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A prospective study of toddlers with ASD: short-term diagnostic and cognitive outcomes

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Abstract

Background—Despite recent increases in the number of toddlers referred for a differential diagnosis of autism spectrum disorders (ASD), knowledge of short-term stability of the early diagnosis as well as cognitive outcomes in this cohort is still limited.

Method—Cognitive, social, and communication skills of 89 clinic-referred toddlers were assessed at the average age of 21.5 (SD = 4.9) months, and reassessed at 46.9 (SD = 7.7) months. Groups with stable and unstable diagnostic presentation were identified and compared on their profile of cognitive and social-communicative skills obtained at the time of initial diagnosis.

Results—Stability of the ASD diagnosis was 100%; diagnosis of autism was stable in 74% of cases as compared to 83% and 81% in PDD-NOS and Non-ASD groups, respectively. Worsening of social disability symptoms resulting in autism diagnosis was noted in 17% of toddlers initially diagnosed with PDD-NOS and in 19% of toddlers with initial diagnosis of non-ASD disorder. However, marked improvement was noted in approximately 1/4 of children initially presenting with autism, warranting diagnostic reassignment to PDD-NOS at follow-up. An analysis of developmental skills profiles suggests particular relevance of the assessment of verbal and nonverbal communication skills to diagnostic differentiation between subtypes within ASD in the second year of life.

Conclusions—Stability of ASD diagnosis in toddlers is high, though marked changes in severity of symptoms is to be expected in a minority of cases. Simultaneous consideration of cognitive, social, and communication skills profiles enhances accuracy of diagnostic classification and prediction of outcome.

Keywords

Autism; ASD; PDD-NOS; toddlers; early diagnosis; assessment; prospective studies

Autism (autistic disorder) is a complex developmental disorder characterized by severe impairments in social interaction and communication and accompanied by a range of repetitive behaviors and restricted interests (DSM-IV, 1994). Along with its less severe variant, pervasive developmental disorder-not otherwise specified (PDD-NOS) and Asperger syndrome, it constitutes what has been increasingly referred to in the literature as the autism

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spectrum disorders (ASD) diagnostic group. Current prevalence of ASD estimates suggest that as many as 116 per 10,000 individuals in the general population might be affected by some form of the disorder (Baird et al., 2006) and that early identification and treatment lead to better outcomes in terms of the overall level of functioning and adaptation (Eikeseth, Smith, Jahr, & Eldevik, 2007; Smith, Groen, & Wynn, 2004; Whalen & Schreibman, 2003; Whalen, Schreibman, & Ingersoll, 2006; Yoder & Stone, 2006). Rising awareness amongst parents and professionals regarding the early signs of ASD, as well as ongoing monitoring of infants who, due to genetic liability, are at risk for developing the disorder, has led in recent years to a rapid increase in the number of very young children referred for a diagnostic evaluation. Considering that in a majority of children with ASD, parents and professionals begin to note first concerns in the second year of life (Chawarska, Paul et al., 2007; De Giacomo & Fombonne, 1998; Ozonoff, Williams, & Landa, 2005), enhancing our understanding of the syndrome expression within this developmental period is essential for both clinical practice and research purposes.

With the growing emphasis on early identification of ASD (Johnson & Myers, 2007), considerable effort has been invested in examining stability of the early diagnosis (e.g., Chawarska, Klin et al., 2007; Cox et al., 1999; Turner & Stone, 2007) and identifying early symptoms of autism prior to the second birthday (Baron-Cohen, Cox, Baird, Sweettenham, & Nighingale, 1996; Bryson et al., 2007; Charman, Baron-Cohen et al., 2003; Charman et al., 1998; Chawarska, Klin, Paul, & Volkmar, 2007; Cox et al., 1999; Landa, 2007; Gamliel, Yirmiya, & Sigman, 2007; Landa, Holman, & Garrett-Mayer, 2007; Mitchell et al., 2006; Nadig et al., 2007; Swettenham et al., 1998; Wetherby et al., 2004; Zwaigenbaum et al., 2007). Amongst the symptoms shared by toddlers later diagnosed with autism and PDD-NOS are limited response to name and to bids for joint attention, poor eye contact, lack of pointing, and delayed functional and symbolic play skills (Chawarska, Klin et al., 2007). The symptoms are typically expressed in the context of severely delayed verbal and moderately delayed nonverbal skills. Several reports suggest that a majority of children who present with symptoms of autism in the second year of life continue to do so at the age of 3 to 4 years (Chawarska, Klin et al., 2007; Cox et al., 1999; Klin et al., 2007; but see Cox et al., 1999; Turner & Stone, 2007). Evidence for stability of milder forms of ASD, however, is less established (Chawarska, Klin et al., 2007; but see Cox et al., 1999; Turner & Stone, 2007).

The first three years of life is a period of rapid development of perception, memory, cognition, verbal and nonverbal communication, as well as reciprocal social interaction skills. While DSM-IV (American Psychiatric Association, 1994) emphasizes the necessity of interpreting symptoms of social dysfunction within the context of cognitive and adaptive functioning, this imperative becomes even more relevant in the case of young children, as symptoms of social disability are likely to be expressed somewhat differently in pre-verbal and pre-intentional children whose representational skills are still very fragile, as compared to those with a better understanding of language and emerging symbolic reasoning skills. Within this framework, different sets of diagnostic features might need to be applied depending, for instance, on the verbal skills level. This notion is reflected in the recent modification of diagnostic algorithms in the *Autism Diagnostic Observation Schedule–Generic* (ADOS-G; Lord et al., 2000), the most commonly used diagnostic instrument in

