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Diagnosing Autism Spectrum Disorder in Children with Low Mental Age

Lauren E. Miller¹, Jeffrey D. Burke¹, Diana L. Robins², and Deborah A. Fein¹

¹Department of Psychological Sciences, University of Connecticut, 406 Babbidge Road, Unit 1020, Storrs, CT 06269, USA

²A.J. Drexel Autism Institute, Drexel University, 3020 Market Street, Suite 560, Philadelphia, PA 19104, USA

Abstract

Autism Spectrum Disorder (ASD) diagnostic tools are not designed for mental ages (MA) below 12 months. Autism Diagnostic Observation Schedule (ADOS) and Childhood Autism Rating Scale (CARS) were examined in 2-year-olds with ASD-low MA ($n = 53$), Global Developmental Delay (GDD; $n = 175$), and ASD-higher MA ($n = 425$). ADOS and CARS demonstrated similar agreement with clinical diagnosis, but ADOS over-classified ASD in low MA, whereas CARS both over- and under-classified. All ADOS items differentiated GDD from ASD. Elementary social behaviors (e.g., eye contact, social interest) were similar across ASD groups, although advanced skills (e.g., pointing, play) were more impaired in ASD-low MA. ASD-low MA, a severe presentation, may require a modified ADOS algorithm to account for developmental delays.

Keywords

Autism spectrum disorder; Low mental age; ADOS; CARS; Symptom profiles

Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by early impairments in socialization and communication, as well as restricted interests and repetitive

Lauren E. Miller, lauren.miller@uconn.edu.

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Conflict of interest Diana Robins and Deborah Fein are part owners of M-CHAT, LLC, which receives royalties from companies that incorporate the M-CHAT(-R) into commercial products and charge for its use. Data reported in this manuscript are from the freely available paper version of the M-CHAT(-R). Lauren Miller and Jeffrey Burke declare that they have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from caregivers of all individual participants included in the study.

behaviors (American Psychiatric Association (APA) 2013). Currently, the Centers for Disease Control and Prevention (CDC) estimate that one in every 59 children has ASD; although most children are diagnosed by age 3 years, approximately 39% are not evaluated for the first time until after age 4 years (CDC 2018). There is clear evidence that ASD-specific symptoms emerge in the first 2 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 and Gillberg 1989; Hazlett et al. 2017; Maestro et al. 2005; Martinez-Pedraza and Carter 2009; Osterling et al. 2002; Ozonoff et al. 2010). Even so, ASD can be difficult to diagnose in very young children, as many of the defining characteristics (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 usually seen in infants and young toddlers, nor are they seen in older individuals with low mental age (low MA), defined as developmental functioning below a 12-month level (Crais et al. 2006; Ventola et al. 2006; Vig and Jedrysek 1999; Watson et al. 2003). Despite these challenges, it is possible to diagnose ASD in children with low MA, and these diagnoses show high stability over a 2-year period (Hinnebusch et al. 2017). To facilitate diagnosis and intervention early 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% (CDC 2018). Further, the percentage of children for whom developmental concerns are raised before age 3 years is significantly higher in children later diagnosed with comorbid ASD and ID, as compared to individuals diagnosed with only ASD, suggesting that children with comorbid cognitive delays may be a particularly severe 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 et al. 2015). In particular, children with ASD and comorbid cognitive delays appear to make limited developmental progress over time and show greater deficits in adaptive functioning, social skills, and disruptive behavior even with intensive intervention, perhaps suggesting that those with low MA may struggle to respond to traditional ASD-specific intervention services (Gardner et al. 2018; Hinnebusch et al. 2017). Intellectual level can be difficult to measure accurately in very young children because developmental domains may undergo rapid changes in early childhood, and because the children may have difficulty complying with the demands of testing. Given that children with ASD and low MA may require more intensive or adapted intervention approaches, however, it is necessary to assess 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 to accurately distinguish children with ASD from those with Global Developmental Delay (GDD) without ASD, who by definition present with delays in more than one developmental domain (APA 2013). This differentiation has strong implications for treatment recommendations and may also inform long-term prognosis (Gardner et al. 2018; Hinnebusch et al. 2017; Riou et al. 2009). For example, current evidence supports intensive ASD-specific intervention services, such as Applied Behavior Analysis (ABA) therapy, for children with ASD to target social

communication skills and challenging behaviors, but toddlers with GDD may instead show greater benefit from special education or rehabilitation services to bolster skills across broad developmental domains (Riou et al. 2009; Zwaigenbaum et al. 2015). Furthermore, individuals with cognitive delays without ASD present with heterogeneous functional outcomes, much like those with ASD. While some young children with GDD no longer show cognitive impairment as they get older, others show persistent deficits in intellectual functioning and are diagnosed with Intellectual Disability (ID), and still others present with emotional or behavioral issues (e.g., aggression; Gardner et al. 2018; Riou et al. 2009). However, children with GDD are more likely to display symptoms associated with ASD than children with average cognitive abilities; therefore, cognitive impairment can present a particular obstacle to accurate diagnosis (Brereton et al. 2002; Gardner et al. 2018).

