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A Comparison Between High-Risk and Low-Risk Children with Autism Spectrum Disorder

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Abstract

Due to the elevated recurrence rates in high-risk younger siblings of children with ASD, the population is frequently used to examine early ASD symptomatology. However, the representative nature of this population compared to the general population of children with ASD is unknown. Previous research also suggests that parents of children with ASD raise concerns about the development of subsequent children earlier than first-time parents or parents of typically developing children. Whether an actual discrepancy exists in the attainment of milestones in these populations has not yet been assessed. The current study proposes to compare high- and low-risk children with ASD with respect to behavioral differences and milestone attainment. A high-risk sample of 23 children with ASD who had an older affected sibling was compared to 23 children with ASD drawn from a low-risk sample. Samples were matched on age, gender, and maternal education. T-tests and chi-squares were utilized to detect differences between groups on ASD symptomatology, cognitive ability, adaptive functioning, and milestone attainment. Few group differences on ASD symptom severity were observed. High-risk children had fewer communication-related symptoms than low-risk children, and significantly higher cognitive scores. Adaptive functioning and milestone attainment appeared similar across groups. High-risk children may be higher functioning than children drawn from the low-risk sample in their communicative skills and cognitive abilities. This may be partially related to high-risk parents' increased sensitivity to early signs of language and cognitive delay and may have implications for the generalizability of results from high-risk samples.

A Comparison Between High-Risk and Low-Risk Children with Autism Spectrum Disorder

Autism Spectrum Disorders (ASDs) are a group of neurodevelopmental disorders characterized by deficits in the domains of reciprocal social interaction and verbal and nonverbal communication, as well as the presence of restricted and repetitive behaviors (American Psychiatric Association; APA, 2000). According to the DSM-IV-TR (APA, 2000), ASDs can be further divided into Autistic Disorder, Asperger's Syndrome, and Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS) based upon the presentation of symptoms in the domains listed above. ASDs are pervasive in that they affect all aspects of an individual's life, from cognitive and social functioning to adaptive skills. As with many other psychological disorders, ASD is currently diagnosed based upon the presence or absence of specific behavioral symptoms. Current estimates from the Centers of Disease Control (CDC) suggest that one in every 88 children in the United States is affected with ASD (CDC, 2012). ASD affects more males than females, such that there are more than four males for every one female affected with the disorder (CDC, 2012).

Relatives of Children with ASD

Additionally, there is evidence of an increased recurrence risk in younger siblings of children with ASD. Early estimates of recurrence risk were extremely low, as they did not take into account the possibility of stoppage, where parents decide to stop procreating due to the possibility of having another child on the autism spectrum. Currently, recurrence risk is estimated to fall between 10 and 20% (Constantino, Zhang, Frazier, Abbacchi, & Law, 2010; Ozonoff et al., 2011; Szatmari, 1999). Recurrence risk is affected by a variety of factors, including the gender of the younger sibling and the number of children in the family with the

disorder, increasing three-fold or two-fold, respectively (Ozonoff et al., 2011). A significant decrease in recurrence risk is often observed in second and third degree relatives suggesting particular patterns of inheritance (i.e., non-Mendelian; Szatmari, 1999).

Siblings of children on the autism spectrum are not only more likely to develop ASD, but also are more likely to present with milder ASD-like behaviors. The presence of subclinical social and communicative deficits and stereotyped behavior in siblings of individuals with ASD is often referred to as the Broader Autism Phenotype (BAP; Piven, Palmer, Jacobi, Childress, & Arndt, 1997). Evidence of BAP is seen not only in siblings of children with ASD, but also in parents, and second-degree relatives (Pickles et al., 2000; Piven et al., 1997). Several researchers have suggested that BAP is more often seen in families with more than one individual on the spectrum (i.e., multiplex families), than in families with only one affected individual (i.e., simplex families; Gerdts, Bernier, Dawson, & Estes, 2012; Schwichtenberg, Young, Sigman, Hutman, & Ozonoff, 2010).

Symptom gradation is also observed in affected siblings. There is evidence of a birth order effect, such that affected younger siblings tend to be more severe than their older sibling with ASD (i.e., proband), specifically with respect to IQ (Goin-Kochel, Mazefsky, & Riley, 2008; Martin & Horriat, 2012; Spiker, Lotspeich, Dimiceli, & Szatmari, 2001) and social abilities (Martin & Horriat, 2012). Birth order effects hold for additional younger siblings as well (Goin-Kochel et al., 2008; Martin & Horriat, 2012).

Genetic Mechanisms in ASD

Evidence from family studies of higher recurrence rates and BAP, as well as twin studies (i.e., Folstein & Rutter, 1977), suggests that ASD is highly heritable. While the genetic etiology of ASD is not yet fully understood, research suggests that heritability estimates of ASD range

from 70 to 80% (Geschwind, 2011). Despite being highly heritable, the etiology of ASD is only known for approximately 10 to 20% of cases (Geschwind, 2011). Recently, there have been increased efforts to study the genetic mechanisms of ASD in the hopes of finding genetic markers that are diagnostic or predictive of later ASD. Many believe that understanding the genetic underpinnings will shed light upon the phenotypic heterogeneity prevalent in ASD. There is some evidence of distinct genetic mechanisms at play in multiplex and simplex ASD families; specifically, that simplex ASD is more likely to be idiopathic (i.e., of unknown cause; Constantino et al., 2010).

Additionally, some studies suggest that there may be different genetic mechanisms at play in higher functioning individuals with ASD and lower functioning individuals with ASD (MacLean et al., 1999). However, MacLean and colleagues (1999) found that ASD subtype (i.e., Autistic Disorder, Asperger's Syndrome, or PDD-NOS) and symptom severity showed minimal familial aggregation. This finding suggests that within individual multiplex families a variety of ASD subtypes and a range of ASD symptom severity can exist. The apparent genetic heterogeneity in ASD may contribute to the difficulties researchers encounter in linkage and other genetic studies.

Behavioral Differences in ASD

If differing genetic mechanisms are at play in multiplex and simplex ASD, there may be phenotypic differences in the presentation of ASD between these two groups as well. Very few studies have considered potential behavioral differences in ASD between multiplex and simplex families. Thus far, studies have focused on differences on the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) with inconsistent findings. At the domain level, there appears to be no difference in ASD symptomatology in multiplex and simplex ASD

families (Cuccaro et al., 2003). When looking at the item level, however, singletons from simplex families had higher scores on restricted interests and compulsions and rituals compared to probands in multiplex families (Lotspeich, 1997, as cited in Cuccaro et al., 2003). Since the ADI-R is a semi-structured parent interview, these findings are based upon parent report of symptoms opposed to clinical observations. It is important to consider direct behavioral measures and clinician ratings in addition to parent report of development and symptomatology.

Pandey (2007) suggested that children with ASD from multiplex families might be higher functioning than children with ASD from the general population with regard to visual reception skills, fine motor skills, daily living skills, and social adaptive skills. Consistent with this finding, Miles et al. (2005) found, similar to intellectual disability literature (i.e., Zigler, Balla, & Hodapp, 1984), that familial autism (i.e., multiplex autism) is associated with higher IQ compared to complex autism (essentially simplex autism). These results suggest that children from multiplex families may in fact differ from singletons when looking beyond simply ASD symptomatology.

Detection of Multiplex and Simplex ASD

Since diagnosis of ASD is made based upon behavioral symptoms, detection of these symptoms is crucial. Parents often spend significantly more time with their infants than healthcare providers, such as pediatricians. Thus, they play a critical role in detection of symptoms. Parents are more apt to notice symptoms such as language delay in subsequent children than in their first child as comparison to other children appears to be more important than knowledge of milestone attainment (Glascoe, Altemeier, & MacLean, 1989). Furthermore, parents of children with ASD tend to voice concerns about subsequent children earlier than first-time parents or parents of typically developing children (Herlihy, Knoch, Vibert, & Fein, 2013; Ozonoff et al., 2009). Herlihy et al. (2013) found that parents of children with ASD voiced

concerns about subsequent infants with ASD approximately six months earlier than first-time parents and approximately four months earlier than parents of typically developing children. In general, parent concerns appear to be warranted, as Ozonoff et al. (2009) found that parent reported ASD-specific concerns at 12 months were predictive of ASD diagnosis at 36 months. These results suggest having older children serves to sensitize parents to delays in subsequent children. While these concerns are predictive of later diagnostic outcome, there is little research in ASD on how these concerns are related to scores on psychometric measures and milestone attainment.