ASD, which specifies separate algorithms for young verbal and nonverbal children (Gotham et al., 2007). Thus, identification of profiles of skills and deficits in the second year of life that predict the diagnostic outcome would allow for more reliable differentiation between children with ASD from those with other disorders and further discrimination between ASD subtypes. This a particularly pressing issue as the most dynamic changes in the clinical presentation are expected during the first three to four years of life (Charman et al., 2005; Lord et al., 2006; Turner, Stone, Pozdol, & Coonrod, 2006), and reports suggest that the diagnostic strategies that are effective in 3-year-olds might not be as effective for those under 30 months of age (Turner & Stone, 2007). While a broadly defined framework for identifying social–communicative deficits and abnormalities in children under the age of 3 has begun to crystallize (Charman & Stone, 2006; Chawarska, Klin, & Volkmar, 2008; Lord & Corsello, 2005; National Research Council, 2001; Wetherby & Prizant, 2000), the vast majority of studies include toddlers with ages ranging from early 2nd to late 3rd year, leaving the youngest group of children presenting for differential diagnosis still not well understood.

A recent study compared social and communicative functioning of a small group of toddlers under the age of 2 years who were later diagnosed either with autism or PDD-NOS (Chawarska, Klin et al., 2007). While all toddlers with ASD shared a set of social–communicative deficits, marked differences in clinical presentation between the two diagnostic groups were already noticeable in the second year of life and were centered on early emerging dyadic interaction and communication skills. Changes in syndrome expression over time were complex and associated with a rate of progress in the verbal and nonverbal cognitive domains. The study also documented both advantages and disadvantages of using the ADOS-G and ADI-R (Rutter et al., 2003) for diagnostic purposes in this population. The grouping approach employed in this study was based on the diagnosis at 3 to 4 years. Thus, the study examined what confirmed cases of autism or PDD-NOS might look like in the second year of life. In the present study we would like to take the opposite approach, that is, examine clinical and cognitive outcomes of children whose symptoms were consistent with autism, PDD-NOS, or a non-ASD diagnosis in the second year of life. The study reports on a large sample of toddlers who presented for a differential diagnosis either before or shortly after their 2nd birthday and were reassessed one to three years later. The main aims of this study were: (1) to examine short-term stability of clinical diagnosis in the second year of life; (2) to examine stability of verbal and nonverbal functioning levels; and (3) to identify profiles of skills that in the second year are predictive of diagnostic outcome in the 3rd to 4th year.

Method

Participants

Eighty-nine[1] infants were evaluated by a multidisciplinary team consisting of a clinical child psychologist, speech and language pathologist, and psychiatrist. Children included in this sample were referred by parents or professionals for a differential diagnosis between 2001

[1]Data on the first 31 toddlers enrolled into the study were included in another report: Chawarska, Klin, Paul, and Volkmar, 2007a.

and 2006. Children were referred to the clinic or to a research project due to concerns regarding their cognitive, language, or social development, both with and without specific concerns regarding ASD. Consecutive referrals that met the inclusion and exclusion criteria were considered in this study. Inclusion criteria were a diagnosis of ASD or other non-autistic developmental disability and chronological age below 28 months. Age at assessment ranged from 13 months to 27 months (M = 21.5, SD = 4.9) at Time 1, and from 30 to 61 months (M = 46.9, SD = 7.7) at Time 2. On average, 24% of toddlers were below 18 months at Time 1. Ethnically, 86% were Caucasian, 3.5% were Asian, 1.3% were African American, 6.9% of parents reported mixed racial heritage, and 3.4% did not provide information regarding ethnicity. Hispanics constituted 5.2% of the entire sample. Mothers were on average 35 years old (SD = 4) and fathers were 36 years old (SD = 4). On average, 82% and 79% of mothers and fathers, respectively, completed college education.

Time 1 provisional diagnosis—A consensus clinical diagnosis was assigned by at least two expert clinicians (KC, AK, FV, and RP) who participated directly in the assessment. Considering findings that experienced clinicians' judgment of children at the age of 2 is a better predictor of later diagnosis than scores on the ADOS-G (Chawarska, Klin et al., 2007; Lord et al., 2006; Gotham et al., 2007), expert opinion prevailed over the ADOS-G diagnostic algorithms. Provisional diagnosis of autism (N = 43) was based on the DSM-IV criteria modified for children under the age of 3 (Chawarska & Volkmar, 2005) with emphasis on the absence of early emerging dyadic and triadic interaction skills, extremely limited nonverbal communication skills, and lesser emphasis on the presence of restricted and repetitive behaviors (RRB). However, most children diagnosed with autism presented with some form of unusual sensory interests or repetitive behaviors; self-injurious behaviors were practically absent (see Chawarska, Klin et al., 2007). A vast majority (91%) of toddlers diagnosed with autism also met diagnostic autism cut-off on the ADOS-G (see Chawarska, Klin et al., 2007 for more details). PDD-NOS provisional diagnosis (N = 18) was assigned in cases where social deficits appeared milder, nonverbal communication skills were more advanced, and children displayed fewer unusual sensory interests and motor mannerisms. In 44% of PDD-NOS cases the ADOS-G classification and clinical diagnosis were congruent, though 50% of cases at Time 1 met the ADOS-G cut-off for autism, and in 6% fell into the non-ASD category. In such cases, a careful examination of their communication patterns (verbal, gestural, use of eye contact and affective expressions), social interaction and symbolic play skills, as well as the pattern of repetitive behaviors aided the diagnostic decision process. The non-ASD group (N = 28) included toddlers given a provisional diagnosis of language delay (LD) or global developmental delay (DD). The Non-ASD category was assigned if at least one of the Mullen Scales domain scores was 1.5 SD below the average and based on consensus clinical diagnosis. Toddlers with Non-ASD met criteria on the ADOS-G for autism in 29% of cases and for PDD-NOS in 21% of cases. In such cases, examination of their dyadic and triadic interaction and nonverbal communication skills within the context of their overall cognitive and motor skills facilitated differential diagnosis.

