and has excellent recovery of known cluster solutions. Therefore, Ward's method was the clustering method chosen for examining empirically derived subgroups of toddlers with ASDs; the cluster solution generated from Ward's method was used in subsequent analyses. However, due to the limitations of Ward's method, as well as consideration of the fact that different clustering methods produce different solutions, complete linkage was also utilized to examine subgroups of children who fail an autism screen. The subgroups produced by Ward's method and complete linkage were compared for consistency across methods.

Determining the number of clusters.

Determining the number of clusters in a cluster solution has been criticized as the most subjective aspect of the cluster process. Indeed, heuristic procedures are the most commonly used procedures for determining the number of clusters in a solution. In fact, the examination of graphical cluster output, otherwise known as the dendogram or tree, is standard practice for deciding cluster structure. Deciding where to "cut" the tree is left to the researcher, who may be biased by his or her own opinions and research hypotheses.

An alternative to determining the number of clusters by examination of graphical output is inspection of the agglomeration schedule, which displays the numerical values at which cases merge to form a cluster. Inspection of the agglomeration schedule typically reveals a "jump" in values, which indicates that two relatively dissimilar clusters have been merged. Therefore, the

number of values prior to the "jump" reveals the most appropriate number of clusters in a given solution (Romesburg, 1984).

An inspection of the agglomeration schedule was used to determine the number of clusters in this study. The number of clusters determined by inspection of the agglomeration schedule was verified by inspection of the cluster dendogram (or cluster tree).

Validating the cluster solution.

It is important to validate the cluster solution produced by a cluster analysis using significance tests on external variables. External variables are defined as variables that were not used to generate the cluster solution. According to Aldenderfer and Blashfield (1984), this validation technique is the most highly regarded because it tests the generality of a cluster solution against a set of pertinent external criteria.

The external variables that were used to validate the cluster solutions are MSEL expressive language scores, MSEL receptive language scores, MSEL visual reception scores, MSEL fine motor scores, VABS communication scores, VABS socialization scores, VABS daily living scores, and VABS motor scores. ADOS social scores, ADOS communication scores, ADOS SIB scores, ADOS play scores, ADI-R social scores, ADI-R communication scores, and ADI-R SIB scores were also used to validate the cluster solutions. Each of these variables were considered dependent variables in ANOVA analyses to assess mean differences between study groups. Since multiple analyses increase the likelihood of Type I error, an alpha level of .01 was chosen for all ANOVA analyses. Tukey's b post-hoc analyses were used to determine difference between cluster subgroups.

Separate ANOVAs were performed to determine subgroup differences on individual SIB item scores included on the ADI-R diagnostic algorithm and individual SIB item scores included

on the ADOS diagnostic algorithm. This analysis was performed to determine whether ASD cluster subgroups differ on additional SIB than those included as cluster variables (i.e., CARS items). Tukey's b post-hoc analyses were used to determine difference between cluster subgroups.

Additional analyses were performed to test whether cluster subgroups differ on potential confounds. Specifically, ANOVA and chi-square analyses were performed to test whether cluster subgroups differ on sex, race, and chronological age at time of evaluation. For the ASD only solution, chi-square analyses were also performed to test whether the same clinician administered the CARS and ADOS and whether the child received a 4-year follow-up evaluation.

Discriminant Function Analyses

Discriminant function analysis (DFA) was used to determine cluster variables that best defined resultant subgroups. DFA is used to determine which variables discriminate between, or are the best predictors of, two or more naturally occurring groups. Thus, each of the CARS items were entered into a DFA as an independent variable and the cluster solution was entered as the grouping variable. Since two cluster analyses were performed, two disciminant function analyses were also performed: one with the cluster solution generated from children diagnosed with ASD only and one with the cluster solution generated from children diagnosed with ASD and DD. Wilk's Lambda was used to test the overall significance of each DFA. Standardized DFA coefficients and structure coefficients were also examined. Standardized DFA coefficients indicate the unique association of each independent variable to the DFA controlling for all other independent variables. In contrast, structure coefficients are similar to correlation coefficients, and reflect the uncontrolled association of each independent variable with the discriminant

functions. Therefore, the standardized DFA coefficients were used to assess the importance of each independent variable's unique contribution to the DFA and the structure coefficients were used to assign meaningful labels to the DFA.

Additional DFAs were conducted to determine which external variables best defined resultant subgroups. It is important to note that the advantage of DFA in these analyses was examination of standardized DFA coefficients and structure coefficients. As stated previously, examination of these two coefficients allows the researcher to assess the unique contribution of each variable's contribution to the DFA and assign meaningful labels to the DFA. The external variables that were entered into the DFA were the same as those that were used to validate the cluster solution: MSEL expressive language scores, MSEL receptive language scores, MSEL visual reception scores, MSEL fine motor scores, VABS communication scores, VABS socialization scores, VABS daily living scores, and VABS motor scores; ADOS social scores, ADOS communication scores, ADOS SIB scores, ADOS play scores, ADI-R social scores, ADI-R communication scores, and ADI-R SIB scores were also included in the DFAs. Furthermore, the discriminant function generated from children diagnosed with an ASD was compared to children diagnosed with DD as an additional validation technique to support the hypotheses that this discriminant function is unique to the autism spectrum.

Sensitivity of Diagnostic Instruments

The psychometric properties of diagnostic instruments are typically evaluated with measures of sensitivity and specificity. Sensitivity is the proportion of children with the disorder correctly identified by the diagnostic instrument, whereas specificity is the proportion of children without the disorder correctly identified by the diagnostic instrument. False negatives (children

with the disorder who score negative) decrease sensitivity, whereas false positives (children without the disorder who score positive) decrease specificity.

Sensitivity for the ADOS and ADI-R, two of the most common diagnostic instruments, was calculated for each ASD cluster subgroup. Specifically, the proportion of children in each ASD cluster subgroup correctly classified by the ADOS and ADI-R was calculated to assess sensitivity. Alternative diagnostic algorithms were explored for measures of sensitivity below acceptable standards (i.e., less than .80). Specifically, it was hypothesized that many children with ASDs, especially those with higher social, language, and intellectual functioning would not meet criteria for the SIB domain of the ADI-R. Therefore, the influence of removing the ADI-R behavioral domain for autism classification was explored. Furthermore, it was felt that several items not currently included on the ADI-R diagnostic algorithm may distinguish young children with ASD from young children with DD, such as loss of previously acquired language, use of other's body to communicate, lack of attention to voice, unusual sensitivity to noise, and unusual attachment to objects. Consequently, ANOVA analyses were conducted to examine whether these items produced means differences between children with ASD and children with DD.

Multinomial Logistic Regression

A multinomial logistic regression was conducted to examine how ASD subgroup membership predicts diagnosis two years later. Specifically, clinical diagnosis around four years of age was coded into three categories: nonASD, PDD-NOS, and Autistic Disorder. These categories were entered as the dependent variable. The categorical, three-level ASD cluster membership was entered as the independent variable. The reference category for four year diagnoses was Autistic Disorder. The Chi-Square statistic and associated p-value were used to test the overall significance of the model (i.e., whether the cluster model predicts diagnosis better

than the intercept-only model); Wald Statistics and associated p-values were used to test the significance of cluster each cluster subgroup in predicting four year diagnoses. The exponentiate of the (b) coefficients were interpreted as odds-ratios, which are differences in the odds likelihood of membership in various diagnostic groups.

CHAPTER 3: RESULTS

Sample Characteristics

The original study sample consisted of 200 toddlers who failed an autism screen; 186 toddlers were subsequently diagnosed with an ASD around two years of age, 102 toddlers were subsequently diagnosed with other DD around two years of age, and 12 were subsequently found to have typical development. Since the focus of these analyses were on toddlers who failed an autism screen and were subsequently found to have developmental concerns, the 12 children with typical development were dropped from the study; leaving a final sample of 288 toddlers. Of the 186 children diagnosed with an ASD, 113 were diagnosed with Autistic Disorder, 72 were diagnosed with PDD-NOS, and one was diagnosed with Asperger's Disorder. Of the 102 toddlers diagnosed with other DD, 57 were diagnosed with a language disorder, 29 were diagnosed with intellectual disability, six were labeled "broader autism phenotype", five were diagnosed with a motor delay, three were diagnosed with a regulatory disorder, one was diagnosed with Attachment Disorder, and one was diagnosed with Attention Deficit Hyperactivity Disorder. It is important to note that the "broader autism phenotype" is not a clinical diagnosis. Rather, the term describes a child that displays some characteristics of ASDs, but these characteristics are not of the quantity or quality to warrant an ASD diagnosis.

The sample was 80% male and 20% female, which constituted a male: female ratio of 4:1. The male: female ratio of this sample is comparable to the male: female ratio of larger

samples of children with ASDs and reflects a higher male prevalence of the disorders (Centers

for Disease Control and Prevention, 2007). One hundred and seventy two children had race data;

143 of these children were White, 11 were Black, seven were Hispanic (including Puerto Rican),

four were Asian, two were bi-racial, one was Hawaiian, and four chose "other" to describe their

race. The average age at time of evaluation and diagnosis was 26 months (range = 13-37

months; *SD* = 5 months). The chronological age at time of evaluation and diagnosis did not

differ by study group (i.e., ASD or DD; *F* (1, 287) = 0.05, *p* = .94).

Two hundred seventy children had cognitive data as assessed by the MSEL (*N* = 226), the

Bayley Scales of Infant Development (Bayley; *N* = 36), or the Differential Abilities Scales

(DAS; *N* = 8). The average cognitive standard score was 66, reflecting mild intellectual

disability. There was a significant difference in average cognitive standard score based on study

group, *F* (1, 269) = 27.1, *p* < .01. Specifically, children with ASDs had an average cognitive

standard score of 61 and children with DD had an average cognitive standard score of 74. Eighty

percent of the ASD sample had cognitive test scores at or below 70 points. Again, this finding is

comparable to results using larger samples and expected rates of the prevalence of intellectual

disability among persons with ASDs (Gillberg & Billstedt, 2000). Furthermore, the range of

cognitive test scores for the ASD sample was 49-127, reflecting a heterogeneous presentation of

intellectual abilities, including a "floor effect" among some children (i.e., a score of 49). Again,

this was expected given population-based studies that suggest the range of intellectual abilities in

the autism spectrum vary widely (Centers for Disease Control and Prevention, 2007).

The mean CARS total score was 29 (range = 16-46); the mean CARS score also differed

significantly based on study group, *F* (1, 287) = 380, *p* < .01. The mean CARS score for

children with ASDs was 33 (range = 20-46), reflecting mild-moderate autistic impairment. The

mean CARS score for children with DD was 22 (range = 16-32.5), reflecting no autistic impairment. It is important to note that 47 children in the ASD sample did not meet the CARS cutoff criteria for autism (i.e., a total score of 30 or above); children diagnosed with PDD-NOS or mild autism are often rated with subthreshold autistic symptomatology on standardized diagnostic instruments. Five children in the DD sample met CARS criteria for autism; four of these children were diagnosed with intellectual disability and one of these children was diagnosed with a language disorder.

Data were initially screened to detect outliers in the total CARS score for the entire study population and for the population of children with ASDs. Again, outliers were defined as scores that were 1.5 times above or below the inter-quartile range as depicted on a box and whiskers plot for the population of interest (i.e., ASD and DD or ASD only). Results did not find any outliers for the entire study population or the ASD population. Therefore, data analyses proceeded as planned.

Each cluster variable (i.e., CARS item) was also screened to detect outliers due to errors in measuring and coding the data. Outliers were detected for items relating to emotional response, object use, resistance to change, sensory response, fear, verbal communication, and intellectual response. Since these outliers reflected true variations in behavioral presentation rather than errors in measuring and coding the data, they were retained for data analysis. Specifically, variations are expected to exist on individual item scores due to differences in specific aspects of behavioral presentation. These variations are especially important in cluster analysis since the purpose of cluster analysis is to describe similarities (and differences) among cases in a particular sample. Therefore, since the item presentation among children in this sample naturally varied from one extreme to another, this is important information to consider

when describing the phenotypic and behavioral manifestations of ASDs in the toddler years and determining which characteristics best distinguish identified subgroups.

Cluster Analyses

Two hierarchical cluster analyses were performed to classify empirically derived subgroups of children who failed an autism screen and subsequently were found to have developmental concerns in the toddler years. The first cluster analysis included children with ASD and DD; the second cluster analysis included children with ASD only. Although the primary interest of the author was the cluster analysis on children with ASD only, the cluster analysis on children with ASD and DD was included in order to identify homogeneous subgroups of children who fail an autism screen and have developmental concerns and variables that most distinguish resultant subgroups.