The differentiation between ASD and GDD without ASD is most difficult in children with mental ages below 2 years; the number of signs differentiating the two disorders appears to increase both with age and developmental level (Dahlgren and Gillberg 1989; Desombre et al. 2006; Vig and Jedrysek 1999). Cognitive level likely influences the emergence of clinical symptomatology, with children functioning at different intellectual levels potentially exhibiting distinct clinical features. It is therefore necessary to determine which specific symptoms can distinguish ASD from GDD in young children with significant intellectual impairment (i.e., low MA).

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). It is important to consider the developmental prerequisites of behaviors that are impaired in ASD, as we do not expect to see these skills in children with mental or chronological ages lower than the age of emergence in typical development (Martinez-Pedraza and Carter 2009). Within the first year of life, typically developing infants show clear social-communicative behaviors (e.g., eye contact, responsiveness to their name, social smiling), whereas more advanced social behaviors (e.g., imitation, pretend play, pointing and following a point) may not appear consistently until the second year of life (Inada et al. 2010). 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).

Consistent with the typical developmental timetable of these behaviors, several features of ASD appear to emerge before 2 years, and even in the first year of life (Baron-Cohen et al. 1996; Crais et al. 2006; Martinez-Pedraza and Carter 2009; Watson et al. 2003). Infants with ASD show fewer facial expressions, specifically fewer directed toward other people, than their typically developing peers by 6 months (Desombre et al. 2006). Parents 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 6 and 18 months, children later diagnosed with ASD show less (or even declining) eye contact, social smiling, and social responsivity compared to their typically developing peers (Jones and Klin 2013; Maestro et al. 2005; Ozonoff et al. 2010).

Behaviors Discriminating Autism and Global Developmental Delay

Consistent with the defining features of ASD, it has been suggested that deficits in social and pre-linguistic behaviors (e.g., response to one's name), reciprocal social engagement, and simple play are more indicative of ASD than delays in nonverbal problem solving, motor skills, and nonsocial adaptive behaviors, which are more associated with GDD (Osterling et al. 2002; Vig and Jedrysek 1999). Given the finding that many children with intellectual impairment present with autism-like deficits, including atypical behaviors and attention problems (Brereton et al. 2002; Einfeld and Tonge 1996; Gardner et al. 2018), it is important to understand specific features that differentiate ASD and 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 and 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 and 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 4 years (Vig and 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 and Jedrysek 1999).

Discriminating ASD from intellectual impairment in the first year of life is especially difficult. Baranek (1999) compared children aged 9–12 months with ASD to those with equivalent developmental delays and to a group with typical development on ASD-related symptoms (i.e., early social communication, atypical motor mannerisms, etc.). Results showed that children with ASD were more likely to display abnormal affect, unusual posturing and mouthing, aversion to social touch, reduced orientation to visual stimuli, and poor responsiveness to name than those with GDD. This study was limited by a small sample size and reliance on children with known genetic disorders (e.g., Down syndrome) in the GDD group, but was consistent with results from Osterling et al. (2002), who also found that 1-year-old infants with ASD demonstrated less social attention and responsiveness to their names than those with GDD. Both groups engaged in repetitive motor behaviors more frequently than typically developing peers. Taken together, these findings suggest that core social communication symptoms may be useful in identifying very young and cognitively delayed children with ASD, whereas atypical imitation, play, and motor movements may be seen in both ASD and GDD.

Differential Diagnosis of Autism and Global 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 appropriate early 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 et al. 2003) has long been considered a gold-standard tool for the diagnosis of ASD across the lifespan, but it is recommended for individuals with a mental age above 2 years. Below the age of 3 years, diagnostic utility is mixed (Gray et al. 2008; Risi et al. 2006; 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, with different modules designed for varying ages and language levels. 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 16–31-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 cognitively impaired children over the age of 3 years (Risi et al. 2006), with particularly poor ability to discriminate ASD from other disorders in mental ages at or below a 15-month level (Gotham et al. 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 developed to address some of these concerns, although it continues to be less valid when used with toddlers who are functioning at or below a 15-month level and not walking independently (Luyster et al. 2009).