Time 2 confirmatory diagnosis—Similarly as at Time 1, the confirmatory diagnosis was carried out by a multidisciplinary team of clinicians and was based on developmental

and health history, direct clinical impressions, the results of the ADI-R (Lord, Rutter, & Le Couteur, 1994; Rutter, Le Couteur, & Lord, 2003) and ADOS-G (Module 1 or 2) (Lord et al., 2000), and assessment of verbal, nonverbal (Mullen, 1995), and adaptive (Sparrow, Balla, & Cicchetti, 1984) skills. Only one out of three clinicians on the team participated in assessments at both times; all three clinicians made independent diagnostic judgments and a full consensus amongst all participating clinicians was necessary for the diagnostic assignment (see Table 1 for sample characterization at Time 2). All clinicians involved in assigning diagnosis were directly involved in the assessment, either evaluating the child directly or supervising and observing the direct assessments sessions. Thus, all clinicians had immediate and firsthand experience with the child's clinical presentation.

Following the initial diagnostic assessment toddlers were referred to their local early intervention agencies for treatment, which for toddlers with ASD included typically up to 15 hours of intervention per week and often consisted of an eclectic combination of the Applied Behavioral Analysis approach with developmental methods (Koegel, Koegel, Fredeen, & Gengoux, 2008; Wetherby & Woods, 2008). Information regarding the average hours per week and duration of the various types of services (special education, speech therapy, behavioral therapy/ABA, occupational therapy, educational therapy, physical therapy, play therapy, social skills therapy, and regular preschool) were gathered at the time of confirmatory diagnosis.

Informed consent was obtained from all parents and the study was conducted in accordance with the Human Investigation Committee of the Yale University School of Medicine.

Procedures

Cognitive skills—Developmental level was assessed at both time points with the Mullen Scales of Early Learning (Mullen, 1995), capturing Gross Motor (GM), Fine Motor (FM), Visual Reception (VR), Receptive Language (RL), and Expressive Language (EL) skills. Levels of functioning in each of the domains were quantified using developmental quotient (DQ) scores ((AE/CA)*100).

Symptom severity—At Time 1 range and severity of symptoms were assessed directly with the ADOS-G Module 1 (Lord et al., 2000). At time 2 a large proportion of toddlers were administered Module 2 of the ADOS-G. Here we present ADOS-G data based on the new and improved algorithms for Module 1 and Module 2 (Gotham et al., 2007): Social Affect (SA) and Restricted and Repetitive Behaviors (RRB). The algorithms are calculated differently for verbal and nonverbal children and have been shown to have a better sensitivity and specificity with regard to the age groups of interest in the present study (Gotham et al., 2007).

Nonverbal communication—Low frequency of communicative bids, impoverished use of communicative gestures, and limited joint attention skills are amongst most frequently cited areas of impairment in young children with ASD (Dawson et al., 1990; Kasari, Sigman, Mundy, & Yirmiya, 1990; Mundy, Sigman, & Kasari, 1990; Mundy & Stella, 2000; Paul, Chawarska, Klin, & Volkmar, 2007; Sigman & Ruskin, 1999; Wetherby et al., 2004). In extreme cases children presenting with ASD in the second year are still in the pre-

intentional stage of communicative development (Bates, 1979) and, thus, are incapable of expressing their basic needs by means other than undirected whining, crying, or simply pursuing goals on their own and abandoning them when they cannot be achieved independently. To capture these aspects of their presentation we isolated the ADOS-G Module 1 items that capture frequency of communication (FC), joint attention skills (JA) or the ability to share experiences through gaze and gestures index, and use of communicative gestures (CG). The FC index was computed based on the child's scores on items A6 (Use of Other's Body), B4 (Integration of Gaze), and B7 (Requesting); the JA score was based on items B1 (Eye Contact), B10 (Response to Joint Attention), B11 (Initiation of Joint Attention), and B9 (Showing). The delay in gestural communication was captured by items A7 (Pointing), A8 (Gestures), and B8 (Giving). If a child received a score of 2 or higher on a given item, their score was converted to 1, otherwise it was assigned the value of 0. The indices represent sum of scores for all relevant items, with higher scores representing greater degree of impairment.

All examiners had previously established reliability with the training center (ADOS-G and ADI-R), and with each other (ADOS-G, ADI-R, Vineland and Mullen Scales).

Analytic strategy—The first part of the analysis is focused on examining stability of clinical diagnosis and levels of verbal and nonverbal skills as they were assessed in the 2nd year. Consequently, the diagnostic grouping employed in these analyses is based on their clinical presentation at the time of the first diagnosis. The second part of the analysis is focused on identifying characteristics of children for whom diagnosis is likely to remain stable over time versus those for whom marked changes in the clinical presentation are to be expected. In this analysis we consider their initial indices of social interaction, nonverbal communication, and repetitive behaviors, as well as their cognitive and verbal skills as potential predictors of short-term diagnostic outcome. Unless otherwise indicated, all significant omnibus effects were followed up with post-hoc tests with the Tukey-Kramer correction for multiple comparisons.

Results

Stability of consensus clinical diagnosis

At the time of the confirmatory diagnosis 36 toddlers were diagnosed with autism, 28 with PDD-NOS, and 25 with Non-ASD difficulties ranging from language ($N = 8$) and global delays ($N = 5$) to a host of other difficulties related to motor delays, articulation problems, mild social difficulties, or attention/hyperactivity problems ($N = 12$) (see Table 1 for the sample characterization at the time of the confirmatory diagnosis). A comparison of the confirmatory and the provisional diagnostic classification (see Table 2) suggests two important findings: (1) a broadly defined ASD diagnosis in this clinic-referred sample was stable between the 2nd and the 3rd-4th years, and (2) there was a considerable amount of change in the diagnostic classification within the spectrum during this time period.