Cluster Analysis for Entire Study Population

The first cluster analysis included children with ASD and DD who failed the M-CHAT in the toddler years. Ward's method revealed two distinct clusters: Cluster 1 consisted of 133 children and Cluster 2 consisted of 155 children. Of the 133 children in Cluster 1, 39 (29%) were diagnosed with an ASD and 94 (71%) were diagnosed with a DD (see Figure 1). Of the 39 children diagnosed with an ASD in Cluster 1, eight were diagnosed with Autistic Disorder, 30 were diagnosed with PDD-NOS, and one was diagnosed with Asperger's Disorder. Cluster 1 also included all six children labeled as "broader autism phenotype."

Of the 155 children placed in Cluster 2, 147 (95%) were diagnosed with an ASD and eight (5%) were diagnosed with DD. Of the 147 children diagnosed with an ASD, 105 were diagnosed with Autistic Disorder and 42 were diagnosed with PDD-NOS. Of the eight children diagnosed with DD, five were diagnosed with intellectual disability, two were diagnosed with a language

disorder, and one was diagnosed with a regulatory disorder (five of these eight children, including four children diagnosed with intellectual disability and one child diagnosed with a language disorder, met CARS cutoff criteria for autism). It was important to assess which cluster variables were most important in distinguishing children placed in Cluster 1 from children placed in Cluster 2 to further elucidate differences between cluster groups.
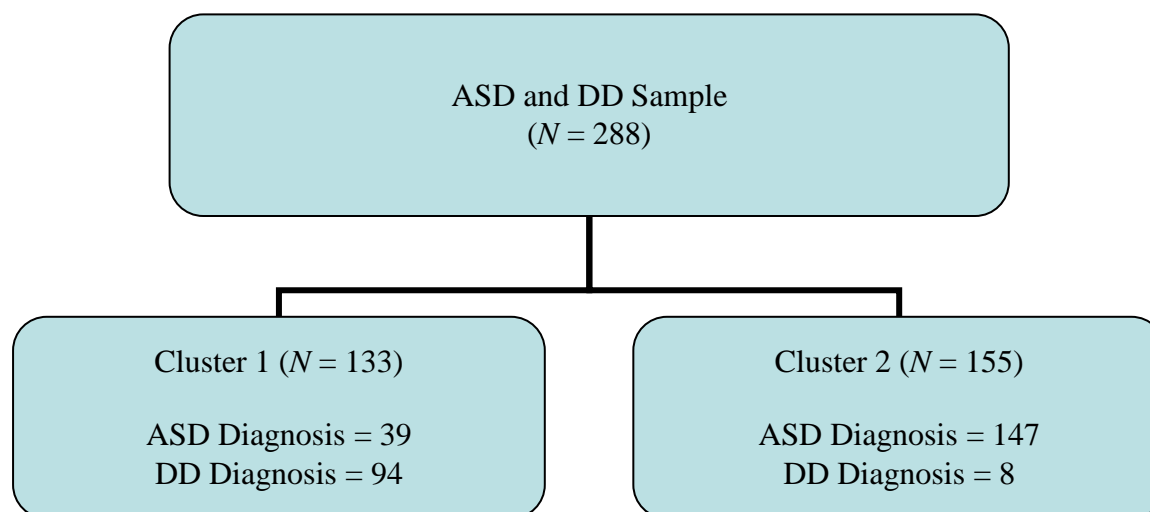
Figure 1. Results of Ward's cluster analysis for the entire study sample (i.e., ASD and DD).

Therefore, a DFA was performed on the entire study population. For this analysis, the cluster solution generated by Ward's method was used as the grouping variable and individual CARS items were used as the independent variables. Results showed that the discriminant function was significant in differentiating cluster groups, Wilks' lambda = .26, χ^2 (15, $N = 300$) = 374, $p < .01$. Standardized DFA coefficients (DFAC) were then examined to determine which independent variables most contributed to cluster group differences. Variables that assessed general impressions of an ASD, emotional response, and imitation most distinguished cluster groups (see Table 2).

Table 2

Variables that Most Contributed to Differences Between Cluster Groups for Entire Study

Sample

	DFAC
General impressions	.36
Emotional response	.30
Imitation	.30
Intellectual response	.23
Relating to people	.23
Nonverbal communication	.20
Object use	.18
Fear	.17
Activity level	.09
Sensory response	.07
Verbal communication	.07
Body use	.06
Visual response	.06
Listening response	.06
Resistance to change	.02

In order to further validate whether these two groups were distinctly different from one

another, the cluster groups were compared on variables that were not used to generate the cluster

solution. There was a significant difference in total cognitive standard score based on cluster

group membership, $F (1, 269) = 49.5, p < .01$. Specifically, Cluster 1 had higher cognitive

standard scores (as measured by the Bayley, DAS, and MSEL; $M = 74$) than Cluster 2 ($M = 68$).

Moreover, there was a significant difference in the proportion of children in each cluster who had a cognitive standard score less than or equal to 70 points, χ^2 (1, $N = 270$) = 43.9, p < .01. Specifically, 49% of Cluster 1 children were intellectually disabled and 87% of Cluster 2 children were intellectually disabled.

Cluster groups were next compared on MSEL domain scores, VABS domain scores, the CARS total score, ADOS domain scores, and ADI-R domain scores. MSEL domain scores are reported as T scores and VABS domain scores are reported as standard scores; higher scores on both measures indicate more advanced skills. In contrast, the CARS total score, ADOS domain scores, and ADI-R domain scores are reported as summary scores; higher scores on all these measures indicate more autistic deficit. As table 3 illustrates, Cluster 1 performed significantly better across all measures except the VABS motor domain than Cluster 2. In addition, effect sizes showed that moderate to large effects for distinguishing cluster groups were found primarily within the social and communication domains; on average, Cluster 2 children met ASD criteria on the ADOS and CARS and autism criteria on the ADI-R whereas Cluster 1 children did not. Therefore, cluster groups for the entire study population were labeled "many ASD symptoms" (Cluster 2) and "fewer ASD symptoms" (Cluster 1).

It is important to note that Cluster 1 children diagnosed with an ASD differed from Cluster 2 children diagnosed with an ASD in that they had more intellectual and adaptive abilities and less autistic symptomatology. Specifically, the 39 children with an ASD placed in the first cluster had a lower CARS total score (i.e., the mean CARS score for these children did not reach cut-off criteria for autism), higher MSEL expressive language, receptive language, visual reception, and fine motor scores, and higher VABS communication, socialization, and daily living scores than the 147 children with an ASD placed in the second cluster (see Table 4).

Table 3

Differences between Cluster 1 ("Many ASD Symptoms") and Cluster 2 ("Fewer ASD Symptoms") Generated from Cluster Analysis

	Cluster 1 (N = 133)	Cluster 2 (N = 155)			
	M (SD)	*M (SD)*	*F*	*p*	*η²*
CARS total score	23.1 (3.66)	34.4 (4.28)	562	<.01	.66
MSEL expressive language	32.7 (11.2)	25.2 (10.9)	27.3	<.01	.10
MSEL receptive language	32.4 (14.1)	23.7 (10.4)	29.4	<.01	.11
MSEL visual reception	35.9 (12.8)	26.9 (10.6)	33.7	<.01	.13
MSEL fine motor	35.3 (13.1)	28.5 (11.6)	17.1	<.01	.07
VABS communication	76.2 (12.1)	64.6 (7.37)	96.4	<.01	.26
VABS socialization	78.8 (10.4)	67.8 (8.56)	95.1	<.01	.25
VABS daily living	77.4 (12.3)	69.1 (10.1)	39.2	<.01	.12
VABS motor	84.8 (12.4)	82.6 (12.6)	2.29	.06	.01
ADOS socialization	2.78 (1.98)	6.01 (1.75)	143	<.01	.43
ADOS communication	4.04 (3.53)	10.2 (2.97)	170	<.01	.47
ADOS play	1.56 (1.41)	3.29 (1.06)	93.4	<.01	.33
ADOS SIB	1.10 (1.33)	3.04 (1.76)	71.2	<.01	.27
ADI-R socialization	8.01 (5.04)	15.2 (3.47)	122	<.01	.41
ADI-R communication	7.23 (3.91)	11.2 (2.44)	68.3	<.01	.28
ADI-R SIB	1.67 (2.27)	2.73 (2.13)	7.98	<.01	.05

Table 4

Differences between Children Diagnosed with ASD Placed in Cluster 1 versus Children

Diagnosed with ASD Placed in Cluster 2 for Entire Study Sample

	Cluster 1 (N = 39)	Cluster 2 (N = 147)			
	M (SD)	*M (SD)*	*F*	*p*	*η²*
CARS total score	26.4 (3.15)	34.6 (4.22)	128	<.01	.41
MSEL expressive language	33.4 (11.9)	24.5 (9.98)	19.1	<.01	.12
MSEL receptive language	28.5 (11.6)	23.1 (9.39)	8.31	<.01	.05
MSEL visual reception	34.2 (10.7)	26.8 (10.8)	12.5	<.01	.08
MSEL fine motor	34.8 (13.9)	28.4 (11.6)	7.53	<.01	.05
VABS communication	75.3 (13.9)	64.6 (7.40)	41.5	<.01	.19
VABS socialization	74.7 (8.57)	67.7 (8.49)	20.6	<.01	.10
VABS daily living	74.1 (10.2)	69.1 (10.3)	7.03	<.01	.04
VABS motor	83.9 (9.55)	82.4 (12.6)	0.44	.51	.00
ADOS socialization	3.89 (1.63)	6.22 (1.51)	49.0	<.01	.28
ADOS communication	6.52 (3.32)	10.5 (2.64)	42.2	<.01	.26
ADOS play	1.89 (1.23)	3.38 (1.00)	44.3	<.01	.27
ADOS SIB	1.70 (1.64)	3.03 (1.80)	11.9	<.01	.09
ADI-R socialization	11.5 (4.29)	15.4 (3.35)	23.5	<.01	.17
ADI-R communication	9.15 (3.02)	11.3 (2.41)	14.4	<.01	.11
ADI-R SIB	1.52 (2.02)	2.70 (2.14)	5.06	<.01	.05

Cluster 1 children who had an ASD also performed significantly better on all ADOS and ADI-R domains (see Table 4). These findings are not particularly surprising given that children with ASDs have a broad range of abilities (including social and communication abilities). Moreover, many children with ASDs are verbal and interested in social relationships, but may not understand the nuances of social interactions (such as social imitation, emotional response, and relating to people). Therefore, if Ward's method divided the sample based on social, communication, and intellectual abilities, it is not remarkable that many children with ASDs were placed in the cluster with fewer ASD symptoms.

Of the 186 children who were diagnosed with an ASD as a toddler, 120 received a repeat clinical evaluation around four years of age. A chi-square analysis revealed a significant difference in the proportion of Cluster 1 and Cluster 2 children with an ASD who were diagnosed with nonASD, PDD-NOS, and Autistic Disorder around their fourth birthday, χ^2 (1, N = 120) = 9.24, p = .01. Specifically, of toddlers with an ASD placed in Cluster 1, 32% received a nonASD diagnosis, 32% received a PDD-NOS diagnosis, and 36% received an Autistic Disorder diagnosis around four years of age. In contrast, of toddlers placed in Cluster 2, 14% received a nonASD diagnosis, 18% received a PDD-NOS diagnosis, and 68% received an Autistic Disorder diagnosis around four years of age.

Additional analyses were performed to test whether cluster groups differed on potential confounds and whether another cluster method yielded a similar solution. Specifically, ANOVA and chi-square analyses were performed to test whether cluster groups differed on sex, race, and chronological age at time of evaluation. Results found no significant differences between cluster groups on any of these variables (p = .26, .68, and .59; respectively). Furthermore, another clustering method (i.e., complete linkage) also found a 2-group solution; this solution found 161

children in Cluster 1 and 127 children in Cluster 2. There was significant overlap between

cluster solutions, χ^2 (1, $N = 288$) = 194, $p < .01$. Specifically, all 133 children placed in Cluster 1

by Ward's method were also placed in Cluster 1 by complete linkage. However, an additional 28

children were also placed in Cluster 1 by complete linkage (see Table 5). Of the 161 children

placed in Cluster 1 by complete linkage, 64 (40%) were diagnosed with an ASD and 97 (60%)

were diagnosed with DD. Of the 127 children placed in Cluster 2, five (4%) were diagnosed

with DD and 122 (96%) were diagnosed with ASD.