An observational research measure, the Autism Observation Scale for Infants (AOSI; Bryson et al. 2008), was specifically designed to detect signs of ASD in children between the ages of 6 and 18 months. Elevated scores on the AOSI by 1 year of age are predictive of social communication symptoms at age 24 months and a diagnosis of ASD at age 3 years (Bryson et al. 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 et al. 1988) combines information from caregiver report and direct observation in a clinician-completed rating scale. Although used with individuals of all ages, the measure is recommended for those over age 2 years. In toddlers with varying mental ages and older children with intellectual impairment, the CARS shows high agreement with clinical judgment and good sensitivity in diagnosing ASD (Morgan 1988; Teal and Wiebe 1986; Ventola et al. 2006). 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 ASD diagnosis and the presentation of autism symptoms in very young and cognitively delayed children. We focused on a subgroup of children with ASD and 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 two standardized diagnostic measures, and to examine whether certain symptoms are particularly useful in discriminating ASD from GDD in young children. 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 2-year-old children functioning below a 12-month cognitive 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 would be most accurate in discriminating the disorders, and that the ADOS might over-classify very low-functioning children.
2. Explore specific features that characterize children with ASD-low MA and ASD-higher MA, compared to those with GDD. 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 both groups of children with ASD from those with GDD only. 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 peers with ASD and milder delays.

Methods

Participants

Participants were 653 children with either ASD or GDD drawn from a large, multi-site investigation of the early detection of ASD. Children screened positive on the Modified Checklist for Autism in Toddlers with Follow-Up (M-CHAT/F; Robins et al. 2001) or its revision (M-CHAT-R/F; Robins et al. 2014) between the ages of 16 and 30 months, or they were referred for autism-specific concerns by their pediatrician or early intervention provider; all children were evaluated at the approximate age of 2 years (Table 1). 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 following Mullen Scales of Early Learning (MSEL) scales: Visual Reception, Receptive Language, and Expressive Language. The GDD group ($n = 175$) was composed of children with DSM-IV-TR Global Developmental Delay, which was operationalized as 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-higher MA 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 previously 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. To be included in the current study, participants had to have a DSM-IV-TR diagnosis of Autistic Disorder or Pervasive Developmental Disorder—Not Otherwise Specified (PDD-NOS), together referred to as ASD, or GDD, as these two diagnostic groups were the primary populations of interest for this project. They also had to have available data on primary study measures (i.e., ADOS and CARS). Of the 744 children with ASD or GDD, 91 were excluded from the current study because they were missing the ADOS and/or CARS in their entirety, leaving a final sample of 653 participants.

Included and excluded children did not significantly differ based on child age ($t(737) = -1.221, p = .223$), child gender ($\chi^2(1, N = 744) = .178, p = .673$), diagnostic group (i.e., ASD-low MA, ASD-higher MA, GDD; $\chi^2(2, N = 744) = 4.874, p = .087$), MSEL Visual Reception ($t(652) = .536, p = .592$), MSEL Receptive Language, $t(649) = .903, p = .367$), or MSEL Expressive Language ($t(653) = -0.083, p = .934$). There was a trend-level difference on MSEL Fine Motor scores ($t(655) = 2.144, p = .032$), with included children ($M = 18.46, SD = 4.44$) achieving age-equivalents 2 months higher, on average, than excluded toddlers ($M = 16.12, SD = 4.57$). Because a large proportion of excluded individuals were missing data on maternal education (i.e., 87%) and race/ethnicity (i.e., 43%), included and excluded groups could not be accurately compared on these variables.

For included participants, there were no differences between diagnostic groups based on child age ($p = .428$), child gender ($p = .614$), or maternal education ($p = .063$). However, groups significantly differed on child race/ethnicity ($p = .017$); specifically, although all three groups were composed of majority White toddlers, the ASD-higher MA group had a slightly larger proportion of White and biracial participants, whereas 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 and the follow-up phone interview (i.e., indicating risk for ASD), or who screened negative on the M-CHAT(-R)/F but were referred for autism-specific concerns by their pediatrician or early intervention provider, 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 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 of the child, developmental history (as obtained from a caregiver-completed history form and clinical interview), and scores on the ADOS, CARS,

MSEL, and VABS. Additional information about core ASD symptomatology was ascertained by a targeted caregiver interview designed by the research team. All diagnoses were assigned based on DSM-IV-TR criteria (APA 2000) given the years in which participants were evaluated (i.e., 2002–2014).

Measures

Autism Diagnostic Observation Schedule—Generic (ADOS; Lord et al. 2000)—

The ADOS is a semi-structured observational assessment designed to measure symptoms of ASD in toddlerhood through adulthood. The ADOS includes four modules based on a participant's expressive language level and chronological age. The current study's participants received 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 has been described as good across all domains, ranging from $r = .82$ to $r = .93$ (Lord et al. 2000).

Childhood Autism Rating Scale (CARS; Schopler et al. 1988) and Childhood Autism Rating Scale, Second Edition (CARS2-ST; Schopler et al. 2010)—

The CARS and CARS2-ST are 15-item clinician rating scales measuring autism symptom severity based on *both* direct observation and caregiver report. Item content and recommended clinical cut-offs did not change from CARS to CARS2-ST, making the measures ideally suited for longitudinal research such as the current study (Schopler et al. 2010). 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 validated for ASD more broadly (Chlebowski et al. 2010). Internal consistency of CARS and CARS2-ST items has been described as high at $\alpha = .94$ and $\alpha = .93$, respectively, and inter-rater reliability has been reported as good at $r = .71$ (Schopler et al. 1995, 2010).