Specifically, diagnosis of autism was stable in 74% of cases, PDD-NOS in 83% of cases, and 89% of those initially meeting criteria for other Non-ASD retained the Non-ASD diagnosis at follow-up. A majority of children presenting with symptoms of autism in the

second year of life continued to do so at follow-up. Also, marked worsening of social dysfunction symptoms was observed in 17% (3 out of 18) of children initially diagnosed with PDD-NOS, warranting diagnosis of autism at follow-up. Eleven percent (3 out of 28) of non-ASD cases were classified as ASD cases at follow-up. There are, however, several encouraging findings regarding the short-term outcome amongst toddlers diagnosed with ASD in the 2nd year. No marked worsening of symptoms was noted in 83% of children given a provisional diagnosis of PDD-NOS, suggesting that toddlers who present with a milder form of social disability early on are unlikely to develop full symptoms of autism within the 1–2-year period. Another encouraging statistic is that 26% of toddlers who presented with severe symptoms of autism in the 2nd year showed marked improvement warranting change of the diagnosis to PDD-NOS.

Stability of verbal and nonverbal levels of functioning

Amongst the best predictors of outcome in ASD are the levels of cognitive and language skills. However, it is not clear how stable these indices of functioning are when ascertained in the second year of life. A mixed model ANOVA with between-group factor of diagnosis and within-group factor of time on the verbal DQ scores indicated a significant effect of time, $F(1, 158) = 38.14$, $p < .001$ and diagnosis, $F(2, 158) = 13.13$, $p < .001$ (see Table 3). Verbal DQ scores increased significantly in all groups from Time 1 to Time 2. The autism group had scores that were significantly lower than the PDD-NOS ($p < .001$) and NON-ASD ($p < .008$) groups and the PDD-NOS and NON-ASD group differed marginally ($p < .070$). An analogous analysis on the nonverbal DQ scores indicated no significant changes over time but significant differences between diagnostic groups, $F(2, 158) = 8.44$, $p < .001$. The autism group had scores lower than PDD-NOS ($p < .001$) and marginally lower than the Non-ASD group ($p < .054$). The PDD-NOS and Non-ASD groups did not differ significantly ($p < .164$). Thus, simple group comparisons reveal significant increase over time in verbal DQ scores, suggesting rapid pace of language development in the third and fourth years of life in children with initial language delays, regardless of the diagnosis. No significant changes over time were noted in DQ scores in the nonverbal domains; notably, however, the delays in this domain at Time 1 were not as profound as in the verbal domain. However, judging from the magnitude of the standard deviations associated with average verbal and nonverbal DQ scores, toddlers in our sample presented with a wide range of levels of functioning at both times. Correlational analysis (see Table 3) suggests that while the association between Time 1 and Time 2 scores in all groups was statically significant, the magnitude of the association differed depending on the group. The association between Time 1 and 2 scores was the lowest in the autism group where the Time 1 scores accounted for approximately 12% and 22% of variance in the nonverbal and verbal domains, respectively at Time 2. A stronger association was found in the Non-ASD group, where Time 1 scores accounted for 26% and 44% in verbal and nonverbal domains, respectively. The greatest stability of DQ scores was noted in the PDD-NOS group, with Time 1 scores accounting for 59% and 46% in the nonverbal and verbal domains, respectively. This suggests that the autism group was the most heterogeneous with respect to the amount of progress made by the time of their confirmatory assessment. We return to this point in the subsequent section.

Characteristics of toddlers with stable and unstable diagnostic outcomes

Our second goal was to identify areas of functioning at Time 1 that were associated with the diagnostic outcome at the age of 3 to 4 years. As seen in Table 2, diagnostic grouping based on the confirmatory diagnosis alone would result in highly heterogeneous groups in terms of their characteristics at the time of their first diagnosis. To reduce hetererogeneity in the sample, we explored a sub-grouping strategy based on a combination of the provisional and confirmatory diagnoses. That is, toddlers were divided into those with a stable diagnosis (e.g., autism at both time points) and those where diagnosis changed over time (e.g., autism to PDD-NOS), resulting in the following breakdown: autism stable group (AUT–AUT, N = 32), PDD-NOS stable group (PDD–PDD, N = 15), Autism–PDD-NOS cross-over group (AUT–PDD, N = 11), and Non-ASD stable group (NON–NON, N = 25), (total N = 83). The remaining 6 children (originally given either PDD-NOS or Non-ASD diagnoses) showed worsening of social dysfunction symptoms over time. Their presentation will be addressed in the Discussion, but the sample was too small and too heterogeneous for meaningful statistical comparisons.

There were no differences, in the time lapsed between the assessments, gender, gestational age, onset of independent walking, and age when parents noted first concerns (see Table 4). On average, 38% of infants were firstborn. There were no differences between groups regarding the average hours of intervention, though the program intensity in the NON– NON group was marginally lower than in the ASD groups.

Social interaction, communication, and stereotyped behaviors—Analysis of the Social Affect scale of the ADOS-G at Time 1 revealed that the groups differed significantly in the extent of social abnormality symptoms, $F(3, 81) = 26.10$, $p < .001$ (see Table 5). Not surprisingly, the autism stable group had higher SA scores than those with stable PDD-NOS, and those with stable Non-ASD diagnosis had lower SA scores than those with PDD-NOS. Though, there were no significant differences between autism stable and autism cross-over groups. The effect of diagnosis was also significant in the RRB domain, $F(3, 81) = 9.53$, $p < .001$, but in this domain autism stable had the highest scores, with the cross-over group showing similar levels of RRBs as the PDD–PDD and NON–NON groups.