Table 5

Differences between Cluster Solutions for Entire Study Sample

Clusters and Totals	Ward's Cluster 1	Ward's Cluster 2	Totals
Complete Linkage Cluster 1	133	28	161
Complete Linkage Cluster 2	0	127	127
Totals	133	155	

Cluster Analysis for Children with ASD

The second cluster analysis included only children with ASD who failed the M-CHAT in

the toddler years. Ward's method revealed three distinct clusters: Cluster 1 consisted of 47

children, Cluster 2 consisted of 44 children, and Cluster 3 consisted of 95 children. As Figure 2

illustrates, of the 47 children in Cluster 1, 35 (74%) were diagnosed with PDD-NOS or

Asperger's Disorder (ASP) and 12 (26%) were diagnosed with Autistic Disorder; of the 44

children in Cluster 2, 22 (50%) were diagnosed with PDD-NOS or ASP and 22 (50%) were

diagnosed with Autistic Disorder; and of the 95 children in Cluster 3, 16 (17%) were diagnosed

with PDD-NOS or ASP and 79 (83%) were diagnosed with Autistic Disorder.
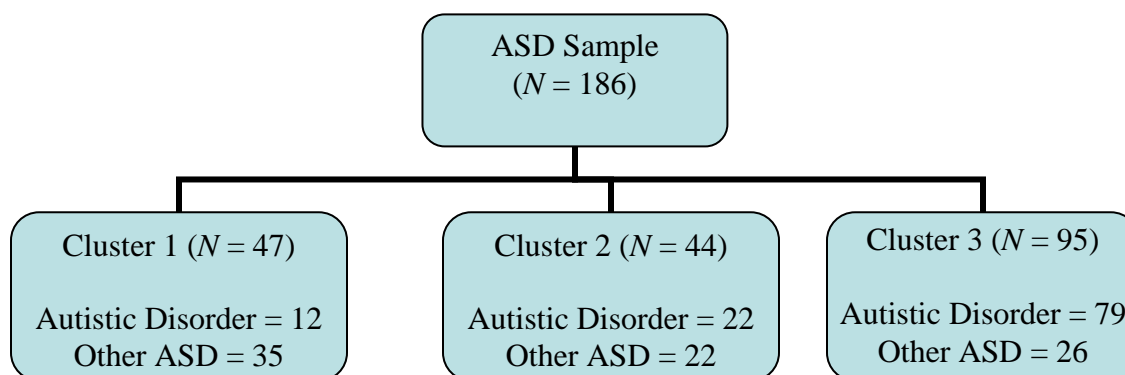
Figure 2. Results of Ward's cluster analysis for children diagnosed with an ASD.

A DFA was performed to assess which cluster variables most distinguished ASD cluster

groups and how to best define resultant discriminant functions. For this analysis, the 3-cluster

solution generated by Ward's method was used as the grouping variable and individual CARS

items were used as the independent variables. Results found that both discriminant functions

were significant in distinguishing ASD cluster groups, Wilks' lambda = .15, χ^2 (30, $N = 186$) =

331.91, $p < .00$ for the first function and Wilks' lambda = .55, χ^2 (14, $N = 186$) = 105.06, $p < .00$

for the second function. The first function accounted for 76% of the variance in differentiating

ASD cluster groups and the second function accounted for 24% of the variance in differentiating

ASD cluster groups. Structure coefficients were examined in order to assign meaningful labels

to each discriminant function. As Table 6 reveals, the first discriminant function included

variables that assessed social, communication, and intellectual functioning and the second

discriminant function included variables that assessed activity level, fear, and SIB. Therefore,

based on commonalities among most variables in each function, the discriminant functions were labeled "social communication" and "SIB." Variables that contributed the most to group differences in the first discriminant function were general impressions of the presence of an ASD, verbal communication, and emotional response, imitation, nonverbal communication, and relating to people; variables that contributed the most to group differences in the second discriminant function were fear, activity level, and object use (see Table 6).

The DFACs for the entire study population were compared to the DFACs for the ASD only population to verify that the ASD DFA is unique to children on the autism spectrum. Table 7 shows CARS items that most contributed to group differences in each of the study populations. As Table 6 reveals, certain variables, such as fear, activity level, verbal communication, object use, nonverbal communication, and relating to people were important in distinguishing ASD subgroups but not ASD and DD subgroups. Therefore, these variables may be more important in distinguishing children on the autism spectrum.

Another DFA was performed on variables not used to generate the cluster solution in order to determine which external variables best define resultant ASD subgroups. Again, it is important to note that the advantage of this DFA was to examine standardized DFA coefficients and structure coefficients. The 3-cluster solution generated by Ward's method was used as the grouping variable and the following were used as independent variables: MSEL expressive language scores, MSEL receptive language scores, MSEL visual reception scores, MSEL fine motor scores, VABS communication scores, VABS socialization scores, VABS daily living scores, VABS motor scores, ADOS social scores, ADOS communication scores, ADOS SIB scores, ADOS play scores, ADI-R social scores, ADI-R communication scores, and ADI-R SIB scores. Results found that one discriminant function was significant in distinguishing ASD

cluster groups, Wilks' lambda = .26, χ^2 (30, N = 89) = 107.77, p < .00, whereas the other

discrimninant function was not significant in distinguishing ASD cluster subgroups, Wilks'

lambda = .76, χ^2 (14, N = 89) = 105.06, p = .08. The first function accounted for 86% of the

variance in differentiating ASD cluster groups.

Table 6

Structure coefficients (SC) and Standardized DFA Coefficients (DFAC) for DFA Performed

on ASD Sample

	Function 1 Social Communication	Function 2 SIB
	SC (DFAC)	*SC (DFAC)*
Imitation	.62 (.36)	
General impressions	.52 (.55)	
Relating to people	.45 (.30)	
Nonverbal communication	.41 (.35)	
Verbal communication	.41 (.53)	
Listening response	.35 (.07)	
Intellectual response	.29 (.26)	
Emotional response	.29 (.40)	.
Visual response	.26 (.14)	
Activity level		.50 (.51)
Object use		.41 (.35)
Fear		.40 (.52)
Resistance to change		.37 (.08)
Body use		.26 (.13)
Sensory response		.21 (.09)

Table 7

Variables that Most Contributed to Differences between Cluster Groups for Each Study Sample

	DFAC for ASD and DD	*DFC for ASD only*
General impressions	.36	.55
Emotional response	.30	.40
Imitation	.30	.36
Intellectual response	.23	.26
Relating to people	.23	.30
Nonverbal communication	.20	.35
Object use	.18	.35
Fear	.17	.52
Activity level	.09	.51
Sensory response	.07	.09
Verbal communication	.07	.35
Body use	.06	.13
Visual response	.06	.14
Listening response	.06	.07
Resistance to change	.02	.08

Structure coefficients were then examined in order to assign meaningful labels to each

discriminant function. As Table 8 reveals, the first discriminant function included variables that

assessed social, communication, play, and SIB and the second discriminant function included

variables that assessed motor functioning and daily living skills. Therefore, based on

commonalities among most variables in each function, the discriminant functions were labeled

"ASD symptoms" and "nonASD symptoms." Variables that contributed most to group differences in the first discriminant function were VABS communication, VABS socialization, ADOS communication, and ADOS socialization scores. These results were commensurate with the DFA yielded from the ASD only population which showed that CARS items that contributed most to group differences assessed communication and social/emotional functioning.

Thus far, results suggest three distinct subgroups of toddlers with ASD that can be distinguished primarily by social and communication abilities. Results also suggest that toddlers with ASD can be distinguished by SIB, including activity level, fear response, resistance to change, object use, body use, and sensory response. In order to gain further clarification on how these three ASD cluster groups differed from one another, groups were compared on total cognitive standard score; MSEL, VABS, ADOS, and ADI-R domain scores; specific CARS items; ADOS algorithm items; and ADI-R algorithm items. There was a significant difference in total cognitive standard score based on cluster group membership, F (2, 171) = 17.10, $p < .00$. Specifically, Cluster 1 had higher cognitive standard scores ($M = 71.35$) than Cluster 2 ($M = 61.20$) or Cluster 3 ($M = 55.55$). There was not a significant difference between Cluster 2 and Cluster 3 in level of intellectual functioning. Moreover, there was a significant difference in the proportion of children in each cluster who had a cognitive standard score less than or equal to 70 points, χ^2 (2, $N = 173$) = 20.88, p < .00. Specifically, 59% of Cluster 1 children were intellectually disabled, 80% of Cluster 2 children were intellectually disabled, and 92% of Cluster 3 children were intellectually disabled.

Table 9 shows that ASD subgroups also differed on all MSEL, VABS, ADOS, and ADI-R domains, except the VABS motor domain and ADI-R SIB domain. Moreover, Table 9 shows the first cluster subgroup performed better on all social and communication domains and had

Table 8

Structure Coefficients (SC) and Standardized DFA Coefficients (DFAC) for DFA Performed

on ASD Sample

	Function 1 ASD Symptoms	Function 2 NonASD Symptoms
	SC (DFAC)	*SC (DFAC)*
ADOS communication	.64 (.52)	
ADOS socialization	.55 (.52)	
ADOS play	.54 (.33)	
MSEL expressive language	.36 (.37)	
MSEL visual reception	.35 (.21)	
ADOS SIB	.34 (.08)	
VABS communication	.33 (.52)	
MSEL receptive language	.31 (.21)	
ADI-R socialization	.31 (.07)	
ADI-R communication	.30 (.45)	
VABS socialization	.27 (.54)	
ADI-R SIB	.22 (.40)	
MSEL fine motor skills		.35 (.27)
VABS daily living skills		.19 (.46)
VABS motor skills		.13 (.34)

fewer SIB symptoms than the second or third cluster subgroups. Therefore, cluster subgroups

were distinguished by social and communication abilities and SIB. Given these differences, the

third cluster subgroup, which was characterized by many social and communication deficits and

many SIB, was labeled "Toddler Autistic Disorder." The second cluster subgroup, which was characterized by many social and communication deficits, few SIB, and intellectual disability was labeled "Toddler PDD-NOS, low-functioning." Conversely, the first cluster subgroup, which was characterized by few social and communication deficits, few SIB, and no intellectual disability was labeled "Toddler PDD-NOS, high-functioning."

ASD cluster subgroups were then compared on CARS items to further clarify group differences; Table 10 reveals results of the CARS analysis. Remember that CARS items are scored on a 7-point Likert scale rated from one to four in half-point increments with higher scores relating to more deficit. Commensurate with previous results, the "Toddler PDD-NOS, high-functioning" cluster performed significantly better on items that assessed intellectual response, verbal communication, nonverbal communication, and relating to people. The "Toddler PDD-NOS, low-functioning" and "Toddler Autistic Disorder" clusters were found to have similar levels of intellectual response, verbal communication, and nonverbal communication; yet the former had significantly fewer abnormalities in body use, object use, visual response, and sensory response. There were no significant group differences in resistance to change. Again, these results support cluster labels as representing toddlers that can be distinguished by level of social and communication abilities and lower-order SIB.

Even though these results support study hypotheses in that ASD cluster subgroups could be distinguished by level of social and communication abilities and lower-order SIB, it was important to further classify cluster subgroups on additional SIB items (to offer additional validation of cluster labels and test whether higher-order or lower-order SIB were more prevalent in one subgroup versus others). Thus, cluster subgroups were compared on ADOS and ADI-R

Table 9

ASD Cluster Subgroup Differences in General Developmental and Autism-specific Domains

	Cluster 1 (*N* = 47)	Cluster 2 (*N* = 44)	Cluster 3 (*N* = 95)			
	M (SD)	*M (SD)*	*M (SD)*	*F*	*p*	η^2
CARS total score	27.3 (3.64)$_a$	30.4 (1.73)$_{\mathbf{b}}$	36.8 (3.43)$_c$	160	<.01	.64
MSEL expressive language	32.6 (12.0)$_a$	23.8 (7.10)$_b$	24.5 (11.1)$_{\mathbf{b}}$	9.65	<.01	.12
MSEL receptive language	27.9 (11.2)$_a$	22.1 (7.07)$_b$	23.3 (10.6)$_b$	4.09	.02	.05
MSEL visual reception	33.5 (11.3)$_a$	29.8 (11.6)$_a$	24.8 (9.51)$_b$	8.85	<.01	.11
MSEL fine motor	34.6 (13.8)$_a$	31.9 (11.4)$_a$	25.9 (11.0)$_b$	7.34	<.01	.09
VABS communication	75.6 (14.3)$_a$	66.5 (5.28)$_b$	63.1 (6.59)$_b$	24.8	<.01	.22
VABS socialization	73.7 (9.35)$_a$	69.8 (6.36)$_b$	66.6 (8.94)$_b$	10.7	<.01	.12
VABS daily living	74.1 (12.3)$_a$	69.3 (6.86)$_b$	68.6 (10.5)$_b$	4.51	.01	.05
VABS motor	83.7 (11.0)$_a$	84.7 (10.3)$_a$	81.3 (13.1)$_a$	1.39	.25	.02
ADOS socialization	7.38 (3.20)$_a$	8.71 (2.78)$_b$	11.6 (2.06)$_c$	34.0	<.01	.33
ADOS communication	4.36 (1.63)$_a$	5.53 (1.75)$_b$	6.63 (1.43)$_c$	25.4	<.01	.27
ADOS play	2.33 (1.26)$_a$	2.78 (1.07)$_a$	3.68 (0.74)$_b$	24.0	<.01	.17
ADOS SIB	1.95 (1.61)$_a$	1.97 (1.48)$_a$	3.40 (1.80)$_b$	12.7	<.01	.16
ADI-R socialization	12.1 (4.19)$_a$	14.0 (3.31)$_b$	15.7 (3.63)$_b$	11.3	<.01	.15
ADI-R communication	8.41 (3.55)$_a$	10.3 (2.42)$_b$	11.2 (2.88)$_b$	10.5	<.01	.14
ADI-R SIB	1.81 (1.98)$_a$	2.30 (1.92)$_a$	2.81 (2.16)$_a$	2.39	.09	.04

Note: Group differences are indicated by subscripts and shading; shaded areas show scores that were not significantly different from one another.

