3-25-2019

The Impact of Developmental Level on the Emergence of Autism Symptoms: Implications for Diagnosing Children with Low Mental Age

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University of Connecticut, 2019

Diagnosis of Autism Spectrum Disorder (ASD) is complicated in children with low mental age (low MA; cognitive functioning below a 12-month level) due to the way in which diagnostic measures function in this group, and due to limited understanding of symptom presentation in children with low MA. Indeed, no commercially available ASD diagnostic tools are designed or recommended for use in children below 12 months. Utility of the Autism Diagnostic Observation Schedule (ADOS) and the Childhood Autism Rating Scale (CARS) in discriminating ASD from Global Developmental Delay (GDD), as well as symptom profiles measured by individual ADOS item scores, were examined in two-year-old children with ASD-low MA (n = 53), GDD (n = 175), and ASD with MA over 12 months (n = 425). Both the ADOS and CARS were similar in their agreement with clinical best estimate (i.e., 79.2% and 83.3%, respectively). Yet, in cases of disagreement, the ADOS over-diagnosed ASD in children with low MA, whereas the CARS both over-classified (though less than the ADOS) and under-classified these children. Reciprocal social interaction (e.g., eye contact, social interest), but not more advanced social behaviors (e.g., pointing or play), best distinguished children with ASD (with *and* without low MA) from those with GDD. ASD-low MA, a more severe autism subtype, may benefit from a modified ADOS algorithm or alternative direct measure of symptoms to facilitate accurate, timely diagnosis.

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B.A., Washington University in St. Louis, 2011

M.S., University of Connecticut, 2016

A Dissertation

Submitted in Partial Fulfillment of the

Requirements for the Degree of

Doctor of Philosophy

at the

University of Connecticut

2019

APPROVAL PAGE

Doctor of Philosophy Dissertation

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ACKNOWLEDGEMENTS

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Funding Support

Maternal and Child Health Bureau (R40 MC00270-04-00) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (5 R01 HD039961-05)

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Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by early impairments in socialization and communication, as well as restricted interests and repetitive behaviors (American Psychiatric Association (APA), 2013). Currently, the Centers for Disease Control and Prevention (CDC) estimate that one in every 59 children has ASD (CDC, 2018), with the average age of diagnosis falling between three and seven years (Crais, Watson, Baranek, & Reznick, 2006; Gray & Tonge, 2005). There is clear evidence that ASD-specific symptoms emerge in the first two years of life, however, and a large proportion of affected children (i.e., up to 87.5%) exhibit both behavioral and neurological signs of ASD prior to their first birthday (Crais et al., 2006; Dahlgren & Gillberg, 1989; Hazlett et al., 2017; Maestro et al., 2005; Martinez-Pedraza & Carter, 2009; Osterling, Dawson, & Munson, 2002; Ozonoff et al., 2010). Even so, ASD can be difficult to diagnose in very young children, as many of the characteristic markers (e.g., poor peer relationships, lack of conversation skills, and restricted or stereotyped interests) are age- or development-specific; that is, these behaviors are not typically seen in infants and young toddlers, nor are they seen in older individuals with low mental age (Crais et al., 2006; Ventola et al., 2006; Vig & Jedrysek, 1999; Watson, Baranek, & DiLavore, 2003). It is possible to diagnose ASD in children functioning below a 12-month cognitive level, though, and these diagnoses show high stability over a two-year period (Hinnebusch, Miller, & Fein, 2017). To facilitate diagnosis and intervention earlier in development, it is important to understand how ASD manifests in very young and cognitively delayed children.

Variations in intellectual functioning contribute to the challenge of diagnosing ASD. Current estimates suggest that the prevalence of comorbid intellectual disability (ID, defined as

IQ ≤ 70) in individuals with ASD is approximately 31.6% (CDC, 2016; CDC, 2018). Further, the percentage of children for whom developmental concerns are raised before age three years is significantly higher in children later diagnosed with ASD and ID, as compared to individuals diagnosed with only ASD, suggesting that children with comorbid cognitive delays may be a particularly severely affected subgroup (CDC, 2016). Cognitive functioning is an important predictor of response to intervention and functional outcomes in individuals with ASD (Hinnebusch et al., 2017; Rivard, Terroux, Mercier, & Parent-Boursier, 2015). Although intellectual level can be difficult to measure accurately in very young children, as developmental domains may undergo rapid changes through school age, and the children may be difficult to evaluate, it is important to screen for possible intellectual impairment in toddlers with ASD in order to design appropriate interventions (Rivard et al., 2015). It is of equal or perhaps greater importance, however, to accurately distinguish children with ASD from those with global developmental delays. Because children with cognitive impairment are more likely to display symptoms associated with ASD than children with average cognitive abilities, cognitive impairment can present a particular obstacle to accurate diagnosis (Brereton, Tonge, MacKinnon, & Einfeld, 2002).

The differentiation between ASD and intellectual impairment is most difficult in children with mental ages below two years; the number of signs differentiating the two disorders appears to increase both with age and developmental level (Dahlgren & Gillberg, 1989; Desombre et al., 2006; Vig & Jedrysek, 1999). Cognitive level likely influences the emergence of clinical symptomatology, with children functioning at different intellectual levels potentially exhibiting distinct behavioral features. It is therefore necessary to determine if certain features, or

symptoms, can distinguish ASD from more global delays in young children with significant intellectual impairment (i.e., low mental age).

Early Emergence of Autism Features

With increasing evidence in support of early intervention for ASD, there has been a push for earlier detection and diagnosis of very young children (Crais et al., 2006). Several features of ASD appear to emerge before two years (Baron-Cohen et al., 1996; Crais et al., 2006; Martinez-Pedraza & Carter, 2009; Watson et al., 2003). It is important to understand the developmental prerequisites of ASD-specific symptoms, as we do not expect to see certain behaviors in children with mental or chronological ages lower than the age of emergence in typical development (Martinez-Pedraza & Carter, 2009). Within the first year of life, typically developing infants show clear social-communicative behaviors, including eye contact, responsiveness to their name, gestures (e.g., reaching to be picked up, pushing away non-preferred objects, pointing), and other signs of early joint attention. Exploratory and object play also emerges by 12 months in typically developing infants. Of note, repetitive behaviors are often seen in typically developing infants and toddlers and thus may not be useful indicators of ASD in early development (Crais et al., 2006).

Infants with ASD show fewer facial expressions, specifically fewer directed toward other people, than their typically developing peers by six months (Desombre et al., 2006). Parents of children with ASD also report abnormal development of language precursors, including babbling and attentiveness to one's name (Watson et al., 2003). As early as 12 months, infants with ASD show less social engagement and play, as well as limited motor and vocal imitation (Rowberry et al., 2015; Watson et al., 2003). Between six and 18 months, children later diagnosed with ASD show less eye contact, social smiling, and social responsivity compared to typically developing

peers (Jones & Klin, 2013; Maestro et al., 2005; Ozonoff et al., 2010). This early emergence of autism symptomatology is supported by Hazlett et al.'s (2017) neuroimaging study, in which infants at high familial risk for ASD, who were later positively diagnosed, showed an increase in cortical surface area growth from six to 12 months, particularly in brain regions related to processing of sensory information. Further, Jones and Klin (2013) found that children later diagnosed with ASD showed a decline in a key social behavior, visual attention to eyes, between two and six months, and Bosl, Tager-Flusberg, and Nelson (2018) demonstrated that infants who were later given ASD diagnoses showed atypical EEG signals in the frontal and temporal lobes as early as three months. These findings suggest that a "prodromal" autism presentation may be detectable very early in child development (Hazlett et al., 2017, p. 351).

Behaviors Discriminating Autism and Developmental Delay

Consistent with the defining features of ASD, it has been suggested that deficits in social and pre-linguistic behaviors (e.g., responsiveness to one's name), reciprocal social engagement, and play are more related to a diagnosis of ASD, in comparison to delays in nonverbal problem solving, motor skills, and nonsocial adaptive behaviors, which are associated with global patterns of cognitive delay (Osterling et al., 2002; Vig & Jedrysek, 1999). Given the finding that many children with intellectual impairment present with autism-like deficits, though, it is important to understand specific features that differentiate ASD and Global Developmental Delay (GDD) in young children. Some researchers have suggested that children with ASD show *deviations* from the typical developmental course, whereas children with global cognitive deficits exhibit *delays*, although this finding is not universal (Vig & Jedrysek, 1999).