Specific Aims

Many ASD research studies are currently being conducted using younger siblings of children with ASD to examine the early emergence of ASD symptomatology and possible predictors of outcome. While this type of research is common among other low base rate disorders, and solves the problem of conducting longitudinal studies of a relatively low base rate condition, it is concerning that findings regarding ASD core deficits and development of symptomatology are based upon this high-risk sample with little evidence as to how representative the sample is of the larger population of children with ASD. There is currently a lack of research on the degree to which multiplex ASD is similar to simplex ASD with respect to symptomatology, cognitive ability, adaptive functioning, and milestone attainment.

The current study proposes to further the research by comparing multiplex and simplex ASD to determine if children with ASD from multiplex families are truly representative of the larger population of individuals with ASD. Since approximately half of the children in the simplex sample are only children, for the purposes of the study, the multiplex and simplex samples will subsequently be referred to as high-risk and low-risk, respectively. Although the

low-risk children are not strictly low-risk given their ASD diagnosis, they will be referred to as such to indicate that they were drawn from a low-risk population.

We propose the following hypotheses. First, since minimal differences were seen between multiplex and simplex ASD on the ADI based on parent report and there is evidence of a continuum of severity in multiplex and simplex families, we hypothesize that ASD symptomatology and severity will not differ between high-risk and low-risk groups with ASD on clinician-rated measures. Secondly, since simplex ASD is associated with lower cognitive functioning, we predict that the high-risk group will be higher functioning with respect to intellectual and adaptive functioning. Lastly, as previously literature suggests that the high-risk group may be less developmentally delayed, we predict that the high-risk group will attain developmental milestones earlier than the low-risk group.

Method

Participants

Children were recruited as part of a larger research study evaluating the effectiveness an autism screening measure, specifically the Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein, & Barton, 1999a) and a second-generation version, the M-CHAT, Revised (M-CHAT-R; Robins, Fein, & Barton, 2009). Children were recruited through three different avenues, including through well-child visits at pediatrician sites in Connecticut and bordering states, through Early Intervention sites, and through clinical services or research involving an older sibling with ASD, as part of an adjunct sibling study. Children who screened positive on the M-CHAT(-R) and continued to screen positive after a follow-up phone interview, were invited to the University of Connecticut (UConn) for a complete diagnostic and behavioral evaluation. See procedure section for more detailed information regarding the recruitment and

screening process. Children with a previous ASD diagnosis from a MD or psychologist, a major medical condition, or a sensory or motor impairment that would render the evaluation invalid, were excluded from the study. Additionally, children recruited through the sibling study were excluded if they were more than three weeks premature, weighed less than 4.4 pounds at birth, or if they did not have an older sibling (full or half-sibling) with ASD. Children who were high-risk for a reason other than having an older sibling on the spectrum (i.e., referred from an early intervention site) were also excluded from both groups. Furthermore, children with missing diagnostic or behavioral data were excluded. Only children who received an ASD diagnosis as a result of the evaluation were included in the current sample. Informed consent was obtained from the child's parents prior to the evaluation being conducted.

High-Risk Sample. The high-risk sample (HR-ASD; n = 23) was composed of children from the larger sample described above, who had an older sibling also diagnosed with ASD. The majority (74%) of the HR-ASD group was recruited through clinical services or research involving an older sibling with ASD, while the remainder (26%) was recruited from pediatrician sites. The HR-ASD group was composed of toddlers (M = 24.9 months, SD = 3.8); 56.5% (n = 13) were male and 43.5% (n = 10) were female. The sample was predominantly (87%) White. Approximately half (65.2%) of the children's mothers had at least a college level education. Diagnosis of the older sibling was confirmed as part of the sibling study through an evaluation comparable to that received by the younger sibling.

Low-Risk Sample. A matching sample of children, the Low-Risk ASD (LR-ASD) group, was selected from a larger sample of children with ASD, who had no evidence of siblings diagnosed with ASD. There were 12 children in the LR-ASD group who had no siblings. The LR-ASD group and the HR-ASD group were matched exactly on gender. The groups were also

matched on age and maternal education and did not differ with regard to ethnicity (See Table 1). All of the LR-ASD group was recruited through pediatrician offices. The LR-ASD group was composed of toddlers (*M* = 24.4 months, *SD* = 4.0); 56.5% (*n* = 13) were male and 43.5% (*n* = 10) were female. As with the HR-ASD sample, the LR-ASD sample was predominantly White (78.3%). The majority (60.9%) of mothers of the LR-ASD group received a college education or higher.

Procedures

Caregivers, typically mothers, of children between the ages of 16 and 30 months completed the M-CHAT(-R) at the pediatrician's office or at home. Completed screeners were mailed to the Early Detection Lab at UConn for scoring. Children who passed the screener were screened again at 48 months of age with the M-CHAT(-R) and the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003). Caregivers of children who failed the screener were contacted for a follow-up phone interview, to review the questions they had failed in more detail. Items that were left blank or answers that were ambiguous were considered failed items for the purposes of qualifying for the follow-up phone interview. If the child continued to screen positive after the follow-up phone interview, the family was invited to UConn for a free developmental and diagnostic evaluation. A licensed clinical psychologist or developmental pediatrician and a graduate student from the UConn clinical psychology PhD program conducted the evaluations.

Prior to the evaluation, parents completed several pencil-and-paper measures. At the evaluation, caregivers were interviewed about their child's development, social and communication skills, and restricted and repetitive behaviors using the Autism Diagnostic Interview (ADI or ADI-Revised) or a similar interview developed by the investigators for use

with toddlers (i.e., Toddler ASD Symptom Interview; TASI; Barton et al., 2012). Caregivers were also asked about their child's adaptive functioning using the Vineland Adaptive Behavioral Scales (Vineland ABS; Sparrow, Balla, & Cicchetti, 1984 or Vineland-II; Sparrow, Cicchetti, & Balla, 2005). Children's cognitive abilities were assessed using the Mullen Scales of Early Learning (MSEL; Mullen, 1995) and their social and communication skills were assessed using the Autism Diagnostic Observation Schedules (ADOS; Lord et al., 2000). Afterwards, the clinician rated autism-related symptoms on the Childhood Autism Rating Scale (CARS) based upon parent report and direct observation of the child. Children were diagnosed based upon scores on diagnostic measures (i.e., ADOS, ADI or ADI-R, and CARS), in conjunction with clinical judgment according to DSM-IV-TR (APA, 2000) criteria. Immediately following the evaluation, short feedback sessions were conducted to provide families with testing results, including diagnoses and preliminary recommendations. Six to eight weeks following the evaluation, a comprehensive report detailing the results of the evaluation, highlighting the child's strengths and weaknesses, as well as appropriate recommendations, was sent to the family by mail. Families were then invited back for a free, follow-up evaluation when their child was four years old, in an effort to collect data on diagnostic stability.

Only children diagnosed with ASD (i.e., Autistic Disorder or PDD-NOS) at the initial evaluation were included in the current study sample. Evaluations of children in the HR-ASD group included an evaluation of the older sibling to confirm diagnosis as well as to measure current cognitive and behavioral functioning.

Measures

Modified Checklist for Autism in Toddlers (M-CHAT). The M-CHAT (Robins, Fein & Barton, 1999a) is a parent-report, autism screening measure, consisting of 23 yes/no questions

pertaining to a child's development. The M-CHAT is a revised version of the Checklist for Autism in Toddlers (CHAT; Baron-Cohen, Allen, & Gillberg, 1992), an ASD screening questionnaire developed to detect ASD in 18-month-old children when administered by a clinician. Higher scores on the M-CHAT are indicative of more ASD-related concerns. In order to screen positive on the M-CHAT, a child must fail three out of the twenty-three items overall or two of the six critical items; cutoffs that were determined to maximize sensitivity and positive predictive value (PPV; Robins, Fein, Barton, & Green, 2001). Critical items were determined to be the best items that distinguish between ASD and non-ASD based upon a discriminant function analysis conducted by Robins et al. (2001). Positive screens on the M-CHAT receive a follow-up phone interview (Robins et al., 1999b) to clarify failed items. Internal reliability has shown to be adequate for both the overall M-CHAT ($\alpha = .85$) and the M-CHAT critical items ($\alpha = .83$; Kleinman et al., 2007; Robins et al., 2001). PPV for the M-CHAT total score is .36, which rises to .68 after the follow-up phone interview, while PPV for the M-CHAT critical item score is .64, which rises to .79 after the follow-up phone interview (Robins et al., 2001). The addition of the follow-up phone interview is particularly important when screening in a low-risk population (Kleinman et al., 2007). The follow-up phone interview has good inter-rater reliability, ranging from .60 to 1.0 across all items (Robins, 2008). Approximately half of the sample (58.7%) completed the M-CHAT and the follow-up phone interview, compared to the revised M-CHAT.