Table 10

ASD Cluster Subgroup Differences in CARS Items

	Cluster 1 (N = 47)	Cluster 2 (N = 44)	Cluster 3 (N = 95)			
	M (SD)	*M (SD)*	*M (SD)*	*F*	*P*	η^2
Relating to people	1.94 (.46)$_a$	2.40 (.44)$_b$	2.91 (.47)$_c$	71.6	<.01	.44
Imitation	1.70 (.44)$_a$	2.56 (.56)$_b$	3.00 (.60)$_c$	84.8	<.01	.49
Emotional response	1.51 (.42)$_a$	1.71 (.55)$_a$	2.27 (.60)$_b$	35.8	<.01	.28
Body use	1.92 (.65)$_a$	1.89 (.74)$_a$	2.31 (.68)$_b$	8.24	<.01	.09
Object use	1.76 (.57)$_a$	1.91 (.46)$_a$	2.55 (.56)$_b$	41.8	<.01	.31
Resistance to change	1.97 (.80)$_a$	2.03 (.85)$_a$	2.15 (.88)$_a$	1.33	.30	.03
Visual response	1.73 (.55)$_a$	1.82 (.66)$_a$	2.34 (.73)$_b$	16.9	<.01	.15
Listening response	1.80 (.45)$_a$	2.27 (.48)$_b$	2.55 (.58)$_c$	32.6	<.01	.26
Sensory response	1.62 (.61)$_a$	1.63 (.58)$_a$	1.94 (.75)$_b$	5.19	.01	.06
Fear	1.61 (.58)$_a$	1.13 (.29)$_b$	1.66 (.69)$_a$	13.1	<.01	.12
Verbal communication	2.21 (.41)$_a$	3.00 (.36)$_b$	3.12 (.55)$_b$	58.9	<.01	.40
Nonverbal communication	1.94 (.41)$_a$	2.59 (.39)$_b$	2.70 (.48)$_b$	48.2	<.01	.35
Activity level	1.80 (.64)$_a$	1.34 (.48)$_b$	1.90 (.74)$_a$	11.0	<.01	.11
Intellectual response	1.90 (.51)$_a$	2.41 (.46)$_b$	2.55 (.51)$_b$	26.8	<.01	.22
General impressions	1.92 (.47)$_a$	2.18 (.31)$_b$	2.90 (.45)$_c$	97.4	<.01	.52

Note: Group differences are indicated by subscripts and shading; shaded areas show scores that were not significantly different from one another.

SIB algorithm items appropriate for toddlers (i.e., all algorithm items except ADI-R

"circumscribed interests," which is only appropriate for children 36 months and older). As Table

11 and Table 12 show, there were no significant group differences in higher-order SIB, such as unusual preoccupations, verbal rituals, and compulsions/rituals; the majority of these high-order items were found in the ADI-R behavioral domain and few children exhibited such behaviors. There were also no significant group differences in the lower-order SIB of hand and finger or other complex body mannerisms on either diagnostic instrument. There were, however, significant group differences in other lower-order SIB, particularly repetitive behaviors and unusual sensory interests. These results support CARS analyses in that similar group differences were found on all instruments (i.e., Cluster 3 had more repetitive behaviors, especially repetitive object use, and abnormal sensory response than Cluster 1 or Cluster 2; see Figure 3). These results support study hypotheses in that cluster subgroups were distinguished by certain lower-order SIB but not higher-order SIB.

Additional analyses were performed to test whether ASD cluster groups differed on potential confounds and whether another cluster method yielded a similar solution. Specifically, ANOVA and chi-square analyses were performed to test whether ASD cluster groups differed on sex, race, chronological age at time of evaluation, whether the same clinician administered the CARS and ADOS, and whether the child received a 4-year follow-up evaluation. Results found no significant differences between cluster groups on any of these variables ($p = .34$, $p = .76$, $p = .56$, $p = .61$, and $p = .57$; respectively). Another clustering method (i.e., complete linkage) found a 2-group solution instead of a 3-group solution; this solution found 34 children in Cluster 1 and 152 children in Cluster 2 (Table 13). Of the 34 children placed in Cluster 1, 30 were diagnosed with PDD-NOS or Asperger's Disorder and four were diagnosed with Autistic Disorder. Of the 152 children placed in Cluster 2, 109 were diagnosed with Autistic Disorder and 43 were diagnosed with another ASD. Chi-square analyses found significant overlap between cluster
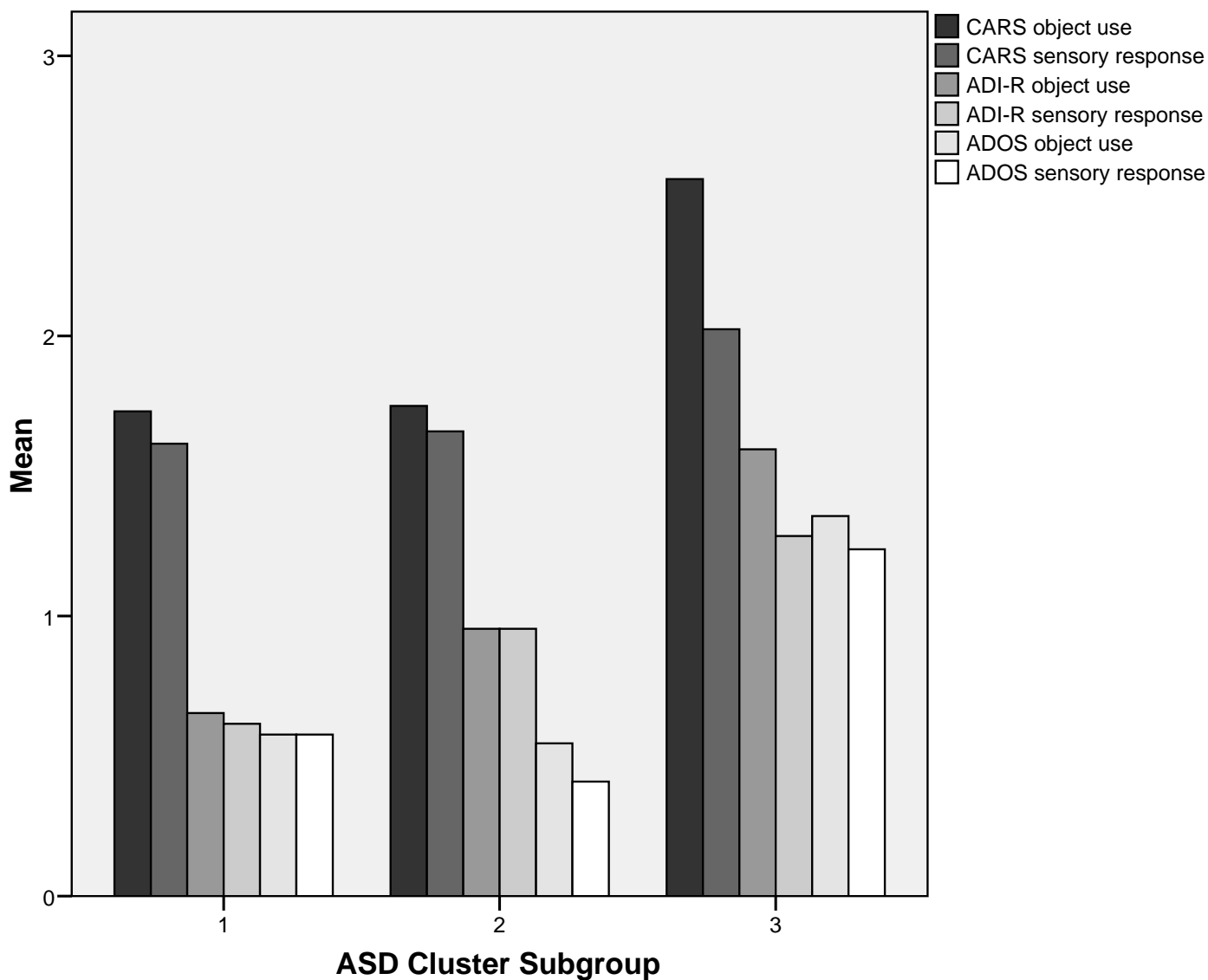
Figure 3. Differences between ASD cluster subgroups on abnormal object use and abnormal

sensory response across measures. CARS items are scored 1-4, ADI-R items are scored 0-2,

ADOS object item is scored 0-3, and ADOS sensory item is scored 0-2; ASD clusters 1 and 2

significantly differed from Cluster 3 but did not differ from one another.

solutions in that all 34 children placed in Cluster 1 by complete linkage were also placed in the

"Toddler PDD-NOS, high functioning" cluster by Ward's Method, χ^2 (2, $N = 186$) = 123.05, $p <$

.00. Therefore, complete linkage classified children with ASD as "high-functioning" and "low-functioning" whereas Ward's method further divided "low-functioning" children into groups characterized by rate and intensity of SIB symptoms.

Table 11

ASD Cluster Subgroup Differences on ADI-R SIB Algorithm Items

	Cluster 1 (N = 47)	Cluster 2 (N = 44)	Cluster 3 (N = 95)			
	M (SD)	*M (SD)*	*M (SD)*	*F*	*p*	η^2
Unusual preoccupations	0.64 (.87)$_a$	0.95 (.95)$_a$	0.98 (1.52)$_a$	0.69	.50	.01
Verbal rituals	0.46 (.98)$_a$	0.13 (.50)$_a$	0.08 (.50)$_a$	2.30	.11	.06
Compulsions/rituals	0.54 (.88)$_a$	0.09 (.29)$_a$	0.49 (1.38)$_a$	1.27	.29	.03
Hand and finger mannerisms	0.71 (.85)$_a$	0.96 (1.02)$_a$	1.24 (.93)$_a$	3.00	.06	.06
Other complex mannerisms	1.16 (1.28)$_a$	0.83 (.94)$_a$	1.07 (1.24)$_a$	0.57	.57	.01
Repetitive use of objects	0.65 (.89)$_a$	0.96 (.88)$_a$	1.72 (1.94)$_b$	4.74	.01	.09
Unusual sensory interests	0.62 (.70)$_a$	0.96 (.71)$_a$	1.23 (.70)$_b$	6.60	<.01	.13

Note: Group differences are indicated by subscripts and shading; shaded areas show scores that were not significantly different from one another.

Sensitivity of Diagnostic Instruments

Sensitivity for the ADOS and ADI-R, two of the most common ASD diagnostic instruments, were calculated for each ASD cluster subgroup. Again, sensitivity was calculated by measuring the proportion of children in each ASD cluster subgroup correctly classified by the ADOS or ADI-R. As Table 14 shows, the ADOS was sensitive in detecting children with ASD in each cluster subgroup (i.e., rates of sensitivity were .80 or higher for all three subgroups).

Table 12

ASD Cluster Subgroup Differences on ADOS SIB Algorithm Items

	Cluster 1 (*N* = 47)	Cluster 2 (*N* = 44)	Cluster 3 (*N* = 95)			
	M (SD)	*M (SD)*	*M (SD)*	*F*	*p*	η^2
Unusual sensory interests	0.55 (.69)ₐ	0.72 (.82)ₐ	1.24 (.80)ᵦ	10.8	<.01	.14
Hand, finger, or other complex mannerisms	0.66 (.82)ₐ	0.58 (.69)ₐ	0.89 (.87)ₐ	1.89	.16	.03
Repetitive interests or stereotyped behaviors	0.66 (.67)ₐ	0.67 (.83)ₐ	1.37 (1.01)ᵦ	10.9	<.01	.14

Note: Group differences are indicated by subscripts and shading; shaded areas show scores that were not significantly different from one another.