Compared to children with purely cognitive delays, children with ASD tend to repeat sounds for non-communicative purposes and ignore bids for social interaction from adults and

same-aged peers (Baron-Cohen et al., 1996). They also exhibit less frequent vocal and gestural imitation and less sophisticated play than their intellectually impaired peers; that is, they may engage in sensorimotor, but not imaginative or cooperative, play (Vig & Jedrysek, 1999). Of note, children with GDD, but not ASD, are more likely to respond to social bids and demonstrate early joint attention behaviors, including gaze monitoring, pointing, showing, and sharing, by four years (Vig & Jedrysek, 1999). However, although stereotyped finger movements (e.g., wiggling and flicking) may be unique to children with ASD, both children with ASD and those with cognitive delays show hand flapping throughout the preschool period (Vig & Jedrysek, 1999).

The research on discriminating ASD from intellectual impairment in the first year of life is limited. Baranek (1999) compared children aged nine to 12 months with ASD to those with developmental delays and typical development using retrospective video analysis. In this study, children with ASD were equally impaired on standardized cognitive measures as those in the developmental delay group. Results indicated several sensorimotor deficits unique to children with ASD, including abnormal affect, unusual posturing and mouthing behaviors, aversion to social touch, reduced orientation to visual stimuli, and poor responsiveness to their name. Although Baranek's (1999) findings provide useful clinical data for the differential diagnosis of ASD and intellectual impairment, particularly in young and cognitively delayed children, this study was limited by a small sample size and reliance on children with known genetic disorders (e.g., Down syndrome) in the developmental delay group.

Again using retrospective video analysis, Osterling et al. (2002) examined differences between children with ASD (i.e., majority cognitively delayed) or intellectual impairment as compared to typically developing one-year-olds. They found that infants with either ASD or

cognitive delays used gestures and looked at objects held by others *less* frequently and engaged in repetitive motor behaviors *more* frequently than typical peers, suggesting that these behaviors may be associated with global developmental delays rather than being autism-specific. However, early social and pre-linguistic skills, including social attention and interest and responsiveness to one's name, appeared to be intact in children with intellectual impairment but largely absent in those with ASD (Osterling et al., 2002). Taken together, these findings suggest that core social-communication symptoms may be useful in identifying very young and cognitively delayed children with ASD, but atypical imitation and play and unusual motor movements may instead be associated with global delays.

Differential Diagnosis of Autism and Developmental Delay

The ability to differentiate ASD from other disorders, including GDD, is a key feature of a strong autism-specific diagnostic instrument, as accurate and timely diagnosis facilitates earlier intervention. Accordingly, it is important to evaluate the diagnostic utility of commonly used measures, particularly in very young and cognitively delayed children. The Autism Diagnostic Interview – Revised (ADI-R; Rutter, LeCouteur, & Lord, 2003) has long been considered a gold-standard tool for the diagnosis of ASD across the lifespan. A clinician-administered semi-structured caregiver interview, the ADI-R adheres to DSM-IV-TR criteria and evaluates functioning in the domains of social reciprocity, verbal and nonverbal communication, and repetitive behaviors. It is recommended for individuals with a mental age above two years. The instrument has yielded mixed results in children below age three years, though, with some researchers showing good performance in this age range (Risi et al., 2006) and others finding relatively poor diagnostic utility, perhaps related to the fact that many toddlers with ASD do not yet display characteristic restricted interests or insistence on sameness often found in older

individuals with ASD (Gray, Tonge, & Sweeney, 2008; Ventola et al., 2006). Moreover, the ADI-R consistently over-diagnoses ASD in cognitively impaired and pre-verbal individuals, regardless of chronological age (Risi et al., 2006).

The Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) aims to evaluate the presence of autism symptoms using a structured play and interview session, dependent on the examinee's age and language level. The ADOS is recommended for use in children and adults with a mental age of at least 12 months. Ventola et al. (2006) found that the ADOS demonstrates high agreement with clinical judgment using DSM-IV-TR criteria in a sample of 16- to 31-month-old children, some of whom were functioning in the borderline to impaired ranges on standardized developmental testing. However, other researchers have shown that the ADOS tends to over-classify profoundly cognitively impaired children over the age of three years (Risi et al., 2006), with particularly poor ability to discriminate ASD from other disorders in children with mental ages at or below a 15-month level (Gotham, Risi, Pickles, & Lord, 2007). It has been suggested that the expectations for interaction in the ADOS are too high for cognitively delayed children (Gotham et al., 2007). A newer Toddler Module of the ADOS was introduced to address some of these concerns, although it continues to be recommended for use with toddlers who are functioning at or above a 12-month level and walking independently. Empirically, scores on the Toddler Module tend to be falsely elevated in children who have not yet attained these developmental milestones, and the measure may be less sensitive in toddlers below age 15 months (Luyster et al., 2009).

An observational research measure, the Autism Observation Scale for Infants (AOSI; Bryson, McDermott, Rombough, Brian, & Zwaigenbaum, 2000), was specifically designed to detect signs of ASD in young children between the ages of six and 18 months. Elevated scores

on the AOSI by one year of age are predictive of social-communication symptoms at age 24 months and a diagnosis of ASD at age three years (Bryson, Zwaigenbaum, McDermott, Rombough, & Brian, 2008). However, despite its potential utility for the very early diagnosis of ASD, the AOSI remains an unpublished research instrument.

The Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1988) builds on the ADI-R and ADOS by combining information from caregiver report and direct observation in a clinician-completed rating scale. Although used with individuals of all ages, the measure is technically recommended for those over age two years. In toddlers with varying mental ages, the CARS shows very high agreement with clinical judgment and good sensitivity in diagnosing ASD (Ventola et al., 2006). Furthermore, CARS total scores demonstrated 100% accuracy in discriminating a sample of children aged three to 13 years with ASD and intellectual impairment from those with global delays and no autism (Morgan, 1988; Teal & Wiebe, 1986). It is possible that, because it incorporates subjective clinical judgment, the CARS is more consistent with clinical best estimate of ASD, particularly in very young and cognitively impaired individuals (Ventola et al., 2006).

Current Study Aims

The present study aimed to examine the impact of developmental level on the diagnosis and emergence of autism symptoms in very young and cognitively delayed children. Building on the existing literature, we focused on a subgroup of children with ASD and low mental age (low MA), defined as verbal and nonverbal functioning below a 12-month level, to determine whether these children can be accurately distinguished from their globally delayed peers using standardized diagnostic measures, and to examine whether certain features, or symptoms, are

particularly useful in discriminating ASD from global developmental delays. Specifically, the current study aimed to:

1. Investigate the diagnostic utility of the ADOS and CARS in the differential diagnosis of ASD and GDD in two-year-old children functioning below a 12-month level. Based on previous literature with slightly older and higher-functioning children (Gotham et al., 2007; Risi et al., 2006; Ventola et al., 2006), we hypothesized that the CARS will be most accurate in discriminating the disorders, and that the ADOS may over-classify very low-functioning children.
2. Explore specific features, or symptoms, that characterize children with ASD-low MA compared to those with GDD, as well as those with ASD and cognitive functioning above a 12-month level. Given prior research findings (Baranek, 1999; Osterling et al., 2002), we expected that early social or pre-linguistic behaviors, such as level of social interest and responsiveness to one's name, but not atypical sensorimotor behaviors (e.g., repetitive motor movements), would distinguish children with ASD from those with global delays. Furthermore, as individuals with ASD and comorbid cognitive impairment may be a particularly severely affected subgroup (CDC, 2016), we hypothesized that children with ASD-low MA would exhibit more severe ASD-related features than their autistic peers without significant cognitive delays.