M-CHAT Revised (M-CHAT-R). The M-CHAT-R (Robins et al., 2009) is a revised version of the M-CHAT that contains 20 yes/no questions. Revisions included the re-wording of some questions as well as the provision of examples in an effort to make the questions more comprehensible. For instance, "Does your child ever bring objects over to you (parent) to show you something?" (Robins et al., 1999a) on the M-CHAT, became "Does your child show you

things by bringing them to you or holding them up for you to see – not to get help, but just to share? (For example, showing you a flower, a stuffed animal, or a toy truck)" (Robins et al., 2009). In order to screen positive on the M-CHAT-R, a child needs to fail three of the twenty items or two of the seven critical items. Again, higher scores are indicative of greater concern. The internal consistency for the M-CHAT-R with the follow-up phone interview (M-CHAT-R/F) was relatively high ($\alpha = .79$; Robins et al., 2014). The PPV for the M-CHAT-R for the total score is .14, which increases to .48 after the follow-up phone interview (Robins et al., 2014). Compared to the original M-CHAT, the M-CHAT-R resulted in significantly reduced initial screen-positive rate (Robins et al., 2014). PPV for the two-stage screening process (i.e., screener and follow-up phone interview) did not differ across versions; however, the rate of ASD detection was significantly higher on the revised version (Robins et al., 2014). Approximately 41.3% of the sample completed the M-CHAT-R and the follow-up phone interview (as opposed to the original M-CHAT).

Autism Diagnostic Interview (ADI). Multiple versions of the ADI were used in the current study, including the original ADI (Le Couteur et al., 1989) and a revised version, the ADI-R (Lord et al., 1994). The ADI(-R) is a semi-structured diagnostic parent interview of ASD symptomatology based upon ICD-10 and DSM-IV criteria, that can be utilized for children with a mental age as low as two years (Lord et al., 1994). It consists of sections asking about early development, social interaction, communication, RRBs, and general behavior. On many items, parents are asked about current behavior as well as if children ever exhibited the symptom. Symptoms are rated as either present or absent and tallied according to a specified algorithm based on the child's age and verbal ability. The ADI has high inter-rater reliability with weighted kappas ranging from .64 to .97 on social interaction items and a mean weighted kappa of .70 on

restricted and repetitive behaviors (Le Couteur et al., 1989). Inter-rater reliability across domains on the ADI-R is also relatively high, with weighted kappas ranging from .64 to .89 on reciprocal social interaction algorithm items, .69 to .89 on communication algorithm items, and .63 to .86 on the restricted repetitive behavior algorithm items (Lord et al., 1994). On the ADI-R, internal consistency was relatively high (Reciprocal social interaction: $\alpha = .95$, Communication: $\alpha = .84$, and RRB: $\alpha = .69$; (Lord et al., 1994). In the current study, the ADI(-R) was utilized for diagnosing the infant siblings and for confirming diagnosis of the proband in the high-risk sample. Additionally, data from the early development section of the ADI(-R) were used in the milestone analyses.

Toddler ASD Symptom Interview (TASI). The TASI (Barton et al., 2012) is an investigator-developed, semi-structured parent interview of ASD symptomatology based on DSM-IV-TR criteria. It was developed to be used in place of the ADI(-R) for children with a mental age less than two years. As with the ADI(-R), items are scored to indicate the presence or absence of symptoms. The measure is currently undergoing reliability testing and validation. In the current study, the TASI was utilized for diagnosing infant siblings.

Autism Diagnostic Observation Schedules (ADOS). The ADOS (Lord et al., 2000) is a semi-structured observational measure used to diagnosis ASD. It consists of a variety of activities designed to interest children and provides opportunities for them to communicate. The ADOS also provides opportunities to observe social interaction and pretend play. Different modules are utilized based upon the child's language level. After all of the activities have been administered, the examiner rates the child's behavior during the ADOS with regard to five main domains (a) language and communication, (b) reciprocal social interaction, (c) play, (d) stereotyped behaviors and restricted interests, and (e) other abnormal behaviors. Higher scores

are thought to be indicative of greater ASD symptomatology. Different algorithms exist for each of the modules based upon ROC curves (Lord et al., 2000). The majority (96%) of toddlers in the current study received Module 1 of the ADOS, and the remainder received Module 2. Based upon analyses run with the standardization sample, inter-rater reliability is high for Module 1, with mean weighted kappas (Mk_w) of .78 (Lord et al., 2000). Inter-rater reliability is also relatively high for Module 2 (Mk_w = .70), Module 3 (Mk_w = .65), and Module 4 (Mk_w = .66; Lord et al., 2000). Internal consistency is best for the Social domain (α = .86 - .91, for each module), lower for the Communication domain (α = .74 - .84, for each module) and the Stereotyped Behaviors and Restricted Interests domain (α = .63 - .65, for Modules 1 and 2; Lord et al., 2000). Classification of autism compared to non-spectrum based upon the ADOS algorithms is 100% for Modules 1 and 3, 91% for Module 2, and 90% for Module 4 (Lord et al., 2000). For the purposes of the current study, an ADOS calibrated severity score (CSS) was calculated according to the algorithms developed by Gotham, Pickles, & Lord (2008).

Childhood Autism Rating Scale (CARS). The CARS (Schopler, Reichler, & Renner, 1988) is a 15-item rating scale measuring autism severity that is completed by a clinician based upon observation and parent report. Items cover areas including verbal and nonverbal communication, relating to people, imitation skills, and sensory responses as well as a general overall impression. Each item is scored on a scale of one to four, with half number increments. A total score is then calculated by adding the scores of all of the individual items. Total scores can be categorized into three groups: Non-Autistic (Total Scores = 15 – 30), Mildly-Moderately Autistic (Total Scores = 30 – 37), and Severely Autistic (Total Scores = 37 – 60). While a cut-off of 30 is typically used for Autistic Disorder, a cutoff of 25.5 has been proposed for ASD more broadly (Chlebowski, Green, Barton, & Fein, 2010). Internal consistency of items on the CARS

is high (α = .94) and inter-rater reliability is good (.71; Schopler, Reichler, & Renner, 1995). Test-retest reliability suggests that CARS scores are relatively stable over time (*r* = .88; Schopler et al., 1995). CARS total scores are correlated with scores from other ASD diagnostic measures (*r* = .84) as well as with clinical judgment of autism diagnosis (*r* = .80; Schopler et al., 1995).

Mullen Scales of Early Learning (MSEL). The MSEL (Mullen, 1995) is a standardized test used to assess cognitive development in children from the age of one-month-old to five years, eight months of age. There are five domains: gross motor, visual reception, fine motor, receptive language, and expressive language. Raw scores in each of these domains can be converted into T-scores or age equivalents (AEs). All domains except for gross motor contribute to an overall standardized cognitive score, which is similar to an IQ score (i.e., Early Learning Composite or ELC). MSEL domain standard scores are internally consistent, with a median split-half reliability ranging from .75 to .85 across all ages (Mullen, 1995). MSEL scores tend to be relatively stable, as test-retest reliability over a one to two week period ranged from .82 to .85 across the domains for children up to 24 months, and ranged from .71 to .79 for children between the ages of 25 and 56 months (Mullen, 1995). Inter-scorer reliability is high, ranging from .91 to .99 across all age ranges. MSEL scores have good convergent validity with other measures of cognitive functioning in young children with ASD, such as the Differential Abilities Scales (DAS; Elliott, 1990), with a reliability of .83 for verbal IQ (based upon AE for receptive and expressive language) and .74 for non-verbal IQ (based upon AEs for visual reception and fine motor; Bishop, Guthrie, Coffing, & Lord, 2011). In the current study, only the four domains that contribute to the ELC were completed – visual reception, fine motor, expressive and receptive language.