Table 13

Differences Between ASD Cluster Solutions

Cluster & totals	Ward's Cluster 1	Ward's Cluster 2	Ward's Cluster 3	Totals
Complete Linkage Cluster 1	34	0	0	34
Complete Linkage Cluster 2	13	44	95	152
Totals	47	44	95	

However, the ADI-R was not sensitive in detecting children with ASD in any cluster subgroup. Specifically, measures of sensitivity for the ADI-R ranged from .16-.38, which reflects poor detection of the population of interest. Thus, the influence of removing the SIB domain as a criterion for ADI-R classification was explored (Wiggins & Robins, 2008). When only social and communication cutoff scores were considered, the sensitivity of the ADI-R improved dramatically. Specifically, sensitivity for the "Toddler PDD-NOS, low-functioning"

and "Toddler Autistic Disorder" subgroups improved from .29-.38 to .84-.87. Yet, even though sensitivity for the "Toddler PDD-NOS, high-functioning" improved, detection was still poor for this particular subgroup. These results suggest that the ADI-R is not as good at detecting toddlers with higher intellectual, language, and social functioning as it is as detecting toddlers with lower intellectual, language, and social functioning.

Table 14

Sensitivity of the ADOS and ADI-R for ASD Cluster Subgroups

Clusters	ADOS Sensitivity	ADI-R Sensitivity with SIB Domain	ADI-R Sensitivity without SIB Domain
Toddler PDD-NOS, high-functioning	.87	.16	.57
Toddler PDD-NOS, low-functioning	.97	.29	.87
Toddler Autistic Disorder	1.00	.38	.84

It is important to note that even though children in the "Toddler PDD-NOS, high-functioning" subgroup were not generally detected by the ADI-R, they did show more autistic symptoms on ADI-R social and communication domains than did children with other DD, $F (1, 184) = 164.58$, $p < .00$ and $F (1, 184) = 88.20$, $p < .00$, respectively. In addition, although many of these children did not meet ADI-R criteria for both the social and communication domains, 90% met criteria for the social domain and 91% met criteria for the communication domain (compared to 25% of children with DD who met ADI-R social criteria and 51% of children with DD who met ADI-R communication criteria). Therefore, the most appropriate way to detect children with ASD who have higher social, communication, and intellectual skills and low SIB

and distinguish them from children with other DD would be to refer all children who meet ADI-R social criteria for further assessment.

Several items not currently included on the ADI-R diagnostic algorithm were next examined to see if mean differences exist between cluster subgroups. ANOVA analyses revealed no significant differences between cluster subgroups on lack of attention to voice, loss of previously acquired language, use of other's body to communicate, unusual sensitivity to noise, and unusual attachment to objects; abnormalities in unusual sensitivity to noise and unusual attachment to objects were particularly rare for all three subgroups ($M = .73$ for overall rating of unusual sensitivity to noise and $M = .50$ for overall rating of unusual attachment to objects; respectively). Thus, it was again concluded that the most appropriate ADI-R diagnostic algorithm for children with lower social-communication skills is meeting criteria for current social and communication cutoffs and the most appropriate ADI-R diagnostic algorithm for high-functioning children is meetings current social cutoffs and being referred for further assessment.

Diagnostic Prediction

A multinomial logistic regression was conducted to examine how ASD subgroup membership (ASD-only cluster analysis) predicted diagnosis two years later. Specifically, clinical diagnosis around four years of age was coded into three categories: nonASD, PDD-NOS, and Autistic Disorder. These categories were entered as the dependent variable and the categorical, three-level ASD cluster membership was entered as the independent variable; (b) coefficients were interpreted as odds-ratios for results that found cluster subgroups were significant in predicting 4-year diagnoses. One hundred twenty of the 186 children diagnosed with ASD as a toddler were assessed again around four years of age. The Chi-Square statistic showed that the overall model was significant (i.e., the cluster model predicted 4-year diagnosis

better than the intercept-only model), χ^2 (4, N = 120) = 18.14, $p < .00$. Specifically, children in

the "Toddler PDD-NOS, high functioning" subgroup were four times as likely than children in

the "Toddler Autistic Disorder" subgroup to receive a nonASD diagnosis as compared to a

diagnosis of Autistic Disorder, Wald = 6.07, $p = .01$. There were no significant differences

between children in the "Toddler PDD-NOS, low-functioning" and "Toddler Autistic Disorder"

subgroups in terms of likelihood of receiving a diagnosis of nonASD compared to a diagnosis of

Autistic Disorder. Furthermore, children in the "Toddler PDD-NOS, high-functioning"

subgroup were eight times as likely than children in the "Toddler Autistic Disorder" subgroup to

receive a diagnosis of PDD-NOS as compared to a diagnosis of Autistic Disorder, Wald = 11.23,

$p = .00$, and children in the "Toddler PSS-NOS, low-functioning" subgroup were six times as

likely than children in the "Toddler Autistic Disorder" subgroup to receive a diagnosis of PDD-

NOS as compared to a diagnosis of Autistic Disorder, Wald = 8.26, $p = .00$. The percent of

children in ASD clusters diagnosed with nonASD, PDD-NOS, and Autistic Disorder at their re-

evaluation are summarized in Table 14 for clarity. These results support study hypotheses given

that children characterized by higher social and communication abilities and fewer SIB were

more likely to receive a nonASD or PDD-NOS diagnosis as compared to a diagnosis of Autistic

Disorder at four years of age.

Table 15

Percent of Children in ASD Clusters Diagnosed with nonASD, PDD-NOS, and Autistic Disorder around Four Years of Age

Diagnoses and Totals	Cluster 1 N (%)	Cluster 2 N (%)	Cluster 3 N (%)
nonASD	9 (28%)	5 (17%)	8 (13%)
PDD-NOS	11 (34%)	10 (33%)	5 (9%)
Autistic Disorder	12 (38%)	15 (50%)	45 (78%)
Totals (N)	32	30	58

CHAPTER 4: DISCUSSION

This project sought to examine empirically derived subgroups of toddlers with ASD and DD who fail an autism screen, empirically derived subgroups of toddlers with ASD only who fail an autism screen, characteristics that define clinically distinct subgroups, how ASD subgroup membership forecasts performance on common diagnostic instruments, and how ASD subgroup membership forecasts diagnosis two years later. Hypotheses revolved around the latter goals; primarily, it was hypothesized that ASD subgroups would be distinguished by social relatedness, verbal ability, nonverbal ability, and SIB. Although this hypothesis was generally supported, results from the first analysis relating to empirically derived subgroups of toddlers with ASD and DD who fail an autism screen will first be addressed.

Subgroups of Toddlers Identified at-risk for Autism

Toddlers with ASD and DD who failed an autism screen were classified into a subgroup marked by many ASD symptoms and a subgroup marked by fewer ASD symptoms. Therefore, subgroups of children who fail an autism screen were primarily distinguished by level of social

and communication abilities, especially social and communication impairments associated with ASDs. This conclusion was supported by moderate to large effect sizes for subgroup differences in social and communication skills, especially social and communication abnormalities found on common ASD diagnostic instruments. Discriminant function analyses showed that the three CARS variables that most distinguished resultant subgroups were general impressions of an ASD, emotional response, and imitation. Moreover, almost all children subsequently diagnosed with a DD were placed in the fewer ASD symptoms subgroup; 39 of 186 children diagnosed with an ASD were also placed in the fewer ASD symptoms subgroup.

Charman and colleagues (1998) correctly note that in order to create theories on ASDs in the first few years of life, data on toddlers must be utilized. Consequently, he and others (1998) studied how toddlers diagnosed with Autistic Disorder and PDD-NOS differ from toddlers diagnosed with other DD in terms of social and communication abilities. Results found that toddlers diagnosed with Autistic Disorder showed deficits in empathic response, pretend play, functional play, joint attention, requesting behaviors, and imitation. Surprisingly, toddlers diagnosed with PDD-NOS did not perform significantly differently from toddlers diagnosed with other DD on any of these measures. In conclusion, social and communication abilities distinguished toddlers with Autistic Disorder from toddlers with other DD, but failed to distinguish toddlers with PDD-NOS from toddlers with other DD.

The results of the current analysis support the aforementioned findings. Remember that CARS items were used to generate cluster subgroups. Although play, joint attention, and requesting are not measured on the CARS, emotional response and imitation are two aspects of social relatedness measured on the CARS. Interestingly, emotional response and imitation were two of the top three variables that most distinguished children with many ASD symptoms from

children with fewer ASD symptoms in the present study. Since most children diagnosed with an ASD were placed in the many ASD symptoms cluster and most children with DD were placed in the fewer ASD symptoms, it can be concluded that certain social and communication abilities (e.g., emotional response and imitation) differentiate most children with ASDs from most children with other DD.

However, it is important to remember that a minority of children diagnosed with an ASD were placed in the group with fewer ASD symptoms; these results are commensurate with previous analyses that found that cluster analyses group some children with milder forms of ASDs with children with developmental language disorders and intellectual disabilitys (Fein et al., 1999). Subsequent analyses in this study showed that a higher proportion of these children were diagnosed with nonASD and PDD-NOS (compared to Autistic Disorder) around four years of age than toddlers with an ASD placed in the many ASD symptoms cluster. Since Charman and colleagues (1998) also found that children with PDD-NOS could not be distinguished from children with other DD on social and communication abilities, it can be concluded that social-communication (specifically; emotional response and imitation) can distinguish most toddlers with Autistic Disorder (who typically have many ASD symptoms) from most toddlers with DD (who typically have fewer ASD symptoms). Yet not all children with Autistic Disorder had many ASD symptoms in this study (i.e., some children diagnosed with Autistic Disorder were placed in the subgroup with fewer ASD symptoms). These findings suggest that even toddlers diagnosed with Autistic Disorder represent a heterogeneous group of children characterized by a range of social and communication skills, or that functional limitation is more important than mere number of symptoms when considering a clinical diagnosis of Autistic Disorder.

These results are somewhat contradictory to Sutera and colleagues (2007) who found very few differences between toddlers diagnosed with an ASD who did and did not "recover" by four years of age. However, study groups utilized must be considered. In the Sutera et al. (2007) report, three study groups were compared: 1) a group of children diagnosed with an ASD at both two and four years of age, 2) a group of children diagnosed with nonASD at both two and four years of age, and 3) a group of children diagnosed with an ASD at two years of age and nonASD at four years of age. When these study groups were compared, very few early social and communication differences were found between the two study groups with children diagnosed with an ASD at two years of age. However, there was a significant difference in children diagnosed with PDD-NOS and Autistic Disorder at two years of age in that toddlers with PDD-NOS were more likely to move off the spectrum by four years of age than were toddlers with Autistic Disorder. Two-year social and communication differences between toddlers diagnosed with PDD-NOS versus Autistic Disorder were not examined. Therefore, significant social and communication differences may have been found if the recovered ASD group was further divided by type of diagnosis (instead of one ASD category) or severity of social and communication deficit at two years of age.

Yet it is still unclear how the social-cognitive variables that distinguished subgroups in this analysis speak to an underlying theory of the development of Autistic Disorder in toddlers. Indeed, some researchers have hypothesized that emotional response and imitation are a part of a shared social-affective deficit present since birth (Hobson, 2000; Dawson et al., 2002; Dawson et al., 2004; Dawson, 2008; Mundy & Neal, 2001). In this view, there are two factors important to the development of autism: 1) a failure to perceive or be rewarded by the social environment and 2) a subsequent disruption of brain development that leads to autistic symptomatology.

Although most social-affective theorists agree on these basic premises, different mechanisms have been proposed.

Hobson (2000) believes that children with autism fail to perceive the emotional expressions of other people. According to this theory, typically developing children directly perceive the emotional expressions of others; this perception encourages imitating, relating, and referencing other people. Furthermore, emotional perception allows a child to understand that emotions reveal attitudes toward certain objects or events. Thus, children learn that one object can lead to several different attitudes by reading the emotional expressions of persons engaged with that object (e.g., pleasure versus displeasure). If children with autism fail to perceive the emotional expressions of other people, they will inherently be disconnected from others' attitudes. In conclusion, a failure to perceive the emotional expressions of others leads to problems disconnecting from personal experiences in order to reflect upon the meanings and attitudes expressed by others.