Methods

Participants

Participants were 653 children drawn from a large, multi-site investigation of the early detection of ASD. All children screened positive on the Modified Checklist for Autism in Toddlers with Follow-Up (M-CHAT/F; Robins, Fein, Barton, & Green, 2001) or its revision (M-

CHAT-R/F; Robins et al., 2014) between the ages of 16 and 30 months and were evaluated through the research project at the approximate age of two years. Participants were classified into three groups based on DSM-IV-TR diagnosis and cognitive status. The ASD-low MA group (n = 53) was composed of children with ASD (i.e., Autistic Disorder or Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS)) who also exhibited functioning *below* a 12-month level on all three of the Mullen Scales of Early Learning (MSEL) Visual Reception, Receptive Language, and Expressive Language scales. The GDD group (n = 175) was composed of children with DSM-IV-TR Global Developmental Delay, as assessed by verbal *and* nonverbal scores at least 1.5 standard deviations below the mean on either the MSEL or the Vineland Adaptive Behavior Scales (VABS); these children did not meet diagnostic criteria for ASD. The ASD group (n = 425) was composed of children with Autistic Disorder or PDD-NOS who exhibited functioning *above* a 12-month level on at least one of the above mentioned MSEL scales.

Exclusion criteria for the broader study included significant sensory impairments (e.g., blindness) or deficits in motor functioning (e.g., severe cerebral palsy) that would impact a child's ability to complete testing. Given that the larger study from which participants were drawn aimed to validate autism-specific screening tools, children were also excluded if they had a prior diagnosis of ASD by a qualified person, as this may have impacted caregiver responding on the screening questionnaire. Additionally, participants were excluded from the current project if they were missing a primary study measure (i.e., ADOS and CARS) in its entirety, as data on these measures were the major focus of analyses.

There were no differences between groups based on child age, child gender, or maternal education. However, groups significantly differed on child race/ethnicity; specifically, although

all three groups were composed of majority White toddlers, the ASD group had a slightly larger proportion of White and biracial participants, whereas compared to the ASD group, the ASD-low MA and GDD groups had larger proportions of Black and Hispanic/Latino children. Additional participant characteristics are presented in Table 1.

Procedures

Participants were screened with either the M-CHAT/F (Robins et al., 2001) or M-CHAT-R/F (Robins et al., 2014) at their pediatrician's office or through their early intervention (i.e., non-ASD services) provider between the ages of 16 and 30 months. Children who screened positive on the initial questionnaire, as well as the follow-up phone interview (i.e., indicating risk for ASD), were offered a free developmental and diagnostic evaluation, which was conducted by a licensed psychologist or a developmental-behavioral pediatrician and a doctoral student in clinical psychology. Most evaluations took place at the research team's university clinics, and families who did not have transportation were provided with a taxi service. In some cases, though, study staff traveled to conduct evaluations at participating screening sites with a high proportion of low income patients. Diagnoses were based on clinical best estimate judgment of symptoms incorporating data from observation, developmental history, and scores on the ADOS, CARS, MSEL, and Vineland Adaptive Behavior Scales (VABS). All diagnoses were assigned based on DSM-IV-TR criteria (APA, 2000) given the years in which participants were evaluated (i.e., 2002 to 2014).

Measures

Primary study measures. The *Autism Diagnostic Observation Schedule – Generic* (ADOS; Lord et al., 2000) is a semi-structured observational assessment designed to measure symptoms of ASD in toddlerhood through adulthood. The ADOS includes four separate modules

based on a participant's expressive language level and chronological age. The current study used Module 1. Behaviors are coded in the domains of communication, reciprocal social interaction, play, and stereotyped behaviors and restricted interests. Combined communication and social interaction scores provide autism (i.e., cut-off = 12), autism spectrum (i.e., cut-off = 7), and non-spectrum classifications. Inter-rater reliability is considered good across all domains, ranging from r = .82 to r = .93 (Lord et al., 2000).

The *Childhood Autism Rating Scale* (CARS; Schopler, Reichler, & Renner, 1988) and its revision, the *Childhood Autism Rating Scale, Second Edition* (CARS2; Schopler, Van Bourgondien, Wellman, & Love, 2010), are 15-item clinician rating scales measuring autism symptom severity based on *both* direct observation and caregiver report. A total score is calculated by summing scores from all individual items and is used to classify a child into one of three groups: non-autistic (total score = 15 – 29.5), mildly-moderately autistic (total score = 30 – 36.5), and severely autistic (total score = 37 – 60). Although a cut-off of 30 is typically used for Autistic Disorder, a cut-off of 25.5 has been proposed for ASD more broadly (Chlebowski, Green, Barton, & Fein, 2010). Internal consistency of CARS and CARS2 items is high at α = .94 and α = .93, respectively, and inter-rater reliability is considered good at r = .71 (Schopler et al., 1995; Schopler et al., 2010).

Clinical best estimate by experienced clinicians is considered to be the gold standard for diagnosis of ASD. The current study used DSM-IV-TR criteria (APA, 2000) on which to base clinical best estimate judgment of symptoms, as well as data from a developmental history and standardized measures (i.e., ADOS, CARS, MSEL, VABS). Diagnoses of Autistic Disorder, PDD-NOS, and GDD were given if a child met DSM-IV-TR criteria.

Secondary study measures. The *Mullen Scales of Early Learning* (MSEL; Mullen, 1995) is a developmental assessment of cognitive, motor, and language abilities in children ages one month to five years, eight months. It was used to confirm low MA status and characterize participants' cognitive functioning. The current study used the Visual Reception, Fine Motor, and Receptive and Expressive Language scales. Raw scores in each domain are converted into T scores or developmental age-equivalent scores. Internal consistency is satisfactory, ranging from $\alpha = .75$ to $\alpha = .83$ across all scales, and inter-rater reliability is considered strong, ranging from $r = .91$ to $r = .99$ (Mullen, 1995).

The *Vineland Adaptive Behavior Scales: Interview Edition, Survey Form* (VABS; Sparrow, Balla, & Cicchetti, 1984) and its revision, the *Vineland Adaptive Behavior Scales, Second Edition: Survey Interview Form* (VABS-II; Sparrow, Cicchetti, & Balla, 2005), are semi-structured caregiver interviews that assess adaptive behaviors (i.e., how a child functions in his or her daily life) in the domains of Communication, Daily Living Skills, Socialization, and Motor Skills. Standard scores in each domain were used in the current study to characterize participants' adaptive skills. Inter-interviewer reliability is adequate across the four domains, ranging from $r = .62$ to $r = .78$ (Sparrow et al., 1984; Sparrow et al., 2005).

Data Analytic Plan

Diagnostic utility. The first aim examined diagnostic utility of the ADOS and CARS, compared to clinical best estimate, in discriminating ASD from GDD in children functioning below a 12-month level. As no GDD children were functioning below a 12-month age equivalence on all verbal and nonverbal cognitive domains, "functioning below a 12-month level" was instead based on nonverbal developmental quotient (DQ), which was defined as a MSEL Visual Reception age-equivalent score below 12 months, as an estimate of core reasoning

ability. GDD participants (n = 16) achieving this criterion were matched to a sub-sample of children with ASD (n = 32), drawn from both the ASD-low MA and ASD groups. Participants were well-matched according to Frick's (1995) criterion for chronological age and age-equivalent scores on each of the MSEL scales (Table 2). ADOS combined communication and social interaction domain scores were used to classify each child as having ASD or not, using a cut-off score of 7 (Lord et al., 2000). Using a cut-off score of 25.5 (Chlebowski et al., 2010), each child was also classified as having ASD or not on the CARS.

Due to low cell counts (i.e., expected cell counts below five), Fisher's exact tests were used to compare (a) clinical best estimate (i.e., ASD vs. non-ASD) to ADOS classification, (b) clinical best estimate to CARS classification, and (c) ADOS classification to CARS classification. Percent agreement was also examined to determine the proportion of children correctly classified, over-classified, or under-classified by the ADOS and CARS. A binary logistic regression predicting diagnostic outcome (i.e., ASD vs. non-ASD) from both ADOS and CARS classifications was conducted to determine the potential differential diagnostic utility of each measure more specifically. Predictors were entered simultaneously. Multicollinearity was assessed through the evaluation of variance inflation factor (VIF) and tolerance; conservative cut-offs of VIF > 4 and tolerance < .20 were used, as described in Menard (1995). No evidence of collinearity was found between ADOS and CARS classifications.