Vineland Adaptive Behavior Scales – Survey Interview Form (VABS) and Vineland Adaptive Behavior Scales, Second Edition – Survey Interview Form (Vineland-II). The Vineland is a semi-structured parent interview used to assess children's adaptive skills with regard to communication, socialization, daily living skills, and motor skills. Both versions of the Vineland work similarly. The clinician administering the interview codes each behavior as a zero, one, or two. Behaviors that are usually performed without help, or a skill that the child has mastered, is scored a two. A behavior that the child still needs help with, or can partially complete on his/her own – essentially a skill that is still being learned – is scored a one. Behaviors that the child never completes on his/her own, or is not allowed to complete because he/she is too young are scored a zero. The purpose of the Vineland is to assess the behaviors that the child usually exhibits, not what the child is capable of doing. Often a child is capable of certain behaviors but does not consistently exhibit these behaviors. Individual item scores are then converted into standard scores for the subdomains and domains as well as an overall standard score, the Adaptive Behavior Composite (ABC). On the VABS (Sparrow et al., 1984), split-half reliability ranges from .70 to .95 across domains and across all age groups (Sparrow et al., 1984). Interclass correlations suggest that VABS scores are relatively stable (ICC = .95 - .99, across domains and subdomains) and inter-rater reliability is high (ICC = .93 - .99; Sparrow et al., 1984). On the Vineland-II (Sparrow et al., 2005), split-half reliability ranges from .91 to .98 for the two-year-old cohort. Vineland-II scores are also stable, with a test-retest reliability ranging from .82 to .96 in the zero to two years of age cohort, and inter-rater reliability was high, ranging from .73 to .87 across domains in the zero to six years of age cohort (Sparrow et al., 2005). Both the VABS and the Vineland-II show low correlations with IQ measures indicating criterion validity by suggesting that adaptive skills and cognitive functioning are two different areas of

functioning (Sparrow et al., 1984; Sparrow et al., 2005). Both versions of the Vineland were used in the current study. As the different versions are highly correlated, scores were collapsed across versions and the measure will subsequently be referred to as the Vineland (Sparrow et al., 2005). The current study focuses on the standard scores of the four main domains – communication, socialization, daily living skills, and motor skills.

History Form. The History Form is an investigator-developed, parent report measure comprised of a combination of open-ended and multiple-choice questions regarding family demographics, pregnancy and labor, developmental, medical, and treatment history. The present study focused on questions related to the attainment of developmental milestones, specifically when the child walked alone without support, said first words (other than "mama" and "dada") and put two words together (for example, "more juice"). For each of the aforementioned skills, parents were asked, "For each skill that the child has done or is doing, please write the age in months when the child first did it." To examine age and type of first concern, parents were asked, "At what age (if ever) were you first worried about your child's development?" and responses were converted into months. Parents were also asked to respond to the open-ended question, "Why were you worried?"

Data Analytic Plan

Matching Procedure. Once the HR-ASD group was selected, HR-ASD participants and a larger sample of LR-ASD participants were each listed in random order, opposed to being listed in order on a matching variable (e.g., from youngest to oldest). Research has shown that ordering samples randomly while matching minimizes selection bias (Rubin, 1973). The HR-ASD and LR-ASD groups were then matched pair-wise on age, gender, and maternal education, such that for each HR-ASD participant, a participant from the LR-ASD group was selected with

the same gender and approximately the same age and maternal education. Essentially, an exact match was found for gender, and a nearest available match was found for age and maternal education. After all of the HR-ASD participants were matched, independent samples t-tests and chi-square tests of independence were run on age and maternal education respectively to confirm that the groups were well matched. Additionally, a Fisher's Exact Test was run to confirm that the groups did not differ with regard to ethnicity, due to expected frequency counts less than five.

Analysis of ASD Symptomatology and Severity. The purpose of the study is to determine whether behavioral differences exist between children with ASD drawn from low-risk and high-risk samples. ASD symptomatology, as measured by a DSM-IV-TR checklist, was compared at a domain level across groups using independent samples t-tests. Additionally, the breakdown of ASD diagnoses across groups was also compared using Fisher's Exact Test due to small expected frequency counts. ASD severity, as measured by the ADOS CSS score and the CARS total score, was then be examined. Independent samples t-tests were used to determine if there are any significant group differences on these measures.

Analysis of Cognitive and Adaptive Functioning. The MSEL was used to assess participants' cognitive functioning. Histograms indicated that MSEL subscale scores were not normally distributed in either group since many children received the lowest possible standard score. The MSEL does not distinguish well among children who are lower functioning with regard to language (Mullen, 1995). In order to use parametric statistical tests without violating their assumptions, age equivalents were used to estimate participants' cognitive levels using a ratio IQ according to the formula mental age (i.e., age equivalent) divided by chronological age multiplied by 100, as has been done previously in the literature (i.e., Reitzel et al., 2013; Rogers et al., 2012). Once transformed, scores approximated a normal distribution, and independent

samples t-tests were utilized to determine whether the HR-ASD group differed from the LR-ASD group on any of the MSEL subscales—Visual Reception, Fine Motor, Receptive and Expressive Language.

Lastly, Vineland domain standard scores were used to assess adaptive behavior levels. Unlike MSEL standard scores, Vineland standard scores were normally distributed, so independent samples t-tests could be used to determine whether the HR-ASD and LR-ASD groups differed on any of the Vineland domains—Communication, Socialization, Daily Living Skills, and Motor skills – without transformation.

Analysis of First Concerns and Milestone Attainment. Age of first concerns was calculated in months and compared across groups using independent samples t-tests. Additionally, the LR-ASD group was broken down into two subgroups, No siblings and only Typically Developing siblings (TD-Sibs), to further examine the pattern of differences. Since type of first concern came from several different data sources including some open-ended questions, responses were categorized into four categories for further analyses: (1) language concern, (2) motor concern, (3) social or ASD specific concern, (4) other concern.

The milestones focused upon in this study were age of first steps, age of first words, and age of first phrases. As there were many children who did not attain these milestones by the time of the evaluation, utilizing age at attainment as a continuous measure did not seem appropriate. Instead, children were divided into three categories based upon age at attainment – within typical limits, delayed, and not yet attained – and then compared using the Freeman-Halton (Freeman & Halton, 1951) extension of the Fisher's Exact Test. The age range for attainment of each milestone for typically developing children was determined based on previous literature. Based upon classifications used in Matson, Mahan, Kozlowski, and Shoemaker (2010), the typical age

range for attainment of first steps was nine to 17 months, of first words was eight to 18 months, and of first phrases was 18 to 24 months. Children who attained the milestone beyond the respective ranges were considered delayed. Children who had not attained the milestone at the time of the evaluation were categorized as such.

Power Analysis

According to Cohen (1988), if the study were powered at .8 with a standard alpha level of .05, 64 subjects would be needed in each group in order to detect a medium effect size ($d \geq .5$). Unfortunately, ASD is a low base rate disorder so sample size was limited. The sample of the current study was further limited by inclusion criteria of our HR-ASD group, which required that the child have an older sibling with a diagnosis of ASD. There were 23 subjects in each group in the current study, which provided a power between .33 and .41, according to Cohen (1988). While there was enough power to detect large effects, small to medium effects may have gone undetected. This should be taken into consideration when drawing conclusions from the results, as null findings do not automatically mean that no differences was present between the HR-ASD and LR-ASD groups. If non-significant but consistent effects were observed, effect sizes were reported.

Results

The two groups were first characterized and then assessed to confirm that they were indeed well matched on age, gender, and maternal education. Detailed demographic information for each of the samples is presented in Table 1. Afterwards, the groups were examined with regard to ASD symptomatology and severity, where predictions suggested that there should be no group differences. Then, the groups were examined with regard to cognitive ability and adaptive skills. In accordance with previous research, the HR-ASD group was predicted to be

higher functioning than the LR-ASD group. Lastly, the groups were examined with respect to first concerns and milestone attainment, where it was predicted that the HR-ASD group would reach developmental milestones earlier and parents would have earlier concerns. An alpha level of .05 was used as the criterion for significance for all statistical tests. All basic analyses were run on IBM SPSS Statistics, Version 22 (SPSS, 2013). Effect sizes for independent samples t-tests were run using the Practical Meta-Analysis Effect Size Calculator developed by David B. Wilson at George Mason University (Wilson, 2001). Freeman-Halton extensions (Freeman & Halton, 1951) of the Fisher's Exact Probability Test were run using an online program developed by Richard Lowry at Vassar College where applicable (Lowry, 2014).

Confirmation of Matched Samples

Either independent samples t-tests, chi-square tests of independence, or Fisher's Exact Test were run, as appropriate, to confirm that the HR-ASD and LR-ASD groups were well matched on age and maternal education. As the samples were matched exactly on gender, no comparison was run. According to criteria set forth by Frick (1995), the HR-ASD (M = 24.9 months, SD = 3.8) and LR-ASD (M = 24.4 months, SD = 4.0) groups were well matched on age, $t(44) = -.408$, $p = .685$, $d = .13$. The groups were also well matched on maternal education ($X^2 = .093$, $p = .760$, $phi = .05$), based upon the number of mothers who had earned a college degree compared to those who had not. The HR-ASD and LR-ASD groups did not differ with regard to ethnicity as indicated by a Fisher's Exact Test ($p = .699$), when comparing individuals who were White to those of other ethnicities.