Clinical Best Estimate—Clinical judgment by experienced clinicians is considered to be the gold standard for diagnosis of ASD (Klin et al. 2000; Ventola et al. 2006). 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). Further data about the presence or absence of ASD symptoms as they pertained to participating children was gathered using a targeted caregiver interview designed by the research team. Diagnoses of Autistic Disorder, PDD-NOS, and GDD were given if a child met DSM-IV-TR criteria.

Mullen Scales of Early Learning (MSEL; Mullen 1995)—The MSEL is a developmental assessment of cognitive, motor, and language abilities in children ages 1 month to 5 years, 8 months. It was used to confirm low MA and GDD status and characterize participants' cognitive functioning but was not an outcome measure for the present study. 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 has been reported as satisfactory, ranging from $\alpha = .75$ to $\alpha = .83$ across all scales, and inter-rater reliability has been described as strong, ranging from $r = .91$ to $r = .99$ (Mullen 1995).

Vineland Adaptive Behavior Scales: Interview Edition, Survey Form (VABS; Sparrow et al. 1984) and Vineland Adaptive Behavior Scales, Second Edition: Survey Interview Form (VABS-II; Sparrow et al. 2005)—The VABS and VABS-II 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. In children up to age 2 years, correlations between the VABS and VABS-II have been reported as moderate ($r = .65$; Communication) to very high ($r = .91$; Motor Skills), suggesting good consistency between the two versions in the measurement of adaptive behaviors (Sparrow et al. 2005). Standard scores in each domain were used in the current study to confirm GDD status and characterize participants' adaptive skills but were not used as outcome measures for the present study. Inter-interviewer reliability has been reported as adequate across the four domains, ranging from $r = .62$ to $r = .78$ (Sparrow et al. 1984, 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 with low MA. As no GDD children were functioning below a 12-month age equivalence on all verbal and nonverbal cognitive domains (i.e., study definition of low MA), a low MA designation for these analyses was instead based on 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 ASD groups, to ensure equivalent cognitive levels; 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 the autism spectrum 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 versus 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 versus non-ASD) from both ADOS and CARS classifications was conducted to determine the potential differential diagnostic utility of each measure. Predictors were entered simultaneously. Multicollinearity was assessed through the evaluation of variance inflation factor (VIF) and tolerance; conservative cut-offs of $VIF > 4$ and $\text{tolerance} < .20$ were used, as described in Menard

(1995). No evidence of collinearity was found when ADOS and CARS classifications were both included in models.

Symptom Profile Analysis—The second aim explored specific symptoms that distinguish children with ASD-low MA, GDD, and ASD-higher MA. 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). Most ADOS items are coded with a score of 0, 1, 2, or 3, with higher scores indicating greater impairment. Six ADOS items (i.e., A1, A3, A4, A5, A6, and A8) assessing language and communication 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 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-higher MA) 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 among the three groups and exploration of specific features discriminating 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 ($p = .006$) (Table 3). However, although ADOS classification agreed with clinical best estimate in 79.2% of cases, most of the remaining participants (i.e., 18.8%) were over-classified as having ASD by the ADOS compared to clinical judgment. Only one child (i.e., 2.1%) fell in the non-spectrum range on the ADOS but was clinically diagnosed with 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 ($p < .001$), with 83.3% agreement. On the CARS, 10.4% of participants were over-classified as having ASD compared to clinical judgment. 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 ($p = .002$), 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, and 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 versus 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 ($\chi^2(2, N = 48) = 17.318, p < .001$), 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-higher MA, a repeated-measures ANOVA was conducted. As shown in Fig. 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-higher MA 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 effectively distinguish between ASD-low MA, GDD, and ASD-higher MA (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 ASD group on *all* ADOS items (all p 's < 0.001), with medium to large effect sizes.

In the communication, reciprocal social interaction, and play domains, children with GDD displayed their most impaired scores on items measuring pointing (A7) and imaginative and creative play (C2), with their performance suggesting mild to moderate impairment on these 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 children in either ASD group, 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; Fig. 1).

Children in the ASD-low MA and ASD-higher MA groups did not differ significantly on any items in the stereotyped behaviors and restricted interests domain (D1–4; all p 's > 0.0025).

In terms of social communication, ASD-low MA participants exhibited more severe impairments than their ASD-higher MA peers on a number of items, including vocalizing (A1), pointing (A2), integrating gaze (B4), sharing enjoyment (B5), requesting (B7), giving (B8), initiating and responding to joint attention (B10, B11), quality of social overtures (B12), and functional and creative play (C1, C2) (all p 's = 0.001). However, certain core social features of ASD appeared less subject to mental age, as participants in the two ASD groups did *not* differ significantly (after correction for multiple comparisons) and showed very small effects 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), and spontaneous showing (B9; p = .003) (Table 4; Fig. 1).