Symptom profile analysis. The second aim explored specific features, or symptoms, that distinguish children with ASD-low MA, GDD, and ASD. The full sample was included in these analyses. Individual item-level data on the ADOS was used to examine features of ASD, as these items are well-defined, specific in what they measure, and reliable (Lord et al., 2000). The majority of items on the ADOS are coded with a score of 0, 1, 2, or 3, with higher scores

indicating greater impairment on that particular behavior. Six items (i.e., A1, A3, A4, A5, A6, and A8) assessing language and communication, however, can be coded with a score of 8; this indicates that a child's skills in that domain (e.g., non-echoed language) are too limited to judge the presence or absence of the symptom. Given the lower-functioning composition of our overall sample, a large number of children, particularly in the ASD-low MA group, received scores of 8 on these ADOS items, suggesting that performance on these items is confounded by cognitive level. Thus, an *a priori* decision was made to exclude these six items from analyses, and the remaining set of 20 ADOS items was included.

Using an approach similar to that described by Jeste et al. (2016), a repeated-measures analysis of variance (ANOVA) was conducted with a between-subjects factor of group (ASD-low MA, GDD, ASD) and within-subjects factors of individual ADOS items in language and communication (A2, A7), reciprocal social interaction (B1-12), play (C1-2), and stereotyped behaviors and restricted interests (D1-4) domains. Post hoc analyses were performed to compare mean ADOS scores and item by group interactions between all possible pairings. The benefit of this approach was that it allowed for both a comparison of overall symptom profiles across all three groups and exploration of specific features discriminating between diagnostic groups. A Bonferroni correction was used for post hoc analyses to reduce the potential for Type I errors due to multiple comparisons; a cut-off of $\alpha = .0025$ (i.e., $p = .05/20$ ADOS items) was set for these analyses.

All analyses were run using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., 2013).

Results

Diagnostic Utility

To determine the diagnostic utility of the ADOS and CARS in classifying young toddlers functioning below a 12-month level (Table 2) as having ASD or not, Fisher's exact tests were conducted. ADOS classification was significantly associated with diagnostic classification based on clinical best estimate (p = .006, Fisher's exact test) (Table 3). However, although ADOS classification agreed with clinical best estimate in 79.2% of cases, a large minority of participants were rated more severely on the ADOS than by clinical judgment. Specifically, 18.8% of children were classified as having ASD by the ADOS, when a GDD diagnosis was given based on clinical best estimate. Conversely, just one child (i.e., 2.1%) fell in the non-spectrum range on the ADOS when he was clinically judged to have ASD, which suggested that in children with low MA, the ADOS is more likely to over-classify than to under-classify.

CARS classification was also significantly associated with diagnostic classification based on clinical best estimate (p < .001, Fisher's exact test), with 83.3% agreement. On the CARS, 10.4% of participants were over-classified, meaning that they were rated as having ASD when clinical judgment indicated a non-spectrum (i.e., GDD) diagnosis. Another 6.3% of children were under-classified by the CARS, indicating that their scores fell within the non-spectrum range, yet based on clinical best estimate they were given diagnoses of ASD.

ADOS and CARS classifications were then directly compared to each other to examine agreement at the overall measure level. Classifications on each measure were significantly associated (p = .002, Fisher's exact test), with the ADOS and CARS agreeing in 83.3% of cases (Table 3). Consistent with the observed pattern of somewhat greater over-classification by the ADOS, 14.6% of children with low MA were rated as having ASD on the ADOS but not on the CARS, yet only a single child (i.e., 2.1%) was given an ASD classification on the CARS but not on the ADOS.

A binary logistic regression predicting outcome of clinical judgment (ASD vs. non-ASD) from both ADOS and CARS classifications was then carried out to explore differential utility of one measure over another. The overall model was significant (X^2 (2, N = 48) = 17.318, $p < .001$), indicating that, taken together, classifications on both the ADOS and CARS were significantly associated with clinical best estimate. However, examination of main effects for predictors in the model showed that the ADOS did not add significantly to the prediction model over and above the significant effect for the CARS in predicting diagnostic group membership from clinical best estimate judgment of symptoms (Table 3).

Symptom Profile Analysis

To explore specific features distinguishing children with ASD-low MA from those with GDD and ASD, a repeated-measures ANOVA was conducted with individual ADOS items as a within-subjects factor and diagnostic group as a between-subjects factor. As shown in Figure 1, scores significantly differed across ADOS items (F(19, 604) = 113.674, $p < .001$, $\eta_p^2 = .781$), with a large effect size. Further, we found a significant and large item by diagnostic group interaction, suggesting that ADOS profiles differed for children in the ASD-low MA, GDD, and ASD groups (F(38, 1208) = 12.430, $p < .001$, $\eta_p^2 = .281$). As expected, average scores on ADOS items also differed between diagnostic groups (F(2, 622) = 304.883, $p < .001$, $\eta_p^2 = .495$).

Post hoc analyses explored group differences at the individual item level to determine if certain symptoms distinguish between ASD-low MA, GDD, and ASD effectively (Table 4). With the exception of self-injurious behaviors (D3), which *no* children in the current sample showed, participants in the GDD group exhibited less ASD symptomatology than those in either the ASD-low MA or ASD groups on *all* measured ADOS items (all p's < .001), with medium to large effect sizes. Notably, children with GDD displayed their highest (i.e., worst) scores on

items measuring pointing (A7) and imaginative and creative play (C2), with their performance suggesting mild to moderate impairment on these particular skills. Otherwise, their ADOS scores were largely below the threshold of concern (i.e., a score below 1). These participants also exhibited a somewhat different ADOS profile as compared to *all* children with ASD, with much "flatter" results on items assessing socialization, including unusual eye contact (B1), responsive social smiling (B2), integrating gaze and facial expressions with other behaviors (B3, B4), and sharing enjoyment in social exchanges (B5), as well as initiation of and response to joint attention (B10, B11) and overall quality of social reciprocity (B12; Figure 1).

Children with ASD-low MA were more severe than both their ASD and GDD peers on a number of items (Table 4, Figure 1). However, certain core features of ASD appeared less subject to mental age, as participants in the two ASD groups did *not* differ significantly on: unusual eye contact (B1; $p = .048$), responsive social smiling (B2; $p = .033$), facial expressions directed toward others (B3; $p = .005$), responsiveness to one's name (B6; $p = .100$), spontaneous showing (B9; $p = .003$), unusual sensory interests (D1; $p = .277$), atypical hand and finger mannerisms (D2; $p = .148$), and unusually repetitive interests or stereotyped behaviors (D4; $p = .006$).

Discussion

The current study aimed to explore the impact of developmental level on the emergence of autism symptoms. Specifically, we examined a sample of children with ASD and low MA, defined here as cognitive functioning below a 12-month level, in comparison to children with either GDD or ASD with MA above 12 months. We sought to determine the diagnostic utility of commonly used measures, the ADOS and CARS, in discriminating ASD from global delays, and to further characterize symptom profiles of toddlers in the three diagnostic groups.

Summary of Findings

Overall, the ADOS and CARS appear to adequately sort cognitively delayed children, particularly those with nonverbal DQs below a 12-month equivalence, into ASD and non-ASD groups, compared to clinical best estimate judgment of symptoms, yet neither measure performs optimally in this population. Specifically, the ADOS agreed with clinical judgment in 79.2% of cases, whereas the CARS agreed with clinical best estimate in 83.3% of cases. Although these values are only marginally different, the ADOS was consistent in over-classifying children with low MA as having ASD, but in cases of disagreement, CARS classifications were distributed between over- and under-diagnosing these children.