Performance on Screener and Follow-up Phone Interview

Independent samples t-tests were run to determine if there were differences between the HR-ASD and LR-ASD groups on age at screening and performance on the screener, as well as

their performance on the follow-up phone interview. As the larger study through which the current subjects were recruited has been ongoing, the subjects completed two different versions of the screener, M-CHAT or M-CHAT-R. The majority (58.7%) of the total sample completed the M-CHAT, specifically 10 children (44%) in the LR-ASD group and 17 children (74%) in the HR-ASD group.

As seen in Table 2, all study subjects completed the screener at age two and completed the follow-up phone interview about one month later, on average, with no differences across groups, $t(44) = -.688$, $p = .495$, $d = .20$ and $t(39) = -.888$, $p = .380$, $d = .26$, respectively. The HR-ASD and LR-ASD groups performed similarly on the screener and the follow-up phone interview when comparing the percentage of critical items failed (Screener: $t(44) = -.570$, $p = .572$, $d = .17$; PI: $t(39) = -.410$, $p = .684$, $d = .13$) as well as the percentage of total items failed (Screener: $t(44) = -.667$, $p = .508$, $d = .20$); PI: $t(39) = -.602$, $p = .556$, $d = .18$; Table 2). The HR-ASD group failed 40.2% of total items on screener and 32.1% of total items on the PI, while the LR-ASD group failed 36.6% and 28.7% of items, respectively. These results suggest that no group differences were evident at the level of screening.

Follow-up phone interviews were not completed for four subjects in the HR-ASD group per the two-stage screening process as described by Robins et al. (2014), where subjects who fail eight or more items on the screener bypass the follow-up phone interview and are immediately evaluated. Additionally, one subject in the LR-ASD group bypassed the follow-up phone interview before being evaluated, through study staff oversight.

ASD Symptomatology and Severity

Distribution of Diagnoses and DSM-IV-TR Symptoms. A Fisher's Exact Test was run to determine if group differences existed with regard to distribution of ASD diagnoses according

to DSM-IV-TR criteria. Participants were diagnosed as having Autistic Disorder (AD), Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS), or Autism Spectrum Disorder with a low mental age (ASD – Low MA), meaning they met criteria for AD or PDD-NOS and had a mental age on all cognitive measures less than 12 months. As seen in Figure 1, the LR-ASD group was composed of 11 children with AD, eight children with PDD-NOS, and four children with ASD – Low MA, while the HR-ASD group was composed of nine children with AD, 12 children with PDD-NOS, and two children with ASD – Low MA. There were no significant differences in diagnostic distribution between groups as indicated by a Fisher's Exact Test ($p = .554$).

Although the diagnostic distribution did not differ by group, a more thorough investigation of DSM-IV symptomatology was conducted using independent samples t-tests. Both the HR-ASD and LR-ASD groups had endorsed between five and six symptoms out of a total of 12 possible symptoms (four symptoms in each of the three domains). No differences existed between the HR-ASD and LR-ASD groups on total number DSM-IV symptoms, $t(44) = .297$, $p = .768$, $d = .09$ (Table 3). Furthermore, the groups did not differ in number of symptoms within the Social Interaction domain ($M_{LR\text{-}ASD} = 2.57$, $SD_{LR\text{-}ASD} = .945$; $M_{HR\text{-}ASD} = 2.43$, $SD_{HR\text{-}ASD} = .843$) or the number of symptoms within the Restricted and Repetitive Behaviors domain ($M_{LR\text{-}ASD} = 1.30$, $SD_{LR\text{-}ASD} = .703$; $M_{HR\text{-}ASD} = 1.61$, $SD_{HR\text{-}ASD} = .891$; p's > .20; Table 3). However, the LR-ASD group ($M = 1.87$, $SD = .458$) had significantly more symptoms in the communication domain than the HR-ASD group ($M = 1.57$, $SD = .507$), $t(44) = 2.137$, $p = .038$, $d = .62$ (Table 3).

Childhood Autism Rating Scale (CARS). An independent samples t-test was run to determine if the severity of ASD differed by group as indicated by the CARS total score. The

HR-ASD (M = 30.4, SD = 5.6) and LR-ASD (M = 31.2, SD = 6.4) groups had similar CARS total scores, suggesting that the groups do not differ by severity of overall ASD symptomatology, $t(44) = .991$, $p = .327$, $d = .13$.

Autism Diagnostic Observation Schedule (ADOS). Severity was also examined using the ADOS Calibrated Severity Score (CSS) based upon the algorithm developed by Gotham et al. (2008). An independent samples t-test was run to detect any group differences. The HR-ASD (M = 6.4, SD = 2.5) and LR-ASD (M = 7.0, SD = 2.0) groups were similar with regard to overall ASD severity as measured by the ADOS CSS, $t(44) = .467$, $p = .643$, $d = .27$.

Cognitive Ability

Since the subscale standard scores of the MSEL were not normally distributed, they were transformed into ratio IQ scores by dividing the age equivalent by the chronological age and multiplying by 100 (i.e., MA/CA*100). Each subscale's ratio IQ score was highly correlated with its respective subscale standard score (r's > .90).

Independent samples t-tests were run on each of the subscale ratio IQs – Visual Reception, Fine Motor, Receptive Language, and Expressive Language – to determine if any group differences existed. As seen in Table 4, both groups were delayed on measures of cognitive ability (that is, had means below 100). However, the HR-ASD group (M = 80.9, SD = 24.1) had higher non-verbal problem solving skills than the LR-ASD group (M = 66.2, SD = 16.4), as measured by the Visual Reception scale, $t(44) = -2.412$, $p = .020$, $d = .71$ (Table 4). Additionally, the HR-ASD group (M = 83.4, SD = 18.2) had better fine motor skills than the LR-ASD group (M = 68.0, SD = 18.7), $t(44) = -2.831$, $p = .007$, $d = .83$ (Table 4).

With regard to language ability, the HR-ASD group (M = 63.2, SD = 27.2) had better receptive language skills than the LR-ASD group (M = 45.5, SD = 15.8), $t(44) = -2.705$, p =

.010, d = .79 (Table 4). The HR-ASD group (M = 68.3, SD = 25.4) had better expressive language skills than the LR-ASD group (M = 43.6, SD = 14.4) as well, $t(43) = -4.023$, $p < .001$, d = 1.19 (Table 4). The expressive language subscale could not be completed for one subject in the LR-ASD group. Overall, the HR-ASD group was higher functioning than the LR-ASD group with respect to cognitive ability as measured on all subscales of the MSEL with large effects ranging from .71 (Visual Reception) to 1.19 (Expressive Language).

Adaptive Functioning

Adaptive functioning skills were examined using the domain standard scores of the Vineland – Communication, Daily Living, Motor, and Socialization. Since the scores were normally distributed, independent samples t-tests were run to determine if any group differences existed between the HR-ASD and LR-ASD groups. Overall, similarly to cognitive scores, both groups scored significantly lower than typically developing children. In the Communication domain, there was a trend for the HR-ASD group to have better communication skills than the LR-ASD group, $t(44) = -1.774$, $p = .084$, $d = .52$ (Table 5). No significant group differences or trends were observed between the HR-ASD and LR-ASD groups with respect to Daily Living skills, Motor skills, or Socialization skills *(p*'s > .69; Table 5). See Table 5 for means and standard deviations of samples.

Age and Type of First Concerns

Age and type of first concerns were examined to determine if any group differences existed. Again, independent samples t-tests were run to look at these potential differences. Parents in the HR-ASD group (M = 9.30 months, SD = 5.32) reported becoming concerned about their child's development significantly earlier than parents in the LR-ASD group (M = 15.39, SD = 7.18), $t(44) = 3.265$, $p = .002$, $d = .96$.

Fisher's Exact Test was used to determine if any differences existed in the type of concerns (i.e., language, social, etc.) first noted by parents in the HR-ASD versus the LR-ASD group. No differences were observed between groups as indicated by the Freeman-Halton extension of the Fisher's Exact Test, $p = .704$. As seen in Figure 2, parents in both groups most frequently identified language concerns, followed by motor or other delayed milestones, then other concerns, which includes behaviors not specific to ASD or a professional raising concern and lastly, social concerns. While parents often noted more than one type of concern, for the purpose of this analysis only the primary concern (i.e., the first one listed) was included. One subject in each group did not have information on type of parental concerns.