Discussion

The current study explored the impact of developmental level on the presentation of autism symptoms. 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 two 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, both the ADOS and CARS demonstrated approximately 80% agreement with clinical best estimate diagnosis of ASD in children with low MA. 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. In cases of disagreement, the ADOS consistently over-classified children with low MA as having ASD, but CARS classifications were distributed between over- and under-classifying these children.

Symptom profile analyses suggested that children with GDD show minimal signs of ASD, with the exception of mild deficits in more advanced behaviors (e.g., pointing and pretend play). ASD-low MA participants were more severely impaired than children with ASD-higher MA on most autism symptoms. In particular, social-communicative skills that typically appear toward the end of the first year of life or into the second year, such as pointing, integrating gaze, sharing enjoyment with others, requesting, giving, initiating and responding to joint attention, making social overtures, and pretend play, differentiated children with ASD-low MA from those with ASD-higher MA. However, certain core social

behaviors that are typically seen early in development (i.e., in the first year of life), specifically eye contact, social smiling, directing facial expressions toward others, and responding to one's name, did not differ between these two groups, nor did the ASD groups differ on atypical sensorimotor behaviors (e.g., unusual sensory interests, hand and finger mannerisms, and repetitive interests or stereotyped behaviors).

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). The diagnostic utility of two widely used measures, the ADOS and CARS, was explored in a well-defined subgroup of toddlers with cognitive functioning below a 12-month age equivalence; in fact, these children were functioning at a 9-month-old level, on average, across both verbal and nonverbal cognitive domains.

Results suggested that the ADOS, although significantly aligned with clinical judgment in most cases, tended to over-classify a large minority of children with low MA as having ASD when they received a clinical diagnosis of GDD. In the context of developing improved ADOS diagnostic algorithms, Gotham et al. (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 or cognitively delayed children).

The newer ADOS-2 Toddler Module (Lord et al. 2012) was not available when the current study began, but given that it was designed to better meet the needs of young toddlers, it is one potential option, at least for children functioning at or above a 15-month level (Luyster et al. 2009). Another option is the AOSI (Bryson et al. 2008), an observational tool with presses to elicit social behavior designed specifically for infants between the ages of 6 and 18 months, although this measure is not yet commercially available.

The CARS' agreement with clinical best estimate showed a significant main effect in a logistic regression prediction model, which was not seen for the ADOS. This measure has also been shown to be somewhat more aligned with clinical diagnosis than the ADOS in previous literature (Gotham et al. 2007; Morgan 1988; Risi et al. 2006; Teal and Wiebe 1986; Ventola et al. 2006). The CARS incorporates multiple sources of information (e.g., expert opinion, parent report, and direct clinical observation) rather than relying on brief observations of behavior in specified situations (i.e., ADOS presses); this may be one reason for the CARS' agreement with clinical judgment. However, clinicians should be aware that this instrument also both over- and under-classifies a small portion of children with low MA.

Impact of Developmental Level on Autism Symptom Presentation

The existing literature on discriminating ASD from GDD is quite limited and has focused on infants in the first year of life (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-low MA, GDD, or ASD-higher MA. Overall, 2-year-old toddlers with GDD, who earned similar cognitive scores to their peers with ASD-higher MA, scored below the autism threshold on most items, and *no* children in any diagnostic group exhibited self-injurious behavior. It is possible that this behavior may not be present in children this young 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 and GDD, may exhibit atypical sensorimotor behaviors (Osterling et al. 2002; Vig and Jedrysek 1999), we hypothesized that *all* children would show these symptoms, and thus items measuring these 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, hand and finger mannerisms, and unusually repetitive interests and stereotyped behaviors. Notably, in our sample, scores on these items were not as severe as scores on social communication items, which suggests that these atypical behaviors are present in young children with ASD, but in a milder form compared to impairments in socialization and communication.

Children with GDD showed elevations on items measuring pointing and creative and imaginative play, suggesting that they, like toddlers with ASD, are delayed in these areas; indeed, participants in both 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 have significant global delays. Although toddlers with GDD demonstrated some impairment 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, which suggested that pretend play is impaired in cognitively delayed children, but early joint attention behaviors (e.g., pointing) are intact even in intellectually impaired individuals (Osterling et al. 2002; Vig and 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 creative play, both of which are observed in typically developing 2-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 are not necessarily indicative of an ASD diagnosis.

Given the 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 developmental 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 Fig. 1, we interpret 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, responsiveness to one’s name, initiation of and response to joint attention, and overall quality of social overtures, consistent with our hypothesis that social and communication markers would be useful indicators of ASD versus global delays in very young and cognitively impaired children (Baranek 1999; Osterling et al. 2002).