Furthermore, symptom profile analyses suggest that children with GDD show minimal to no signs of ASD, with the exception of deficits in more advanced behaviors (e.g., pointing and pretend play), indicating that these symptoms may not be useful identifiers of ASD in toddlers with low MA. In addition, ASD-low MA participants are more severely impaired in terms of autism-specific features than their peers with ASD and higher mental ages, although certain core symptoms did not differ between these groups. Specifically, the two ASD groups did not differ significantly on early social communication and joint attention behaviors, including eye contact, social smiling, directing facial expressions toward others, and responding to one's name, nor did they differ on atypical sensorimotor behaviors (e.g., unusual sensory interests, hand and finger mannerisms, and repetitive interests or stereotyped behaviors). Taken together, these findings have significant implications for the diagnosis of ASD in very young and cognitively delayed children.

Diagnosis of Autism in Children with Low Mental Age

Despite the recent push to identify ASD earlier, perhaps within the first year of life, no commercially available diagnostic tools are recommended for use in children under 12 months (Crais et al., 2006). Thus, diagnostic utility of two widely used measures, the ADOS and CARS, was explored in a well-defined subgroup of toddlers with nonverbal DQs below a 12-month age equivalence; in fact, these children were functioning at a nine-month-old level, on average, across both verbal and nonverbal cognitive domains. Results suggest that, although the ADOS significantly aligns with clinical judgment (i.e., 79.2% agreement) in this sample of cognitively impaired children, the measure over-classifies a large minority of these children as having ASD when they are globally delayed, not autistic, per clinical best estimate judgment of symptoms. The CARS' agreement with clinical judgment was somewhat higher (i.e., 83.3%) and showed a significant main effect in a logistic regression prediction model, which was not found for the ADOS. These results are consistent with our hypothesis and the small literature indicating that the ADOS performs questionably in discriminating ASD from other developmental disorders in children functioning below a 15-month level, whereas the CARS is more aligned with clinical diagnosis (Gotham et al., 2007; Morgan, 1988; Risi et al., 2006; Teal & Wiebe, 1986; Ventola et al., 2006). Even so, it should be stated that the CARS also over-diagnosed several children with low MA, but to a lesser degree than the ADOS.

Notably, just one child with cognitive delays was missed by the ADOS, indicating that he was classified as non-ASD when in fact he had ASD based on clinical best estimate judgment of symptoms. Three children were missed by the CARS. For any diagnostic measure, it is important to minimize both the number of misses and false positives; findings suggest that the ADOS accomplishes that first goal, but at the expense of a larger percentage (18.8%) of over-classified children. In the context of developing improved diagnostic algorithms, Gotham and colleagues

(2007) indicated that the task demands of the ADOS may be too challenging for lower-functioning children. All toddlers in our sample were administered Module 1, which is intended for pre-verbal children and those with single words (Lord et al., 2000). In addition to simple to-and-fro activities, such as bubble play and interaction games (e.g., peekaboo), Module 1 asks toddlers to both initiate and respond to joint attention by social referencing, as well as to engage in functional and symbolic imitation and creative pretend play (e.g., acting out a birthday party scenario, which may be unfamiliar for very young children). It is possible that these more complex behaviors are confounded by low MA, as supported by our item profile analyses. Thus, the need for an autism-specific *direct* measure to aid in the diagnosis of children functioning below a 12-month level, either due to low MA or chronological age, remains unmet. Clinicians should be mindful that ADOS classifications based on current algorithms may over-diagnose a subset of cognitively delayed children. An *indirect* measure that incorporates clinical subjectivity (e.g., expert opinion, observation, and parent report), such as the CARS, may be one alternative (Ventola et al., 2006); however, clinicians should be aware that this measure, too, misclassifies a small portion of children with low MA, and in a less predictable manner than the ADOS.

Impact of Developmental Level on Autism Symptom Presentation

To more specifically examine the presentation of autism symptoms in cognitively delayed children, we explored whether certain behavioral features, or symptoms, distinguish participants with ASD-low MA from those with GDD or ASD with cognitive functioning above a 12-month level. The existing literature on markers discriminating ASD from global delays is quite limited and has investigated infants (e.g., nine to 12 months), as compared to slightly older toddlers with low mental ages; further, these studies have relied on small samples and intensive data collection methodology (e.g., retrospective video analysis) (Baranek, 1999; Osterling et al.,

2002). To build upon this work, we examined symptom profiles, as defined by ADOS item scores (i.e., valid and reliable scaled measures of core autism symptoms and related behaviors; Lord et al., 2000), in a large sample of children with ASD, some with low MA, or GDD. Overall, two-year-old toddlers with GDD, who earned similar cognitive scores to their peers with ASD only, scored below the autism threshold on most items, and *no* children in any diagnostic group exhibited self-injurious behavior (D3). It is possible that this behavior may not be present in young children with or without ASD or, given that ADOS scoring is based only on behaviors seen during the testing session, these low scores may be a product of testing demands or the testing context. However, the consistency with which low scores were observed on this item lends support to the former interpretation. Based on previous research indicating that delayed children, both those with ASD or global deficits, may exhibit atypical sensorimotor behaviors (Osterling et al., 2002; Vig & Jedrysek, 1999), we hypothesized that *all* children would show these behaviors, and thus items measuring those features would not discriminate between ASD and GDD. However, participants in both ASD groups displayed higher scores than children with GDD on items assessing unusual sensory interests (D1), hand and finger mannerisms (D2), and unusually repetitive interests and stereotyped behaviors (D4). Notably, in our sample, scores on these items were lower than for social communication items, which suggests that these atypical behaviors are present in young children with ASD, but in a milder form compared to moderate to severe impairments in socialization and communication.

Children with GDD showed elevations on items measuring pointing (A7) and creative and imaginative play (C2), suggesting that they, like toddlers with ASD, are delayed in these areas; indeed, participants in both the ASD-low MA and ASD groups displayed their highest scores on these two items, indicating significant impairment. These findings suggest that more

advanced social behaviors are particularly subject to developmental level and thus may not be as useful in distinguishing children with ASD from those who are more globally delayed. To be clear, although toddlers with GDD demonstrated elevated scores on these skills, on average their scores were between 1 and 1.5; this suggests inconsistent or inflexible pointing and pretend play, but not a complete absence of either behavior, in support of Vig and Jedrysek's (1999) claim that globally delayed children show *delays*, but not *deviations*, in their development. This result, that toddlers with GDD exhibit impaired pointing and imaginative play, is contrary to our hypothesis and somewhat inconsistent with previous research suggesting that atypical play, but *not* a lack of early joint attention behaviors (e.g., pointing), is confounded by intellectual abilities (Osterling et al., 2002; Vig & Jedrysek, 1999). Perhaps because our children with GDD were older than those studied earlier (i.e., approximately 26 months versus 12 months in Osterling et al., 2002), delays in pointing and emerging creative play, both of which are observed in typically developing two-year-old children, were more apparent and thus more likely to be coded as impaired. However, it is also possible that our participants did not demonstrate these particular behaviors during testing but do point and play imaginatively at home, resulting in inflated ADOS scores. Even so, limited variability in scores on these two items in our fairly large GDD sample supports the notion that these skills are impacted by developmental level, and delays in pointing and pretend play may not be solely indicative of an ASD diagnosis.

It is important to determine what autism-specific features can be reliably assessed before 12 months to inform diagnosis in individuals with low MA and in infants in the first year of life. One core domain of impairment in ASD is communication. Given the typical developmental course of language in normative development, in which many children do not say their first words until late in their first year, it can be difficult to evaluate atypical language development in

very young children (Crais et al., 2006). For example, even though the ADOS Module 1 is designed for non-verbal children, at least six items in the communication domain rely on some language to allow for accurate determination of the presence or absence of the symptom (e.g., intonation, echolalia, idiosyncratic language); thus, given that these items are highly confounded with cognitive level, we chose to exclude them from analyses. Of the remaining items examined in symptom profile analyses, children with GDD showed a "flatter" profile than toddlers in either ASD group for certain features in the domain of reciprocal social interaction. That is, where a particularly large gap existed between an average GDD item score and an average ASD item score, as seen in Figure 1, we interpreted this to suggest that these are autism-specific symptoms *that can be reliably measured very early in development*. This split between GDD and ASD participants was evident for items assessing eye contact (B1, B4), responsiveness to one's name (B6), initiation of and response to joint attention (B10, B11), and overall quality of social overtures (B12), consistent with our hypothesis that social and communication markers would be useful indicators of ASD versus global delays in cognitively impaired and very young children (Baranek, 1999; Osterling et al., 2002).