Achievement of Developmental Milestones

Finally, Fisher's Exact Test was used to assess whether group differences existed with respect to specific developmental milestones (age of first steps, age of first words, and age of first phrases). For age at first steps, most children in both groups attained the milestone within normal limits, with no significant difference between groups, as indicated by the Freeman-Halton extension of the Fisher's Exact Test, $p = .835$ (Table 6). For language milestones, differences between age of first words and age of first phrases did not differ significantly between the HR-ASD and LR-ASD groups, as indicated by the Freeman-Halton extension of the Fisher's Exact Test ($p = .439$ and $p = .999$, respectively; Table 6). Attainment of first words was relatively evenly distributed across attainment categories in both groups. The large majority of children had not yet attained first phrases by the time of evaluation, which was approximately at age two (71.4% and 68.6% for LR-ASD and HR-ASD groups, respectively; Table 6). Due to missing data, sample sizes were smaller for later milestones, such that there were 14 children from the

LR-ASD group and 16 children from the HR-ASD group included in the age at first phrases analysis.

Post-Hoc Analyses

As mentioned previously, the LR-ASD group was a mixed group composed of children who have no siblings (No Sibs; $n = 12$) and children who only have typically developing siblings (TD Sibs, $n = 11$). We make the assumption that the children with only typically developing siblings are from simplex families. However, the same assumption cannot be made for the subgroup of only children. In order to determine that the findings here were not driven by the subset of the LR-ASD sample whose family type was unknown, post-hoc analyses were run comparing children with only typically developing siblings to children with ASD siblings (i.e., LR-ASD TD Sibs Only vs. HR-ASD).

As seen in Table 7, the two samples remain well matched even when the No Sibs subgroup was removed from the LR-ASD sample. All of the initial findings continued to remain significant after only children were removed from the LR-ASD sample, except for DSM-IV-TR symptom distribution (Table 8). The TD Sibs group no longer differed from the HR-ASD group on the Communication Domain ($t(32) = .893$, $p = .378$, $d = .32$), but on the RRB domain, children with only TD Sibs ($M = 1.00$, $SD = .63$) tended to have fewer restricted and repetitive behaviors compared to the HR-ASD group ($M = 1.61$, $SD = .89$), $t(26.96) = 2.28$, $p = .030$, $d = .75$). These findings suggest that the subgroup of only children within the LR-ASD sample were not driving the initial results. In fact, they may have been masking differences between the LR-ASD and HR-ASD groups, as differences between groups became more pronounced when the subgroup of only children were removed, especially with respect to adaptive functioning (Table 8), diagnostic distribution (Table 7), and attainment of developmental milestones (Table 7).

Discussion

The current study compared children with ASD drawn from a low risk sample to children with ASD from a high-risk sample, defined by having an older sibling on the spectrum. The LR-ASD and HR-ASD samples were compared with respect to ASD symptomatology and severity, cognitive ability, adaptive functioning, and milestone attainment. Consistent with previous research and our first hypothesis, the two samples did not differ with regard to distribution of ASD diagnoses and overall ASD symptom severity, as assessed by clinician-rated measures. However, the LR-ASD group had significantly more communication-related symptoms, which appeared to be driven by the large proportion of children in the LR-ASD group who had delayed or lack of spoken language compared to the HR-ASD group.

With respect to cognitive ability, consistent with previous research and our second hypothesis, the HR-ASD group was higher functioning (i.e., less developmentally delayed) than the LR-ASD group with respect to non-verbal problem solving, fine motor skills, and language abilities, as assessed by standardized developmental measures. As the age at evaluation was highly similar across groups, the cognitive findings cannot solely be explained by maturity. While at first glance these findings may appear counter-intuitive, there are numerous reasons why the HR-ASD group may be higher functioning. These behavioral differences may result from differing underlying genetic mechanisms in simplex and multiplex ASD (See Geschwind, 2011 for review). These findings are consistent with research in the field of intellectual disabilities (IDs) where ‘organic’ or simplex ID is associated with lower IQ compared to multiplex or familial ID (i.e., Zigler et al., 1984), presumably because the simplex cases result from a *de novo* genetic or early injury insult, while the multiplex families may include milder problems shared by the parents. Furthermore, there may be environmental factors at play as well

in the ASD children with affected older sibs, such as exposure to therapy in the home that was meant for their older sibling with ASD or even exposure to differing parenting styles due to having an older child on the spectrum.

In terms of adaptive functioning, a trend existed in parent-reported communication skills in the same direction as the cognitive findings, suggesting that the HR-ASD group may have better communication skills than the LR-ASD group. No other significant group differences were observed in parent-reported adaptive functioning between groups. Thus, the second half of our second hypothesis was not proved. It is important to consider that adaptive functioning was measured through parent interview, and thus parents may be over-reporting their child's skills.

Finally, consistent with previous research (i.e., Ozonoff et al., 2009), parents of HR-ASD children reported concerns almost six months earlier than parents of LR-ASD children. The most frequently reported concerns were in the area of language and communication. Contrary to our third hypothesis and despite differences seen in cognitive measures, the LR-ASD group and the HR-ASD group did not differ by age of attainment for the developmental milestones of first steps, first words, and first phrases. However, it is not surprising to observe a discrepancy between these two measures, as they assess different concepts. That is, age of attainment of a milestone assesses at what age a child met the specified benchmark, but it does not address how the child progressed from there, or how functionally the child uses the skill in their daily life, which is assessed by standardized developmental measures such as the Mullen and Vineland. Furthermore, past research has shown that there is often evidence of a learning plateau or even loss of skills in ASD, specifically with regard to language (i.e., Pickles et al., 2009). For instance, a child may speak his/her first word and maybe develop a few more words, but then may not progress to using more words or using words together until significantly later. Therefore, the

difference in findings between the milestone and cognitive analyses may simply reflect the measurement of different aspects of language development.

Limitations

There are several limitations that must be considered. The current study had a relatively small sample size of only 23 children per group, as there were a limited number of high-risk ASD children due the manner in which samples were ascertained. LR-ASD children were drawn from a sample of children screened at pediatrician offices during well-child visits, while the HR-ASD children were screened after parents were notified about the study through clinical services or research involving the older sibling with ASD. As such, there is the possibility that findings of the current study may reflect ascertainment differences, instead of true underlying differences between simplex and multiplex samples. Future studies should enroll larger numbers of children using a cohort approach in order to address these issues.

Composition of the HR-ASD sample also constrained the gender distribution in the present study. In order to match the HR-ASD sample with children in the LR-ASD sample on gender, an atypical gender distribution for ASD samples had to be selected. The gender ratio in the current study was 1.3 males to every 1 female with ASD, while the gender ratio in the general population is 4.6 males to every 1 female (CDC, 2012). This difference in gender ratio may have affected the results; although, recent research by Reinhardt, Wetherby, Schatschneider, and Lord (2014) suggests minimal sex differences in ASD symptomatology, verbal and nonverbal developmental level, and adaptive functioning in young children with ASD.

It is important to note that the current study compared HR-ASD and LR-ASD children at approximately two years of age. Since children were not followed from birth, this study does not address potential differences that may exist in the development of ASD symptoms, cognitive

ability, or adaptive functioning for simplex and multiplex children with ASD; instead, it provides a snapshot of their current functioning. The current findings should be interpreted as such.

Age and type of first concerns and milestone analyses based upon retrospective parent report is another limitation. Past research has shown that parent recall of motor milestones (Bodnarchuk & Eaton, 2004; Hus, Taylor, & Lord, 2011) and age of first concerns (Hus et al., 2011) is relatively accurate. Conversely, parent recall of language milestones is often less accurate due to telescoping effects (Hus et al., 2011). We can assume that telescoping effects were minimal in this study due to the young age of the subjects, so the attainment of the milestone was relatively recent.

As mentioned above, the LR-ASD group was composed of two subgroups – only children and children with just typically developing siblings. Since only children by definition had no siblings, there is the possibility that once a subsequent child was born, the family might be revealed as multiplex. As such, these results may be an underestimate of the true differences between simplex and multiplex families. To test this possibility, post hoc analyses were run in which the only children subgroup was removed from the LR-ASD group. All findings except differences in communication DSM-IV-TR symptoms held. Many in fact showed stronger effect sizes, suggesting that the differences reported may be an underestimate. Regardless, caution should be taken when generalizing the results of this study to all simplex cases.