Other social-affective theorists believe a failure to be rewarded by the social environment better accounts for the deficits seen in autism (Dawson et al., 2002; Dawson, 2008). As a consequence of failed motivation due to lack of intrinsic reward, infants later diagnosed with autism do not attend to and engage with socially relevant stimuli. Instead, these infants have more interest and engagement with inanimate objects (Dawson et al., 2004; Zwaigenbaum et al., 2005). This preference for non-social stimuli robs the infant of social input, which further disrupts brain development and leads to a variety of negative developmental outcomes (Dawson, 2008; Mundy & Neal, 2001). For instance, Dawson and colleagues (2008) claim that reduced attention to people leads to less efficient functioning of brain systems that mediate social cognition. Both the orbitofrontal cortex and the amygdala are involved in social-emotional

cognition and behavior (Bachevalier & Loveland, 2003); interestingly, both the orbitofrontal cortex and the amygdala have been implicated in autistic deficit (Adolphs, Sears, & Piven, 2001; Baron-Cohen et al., 2000; Loveland, K., Bachevalier, J., Pearson, D., & Lane, D., 2008; Sabbagh, M., 2004). For instance, Adolphs, Sears, and Liven (2001) found that high-functioning subjects with an ASD made abnormal social judgments when viewing faces; these judgments were similar to those made by subjects with amygdala damage without an ASD. They concluded that amygdala dysfunction in autism is responsible for failure to associate social stimuli with retrieval of social knowledge and production of social behavior.

A failure to be rewarded by the social environment and subsequent lack of attention and engagement with socially relevant stimuli would explain why emotional response was one of the variables that most distinguished toddlers with many ASD symptoms from other children with fewer ASD symptoms in this sample. This process would also explain why imitation differentiated cluster subgroups (i.e., in order to imitate, one must first attend to others and then reproduce their actions and behaviors). However, it is important to remember that children with ASD may have great difficulty imitating social behaviors, but they have little difficulty imitating actions with objects (Rogers et al., 2003). Hence, there may be more than one process responsible for the imitation deficit seen in ASD. One process may involve the aforementioned social-affective system that mediates social exchanges; the other process may involve a cognitive system that teaches means-ends relations. Since the imitation deficit in ASD seems to be restricted to social imitation, it may be that persons with ASD learn to use the second, cognitive system at the exclusion of the first, affective system (Rogers et al., 2003).

Again, it is important to remember that some toddlers diagnosed with an ASD were placed in the cluster with fewer ASD symptoms. These toddlers were more likely to receive a

nonASD or PDD-NOS diagnosis around four years of age than toddlers placed in the cluster with many ASD symptoms. This finding suggests that the variables found to most distinguish ASD and DD cluster subgroups in the first few years of life are more related to the development of extreme forms of autistic impairment. It may be that the social-affective deficit that leads to the development of ASDs exists on a continuum and that less severe deficit does not distinguish itself from other DD until after the toddler years. Or, other variables may be at play in the development of milder forms of ASDs, such as the aforementioned failure to associate social stimuli with retrieval of social knowledge and production of social behavior (Adolphs, Sears, & Liven, 2001). Clarification of variables that distinguish toddlers with milder forms of ASDs from toddlers with other DDs (as well as mechanisms of development) is needed in future research.

Subgroups of Toddlers with an ASD

Subgroups of toddlers who failed an autism screen and were subsequently diagnosed with an ASD were classified into three distinct subgroups: one subgroup marked by higher social and communication abilities and fewer SIB, one subgroup marked by lower social and communication abilities and fewer SIB, and one subgroup marked by lower social and communication abilities and more SIB. Therefore, subgroups of toddlers with an ASD were primarily distinguished by level of social and communication abilities and the rate and intensity of SIB. This hypothesis was further supported by a discriminant function analysis that revealed two discriminant functions: a social and communication function and a SIB function. Variables that contributed the most to group differences in the social and communication function were general impressions of the presence of an ASD, verbal communication, emotional response,

imitation, nonverbal communication, and relating to people; variables that contributed the most to group differences in the SIB function were fear, activity level, and object use.

The fact that CARS social and communication items all correlated with one discriminant function is significant for future classifications of children with ASDs. Although listed separately in current diagnostic manuals, social and communication impairments noted on standardized ASD diagnostic instruments have often been found to load onto a single social-communication domain (Gotham, Risi, Pickles, & Lord, 2007; Lord et al., 1999; Lord et al., 2000). This is probably due to the fact that many communication items found on standardized ASD diagnostic instruments involve a social component rather than merely delayed expressive or receptive communication skills (e.g., pointing to express interest, use of gestures, and reciprocal conversation). In fact, it has been proposed that separate social and communication domains on gold-standard ASD assessments be combined to represent a unitary factor that represents social and communicative impairments associated with ASDs (Gotham, Risi, Pickles, & Lord, 2007). Further, including an appropriate SIB factor in diagnostic algorithms improves sensitivity and specificity of diagnostic instruments (Gotham, Risi, Pickles, & Lord, 2007); although some SIB factors may be inappropriate for use in toddler populations (Wiggins & Robins, 2008). Therefore, the two discrimnant functions found in the present study relate to the two domains of autistic development implicated in previous research. It makes sense, then, that these two factors are important in considering the diagnosis of an ASD as well as in creating subtypes based on level of social-communicative impairment and SIB.

It is not surprising that social and communication variables were responsible for distinguishing ASD subgroups since social and communication impairments are defining feature of ASDs and ASDs are a very heterogeneous group of disorders (American Psychiatric

Association, 1994). Therefore, although all children with ASDs have some level of social or communication impairment, the level of impairment varies greatly within the autism spectrum. The results of this analysis support past research in that 76% of the variance in distinguishing ASD cluster subgroups was accounted for by a social-communicative function. Furthermore, there was a clear distinction in social and communicative abilities based on ASD subgroup membership. Specifically, Cluster 1 children (i.e., children classified as Toddler PDD-NOS, high functioning) consistently performed better than Cluster 2 children and Cluster 3 children on social and communication measures. These results were not dependent on type of measurement or method of data collection (e.g., direct observation versus parent report). Yet, even though Cluster 1 children showed clear social and communication advantages, they still performed below average on standardized measures of both social and communication skills. Moreover, Cluster 1 children meet average social and communication cut-off scores on standardized ASD diagnostic instruments. In summary, although there was an apparent distinction between ASD cluster subgroups in terms of social and communicative abilities, those with more social and communication skills ability still showed impairments in both domains. These results support previous research that identifies social and communication impairments as being particularly relevant for the definition and classification of children with ASDs.

These findings, as well as cluster labels employed, bring into question whether current diagnostic definitions of PDD-NOS and Autistic Disorder are appropriate in toddler populations. The diagnosis of PDD-NOS is typically reserved for individuals with fewer social and communication impairments than individuals with Autistic Disorder or similar social and communication impairments and fewer SIB. Thus, the diagnostic category of PDD-NOS is heterogeneous and may not represent a clinically distinct subtype of toddlers with ASDs.

According to the results of this analysis, the diagnostic category of PDD-NOS may be better defined by level of social, communication, and intellectual skills rather than focusing on SIB. For instance, toddlers with many social and communication impairments, below average intellectual functioning, and few SIB could be defined as Toddler PDD-NOS, low-functioning, and toddlers with few social and communication impairments, average intellectual functioning, and few SIB could be defined as Toddler PDD-NOS, high-functioning. Toddlers with many social and communication impairments and many SIB could be defined as having Autistic Disorder. These revised diagnostic categories may better represent subtypes of toddlers with ASDs that enhance understanding of etiology and developmental course.

Again, one theory that accounts for the importance of social and communication skills in the development of ASDs is a social-affective approach that assumes a failure to perceive or be rewarded by the social environment and subsequent disruption of brain development. Specifically, this theory helps explain variables that contribute most to cluster group differences in toddlers with an ASD and toddlers with an ASD and other DD. Remember that emotional response and imitation contributed most to group differences in a cluster analysis on the entire study population. These same variables were also important in distinguishing groups of children when the analysis was restricted to children with a 2-year diagnosis of an ASD. Validation analyses found moderate to large differences between cluster subgroups (for both the cluster analysis on the entire study population and the cluster analysis on toddlers with an ASD diagnosis) on standardized social and communication measures, especially measures that assessed social and communication deficits commonly found in children with ASDs. Therefore, it can be assumed that these variables are important in distinguishing children with more severe

social and communicative autistic deficit from children with less severe social and communicative autistic deficit.

Fear, activity level, verbal communication, object use, nonverbal communication, and relating to people were important in distinguishing ASD subgroups but not ASD and DD subgroups, which suggests these variables are more important in subtyping samples of toddlers with an ASD. This finding is not particularly surprising given that most of these variables represent diagnostic symptoms of ASDs or common comorbid conditions. Conversely, whereas some of these variables may be present in toddlers with other DDs, toddlers with other DDs typically don't display symptoms within all three diagnostic domains of ASDs and the associated features listed above. For instance, almost 50% of the DD sample was diagnosed with a language disorder. All of language disordered children except one (who had profound intellectual disability) were placed in the less severe social-communication cluster. Although impaired verbal communication defines some language disorders, impaired nonverbal communication, impaired social relations, and atypical object use do not define language disorders. Yet these variables are often found among children with ASDs and are considered in diagnostic algorithms. Further, a high activity level is one of the most common conditions associated with ASDs (Gillberg & Billstedt, 2000; Simonoff, et al., 2008).

One interesting finding was that fear was important in distinguishing ASD subgroups but not ASD and DD subgroups. Although this finding may seem incongruous, fear has been related to impaired social functioning and cognitive theories of autism in previous research (Gaigg & Bowler, 2007; Markram et al., 2008). For instance, Markram and colleagues (2008) tested a rat model of autism to see if alterations in amygdala functioning were responsible for producing autism-like symptoms and abnormal fear response. Rats were given valproic acid (VPA) in

order to alter amygdala functioning. VPA treated animals showed more impairments in social interaction (and more repetitive behaviors) than non-VPA treated animals. Moreover, VPA treated rats were more fearful than non-VPA treated rats; these heightened fear reactions were overgeneralized and difficult to extinguish. The amygdala of VPA treated rats was subsequently found to be more reactive to electrical stimulation and was associated with impaired inhibition. The authors concluded that hyperreactivity and impaired inhibition of the amygdala could create an "aversive world" view that results in heightened fear and impaired social interactions. However, the exact mechanisms that link amygdala dysfunction and autism remains unclear and controversial findings are still reported. Therefore, additional research exploring how the amygdala and fear response relate to autistic symptomatology is warranted. Further, abnormal fear response on the CARS is rated as having too much or too little fear; therefore, findings do not necessarily suggest that one ASD cluster subgroup showed more fear than other ASD cluster subgroups. Again, the relationship between fear response and autistic symptomology should be explored in future research.

As predicted, the rate and intensity of SIB also distinguished ASD cluster subgroups. This finding is particularly interesting since many previous studies failed to include SIB as cluster variables, even though some SIB are consistently found in toddlers with ASDs. Specifically, SIB have been categorized into "lower-order SIB" which include sensorimotor behaviors and "higher-order SIB" which includes cognitive rigidity. Some researchers claim that toddlers with an ASD show lower-order SIB but not higher-order SIB (Moore & Goodson, 2003; Richler et al., 2007). The results of the current analysis show that a significant 24% of the variance in distinguishing ASD cluster subgroups was accounted for by a SIB function. The one cluster subgroup that consistently had higher rates of SIB also had more social and

communication deficits. Further, the SIB consistently found in this population were restricted to lower-order SIB. Therefore, lower-order SIB (but not higher-order SIB) distinguished two groups of toddlers with an ASD who had fewer social and communication abilities.

The ability of lower-order SIB to distinguish subgroups of toddlers with an ASD is important for theories related to the development of ASDs in the first few years of life. Previously, a social-affective approach that assumes a failure to perceive or be rewarded by the social environment and subsequent disruption of brain development was used to explain the social and communication differences between cluster subgroups in this analysis. Indeed, a very similar approach has also been used to explain the presence of repetitive behaviors in animal models of autism. For instance, Lewis and colleagues (2007) note that repetitive behaviors seem to be a consequence of social deprivation among all species tested (e.g., pacing in birds, somersaulting in deer mice, and body rocking in rhesus monkeys). This observation is important to the study of autism since early social-affective deficits could attenuate brain development dependent on early social experiences. Thus, an early social-affective deficit that prevents a child from perceiving or attending to social stimuli could result in a cascade of alternative developmental events that result in social-communication impairments as well as SIB.