Nonverbal communication—Analysis of frequency of communicative bids indicated a significant effect of group, $F(3, 82) = 5.16$, $p < .003$ (see Table 6). Planned contrasts suggest that the autism cross-over group had more profound impairments in this area compared to the autism stable group. Frequency of communicative bids was significantly higher in the PDD–PDD and NON–NON groups than the autism groups. Both Joint Attention ($F(2, 82) = 19.07$, $p < .001$) and gestural communication ($F(3, 82) = 9.06$, $p < .001$) were impaired differentially, with both autism groups having greater impairments in this area than the PDD-NOS stable and Non-ASD stable groups.

Developmental profiles—A 4 (group) × 4 (scale) ANO-VA with repeated measures on the last factor indicated a significant effect of group, $F(3, 77) = 6.29$, $p < .001$, scale, $F(3, 231) = 90.27$, $p < .001$, and group × scale interaction, $F(9, 231) = 4.71$, $p < .001$. Analysis of the developmental profiles at Time 1 (see Figure 1) suggest significant differences

between children with stable autism, PDD-NOS, and Non-ASD diagnoses, but not between the autism stable and cross-over groups. Profile analysis in the AUT–AUT group indicated a significant effect of scale, $F(3, 93) = 53.29$, $p < .001$; planned contrast comparing VR with FM, FM with EL, and EL with RL scales indicated a significant advantage of nonverbal over verbal skills and higher scores in the expressive than receptive language domains (VR = FM > EL > RL). Analysis of correlations between scores at Time 1 and Time 2 indicates significant associations between scores (see Table 6) with effect sizes ranging from medium to large (Cohen, 1988; 1992).

In the AUT–PDD group the effect of scale was also significant, $F(3, 30) = 68.09$, $p < .001$, with a very similar profile as in the AUT–AUT group, VR = FM > EL > RL. However, the pattern of correlations between scores at Time 1 and Time 2 indicates that in this group DQ scores at Time 1 were the least predictive of their scores at Time 2 (see Table 6).

Significant differences between scales were also noted in the PDD–PDD ($F(3, 42) = 5.34$, $p < .003$) and NON–NON ($F(3, 72) = 25.74$, $p < .001$) groups; though the profiles were different in each group. In the PDD– PDD group the advantage of nonverbal over verbal skills was also significant; however, their expressive and receptive skills were comparable (VR = FM > EL = RL). Similarly as in the autism stable group, the correlations between DQ scores at Times 1 and 2 were large (see Table 6).

In comparison, in the NON–NON group nonverbal skills exceeded verbal skills, but expressive language skills tended to be lower than receptive skills, a pattern that was reversed in the two autism groups (VR = FM > EL < RL). In this group the scores at Time 1 were also moderately predictive of their levels of functioning at Time 2 (Table 6).

Thus, the primary differences in developmental skill profiles that seemed to differentiate between the autism stable, PDD-NOS, and Non-ASD diagnostic groups were the relationship between the ability to understand and respond to speech and the level of expressive language. Notably, the profiles were very similar in the autism stable and autism cross-over groups. DQ scores at Time 1 constituted moderately good predictors of the levels of functioning in all areas at Time 2 in all groups, except for the autism cross-over group.

Discussion

Stability of the clinical diagnosis

The study addresses diagnostic and developmental outcomes of toddlers diagnosed with ASD and Non-ASD disorders in the second year of life. Assembling the sample at the time of the first diagnosis allowed for the inclusion of children with both rapid and slow improvement rates as well as with a wide range of severity of symptoms and cognitive impairments, enhancing the generalizability of the results to the broader population of same-age children presenting for a differential diagnosis. Syndrome expression was quantified prospectively through a direct assessment procedure eliminating confounds associated with retrospective data collection or repeated parental reporting on the severity of symptoms. Furthermore, inclusion of a Non-ASD group allowed for examining specificity of the impairments observed in the early stages of ASD.

All children who presented with symptoms of ASD at the time of their first diagnosis continued to display symptoms of social disability at the age of 3 to 4 years. Provisional clinical diagnosis of autism was stable in 74% of cases as compared to 83% of PDD-NOS. Amongst children who initially exhibited language or other developmental delays, 81% continued to have difficulties not related to ASD at follow-up, though in many cases the difficulties were considered minor or residual. Stability of autism diagnosis is roughly consistent with a majority of previous reports on both short-term (i.e., from 2–3 to 4 years: 72–87%) (Cox et al., 1999; Eaves & Ho, 2004; Lord, 1995; Stone et al., 1999) and long-term outcome (i.e., from 2 to 7 or 9 years: 85–89%) (Charman et al., 2005; Lord et al., 2006; Turner et al., 2006). However, stability of the PDD-NOS diagnosis was higher than in previous studies where low stability has been associated either with true PDD-NOS cases being missed at Time 1 (Cox et al., 1999) or true autism cases being classified initially as PDD-NOS (Eaves & Ho, 2004; Lord, 1995; Stone et al., 1999).