Clinical Implications

The findings of the current study suggest that HR-ASD children may be higher functioning than their LR-ASD peers. Also, the findings support previous research suggesting that parents of HR-ASD children report concerns earlier than parents of LR-ASD children, even when their milestone attainment is very similar. Taken together, these findings suggest that

parents of children with ASD are more sensitive to milder signs of cognitive and language delay. This sensitivity may in turn learn to earlier detection and earlier intervention for children who could greatly benefit, due to the skills they already have in place. Furthermore, these findings underscore the importance of ASD screening for first-born children. Future research should be conducted to examine how this increased sensitivity translates to screening measures for ASD, such as the M-CHAT(-R).

Conclusions

In sum, the results of the current study suggest that findings from infant siblings can be used to generalize to the broader population of children with ASD, depending upon the question asked. As few significant differences in ASD severity and symptomatology existed between infant siblings with ASD and children with ASD drawn from a low-risk sample, findings about ASD symptomatology can be generalized. However, caution should be used when generalizing findings about cognitive ability and adaptive functioning, as significant differences do exist between the two samples.

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Table 1

Demographics of Low Risk-ASD (LR-ASD) and High Risk-ASD (HR-ASD) Samples

	LR-ASD (n = 23)	HR-ASD (n = 23)
Age in Months (*M, SD*)	24.4 (4.0)	24.9 (3.8)
Gender (*N*, %)		
Males	13 (56.5%)	13 (56.5%)
Females	10 (43.5%)	10 (43.5%)
Maternal Education (*N*, %)		
No College Degree	9 (39.1%)	8 (34.8%)
College Degree or Higher	14 (60.9%)	15 (65.2%)
Race/Ethnicity (*N*,%)		
White	18 (78.3%)	20 (87.0%)
Non-White	5 (21.7%)	3 (13%)

Note. The racial categories of US Census (*Hispanic/Latino, Asian or Pacific Islander, Black or African American, and Biracial*) have been collapsed to form a "*non-White*" category.

Table 2

Age and Performance on Screener and Follow-up Phone Interview (PI)

(*M*, *SD*)	LR-ASD (*n* = 23)	HR-ASD (*n* = 23)	*t*	*p*	Cohen's *d*
Age in Months					
Screener	21.2 (4.0)	22.0 (4.0)	-.688	.495	.20
PI	22.3 (3.7)[a]	23.3 (4.0)[b]	-.888	.380	.26
Screener Critical Score	46.7 (29.6)	51.8(30.8)	-.570	.572	.17
Screener Total Score	36.6 (18.8)	40.2 (17.9)	-.667	.508	.20
PI Critical Score	40.7 (32.9)[a]	44.6 (27.5)[b]	-.410	.684	.13
PI Total Score	28.7 (19.8)[a]	32.1 (16.6)[b]	-.602	.556	.18

Note. Screener refers to M-CHAT and M-CHAT-R. Scores are presented as percentages so that they could be collapsed across screener versions. M-CHAT has 6 critical items and 23 total items. M-CHAT-R has 7 critical items and 20 total items.

[a]*N* = 22. [b]*N* = 19.

Table 3

Number of DSM-IV-TR Symptoms by Domain

Domain (*M*, *SD)*	LR-ASD (*n* = 23)	HR-ASD (*n* = 23)	*t*	*p*	*d*
Social Interaction	2.57 (.945)	2.43 (.843)	.494	.624	.16
Communication	1.87 (.458)	1.57 (.507)	2.137	.038	.62
RRBs	1.30 (.703)	1.61 (.891)	-1.285	.205	.39
Total DSM-IV-TR Symptoms	5.74 (1.54)	5.61 (1.44)	.297	.768	.09

Note. There is a maximum of four possible symptoms in each domain, 12 total.

RRBs: Restricted and Repetitive Behaviors

Table 4

Average Ratio IQ Scores on the Mullen Scales of Early Learning by Sample

Mullen Subscale (*M*, *SD*)	LR-ASD (*n* = 23)	HR-ASD (*n* = 23)	*t*	*p*	*d*
Visual Reception	66.2 (16.4)	80.9 (24.1)	-2.412	.020	.71
Fine Motor	68.0 (18.7)	83.4 (18.2)	-2.831	.007	.83
Receptive Language	45.5 (15.8)	63.2 (27.2)	-2.705	.010	.79
Expressive Language	43.6 (14.4)[a]	68.3 (25.4)	-4.023	<.001	1.19

Note. Average score is 100.

[a]*N* = 22.

Table 5

Average Vineland Domain Standard Scores by Sample

Vineland Domain (*M*, *SD*)	LR-ASD (*n* = 23)	HR-ASD (*n* = 23)	*t*	*p*	*d*
Communication	70.3 (8.38)	75.9 (12.6)	-1.774	.084	.52
Daily Living	78.0 (12.5)	76.9 (10.2)	.336	.739	.10
Motor	83.6 (10.1)	83.6 (11.1)	<.001	>.99	<.01
Socialization	73.2 (8.46)	74.1 (7.04)	-.398	.693	.12

Note. Average score is 100 and standard deviation is 15.

Table 6

Attainment of Milestones by Category Within Samples

(*N*, %)	LR-ASD (*n* = 23)	HR-ASD (*n* = 23)	*Significance*
First Steps			.835
Within Normal Limits	19 (82.6%)	16 (80.0%)[a]	
Delayed	3 (13.0%)	4 (20.0%)[a]	
Not Yet Attained	1 (4.3%)	0 (0.0%)[a]	
First Words			.439
Within Normal Limits	9 (56.3%)[b]	6 (42.9%)[c]	
Delayed	3 (18.8%)[b]	6 (42.9%)[c]	
Not Yet Attained	4 (25.0%)[b]	2 (14.3%)[c]	
First Phrases			.999
Within Normal Limits	2 (14.3%)[c]	3 (18.8%)[b]	
Delayed	2 (14.3%)[c]	2 (12.5%)[b]	
Not Yet Attained	10 (71.4%)[c]	11 (68.6%)[b]	

Note. Due to small expected frequency counts all results presented in the table above were obtained from Fisher's Exact Tests using the Freeman-Halton extension.

[a]N = 20. [b]N = 16. [c]N = 14.

Table 7

Post-Hoc Analyses – Prior Analyses with Re-Run with No Sibling Subgroup Removed from LR-ASD Sample (Categorical Variables Only)

(*N*, %)	LR-ASD TD-Sibs Only (*n* = 11)	HR-ASD (*n* = 23)	*Significance*
	Demographics		
Gender			> .99
Males	7 (63.6%)	13 (56.5%)	
Females	4 (36.3%)	10 (43.4%)	
Maternal Education			> .99
No College Degree	4 (36.3%)	8 (34.8%)	
College Degree or Higher	7 (63.6%)	15 (65.2%)	
Race/Ethnicity			> .99
White	9 (81.8%)	20 (87.0%)	
Non-White	2 (18.1%)	3 (13.0%)	
Diagnosis			.464[a]
Autistic Disorder	3 (27.3%)	9 (39.1%)	
PDD-NOS	5 (45.4%)	12 (52.2%)	
ASD – Low Mental Age	3 (27.3%)	2 (8.7%)	

(*N*, %)	LR-ASD TD-Sibs Only (*n* = 11)	HR-ASD (*n* = 23)	*Significance*
Attainment of Milestones			
First Steps			.473[a]
Within Normal Limits	7 (63.6%)	16 (80.0%)[b]	
Delayed	3 (27.3%)	4 (20.0%)[b]	
Not Yet Attained	1 (9.1%)	0 (0.0%)[b]	
First Words			.483[a]
Within Normal Limits	5 (71.4%)[c]	6 (42.9%)[d]	
Delayed	1 (14.3%)[c]	6 (42.9%)[d]	
Not Yet Attained	1 (14.3%)[c]	2 (14.3%)[d]	
First Phrases			.522[a]
Within Normal Limits	0 (0.0%)[c]	3 (18.8%)[e]	
Delayed	2 (28.6%)[c]	2 (12.5%)[e]	
Not Yet Attained	5 (71.4%)[c]	11 (68.8%)[e]	

Note. Due to small expected frequency counts all results presented in the table above were obtained from Fisher's Exact Tests.

[a]The Freeman-Halton extension was used. [b]*n* = 20. [c]*n* = 7. [d]*n* = 14. [e]*n* = 16.