It is important to remember, however, that it is not the presence of lower-order SIB that distinguishes ASD subgroups, but the rate and intensity at which SIB occur. For instance, even though repetitive body use was more frequently observed in children with an ASD placed in Cluster 3, children with an ASD placed in other cluster subgroups still showed "mildly abnormal body use" associated with "minor peculiarities" (Schopler, Reichler, & Renner, 1988). The same is true for repetitive use of objects and unusual sensory interests on the ADI-R and stereotyped behaviors and unusual sensory interests on the ADOS: Cluster 1 and Cluster 2 children showed

mildly abnormal responses compared to Cluster 3 children who showed clearly abnormal responses. These findings support the hypothesis that SIB represent a continuum of behaviors that may or may not reach clinical significance (Richler et al., 2007). In fact, some ASD researchers (Leekam et al., 2007; Watt, Wetherby, Barber, Morgan, 2008) have noted that SIB are frequently reported in typically developing toddlers; although it is extremely rare these SIB occur to a marked or notable degree. Others note that, on average, parents of children with typical or delayed development endorse one lower-order SIB, whereas parents of children with ASDs endorse three SIB when interviewed about symptoms of autism in their children (Richler et al., 2007). Furthermore, parents of toddlers with autism report more unusual sensory interests and more complex mannerisms than parents of toddlers with PDD-NOS or typical development (Richler et al., 2007). Therefore, it is not the presence of SIB that distinguish children with ASDs, but the rate and intensity at which certain SIB occur.

However, not all lower-order SIB distinguished children with an ASD who had fewer social and communication abilities in this sample. Specifically, hand, finger, and other complex mannerisms failed to distinguish any of the ASD cluster subgroups in the present study. This finding contradicts previous research that found toddlers with Autistic Disorder have significantly more complex mannerisms than toddlers with PDD-NOS (Richler et al., 2007). Differences in complex mannerisms between studies could be due to differences in study sample and study groups utilized. In particular, studies that found more differences in this particular SIB between children with Autistic Disorder and children with PDD-NOS used samples of children suspected of having an ASD. In contrast, this study used a sample of children who failed an autism screen but may not have been suspected of having an ASD. Moreover, previous studies compared toddlers with an ASD to toddlers with DD or typical development. In this study,

toddlers diagnosed with an ASD were placed in empirically created groups based on level of social, communication, and intellectual skills and SIB. Therefore, although hand, finger, and other complex mannerisms may differentiate toddlers with an ASD from toddlers with DD or typical development, they may not differentiate toddlers with an ASD from each other.

Two lower-order SIB that consistently distinguished subgroups of toddlers with an ASD who had fewer social and communication abilities were repetitive behaviors and abnormal sensory response. This finding supports past research that suggests these two lower-order SIB are important in the classification and diagnosis of young children with ASDs (Watt, Wetherby, Barber, & Morgan, 2008). Individual repetitive behaviors implicated in past research are "repetitively banging or tapping objects on a surface; rocking or flipping objects back and forth; swiping objects away repetitively; spinning, wobbling, or rolling objects; moving or placing objects in a stereotypical manner or place; and clutching objects for longer than expected" (Watt et al., 2008). Individual sensory behaviors implicated in past research are licks objects, smells object, feels objects, fixates on objects, and sucks fingers" (Watt et al., 2008). Therefore, including these specific SIB on screening and diagnostic algorithms for children with an ASD is important for early identification efforts.

The fact that repetitive behaviors and abnormal sensory response distinguished subgroups of children with an ASD who had fewer social and communication abilities begs the question of how else these groups of children are similar and different from one another. Careful analysis of MSEL domains shows that ASD Cluster 2 and Cluster 3 children had similar expressive and receptive language abilities, but Cluster 2 children had significantly higher visual reception scores. Subgroups also differed in that Cluster 2 children had less autistic deficit as measured by the ADOS socialization domain, ADI-R socialization domain, ADOS play domain, ADOS SIB

domain, and total CARS score. Therefore, Cluster 2 children had higher nonverbal problem-

solving abilities than Cluster 3 children and less autistic deficit. Past research has found

repetitive behaviors, but not abnormal mannerisms or abnormal sensory response, were

significantly and negatively correlated with developmental level (Watt et al., 2008). The fact

that the ASD cluster subgroup associated with the lowest developmental level consistently had

more repetitive behaviors, while differences in abnormal sensory response and abnormal

mannerisms were less significant, supports this finding. It may be, then, that developmental

level (especially nonverbal problem solving) may be responsible for the initial appearance of

certain SIB and then continued engagement with these SIB may further disrupt social

development which leads to more impaired functioning (Bishop et al., 2006). This hypothesis

would also explain why the ASD cluster subgroup with more lower-order SIB was more likely to

be diagnosed with Autistic Disorder (as compared to nonASD or PDD-NOS) at four years of

age.

Higher-order SIB, such as unusual preoccupations and compulsions and rituals, did not

distinguish ASD subgroups in this study. Further, these SIB occurred at a low frequency for all

ASD subgroups. These findings support the hypothesis that higher-order SIB are not particularly

relevant to younger cohorts and are not useful in classifying and diagnosing toddlers with autism

spectrum conditions. This perspective is shared among others who have also failed to find

significant group differences based on higher-order SIB in younger cohorts (e.g., group

differences between toddlers with various forms of ASDs as well as toddlers with ASD and DD;

Moore & Goodson, 2003; Richler et al., 2007). Yet higher-order SIB are consistently found in

older cohorts and do distinguish older children and adults with ASDs. Therefore, higher-order

SIB may be related to advanced skills not typically found in toddlers with an ASD. For instance,

some previous studies have found that certain high-order SIB are positively correlated with nonverbal intelligence (Bishop, Richler, & Lord, 2006). Yet studies of toddlers with ASDs often utilize children with significantly below average nonverbal abilities. For instance, in the present study, the ASD cluster associated with the highest scores on cognitive, social, and communicative measures still had significantly below average MSEL receptive language and visual reception scores. So, if higher-order SIB are related to nonverbal intelligence, they would not be expected in this particular sample.

Moreover, nonverbal IQ was found to be the most important discriminator in some ASD subtype analyses in older children and adults (Fein et al., 1999; Stevens et al., 2000) but was less important in distinguishing ASD subtypes in this group of toddlers. This discrepancy could be accounted for by the fact that other ASD subtype analyses (in older children and adults) found at least one subgroup with average nonverbal intellectual skills. In contrast, although ASD subgroups found in this study differed in terms of nonverbal problem solving, the subgroup with higher nonverbal problem solving skills still had significantly below average standard scores in visual reception (i.e., average T-scores of 33). These findings suggest that most toddlers identified with an ASD have significantly below average nonverbal problem solving skills and identification of children with ASD and average nonverbal problem solving skills may not occur until after the toddler years. Further, although few discriminant function analyses have been conducted in previous ASD subtype research, subgroups have been described in terms of characteristics that define subgroup membership. In older populations, lower intellectual functioning has consistently been associated with repetitive motor behaviors and unusual sensory response (Eaves et al., 1994; Sevin et al., 1995; Siegel et al., 1986) whereas high intellectual functioning has been associated with unusual preoccupations (Siegel et al., 1986). In this sample

of toddlers, lower nonverbal problem solving was associated with more repetitive motor behaviors and unusual sensory response but higher nonverbal problem solving was not associated with unusual preoccupations. These findings suggest that unusual preoccupations may not develop until after the toddler years or that unusual preoccupations only exist in toddlers with ASD who are not typically identified in the first few years of life (i.e., those with average nonverbal problem solving skills).

Findings from this study could have important intervention implications for children with ASDs. First, ASD cluster subgroups were primarily distinguished by level of social and communication skills; although the subgroup with more social and communicative skills still showed clinically significant deficits. Therefore, developing intervention strategies that target social-communication is important. Several research groups have shown that certain intervention programs are successful in teaching social-communication skills to toddlers; including programs that use therapist trained interventions (Kasari, Freeman, & Paparella, 2006) and parent trained interventions (Wetherby & Woods, 2006). Concerning the latter, Wetherby and colleagues (2006) recently found that 11 of 13 social communication variables significantly improved when parents taught to social-communication skills to their toddlers with an ASD. However, these same results were not found when parents taught social-communication to their 3-year-olds with an ASD. These results suggest that very early identification and social-communication intervention is crucial for the future development of toddlers with an ASD.

Interventions that focus on SIB in toddlers with an ASD should also be considered. If developmental level is responsible for the initial appearance of repetitive behaviors and continued engagement further disrupts social development, then increasing appropriate play with objects is a critical intervention target. In fact, preliminary research shows that toddlers who

received play therapy show higher level play skills (including symbolic play) in interactions with their mothers than toddlers who did not receive play therapy; significant group differences were found after only six weeks of therapy (Kasari, Freeman, & Paparella, 2006). This type of research is important in showing that play skills can be taught to very young children with ASDs in a relatively brief period of time. However, this study did not examine the effects of play therapy of the reduction of lower-order SIB. In fact, there is no published study that examines specific triggers for lower-order SIB and the influence of specific interventions. Identifying triggers for lower-order SIB and methods to replace these triggers is an important direction for future research.

Sensitivity of Gold-standard ASD Diagnostic Instruments

Sensitivity of two of the most common gold-standard ASD diagnostic instruments, the ADOS and ADI-R, was examined for each ASD cluster subgroup. Sensitivity for the ADOS, a child observation instrument, was appropriate for every cluster subgroup (0.87-1.00). These results could be explained by the fact that the ADOS is a child observation instrument administered by a trained clinician who has established reliability in detecting social and communication deficits commonly seen in children with varying forms of ASDs. Results could also be explained by the fact that the ADOS diagnostic algorithm does not consider SIB and, instead, focuses on impairments in social-communicative skills. However, the ADI-R does consider SIB; inclusion of SIB in the ADI-R diagnostic algorithm could explain why ADI-R sensitivity was not appropriate for any cluster subgroup (0.16-0.38). Furthermore, previous studies have found that removal of the ADI-R behavioral domain improved diagnostic agreement in toddlers (Wiggins & Robins, 2008). Therefore, the influence of removing the ADI-R behavioral domain was examined. As predicted, removal of the ADI-R behavioral domain

significantly improved sensitivity (0.57-0.87). Since ADOS classification of ASD does not consider SIB, and removal of the ADI-R behavioral domain improved sensitivity, these results suggest that the current ADI-R SIB algorithm should not be considered when classifying toddlers with ASDs.

Yet at least one previous study shows that including a SIB factor in diagnostic algorithms improves sensitivity and specificity of diagnostic instruments (Gotham, Risi, Pickles, & Lord, 2007). However, this study was not restricted to a sample of toddlers with an ASD and therefore cannot be generalized to toddler populations. Moreover, the current ADI-R algorithm that reduces sensitivity includes many high-order SIB that are not found in younger cohorts. For instance, three out of seven items on the ADI-R behavioral domain failed to produce significant group differences in this analysis; these behaviors (i.e., unusual preoccupations, verbal rituals, and compulsions) rarely occurred for any cluster subgroup. Consequently, diagnostic algorithms for toddlers suspected of having an ASD may become less sensitive when higher-order SIB are included.

Even if only lower-order SIB are included in diagnostic algorithms, the frequency and clinical significance of these SIB need to be further explored to ensure that most toddlers with ASD are being correctly classified. The results of this study suggest that most toddlers with ASD and higher social-communicative functioning and some toddlers with ASD and lower social-communicative functioning may have been missed if an SIB domain was needed for ASD classification on the ADI-R. Therefore, the influence of implementing an appropriate SIB domain on both the ADOS and ADI-R needs more study. Previous analyses suggest that repetitive behaviors, hand, finger, and other complex mannerisms, and abnormal sensory response differentiate toddlers with ASDs from toddlers with other DD and typical development.

This analysis suggests that repetitive behaviors and abnormal sensory response further differentiate subgroups of toddlers with ASDs from one another. Therefore, perhaps future research should focus on these lower-order SIB and which specific behaviors from within these categories improve sensitivity and specificity of diagnostic instruments. At present, however, it appears the most appropriate way to detect high-functioning children with ASD and low SIB and distinguish them from children with other DD would be to refer all children who meet ADI-R social criteria for further assessment.