Despite the high overall stability of the ASD diagnosis, considerable changes in clinical presentation were noted within the spectrum. We observed marked worsening of symptoms in 17% of toddlers who initially met criteria for PDD-NOS, and noted emergence of frank social disability symptoms in 11% of cases initially diagnosed with a Non-ASD disorder. A careful examination of the individual scores of three children with PDD-NOS who received diagnosis of autism at follow-up suggests that the severity of social disability symptoms increased over time despite marked progress in verbal and nonverbal skills. In the Non-ASD cohort, in one case the symptoms of autism were masked at Time 1 by severe developmental delays (MA < 12 months), in two others, development of social skills failed to progress at the anticipated rate, leading to a PDD-NOS diagnosis at follow-up. However, we also found that due to a major improvement in social–communicative functioning, approximately 1/4 of children who were initially diagnosed with autism received a diagnosis of PDD-NOS at follow-up. While the phenomenon of shifting between diagnostic categories might be attributed to a limited sensitivity and specificity of the diagnostic criteria employed by the clinicians involved in the assessment, we would like to argue that these changes can instead be attributed to the natural variation in the course of ASD. The results of the standardized assessment support this notion, documenting significant changes in severity of social-affective, repetitive and stereotyped behaviors as well as the levels of verbal and nonverbal functioning occurring within the first years of life in this sample.

While dramatic improvements in social– communicative functioning was noted in the group with provisional diagnosis of autism and a vast majority of children presenting with milder symptoms did not worsen over time, none of the children in our sample appeared symptom-free at follow-up. Many made remarkable progress in multiple areas and some appeared quite competent when interacting with highly supportive adults in a context of structured interactions. Nonetheless, their social impairments persisted, manifesting primarily in limited grasp of the pragmatics of communication, limited motivation or ability to initiate and sustain reciprocal social interactions, rigid or repetitive play schemas, and inflexible adherence to routines. While a small minority of children might not meet full ASD criteria in middle childhood (Charman et al., 2005; Lord et al., 2006; Turner et al., 2006), the ultimate test of their fragile social–communicative skills is still to come as they enter kindergarten and face challenges of a complex peer and academic environment.

Developmental profiles of children with stable and unstable diagnosis

Toddlers with a stable autism presentation exhibit marked social impairments accompanied by clinically relevant levels of restricted and repetitive behaviors already in the second year of life. Their social impairments often manifest in a context of relatively spared nonverbal skills and profoundly delayed verbal skills. Their ability to understand and respond to language is typically more impaired than their expressive skills. The latter finding is not surprising as the early receptive language items of the Mullen Scales probe for orienting to name, responsivity to speech, and understanding of simple requests and gestures, the skills which are typically deficient in infants and toddlers with autism (Nadig et al., 2007; Paul et al., 2007; Wetherby et al., 2004). At the same time, toddlers with autism are often capable of producing a range of consonant sounds as well as word approximations (Charman, Baron-Cohen et al., 2003; Charman, Drew, Baird, & Baird, 2003), which is reflected in the expressive language scores, even though these vocalizations may be rarely used communicatively (Paul et al., 2007; Wetherby et al., 2004). Our results indicate that the verbal-nonverbal discrepancy and severe impairments in receptive language that have been reported in older children with autism (Charman, Drew et al., 2003; Joseph, Tager-Flusberg, & Lord, 2002; Lord & Paul, 1997) can already be detected in late infancy.

Children with a consistent PDD-NOS presentation differed in the 2nd year from those with autism-stable diagnosis along a number of dimensions, including two obvious ones: lower level of repetitive and restricted behaviors and less severe social-affective impairments. Amongst the others were: higher level of verbal and nonverbal cognitive skills, as well as comparable levels of receptive and expressive language skills, higher frequency of communicative bids and joint attention acts, and more frequent use of communicative gestures. These findings suggest the relative advantage of toddlers with PDD-NOS over those with autism in the early development of verbal and nonverbal communication (Charman, Baron-Cohen et al., 2003).

Perhaps the most intriguing was the group of toddlers in the autism cross-over group. Neither the standard assessment instruments nor expert clinicians differentiated between this group and the autism-stable group at Time 1. Their social deficits were severe and their developmental profiles indicated relatively spared non-verbal skills and profoundly delayed language skills. However, careful examination of their performance suggested several important differences from the autism-stable group. They displayed fewer stereotyped behaviors, which we have shown previously to be related to more positive language outcomes in our cohort (Paul, Chawarska, Cicchetti, & Volkmar, 2008). Nonetheless, their overall frequency of spontaneous communication was very low. They also showed more profound difficulties in understanding and responding to language: their age equivalent scores in the receptive language domain was 5.2 months (SD = 2.5) as compared to 10.4 months (SD = 6.6) in the autism-stable group, with expressive skills at a 9-month level (M = 8.7, SD = 4.2), while those of the AUT–AUT group were approximately at a 12-month level (M = 12.2, SD = 6.6). Thus, it appears that most of the toddlers in the cross-over group were still in the pre-intentional stage of communication (Bates, 1979) at the time of their first assessment, whereas those in the autism-stable group, while still delayed, were beginning to show emerging communication skills as seen in children between 8 and 12 months of age.

The notion that this very impaired group would make such striking progress is counterintuitive, as one might expect that children with more profound delays in communication would have a poorer outcome than those with less severe impairments. While the hypothesis will need to be examined directly in the future, it could be the case that in a minority of toddlers experiencing extreme delays in communication, symptoms of social dysfunction are exacerbated by their profound difficulty in consistently directing attention to, and deriving meaning from, spoken language along with a rudimentary grasp of intentional communication. Once these toddlers begin to derive some meaning from the language around them, and to see the effects on others of their emerging communicative actions, the rewarding outcomes of these behaviors may propel their social development by rendering exchanges with others more functional and relevant for adaptation. Acquisition of communication skills by no means 'resets' their development to a typical trajectory, but did seem to result in gains that were consequential for their overall level of cognitive and social functioning. This finding suggests that caution should be taken when making predictions regarding diagnostic and cognitive outcomes of children under the age of 2 years who present with profound delays in responsivity to, and understanding of, language combined with very low frequency of communication, particularly if marked social-affective impairments are not paired with pronounced stereotyped and repetitive behaviors. Since our findings suggest that increases in communicative skills may pave the way for significant improvements in social skills, intense intervention in nonverbal communication may be especially effective for such children. The identification of the group of toddlers whose presentation can change markedly within a short period of time might index the presence of a specific subtype within the spectrum, possibly associated with different etiological factors. Future studies will have to address in a systematic and prospective manner genetic, neurobehavioral and clinical factors associated with this developmental pattern.