Results indicated that toddlers with ASD-low MA earned higher ADOS item scores on than their peers with ASD-higher MA, who also scored higher than those with GDD. A similar pattern of higher scores in the ASD-low MA group compared to children in both other groups was observed for the CARS. As expected, these findings suggest that children with ASD-low MA are a more severely affected subgroup. This is consistent with the extant literature suggesting that individuals 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 autism features appeared to present similarly between participants in both ASD groups, however, suggesting that mental age may exert less influence on these skills, or that developmental level was high enough for children to engage in these skills, even in our ASD-low MA group. Children in both ASD groups exhibited remarkably similar ADOS item profiles, 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 eye contact, social smiling, direction of facial expressions toward others, and responsiveness to one’s name, nor did they differ on atypical sensorimotor behaviors. Overall, such findings are consistent with prior research (Baranek 1999; Baron-Cohen et al. 1996; Osterling et al. 2002; Vig and Jedrysek 1999). These features, then, appear to be indicative of ASD, even in children who are functioning below a 12-month developmental 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 specific 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. It is also important to elicit these social behaviors through activities designed specifically to meet the developmental level of infants and young toddlers and to capture their interest. For example, the ADOS-2 Toddler Module (Lord et al. 2012), in contrast to ADOS Module 1, includes a variety of developmentally appropriate testing stimuli, such as a toy mobile telephone and bathtub, to promote emerging pretend play. Further development of the AOSI may also be promising (Bryson et al. 2008).

Limitations and Future Directions

Although this study contributes to the relatively limited literature on children with ASD and low MA 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 2-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 sample ($n = 48$); this is a product of the very low number of children in our larger GDD group with nonverbal functioning 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 with some caution.

Clinical judgment was used as a measure of “accurate” diagnosis, as is widely accepted in the field, with any discrepancy suggesting that the ADOS or CARS, but not expert opinion, was “inaccurate.” Even so, clinical best estimate is by its very nature subjective. Although all of the clinicians involved in the current study had considerable experience in the field of autism, with particular expertise in early detection and diagnosis and familiarity with diagnostic criteria, diagnosis is always vulnerable to error. 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 is basing symptom profile analyses on ADOS item scores. The ADOS is based only on behaviors observed during the testing session; because toddlers can be difficult to test, reliance only on behaviors directly observed during a relatively brief (i.e., under an 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 most participant data were collected prior to the release of the ADOS-2 Toddler Module, which is designed specifically for use in toddlers from 12 to 30 months, we continued to use the older version for consistency within our sample. 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. For example, one of the key ADOS items GDD participants scored particularly high on, pretend play, has been updated in the Toddler Module to reflect a more developmentally-appropriate prompt (i.e., bath time versus birthday party script). Reliance on the ADOS also reduced the ability to explore communication symptoms, as many of the items in that domain were not applicable to children with very limited verbal skills. Alternative means of evaluating communication skills in young, minimally verbal children such as those in the ASD-low MA group are indicated.

In addition, 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-higher MA 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, and maternal education was also provided inconsistently. 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.

Finally, participants in all three diagnostic groups were ascertained by either screening positive on an ASD screening tool (i.e., M-CHAT(-R)/F) or being referred by their pediatrician or early intervention provider because of concern about ASD; results may not generalize to the same diagnostic groups ascertained by different methods (e.g., at an older age, or by caregiver or teacher concern).

Conclusions

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 Module 1 as currently scored tends to over-classify ASD in this population. Thus, development of a revised ADOS algorithm, in which social communication skills requiring mental ages of 12 months or higher are less weighted, may be useful. As an alternative, further development of a direct measure of autism symptomology for individuals with intellectual functioning below a 12-month level and infants in the first year of life, with reduced demands for complex social behaviors, including imaginative play, is strongly indicated. Because the AOSI (Bryson et al. 2008) has shown promise in accurately predicting later ASD diagnoses in 6–18-month-olds, further work to norm and publish this measure for clinical use may fill this need. In contrast to the ADOS, which systematically over-classifies children with low MA, the CARS both over- and under-classifies 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 early 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 and Klin 2013). More importantly, such symptoms seem to discriminate children with ASD from their peers with non-autistic global developmental delays accurately. While mild restricted and repetitive behaviors did differentiate ASD from GDD, they may be more useful in slightly older children, when these features tend to become more apparent and potentially 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. Given our results, 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 limit progress, failure to diagnose individuals with low MA may contribute to even poorer outcomes for this subgroup.