Results indicate that toddlers with ASD-low MA earned higher item scores on the ADOS than their peers with ASD and cognitive functioning above a 12-month level, who also scored higher than those with GDD. A similar pattern of higher scores in the ASD-low MA group as compared to children in both additional groups was observed for the CARS. As expected, these findings suggest that children with ASD-low MA are a more severely affected subgroup, which is consistent with the extant literature suggesting that individuals across the age range with ASD and comorbid intellectual impairment exhibit greater symptom severity, fewer developmental

gains, and greater diagnostic stability despite early intervention (CDC, 2016; Hinnebusch et al., 2017; Rivard et al., 2015).

Certain key features of ASD appear to present similarly across all children with the disorder, however, suggesting that mental age may exert less influence on these skills. Children in the ASD-low MA and ASD groups exhibited remarkably similar item profiles (i.e., their lines in Figure 1 follow a similar up-and-down course), with many scores above 1.5. In particular, participants in both ASD groups showed this severity of deficit in pre-linguistic skills, nonverbal communication, and joint attention skills, as well as social communication and social interaction. Specifically, the two ASD groups did not differ on items measuring unusual eye contact (B1), social smiling (B2), direction of facial expressions toward others (B3), responsiveness to one's name (B6), showing (B9), sensory interests (D1), hand and finger movements (D2), or repetitive behaviors (D4). Overall, such findings are consistent with prior research (Baranek, 1999; Baron-Cohen et al., 1996; Osterling et al., 2002; Vig & Jedrysek, 1999). These particular features, then, appear to be indicative of ASD, even in children who are functioning below a 12-month cognitive level, although stereotyped behaviors and restricted interests may be less severe than social communication impairments in young and cognitively delayed toddlers. Given prior research indicating that toddlers with ASD-low MA not only maintain their autism diagnosis over time, but also exhibit more severe symptoms and much less developmental growth (Hinnebusch et al., 2017), it is essential that clinicians are able to diagnose these children early and accurately.

Based on our findings indicating that select symptoms of ASD can be assessed early in development and can discriminate reliably between ASD and GDD, as well as data suggesting that the ADOS, with its existing algorithm, may over-classify a large minority of children with

low MA, we propose that a new ADOS algorithm be developed for use specifically in these very young and cognitively delayed individuals. Because more advanced behaviors, including pretend play and flexible use of pointing for social communicative purposes, appear to be influenced by global delays, items assessing these skills (i.e., A7 and C2) should not be weighted heavily in the calculation of a diagnostic cut-off score. Rather, our data support the utility of certain key items measuring reciprocal social interaction in discriminating ASD from GDD, and these features are likely to be effective in determining a diagnostic classification for children with low MA on the ADOS: eye contact (B1, B4), response to name (B6), initiation of and response to joint attention (B10, B11), and overall social interest and motivation (B12). Additional investigation to validate a proposed new algorithm and ascertain appropriate cut-off scores for this group is indicated.

Limitations and Future Directions

Although this study contributes to the relatively limited literature on children with autism and low mental age, namely by examining diagnosis and symptom presentation in a large and well-characterized sample, several limitations must be considered. Foremost, even though our full sample is quite large (n = 653), and our ASD-low MA group is adequately sized (n = 53) given the difficulty of finding a large number of two-year-old toddlers functioning below a 12-month level across both verbal *and* nonverbal cognitive domains, diagnostic utility analyses were based on a relatively small sub-sample (n = 48); this is a product of the very low number of children in our larger GDD group with nonverbal DQs below a 12-month age equivalence (n = 16). Thus, although our findings regarding the diagnostic utility of the ADOS and CARS in this population are consistent with the existing literature, they should be generalized and interpreted with some caution.

Additionally, like others in clinical practice, we consider clinical best estimate judgment of symptoms to be the gold standard for the diagnosis of ASD and other developmental delays. Accordingly, clinical judgment was used as a measure of the "accurate" diagnosis in diagnostic utility analyses, in that ADOS and CARS classifications were compared to classification based on clinical best estimate, with any discrepancy suggesting that the ADOS or CARS, but not expert opinion, was "inaccurate." Clinical best estimate, or expert judgment on the presence or absence of a disorder, is by its very nature subjective, and thus potentially prone to error. However, all of the clinicians involved in the current study were experts with considerable experience in the field of autism, with particular expertise in early detection and diagnosis, and familiarity with diagnostic criteria. Thus, even though we consider it necessary to acknowledge the inherent subjectivity of clinical judgment and the potential that this subjectivity may have confounded our results, this is widely accepted within the field as the best approach for diagnosis of ASD. Furthermore, given the time frame of our recruitment years, DSM-IV-TR criteria was used to diagnose participating children. Because ICD-10 criteria approximate those of DSM-IV-TR, the results of a similar study using ICD-10 are likely to be comparable to the current results, but findings may not generalize to a study using DSM-5.

Another limitation to consider is the decision to base symptom profile analyses on ADOS item scores. As previously stated, scoring of the ADOS is based only on the behaviors observed during the testing session; because young toddlers can be difficult to test, due to limited attention spans, anxiety, and other behavioral difficulties that may present in an unfamiliar testing setting, reliance only on behaviors directly observed during a relatively brief (i.e. under one hour) ADOS administration may not capture the full range and severity of the child's symptoms. The decision to use ADOS item scores was based on the breadth of behaviors and symptom domains assessed

by the measure, the inclusion of severity ratings at the item level (i.e., ordinal scoring), as well as demonstrated reliability of items (Lord et al., 2000). In addition, all children in the present study were tested using the ADOS Module 1. Since data collection was completed, a newer version of the ADOS with a module designed specifically for use in toddlers (i.e., Toddler Module) from 12 to 30 months was published. Although Module 1 and the Toddler Module measure similar skills, because the Toddler Module was developed to better meet the developmental needs of younger children, a parallel study using the Toddler Module may yield different results. Reliance on the ADOS also reduced the ability to explore communication symptoms, as many of the items in that domain were excluded because a large number of participants received scores of 8, meaning that those items were not applicable to them due to their very low verbal skills. Alternative means of evaluating communication skills in young, minimally verbal children such as those in the ASD-low MA group are indicated.

Finally, we were unable to account for the potential influence of sociocultural factors on differences in symptom presentation. As the primary focus of the current study was to determine how commonly used diagnostic tools operate in children with low MA, and to further explore the influence of developmental level on symptom presentation, groups were divided on the basis of DSM-IV-TR diagnosis and functional level. Descriptive analyses indicated that children in the ASD-low MA, GDD, and ASD groups significantly differed on race/ethnicity. Small cell counts for a number of racial groups limited our ability to explore differential symptom presentation by race/ethnicity. Further, although not significant, a trend level difference was observed between groups for maternal education, but this finding was confounded by a very high proportion of missing data; unfortunately, these data were provided inconsistently by parents. Future research

in a large and diverse sample should consider the role of race/ethnicity and other sociocultural variables on symptom presentation in children of varying mental ages with ASD.

Overall, these results support the diagnosis of ASD in children with low mental age, as these children appear to be a particularly severe subgroup of the broader population with autism. Efforts to facilitate timely and accurate diagnosis of these children are encouraged. Clinicians are advised to understand how commonly-used diagnostic tools function in this subgroup in order to inform clinical decision-making. The ADOS may not be a suitable measure for children with low MA, as it tends to over-diagnose ASD in this population. Thus, development of a revised ADOS algorithm for these children, in which features particularly subject to mental age (i.e., pointing, creative play, verbal communication) are less weighted in calculation of a cut-off score, may be useful and necessitates further investigation. As an alternative, development of a different direct measure of autism symptomology for use in individuals with intellectual functioning below a 12-month level and infants in the first year of life, in which testing activities are designed with the unique needs and limitations of very young and low-functioning children (e.g., reduced demands for complex social behaviors, including imaginative play) in mind, is strongly indicated. Because the AOSI (Bryson et al., 2000) has shown promise in accurately predicting later ASD diagnoses in six- to 18-month-olds, further work to norm and publish this measure for clinical use may fill the need for an appropriate diagnostic tool, thus promoting access to early intervention services for these high-need populations. In contrast to the ADOS, which systematically over-classifies children with low MA, the CARS both over- and under-diagnoses these individuals, but to a lesser degree; classifications based on this measure, too, should be interpreted carefully.