Differentiation between toddlers with ASD from toddlers affected by a variety of developmental non-ASD difficulties is critical both for clinical practice and research applications. Toddlers with non-ASD disorders differed primarily in the level of social functioning from all of the ASD groups, but not in the level of repetitive behaviors. However, their expressive-receptive language pattern was unlike in any of the ASD groups and it was characterized by better understanding and responsivity to language than production of language.

Conclusions

Stability of broadly defined ASD diagnosis is very high in toddlers referred for a differential diagnosis prior to or shortly after their second birthday, though marked changes in the severity of social disability symptoms are to be expected in a minority of the sample. Toddlers with autism and PDD-NOS present with distinct profiles of skills and disabilities, which appreciation can greatly enhance the accuracy of the diagnostic classification in the second year of life and prediction of their cognitive and language outcomes. Clinicians can reassure parents that marked symptoms of social disability and cognitive delays in toddlers are not necessarily predictive of their later functioning, and that milder symptoms and higher cognitive skills in the second year of life bode well with the short-term outcome. Clinicians should also stress the importance of intervention focused on development of intentional

communication, as well as on development of attention to language and receptive language skills. Finally, considering that the field of early diagnosis is emerging and that sensitivity and specificity of the diagnostic criteria for children under the age of 2 are still to be fully examined and codified, we hope that these results will contribute to the ongoing discussion of the best practices regarding early diagnosis of developmental disorders.

Limitations

Toddlers described in this study were referred to a specialized university-based clinic due to history of developmental problems; thus, the findings might not generalize fully to populations of toddlers ascertained though primary screening procedures or prospective monitoring of younger siblings with ASD. Such samples are likely to include a greater proportion of children with sub-clinical and less stable clinical presentation (Zwaigenbaum et al., in press). The sample, however, included children who, due to history of developmental delays and atypical behaviors, triggered concerns amongst parents, pediatricians, early intervention or daycare providers, which represents a typical cohort presenting for a differential diagnosis in infancy. While confirmatory clinical diagnosis was not entirely independent from the provisional diagnosis, only one clinician participated in both assessments and a consensus among three clinicians was necessary for the diagnostic assignment.

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Key points

- In toddlers referred for a differential diagnosis before or around their second birthday, stability of a broadly defined ASD diagnosis is high.
- A majority of toddlers who exhibit symptoms of autism early on continue to do so during preschool years; however, in a minority of these cases, marked improvement in social-affective skills can be expected.
- A majority of toddlers presenting with milder symptoms consistent with a PDD-NOS diagnosis continue to display less severe social disability symptoms and maintain good rate of progress in terms of verbal and nonverbal skills in preschool.
- Analysis of developmental skills profiles in conjunction with type and severity of social-affective and stereotyped and repetitive symptoms can greatly enhance the accuracy of both the clinical diagnosis in the second year of life and the prediction of diagnostic and developmental outcomes in preschool.
- Results emphasize the importance of early intervention focused on developing attention and responsivity to language and fostering intentional communication in young children with ASD.

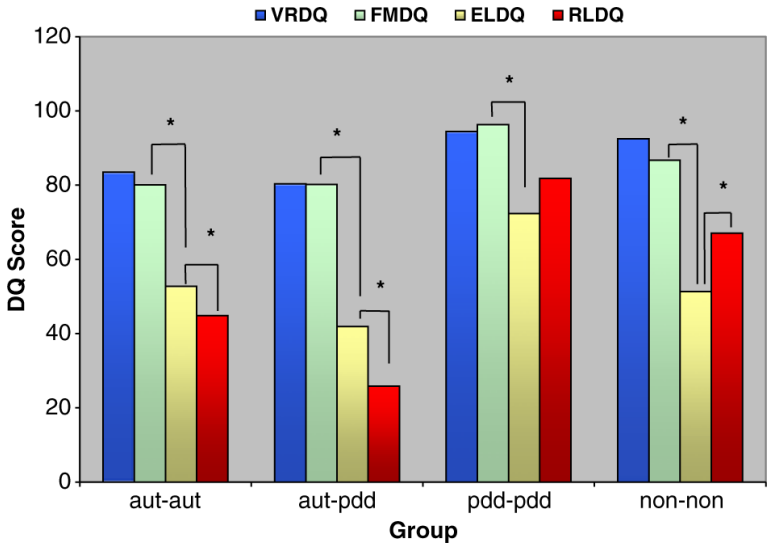

Figure 1.

Mullen Scores profiles in the outcome groups at Time 1 in the groups based on a combination of provisional and confirmatory diagnosis

Table 1

Sample characterization at the time of confirmatory diagnosis

	Time 2 confirmatory diagnosis		
Measure	**Autism *N* = 36**	**PDD-NOS *N* = 28**	**Non-ASD *N* = 25**
ADOS-G * Social Affect [#Module 2 / #Module 1]	13.6 (3.8)[a] [13/23]	8.6 (3.1)[b] [22/6]	4.5 (5.4)[c] [16/9]
ADOS-G * Restricted/Repetitive	5.2 (1.8)[a]	2.9 (1.9)[b]	1.9 (1.9)[b]
ADI Social	13.4 (6.3)[a]	7.4 (4.7)[b]	5.0 (4.5)[c]
ADI Communication	10.5 (4.5)[a]	8.2 (5.2)[b]	6.3 (4.1)[b]
ADI Restricted/Repetitive	5.8 (2.7)[a]	5.01 (2.2)[b]	3.0 (2.4)[b]
Verbal DQ **	68 (29)[a]	99 (18)[b]	91 (31)[b]
% with VDQ > 70	42	96	88
Nonverbal DQ **	75 (21)[a]	99 (16)[b]	89 (25)[b]
% with NVDQ > 70	56	96	88
Vineland Communication	80.8 (19)[a]	94.3 (14)[b]	88.2 (18)[ab]
Vineland Daily Living	64.2 (8)[a]	71.9 (9)[b]	73.3 (12)[b]
Vineland Socialization	66.3 (10)[a]	76.9 (9)[b]	78.2 (13)[b]
Vineland Motor	67.6 (14)[a]	78.7 (12)[b]	73.4 (18)[ab]
Intervention (hrs/week)	14.5 (7.5)[a]	12.4 (10.1)[a]	8.9 (10.9)[a]