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Fig. 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

Table 1

Participant characteristics by diagnostic group

Variable	ASD-low MA (<i>n</i> = 53)	GDD (<i>n</i> = 175)	ASD-higher MA (<i>n</i> = 425)	<i>p</i>
Age in months [<i>M</i> (<i>SD</i>)]	25.34 (4.96)	26.32 (4.82)	26.10 (4.77)	.428
Gender [<i>N</i> (%)]				
Male	38 (71.70)	128 (73.14)	324 (76.24)	.614
Female	15 (28.30)	47 (26.86)	101 (23.76)	
Race/ethnicity [<i>N</i> (%)]				
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 [<i>N</i> (%)]				
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 [<i>M</i> (<i>SD</i>)]				
Visual reception (<i>n</i> = 638)	8.57 (2.18) ^a	17.05 (5.00)	17.93 (4.84)	< .001
Fine motor (<i>n</i> = 640)	13.16 (3.76) ^a	18.47 (4.54)	19.09 (4.04)	< .001
Receptive language (<i>n</i> = 635)	5.79 (3.27)	14.94 (5.41)	12.31 (6.05)	< .001
Expressive language (<i>n</i> = 637)	6.80 (1.96) ^a	13.87 (5.50)	13.32 (5.51)	< .001
VABS standard score [<i>M</i> (<i>SD</i>)]				
Communication (<i>n</i> = 648)	63.38 (8.10)	76.52 (10.28)	70.63 (11.92)	< .001

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Variable	ASD-low MA (<i>n</i> = 53)	GDD (<i>n</i> = 175)	ASD-higher MA (<i>n</i> = 425)	<i>p</i>
Daily living skills (<i>n</i> = 648)	70.38 (12.14)	80.36 (12.84)	75.96 (12.86)	< .001
Socialization (<i>n</i> = 648)	69.34 (11.09)	81.41 (10.26)	74.51 (10.87)	< .001
Motor skills (<i>n</i> = 644)	76.83 (13.38) ^a	83.22 (12.74)	85.00 (11.81)	< .001
ADOS A + B total score [<i>M</i> (<i>SD</i>)]	17.85 (2.19)	5.47 (3.76)	14.76 (4.32)	< .001
CARS total score [<i>M</i> (<i>SD</i>)]	35.81 (5.61)	22.91 (3.08)	32.10 (4.73)	< .001

MSEL Mullen Scales of Early Learning, *VABS* Vineland Adaptive Behavior Scales, *ADOS* Autism Diagnostic Observation Schedule, *CARS* Childhood Autism Rating Scale

^aOnly the ASD-low MA group significantly differed from the other groups on post hoc analyses

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

Table 2

Diagnostic utility subgroup performance on matching variables and primary study measures

Variable	GDD (<i>n</i> = 16)	ASD (<i>n</i> = 32)	<i>p</i>
Age in months [<i>M</i> (<i>SD</i>)]	25.04 (4.85)	25.51 (5.39)	.768
MSEL age equivalent [<i>M</i> (<i>SD</i>)]			
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 [<i>M</i> (<i>SD</i>)]	9.56 (4.24) ^a	17.47 (2.96)	< .001
CARS total score [<i>M</i> (<i>SD</i>)]	25.19 (2.74)	35.80 (6.26)	< .001

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

^aGDD children with low MA scored, on average, in the autism spectrum range on the ADOS

Table 3
Agreement of ADOS, CARS, and clinical best estimate in children with low mental age

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

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 versus ASD-higher MA	.50 (.12)	4.101	< .001	.026
GDD versus ASD-low MA	– 1.49 (.13)	– 11.458	< .001	.174
GDD versus ASD-higher MA	– .99 (.07)	– 13.344	< .001	.223
Socially-directed pointing [A7]				
ASD-low MA versus ASD-higher MA	.59 (.15)	4.081	< .001	.026
GDD versus ASD-low MA	– 1.65 (.16)	– 10.528	< .001	.151
GDD versus ASD-higher MA	– 1.05 (.09)	– 11.752	< .001	.182
Unusual eye contact [B1]				
ASD-low MA versus ASD-higher MA	.21 (.11)	1.982	.048	.006
GDD versus ASD-low MA	– 1.61 (.12)	– 13.834	< .001	.235
GDD versus ASD-higher MA	– 1.39 (.07)	– 20.937	< .001	.413
Responsive social smiling [B2]				
ASD-low MA versus ASD-higher MA	.27 (.13)	2.134	.033	.007
GDD versus ASD-low MA	– 1.14 (.14)	– 8.215	< .001	.098
GDD versus ASD-higher MA	– .86 (.08)	– 10.878	< .001	.160
Facial expressions directed toward others [B3]				
ASD-low MA versus ASD-higher MA	.25 (.09)	2.832	.005	.013
GDD versus ASD-low MA	– 1.07 (.09)	– 11.334	< .001	.171
GDD versus ASD-higher MA	– .82 (.05)	– 15.190	.001	.271
Integration of gaze with other behaviors [B4]				
ASD-low MA versus ASD-higher MA	.49 (.12)	3.963	< .001	.025
GDD versus ASD-low MA	– 1.66 (.13)	– 12.480	< .001	.200
GDD versus ASD-higher MA	– 1.17 (.08)	– 15.354	< .001	.275
Shared enjoyment [B5]				
ASD-low MA versus ASD-higher MA	.34 (.10)	3.557	< .001	.020
GDD versus ASD-low MA	– 1.04 (.10)	– 9.983	< .001	.138
GDD versus ASD-higher MA	– .69 (.06)	– 11.652	< .001	.179