Furthermore, these findings suggest that certain core features of ASD, particularly socialization and communication skills (e.g., eye contact, social smiling, responsiveness to one's

name, and showing), are present and detectable early in development, consistent with previous research with high-risk siblings (Jones & Klin, 2013). More importantly, such symptoms seem to discriminate children with ASD from their peers with global delays accurately. Advanced social behaviors, including pointing and pretend play, are impaired in children with GDD and therefore may not be useful indicators of ASD in lower-functioning toddlers. Additionally, our sample exhibited mild restricted and repetitive behaviors, which suggests that, though these symptoms distinguish ASD from global delays, they may be more useful in slightly older children, when these types of behaviors become more severe.

Our findings replicate and extend earlier research on children with ASD and comorbid cognitive delays, yet further replication would be beneficial to clarify and characterize the ASD-low MA profile, because these children appear to be a unique and severe autism subtype. Future investigation of these children, and infants below 12 months with ASD more broadly, would also support the development of appropriate diagnostic tools for use in these groups. Given these results, autism-focused clinicians should have greater confidence in diagnosing ASD regardless of mental age at the time of evaluation. Although the addition of comorbid intellectual delays exacerbates the child's autism symptoms and may complicate prognosis, failure to diagnose individuals with low mental age may contribute to even poorer outcomes for this subgroup.

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Table 1

Participant Characteristics by Diagnostic Group

Variable	**ASD-low MA** (*n* = 53)	**GDD** (*n* = 175)	**ASD** (*n* = 425)	***p***
Age in months [*M* (*SD*)]	25.34 (4.96)	26.32 (4.82)	26.10 (4.77)	.428
Gender [*N* (%)]				
Male	38 (71.70)	128 (73.14)	324 (76.24)	.614
Female	15 (28.30)	47 (26.86)	101 (23.76)	
Race/ethnicity [*N* (%)]				
White	25 (47.17)	93 (53.14)	269 (63.29)	.017
Black	14 (26.42)	36 (20.57)	63 (14.82)	
Asian	2 (3.77)	6 (3.43)	20 (4.71)	
American Indian	0	2 (1.14)	0	
Biracial	2 (3.77)	5 (2.86)	22 (5.18)	
Hispanic/Latino	8 (15.09)	28 (16.00)	38 (8.94)	
Other	1 (1.89)	1 (0.57)	4 (0.94)	
Missing data	1 (1.89)	4 (2.29)	9 (2.12)	
Maternal education [*N* (%)]				
No degree	3 (5.66)	16 (9.14)	18 (4.24)	.063
High school diploma/GED	1 (1.89)	20 (11.43)	24 (5.65)	
Vocational/technical degree	0	4 (2.29)	4 (0.94)	
Some college	7 (13.21)	18 (10.29)	60 (14.12)	
Bachelor's degree	3 (5.66)	24 (13.71)	56 (13.18)	
Advanced degree	8 (15.09)	19 (10.86)	47 (11.06)	
Missing data	31 (58.49)	74 (42.29)	216 (50.82)	
MSEL age equivalent [*M* (*SD*)]				
Visual reception (*n* = 638)	[a]8.57 (2.18)	17.05 (5.00)	17.93 (4.84)	< .001
Fine motor (*n* = 640)	[a]13.16 (3.76)	18.47 (4.54)	19.09 (4.04)	< .001
Receptive language (*n* = 635)	5.79 (3.27)	14.94 (5.41)	12.31 (6.05)	< .001
Expressive language (*n* = 637)	[a]6.80 (1.96)	13.87 (5.50)	13.32 (5.51)	< .001
VABS standard score [*M* (*SD*)]				
Communication (*n* = 648)	63.38 (8.10)	76.52 (10.28)	70.63 (11.92)	< .001
Daily living skills (*n* = 648)	70.38 (12.14)	80.36 (12.84)	75.96 (12.86)	< .001
Socialization (*n* = 648)	69.34 (11.09)	81.41 (10.26)	74.51 (10.87)	< .001
Motor skills (*n* = 644)	[a]76.83 (13.38)	83.22 (12.74)	85.00 (11.81)	< .001
ADOS A+B total score [*M* (*SD*)]	17.85 (2.19)	5.47 (3.76)	14.76 (4.32)	< .001
CARS total score [*M* (*SD*)]	35.81 (5.61)	22.91 (3.08)	32.10 (4.73)	< .001

Note. MSEL = Mullen Scales of Early Learning; VABS = Vineland Adaptive Behavior Scales; ADOS = Autism Diagnostic Observation Schedule; CARS = Childhood Autism Rating Scale. MSEL age equivalents are presented in months. VABS standard scores have a mean of 100 and standard deviation of 15. ADOS A+B total score is combined communication/social interaction total score. Missing data for categorical and continuous variables are listed as 'missing data' or number of participants with complete data, respectively; where missing data are not presented, complete data was available for all participants.

[a] Only ASD-low MA significantly differed from GDD and ASD on post hoc analyses.

Table 2

Diagnostic Utility Subgroup Performance on Matching Variables and Primary Study Measures

Variable	**GDD** (n = 16)	**ASD** (n = 32)	***p***
Age in months [*M* (*SD*)]	25.04 (4.85)	25.51 (5.39)	.768
MSEL age equivalent [*M* (*SD*)]			
Visual reception	8.69 (1.82)	9.00 (1.83)	.579
Fine motor	12.50 (3.72)	12.84 (3.02)	.732
Receptive language	9.00 (3.56)	8.25 (3.47)	.488
Expressive language	8.00 (3.83)	7.72 (2.98)	.781
ADOS A+B total score [*M* (*SD*)]	[a]9.56 (4.24)	17.47 (2.96)	< .001
CARS total score [*M* (*SD*)]	25.19 (2.74)	35.80 (6.26)	< .001

Note. MSEL = Mullen Scales of Early Learning; ADOS = Autism Diagnostic Observation Schedule; CARS = Childhood Autism Rating Scale. MSEL age equivalents are presented in months. ADOS A+B total score is combined communication/social interaction total score.

[a] GDD children with low MA scored, on average, in the autism spectrum range on the ADOS.

Table 3

Diagnostic Utility of ADOS and CARS in Children with Low Mental Age

Analysis	**Statistics**			
Fisher's exact comparison	**Agreement (%)**		***p***	**Φ**
ADOS vs. clinical best estimate	79.17		.006	.450
CARS vs. clinical best estimate	83.33		< .001	.582
ADOS vs. CARS	83.33		.002	.509
Logistic regression predictor	***B* (SE)**	**Wald**	***p***	**Odds Ratio**
ADOS classification	1.73 (1.33)	1.696	.193	5.660
CARS classification	2.46 (0.88)	7.920	.005	11.757

Note. ADOS = Autism Diagnostic Observation Schedule; CARS = Childhood Autism Rating Scale.