Table 8

Post-Hoc Analyses – Prior Analyses with Re-Run with No Sibling Subgroup Removed from LR-ASD Sample (Continuous Variables Only)

(*M*, *SD*)	LR-ASD TD-Sibs Only (*n* = 11)	HR-ASD (*n* = 23)	*t*	*p*	*d*
Screener and PI Performance					
Age at Screener in Months	22.1 (4.4)	22.0 (4.0)	.027	.978	.02[a]
Age at PI in Months	23.1 (4.5)	23.3 (4.0)[c]	-.132	.896	.05[a]
Screener Critical	65.8 (26.7)	51.8 (30.8)	1.30	.204	.47[b]
Screener Total	48.1 (17.0)	40.2 (17.9)	1.23	.227	.45[b]
PI Critical	61.7 (31.0)	44.6 (27.5)[c]	1.57	.129	.59[b]
PI Total	39.8 (20.2)	32.1 (16.6)[c]	1.12	.271	.43[b]
Age at Evaluation in Months	24.87 (4.52)	24.87 (3.81)	<.001	>.99	<.01[a]
Number of ASD Symptoms					
DSM-IV-TR SI	2.45 (1.04)	2.43 (.84)	.059	.953	.02[a]
DSM-IV-TR Com	1.73 (.47)	1.57 (.51)	.893	.378	.32[a]
DSM-IV-TR RRB	1.00 (.63)	1.61 (.89)	2.28	.030	.75[b]
DSM-IV-TR Total	5.18 (1.83)	5.61 (1.44)	.741	.464	.27[b]
ASD Severity					
CARS	30.77 (6.84)	30.37 (5.58)	.183	.856	.07[a]
ADOS CSS	7.00 (1.90)	6.35 (2.48)	.769	.447	.28[b]

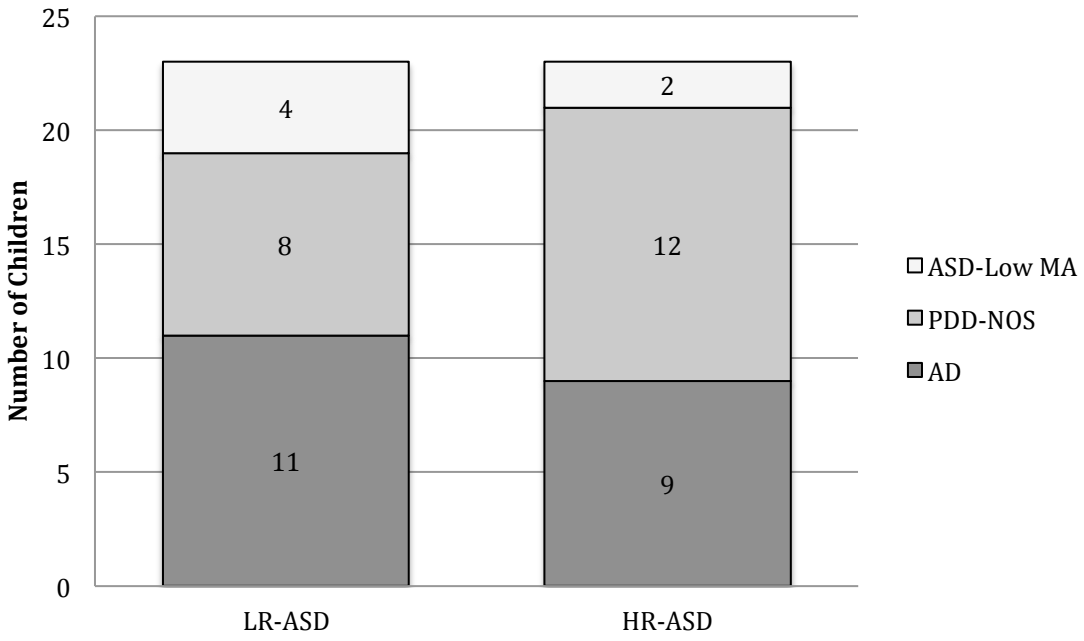
(*M*, *SD*)	LR-ASD TD-Sibs Only (*n* = 11)	HR-ASD (*n* = 23)	*t*	*p*	*d*
Cognitive Abilities					
Mullen VR	61.98 (18.35)	80.86 (24.15)	2.28	.029	.84[b]
Mullen FM	64.89 (22.66)	83.36 (18.23)	2.55	.016	.94[b]
Mullen RL	43.90 (20.99)	63.23 (27.17)	2.07	.046	.76[a]
Mullen EL	45.79 (14.58)	68.28 (25.41)[d]	2.70	.011	1.00[a]
Adaptive Functioning					
Vineland Com	66.82 (6.54)	75.91 (12.63)	2.76	.009	.82[b]
Vineland DL	69.45 (5.68)	76.91 (10.19)	2.73	.010	.83[b]
Vineland Mot	79.64 (10.04)	83.61 (11.12)	1.00	.323	.37[b]
Vineland Soc	69.55 (9.14)	74.09 (7.04)	1.59	.120	.59[b]
Other Analyses					
Age of First Concerns	14.64 (6.19)	9.30 (5.32)	2.60	.014	.95[a]

Note. Screener refers to M-CHAT(-R) Screener and Phone Interview (PI) Performance scores are reported as percentages. DSM-IV-TR: Social Interaction (SI), Communication (Com), Restricted and Repetitive Behaviors (RBB); CARS: Childhood Autism Rating Scale; ADOS CSS = ADOS Calibrated Severity Score; Mullen Scales of Early Learning Domains: Visual Reception (VR), Fine Motor (FM), Receptive Language (RL), Expressive Language (EL); Vineland Domains: Communication (Com), Daily Living (DL), Motor Skills (Mot), Socialization (Soc).

[a]Decrease in effect size seen when no sibling subgroup removed from LR-ASD. [b]Increase in effect size seen when no sibling subgroup removed from LR-ASD.[c]*n* = 19.[d]*n* = 22.

Figure 1

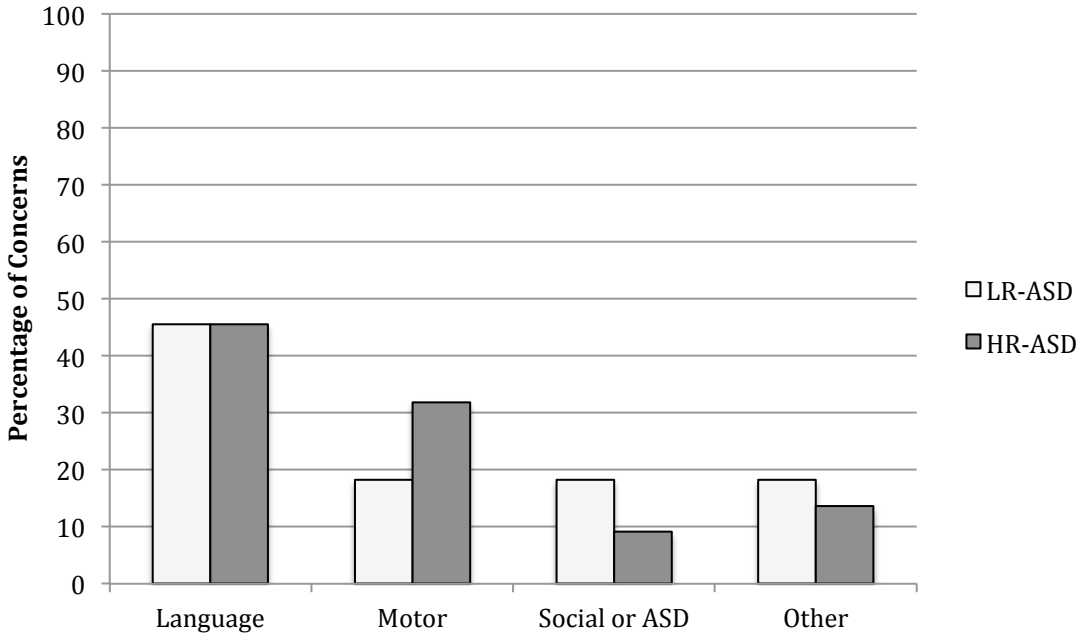
Diagnostic Distribution Within LR-ASD and HR-ASD Samples



ASD-Low MA = Autism Spectrum Disorder with Low Mental Age; PDD-NOS = Pervasive Developmental Disorder – Not Otherwise Specified; AD = Autistic Disorder

Figure 2

Type of First Concerns by Risk Group



Note. Fisher's Exact Test with Freeman-Halton Extension p = .70. ASD = Autism Spectrum Disorder.