Variable	<i>B</i> (SE)	<i>t</i>	<i>p</i>	η_p^2
Responsivity to one's name [B6]				
ASD-low MA versus ASD-higher MA	.24 (.15)	1.649	.100	.004
GDD versus ASD-low MA	– 1.28 (.16)	– 8.084	<.001	.095
GDD versus ASD-higher MA	– 1.03 (.09)	– 11.436	<.001	.174
Requesting [B7]				
ASD-low MA versus ASD-higher MA	.55 (.12)	4.442	<.001	.031
GDD versus ASD-low MA	– 1.14 (.13)	– 8.647	<.001	.107
GDD versus ASD-higher MA	– .60 (.08)	– 7.882	<.001	.091
Giving [B8]				
ASD-low MA versus ASD-higher MA	.35 (.10)	3.498	.001	.019
GDD versus ASD-low MA	– .90 (.11)	– 8.380	<.001	.101
GDD versus ASD-higher MA	– .55 (.06)	– 8.949	<.001	.114
Showing [B9]				
ASD-low MA versus ASD-higher MA	.27 (.09)	2.946	.003	.014
GDD versus ASD-low MA	– 1.15 (.10)	– 11.666	<.001	.180
GDD versus ASD-higher MA	– .88 (.06)	– 15.584	<.001	.281
Initiation of joint attention [B10]				
ASD-low MA versus ASD-higher MA	.40 (.10)	3.861	<.001	.023
GDD versus ASD-low MA	– 1.34 (.11)	– 12.158	<.001	.192
GDD versus ASD-higher MA	– .94 (.06)	– 14.956	<.001	.264
Response to joint attention [B11]				
ASD-low MA versus ASD-higher MA	.47 (.14)	3.481	.001	.019
GDD versus ASD-low MA	– 1.38 (.15)	– 9.493	<.001	.127
GDD versus ASD-higher MA	– .91 (.08)	10.922	<.001	.161
Quality of social overtures [B12]				
ASD-low MA versus ASD-higher MA	.58 (.11)	5.274	<.001	.043
GDD versus ASD-low MA	– 1.80 (.12)	– 15.295	<.001	.273
GDD versus ASD-higher MA	– 1.22 (.07)	– 18.139	<.001	.346
Functional play with objects [C1]				
ASD-low MA versus ASD-higher MA	.62 (.12)	5.093	<.001	.040
GDD versus ASD-low MA	– 1.29 (.13)	– 9.790	<.001	.134
GDD versus ASD-higher MA	– .66 (.08)	– 8.819	<.001	.111

Variable	<i>B</i> (SE)	<i>t</i>	<i>p</i>	η_p^2
Imaginative and creative play [C2]				
ASD-low MA versus ASD-higher MA	.65 (.14)	4.810	<.001	.036
GDD versus ASD-low MA	– 1.38 (.15)	– 9.529	<.001	.127
GDD versus ASD-higher MA	– .73 (.08)	– 8.824	<.001	.111
Unusual sensory interests [D1]				
ASD-low MA versus ASD-higher MA	.12 (.11)	1.088	.277	.002
GDD versus ASD-low MA	– .65 (.12)	– 5.404	<.001	.045
GDD versus ASD-higher MA	– .53 (.07)	– 7.668	<.001	.086
Hand and finger mannerisms [D2]				
ASD-low MA versus ASD-higher MA	.16 (.11)	1.450	.148	.003
GDD versus ASD-low MA	– .67 (.12)	– 5.621	<.001	.048
GDD versus ASD-higher MA	– .51 (.07)	– 7.460	<.001	.082
Self-injurious behavior [D3]				
ASD-low MA versus ASD-higher MA	.11 (.06)	1.911	.056	.006
GDD versus ASD-low MA	– .14 (.06)	– 2.216	.027	.008
GDD versus ASD-higher MA	– .03 (.04)	– 0.764	.445	.001
Repetitive interests/stereotyped behaviors [D4]				
ASD-low MA versus ASD-higher MA	.33 (.12)	2.744	.006	.012
GDD versus ASD-low MA	– .93 (.13)	– 7.188	<.001	.077
GDD versus ASD-higher MA	– .60 (.07)	– 8.092	<.001	.095

With Bonferroni correction, cut-off for significance is $\alpha = .0025$

ADOS Autism Diagnostic Observation Schedule