Table 4

Post Hoc ADOS Item Comparisons Between Diagnostic Groups

Variable	***B* (SE)**	***t***	***p***	η_p^2
Vocalizations directed toward others [A2]				
ASD-low MA vs. ASD	.50 (.12)	4.101	< .001	.026
GDD vs. ASD-low MA	-1.49 (.13)	-11.458	< .001	.174
GDD vs. ASD	-.99 (.07)	-13.344	< .001	.223
Socially-directed pointing [A7]				
ASD-low MA vs. ASD	.59 (.15)	4.081	< .001	.026
GDD vs. ASD-low MA	-1.65 (.16)	-10.528	< .001	.151
GDD vs. ASD	-1.05 (.09)	-11.752	< .001	.182
Unusual eye contact [B1]				
ASD-low MA vs. ASD	.21 (.11)	1.982	.048	.006
GDD vs. ASD-low MA	-1.61 (.12)	-13.834	< .001	.235
GDD vs. ASD	-1.39 (.07)	-20.937	< .001	.413
Responsive social smiling [B2]				
ASD-low MA vs. ASD	.27 (.13)	2.134	.033	.007
GDD vs. ASD-low MA	-1.14 (.14)	-8.215	< .001	.098
GDD vs. ASD	-.86 (.08)	-10.878	< .001	.160
Facial expressions directed toward others [B3]				
ASD-low MA vs. ASD	.25 (.09)	2.832	.005	.013
GDD vs. ASD-low MA	-1.07 (.09)	-11.334	< .001	.171
GDD vs. ASD	-.82 (.05)	-15.190	< .001	.271
Integration of gaze with other behaviors [B4]				
ASD-low MA vs. ASD	.49 (.12)	3.963	< .001	.025
GDD vs. ASD-low MA	-1.66 (.13)	-12.480	< .001	.200
GDD	-1.17 (.08)	-15.354	< .001	.275
Shared enjoyment [B5]				
ASD-low MA vs. ASD	.34 (.10)	3.557	< .001	.020
GDD vs. ASD-low MA	-1.04 (.10)	-9.983	< .001	.138
GDD vs. ASD	-.69 (.06)	-11.652	< .001	.179
Responsivity to one's name [B6]				
ASD-low MA vs. ASD	.24 (.15)	1.649	.100	.004
GDD vs. ASD-low MA	-1.28 (.16)	-8.084	< .001	.095
GDD vs. ASD	-1.03 (.09)	-11.436	< .001	.174
Requesting [B7]				
ASD-low MA vs. ASD	.55 (.12)	4.442	< .001	.031
GDD vs. ASD-low MA	-1.14 (.13)	-8.647	< .001	.107
GDD vs. ASD	-.60 (.08)	-7.882	< .001	.091
Giving [B8]				
ASD-low MA vs. ASD	.35 (.10)	3.498	.001	.019
GDD vs. ASD-low MA	-.90 (.11)	-8.380	< .001	.101
GDD vs. ASD	-.55 (.06)	-8.949	< .001	.114
Showing [B9]				
ASD-low MA vs. ASD	.27 (.09)	2.946	.003	.014

GDD vs. ASD-low MA	-1.15 (.10)	-11.666	< .001	.180
GDD vs. ASD	-.88 (.06)	-15.584	< .001	.281
Initiation of joint attention [B10]				
ASD-low MA vs. ASD	.40 (.10)	3.861	< .001	.023
GDD vs. ASD-low MA	-1.34 (.11)	-12.158	< .001	.192
GDD vs. ASD	-.94 (.06)	-14.956	< .001	.264
Response to joint attention [B11]				
ASD-low MA vs. ASD	.47 (.14)	3.481	.001	.019
GDD vs. ASD-low MA	-1.38 (.15)	-9.493	< .001	.127
GDD vs. ASD	-.91 (.08)	-10.922	< .001	.161
Quality of social overtures [B12]				
ASD-low MA vs. ASD	.58 (.11)	5.274	< .001	.043
GDD vs. ASD-low MA	-1.80 (.12)	-15.295	< .001	.273
GDD vs. ASD	-1.22 (.07)	-18.139	< .001	.346
Functional play with objects [C1]				
ASD-low MA vs. ASD	.62 (.12)	5.093	< .001	.040
GDD vs. ASD-low MA	-1.29 (.13)	-9.790	< .001	.134
GDD vs. ASD	-.66 (.08)	-8.819	< .001	.111
Imaginative and creative play [C2]				
ASD-low MA vs. ASD	.65 (.14)	4.810	< .001	.036
GDD vs. ASD-low MA	-1.38 (.15)	-9.529	< .001	.127
GDD vs. ASD	-.73 (.08)	-8.824	< .001	.111
Unusual sensory interests [D1]				
ASD-low MA vs. ASD	.12 (.11)	1.088	.277	.002
GDD vs. ASD-low MA	-.65 (.12)	-5.404	< .001	.045
GDD vs. ASD	-.53 (.07)	-7.668	< .001	.086
Hand and finger mannerisms [D2]				
ASD-low MA vs. ASD	.16 (.11)	1.450	.148	.003
GDD vs. ASD-low MA	-.67 (.12)	-5.621	< .001	.048
GDD vs. ASD	-.51 (.07)	-7.460	< .001	.082
Self-injurious behavior [D3]				
ASD-low MA vs. ASD	.11 (.06)	1.911	.056	.006
GDD vs. ASD-low MA	-.14 (.06)	-2.216	.027	.008
GDD vs. ASD	-.03 (.04)	-0.764	.445	.001
Repetitive interests/stereotyped behaviors [D4]				
ASD-low MA vs. ASD	.33 (.12)	2.744	.006	.012
GDD vs. ASD-low MA	-.93 (.13)	-7.188	< .001	.077
GDD vs. ASD	-.60 (.07)	-8.092	< .001	.095

Note. ADOS = Autism Diagnostic Observation Schedule. With Bonferroni correction, cut-off for significance is $\alpha = .0025$.

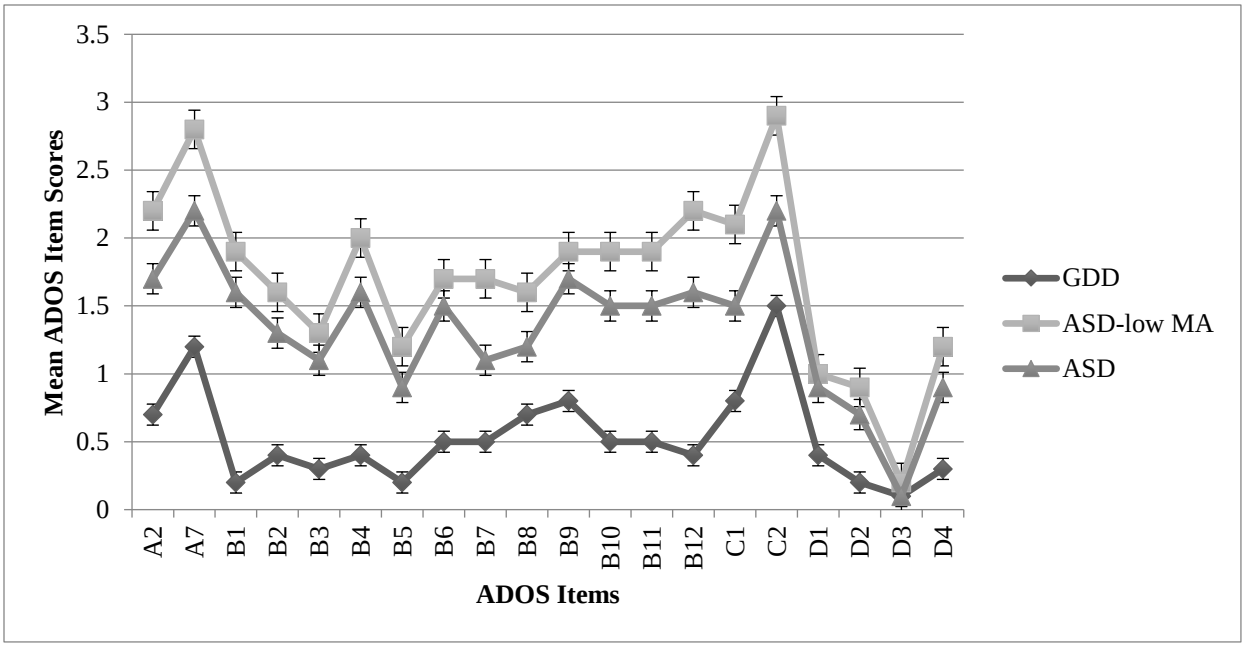

Figure 1. Mean ADOS item scores by diagnostic group. Symptom profiles for each diagnostic group across Autism Diagnostic Observation Schedule (ADOS) items measuring communication (A2, A7), reciprocal social interaction (B1-12), play (C1-2), and stereotyped behaviors and restricted interests (D1-4) are presented; scores of 0 = typical, 1 = atypical and mild, 2 = atypical and moderate, and 3 = atypical and severe. Standard error bars are displayed for each item.