Within each domain, group means marked by different superscripts differ significantly at least at the $p < .05$ level.

* ADOS-G scores reflect either Module 1 or Module 2, depending on the child's level of functioning. The numbers in brackets reflect the number of Module 2 and Module 1 assessments administered in a given group.

** Verbal DQ is based on EL and RL domains; Nonverbal DQ is based on VR and FM domains of the Mullen Scales.

Table 2

Stability of the provisional clinical diagnosis of autism, PDD-NOS, and Non-ASD

Provisional diagnosis at Time 1	Confirmatory diagnosis at Time 2 *N* (%*)			
	Autism	**PDD-NOS**	**Non-ASD**	**Total**
Autism	**32 (74%)**	11 (26%)	0 (0%)	**43**
PDD-NOS	3 (16%)	**15 (83%)**	0 (0%)	**18**
Non-ASD	1 (4%)	2 (7%)	**25 (89%)**	**28**
Total	**36**	**28**	**25**	**89**

* Percentage represents an index of stability of the Time 1 provisional diagnosis.

Table 3

Stability of the verbal and nonverbal DQ scores in toddlers diagnosed in the second year

	Verbal DQ			Nonverbal DQ		
Time 1 provisional diagnosis	**Time 1 M(SD)**	**Time 2 M(SD)**	**Pearson's *r***	**Time 1 M(SD)**	**Time 2 M(SD)**	**Pearson's *r***
Autism *N* = 43	45 (24)	76 (29)	.35 *	81 (13)	81 (22)	.47 **
PDD-NOS *N* = 18	72 (29)	97 (21)	.70 ***	97 (19)	100 (20)	.73 ***
Non-ASD *N* = 28	59 (27)	89 (31)	.51 **	88 (21)	88 (25)	.66 ***

* $p < .05$,

** $p < .01$,

*** $p < .001$.

Table 4

Sample characteristics based on the combination of provisional and confirmatory diagnoses

	Outcome group			
	AUT–AUT	**AUT–PDD**	**PDD–PDD**	**NON–NON**
	***N* = 32**	***N* = 11**	***N* = 15**	***N* = 25**
Age at Time 1 (mo)	23.2 (4)	20.6 (3)	22.1 (4)	20.9 (5)
Age at Time 2 (mo)	48.8 (7)	48.5 (9)	47.5 (8)	44.1 (7)
Time between T1 and T2 assessments (yrs)	2.2 (.63)	2.33 (.51)	1.93 (.38)	2.12 (.51)
Gender (% Male)	75	90	87	74
First concern (mo)	11.6 (5.3)	12.0 (5.4)	11.4 (4.8)	9.0 (4.8)
Firstborn (%)	41	27	47	35
Children receiving intervention[1]	100%	100%	100%	86%
Intervention[2] (hrs/week)	14.5 (8)	14.2 (11)	11.2 (10)	8.5 (10)
	Min: 4	Min: 2	Min: 3	Min: 0
	Max: 32	Max: 36	Max: 35	Max: 30

[1] Intervention including ABA, special education, speech and language, play therapy, social skills therapy, occupational and physical therapy.

[2] Averages calculated over the entire period elapsing between provisional and confirmatory diagnosis. Intensity of intervention differed within this period for each child.

Table 5

Mean (SD) algorithm ADOS-1 scores and communication indices at Time 1 in the groups based on a combination of provisional and confirmatory diagnoses

ADOS-G Module 1	AUT–AUT (A)	AUT–PDD (B)	PDD–PDD (C)	NON–NON (D)	Planned contrast
Social affect	17.06 (2.7)	17.09 (3.1)	11.33 (4.5)	7.88 (5.7)	A = B
					B > C
					C > D
Restricted and repetitive behaviors	4.34 (1.9)	2.81 (2.1)	2.60 (1.8)	1.58 (1.9)	A < B
					B = C
					C = D
Frequency of communication	.72 (.96)	1.45 (.1.3)	.13 (.35)	.40 (.86)	A < B
					B > C
					C = D
Joint attention	3.38 (.89)	3.27 (1.2)	1.73 (1.5)	1.24 (1.5)	A = B
					B > C
					C = D
Gestural communication	1.69 (1.1)	1.81 (.98)	.60 (.74)	.60 (.95)	A = B
					B > C
					C = D

Table 6

Pearson's r correlation coefficients between Mullen Scales scores at the time of provisional (Time 1) and confirmatory (Time 2) diagnostic assessments in four groups with stable and unstable diagnostic outcomes

Mullen Scales of Early Learning	AUT-AUT	AUT-PDD	PDD-PDD	NON-NON
Visual Reception	.68***	−.47	.56*	.53**
Fine Motor	.41*	.47	.58*	.57**
Expressive Language	.49**	.25	.70**	.43*
Receptive Language	.56***	−.11	.59*	.43*

* $p < .05$,

** $p < .01$,

*** $p < .001$.