Predicting ASD Diagnoses at Four Years of Age

As predicted, children with ASD and less severe social and communication impairments were more likely to receive a nonASD or PDD-NOS diagnosis at four years of age as compared to a diagnosis of Autistic Disorder than the other cluster subgroups. Conversely, children with ASD and more severe social communication impairments and more SIB were more likely to receive a diagnosis of Autistic Disorder at four years of age as compared to a diagnosis of nonASD or PDD-NOS than other cluster subgroups. These findings suggests that lower developmental levels and higher rates of lower-order SIB in the toddlers years can predict more severe diagnoses two years later. Current analyses cannot speak to whether lower developmental levels or higher rates of lower-order SIB are more important in predicting future diagnosis since these two variables are highly correlated and both variables characterized the cluster most likely to receive a diagnosis of Autistic Disorder at four years of age. However, results do support past research that shows that SIB in the toddler years are one of the more important predictors of a diagnosis of Autistic Disorder in young children (Lord, 1995).

The finding that lower developmental levels and higher rates of SIB are related to more severe forms of ASDs two years later is not particularly surprising if the hypothesis that

continued engagement in SIB that emerge in first few years of life further disrupts social development. For instance, if repetitive behaviors initially emerge due to lower developmental levels (particularly lower nonverbal problem solving levels, as was found in this study), then toddlers with ASDs, lower developmental levels, and repetitive behaviors are more likely to have further brain insult due to more extensive social deprivation. The same may also be true for abnormal sensory behaviors: toddlers with ASDs, lower developmental levels, and unusual sensory interests may have more social deprivation due to their intense focus on sensory stimuli instead of the social environment.

This study found that when a cluster analysis was performed on the entire study population, of toddlers with ASDs placed in the less severe cluster, 32% received a nonASD diagnosis, 32% received a PDD-NOS diagnosis, and 36% received an Autistic Disorder diagnosis around four years of age. In contrast, of toddlers placed in the more severe cluster, 14% received a nonASD diagnosis, 18% received a PDD-NOS diagnosis, and 68% received an Autistic Disorder diagnosis around four years of age. Therefore, toddlers with ASDs and less severe social-communication impairments were more likely to be diagnosed with nonASD and PDD-NOS around four years of age. Moreover, toddlers with ASDs, less severe social-communication impairments, and cognitive standard scores outside of the intellectually disabled range (e.g., toddlers placed in ASD Cluster 1) were more likely to no longer meet ASD criteria at four years of age. These results suggest that social, communication, and cognitive skills predict whether a toddler with ASD will show significant symptom improvement over the next two years. Again, these results are somewhat contradictory to Sutera and colleagues (2007) who found very little differences between toddlers diagnosed with an ASD who did and did not "recover" by around four years of age. However, as mentioned previously, significant social and

communication differences may have been found if the recovered ASD group was further divided by type of diagnosis (instead of one ASD category) or severity of social and communication deficit at two years of age. Moreover, the fact that eight toddlers with ASD placed in the more severe cluster moved off the spectrum by age four again speaks to the heterogeneous nature of ASDs and the potential impact of early intervention (i.e., four of these children were later diagnosed with intellectual disability and four were later diagnosed with typical development; the type and intensity of intervention received was not measured in the early screening studies).

Strengths, Limitations, and Future Directions

This study has several strengths. First, it is the first study of its kind to explore empirically derived subgroups of toddlers using a standardized instrument that represents behaviors commonly found in toddlers. This type of analysis is important to develop theories on the development of ASDs in the first few years of life, how diagnostic algorithms can be improved, and how we can better understand predictors of future diagnoses. The current analysis addressed all of these areas. Specifically, social-cognitive variables most distinguished cluster subgroups in toddlers; this finding supports a social-affective theory of ASDs. Current SIB diagnostic algorithms (i.e., for the ADI-R) were found to be inappropriate for this population; maybe because many high-order SIB that rarely occur in toddlers were included. Thus, it was suggested that SIB algorithms focus more on lower-order SIB, especially individual behaviors within the repetitive motor behavior domain and abnormal sensory response domain. Moreover, the best approach for identifying children with an ASD and more social-communicative abilities was felt to be referral of every child who meets ADI-R social criteria for further assessment. In

regards to future diagnosis, children who had more lower-order SIB were more likely to be diagnosed with more severe forms of ASDs two years later. Thus, significant engagement in SIB seems to be related to further disruption of developmental processes and may be an early marker for ASDs.

Second, it was suggested that targeting variables that relate to future diagnoses can also help inform early intervention efforts (i.e., these variables can become targets for early intervention programs). For example, intervention programs that focus on social communication skills (such as that developed by Wetherby and colleagues) can enhance an area of functioning that is impaired in all subgroups of toddlers with ASDs. Additionally, if engagement in lower-order SIB results in further disruption of developmental processes, then these SIB should also be targets of early intervention programs.

The primary limitation of this study was the study sample utilized. In particular, children who fail an autism screen may not accurately represent all children with ASD and other DD in the general population. For instance, the cluster analysis on all children included in this sample divided children based on social-communicative maturity; this division may not have been replicated if a sample of children who did not fail an autism screen were used. Thus, this particular sample may have represented children who had varying levels of social-communication difficulties and this shared characteristic could have influenced cluster divisions. However, despite this possibility, discriminant function analyses showed that certain social-cognitive variables implicated in past research most contributed to subgroup differences (i.e., imitation, relating to people, and emotional response). The validity of subgroup divisions was further supported with analyses that supported past research and study hypotheses that suggest social-communication and SIB domains represent separate but related aspects of ASDs that are

important in classifying and diagnosing toddlers with the disorders. Moreover, these domains are important in predicting future diagnoses. Therefore, limitations of the study sample do not negate study results.

Another limitation of the study was that ADOS scores and CARS scores were based on the same behavioral sample and clinical diagnosis was partially based on CARS ratings. However, previous analyses on some of the participants in this sample suggest that inter-rater reliability for the CARS differed on average of 2.8 out of 60 points; reflecting standardized scoring for cluster variables. In addition, ASD cluster subgroups were not replicated when another cluster method was employed. Instead, an alternative cluster method divided groups based on social-communication skill, but did not further divide groups based on rates and intensity of lower-order SIB. As mentioned previously, Ward's method (the method used to create cluster subgroups) is a method that causes clusters to recede on formation, thus producing distinct subgroups of relatively equal size. Since the ASD clusters with lower social-communication skills represented significantly more children than the ASD cluster with higher social-communication skills (i.e., 143 versus 47, respectively), Ward's method could have further divided the former cluster in order to create more equal groups. Yet the groups created by Ward's method represented groups defined by ASD symptoms that have been found to distinguish children with an ASD and relate to correct classification and future diagnosis. Therefore, as with the study sample utilized, limitations of the clustering method used do not negate study results.

Future research studies should attempt to replicate these analyses and utilize different cluster variables. Future research studies also should clarify variables that distinguish toddlers with PDD-NOS from toddlers with other DDs and cognitive mechanisms regarding the

development of ASDs. Concerning the latter, amygdala theories of autism, as well as theories on

other cognitive processes involved in the development of ASDs (e.g., disruption of the

orbitofrontal cortex) deserve more research attention. Furthermore, diagnostic algorithm

appropriate for toddlers that incorporate individual lower-order SIB behaviors and domains

should be explored. Another area of empirical exploration is specific triggers for lower-order

SIB and ways to replace those triggers with more adaptive ways of functioning.

In conclusion, this dissertation was useful in that distinct subgroups of toddlers with

ASDs were identified; these subgroups were primarily distinguished by level of social and

communication skills and the rate and intensity of lower-order SIB. Results suggest that these

variables (e.g., social-communication and lower-order SIB) are important to the development of

ASDs in the first few years of life. Additionally, results helped generate hypotheses on theories

regarding the development of ASDs, how to improve diagnostic algorithms for toddlers, how to

better understand diagnostic prediction, and how to tailor early intervention efforts. Such

hypotheses will help inform future research that can maximize the potential and development of

toddlers with ASDs.

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Appendix A: Childhood Autism Rating Scale Item Labels and Scoring Examples

1. Relating to people (1 = behavior appropriate for age; 4 = consistently aloof; almost never responds or initiates contact)

2. Emotional response (1 = appropriate type and degree of emotional response as indicated by change in facial expression, posture, and manner; 4 = responses are seldom appropriate to the situation; difficult to change mood; wildly different emotions)

3. Imitation (1 = child can imitate sounds, wods, and movements; 4 = child rarely or never imitates sounds, words, or movements)

4. Body use (1 = child moves with the same ease, agility, and coordination of a normal child of the same age; 4 = frequent clumsiness, repetitive movements, and unusual movements)

5. Object use (1 = child shows normal interest in toys and other objects; 4 = child shows little interests in toys or may become preoccupied with toys or use toys in strange ways)

6. Adapting to change (1 = child accepts changes in routine without undue distress; 4 = child shows severe reactions to change (e.g., tantrums))

7. Visual response (1 = vision is used together with other senses to explore objects; 4 = avoids looking at people or objects or shows other forms of visual peculiarities)

8. Listening response (1 = listening is used together with other senses; 4 = child overreacts or underreacts to sounds to an extremely marked degree)

9. Taste, smell, and touch response and use (1 = child explores new objects in an age appropriate manner, by feeling and looking; 4 = preoccupied with smelling, tasting, or feeling objects or touching people)

10. Fear or nervousness (1 = behavior is appropriate to situation and age; 4 = fear persists after repeated experience with harmless objects or events or child shows inappropriate regard for hazards)

11. Verbal communication (1 = normal verbal communication; 4 = meaningful speech is not used; bizarre use of some recognizable words or phrases)

12. Nonverbal communication (1 = normal use of nonverbal communication; 4 = only uses bizarre gestures that have no apparent meaning and shows no awareness of meaning associated with gestures)

13. Activity level (1 = neither more or less active than a normal child the same age; 4 = extremes of activity or inactivity and may shoft from one extreme to the other)

14. Level and consistency of intellectual response (1 = as intelligent as typical children the same age; 2 = not as smart as typical children of the same age)

15. General impressions (1 = no symptoms of autism; 4 = child shows many symptoms of autism)

Note that CARS items are scored on a 7-point Likert scale rated from one to four in half-point increments.

Appendix B: The Modified Checklist for Autism in Toddlers

Please fill out the following about how your child **usually** is. Please try to answer every question. If the behavior is rare (e.g., you've seen it once or twice), <u>please answer as if the child does not do it</u>.

1. Does your child enjoy being swung, bounced on your knee, etc.?   Yes   No
2. Does your child take an interest in other children?   Yes   No
3. Does your child like climbing on things, such as up stairs?   Yes   No
4. Does your child enjoy playing peek-a-boo/hide-and-seek?   Yes   No
5. Does your child ever pretend, for example, to talk on the phone or take care of a doll or pretend other things?   Yes   No
6. Does your child ever use his index finger to point, to ask for something?   Yes   No
7. Does your child ever use his/her index finger to point, to indicate interest in something?   Yes   No
8. Can your child play properly with toys (e.g., cars or bricks) without just mouthing, fiddling, or dropping them?   Yes   No
9. Does your child ever bring objects over to you (parent) to show you something?   Yes   No
10. Does your child look you in the eye for more than a second or two?   Yes   No
11. Does your child ever seem oversensitive to noise? (e.g., plugging ears)   Yes   No
12. Does your child smile in response to your face or your smile?   Yes   No
13. Does your child imitate you? (e.g., you make a face-will your child imitate it?)   Yes   No
14. Does your child respond to his/her name when you call?   Yes   No
15. If you point at a toy across the room, does your child look at it?   Yes   No
16. Does your child walk?   Yes   No
17. Does your child look at things you are looking at?   Yes   No
18. Does your child make unusual finger movements near his/her face?   Yes   No
19. Does your child try to attract your attention to his/her own activity?   Yes   No
20. Have you ever wondered if your child is deaf?   Yes   No
21. Does your child understand what people say?   Yes   No
22. Does your child sometimes stare at nothing or wander with no purpose?   Yes   No
23. Does your child look at your face to check your reaction when faced with something unfamiliar?   Yes   No

Have you ever filled out this form for this child before?   Yes   No

Appendix C: Modified Checklist for Autism in Toddlers Follow-up Interview Example

1. You reported that _____ does not take an interest in other children. (Critical)

Is this still true?

No

Yes

Then your child does take an interest in other children?

Yes

No

Is he/she interested in children who are not his/her brother or sister?

When you are at the playground or supermarket, does your child usually respond to the presence of another child?

No

Yes

No

Yes

How does your child respond?

PASS

Ask all:

Plays with the other child	Yes ❑	No ❑
Talks to the other child	Yes ❑	No ❑
Aggressive behavior	Yes ❑	No ❑
Vocalizes	Yes ❑	No ❑
Looks at the other child	Yes ❑	No ❑
Smiles at the other child	Yes ❑	No ❑

NO to all

FAIL

If yes to any:

Does s/he (fill in responses given here- e.g. plays, talks, smiles, looks, or vocalizes) more than half of the time?

NO

FAIL

YES

PASS