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Early diagnosis of children with autism spectrum disorders

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Abstract

Research focusing on early development in children with Autism Spectrum Disorders (ASD) has been of particular interest in recent years. A greater understanding of the accuracy of early diagnosis, as well as the developmental pathways that are observed in young children with ASD, is of both theoretical and practical importance. In accordance with these concerns, this review addresses questions about three topics: the reliability of early diagnosis, the validity of using narrow versus broad diagnostic categories, and trajectories of development in children with ASD. Findings from two prospective longitudinal studies are reviewed. The first investigation included children referred for ASD at age 2 who were followed for one year. The second study followed children referred for ASD at age 2 until age 9. Results suggested that early diagnoses can be made reliably, that there is no empirical evidence for using narrowly defined diagnostic categories within ASD and that trajectories of development showed considerable heterogeneity.

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1. Introduction

In the last 10 years, there has been a tremendous interest in whether children with autism and autism spectrum disorders (ASD) can be identified at younger ages. This interest has arisen from consistent findings that many parents of children with ASD are aware of differences in their child's development long before the children receive appropriate diagnoses [1,2]. The path from a parent's early concerns to a diagnosis often takes several years as parents seek help from different sources and parents and professionals begin to recognize the specific symptoms of ASD. In addition, the focus on early identification and diagnosis has also been fueled by claims by interventionists that early entry into treatments can change the trajectory of development in ways that may not be possible in later years [3–5].

Three general issues are at the heart of research concerning early diagnosis in ASD. Each stems from the conceptualization of ASD as a *developmental* disorder. First, it is important to recognize that the symptoms manifested in ASD influence underlying developmental processes. That

is, mechanisms and patterns of learning and change are likely to be disrupted by the presence of ASD [6]. Developmental pathways in children with ASD may differ qualitatively or quantitatively or both from those with other developmental disabilities or typical development [7–9].

Second, the symptoms of ASD change with development. Just as we recognize development as a dynamic progression with changing behaviors and explanations, we must also recognize that this principle applies to profiles in ASD. For example, a 3 year-old with ASD may be diagnosed in part because of very limited pretend play. At age 10, the same child may have elaborate play schemes involving a cast of aliens he has invented, but his activity may be different from that of other 10 year-olds in its intensity and inflexibility. Theoretical models of ASD must accommodate this continuity and discontinuity.

Third, children with ASD are characterized by both the presence of abnormal behaviors, as well as the absence of typical behaviors [10,11]. Accurately assessing both positive and negative symptoms is central to identification and diagnosis of ASD. It is necessary to consider these traits in a broader developmental context, as well as their pervasiveness across a range of circumstances. That is, deficits in social reciprocity or communication, as well as

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the presence of restricted or repetitive behaviors, should be considered in terms of the child's overall level of cognitive and language skill, since many of the symptoms of autism can occur in nonASD conditions, such as severe mental retardation or language delay [8,12]. Furthermore, the child's behavior across different environments must be considered, because the deficits characteristic of ASD are not limited to one context (i.e., as one might see poor eye contact with strangers in a very shy typically developing child), though context may affect behaviors in children with ASD just as in other children [13,14].

Empirical findings regarding early trajectories of development in ASD are somewhat conflicted. Studies exploring the efficacy of treatment (i.e., applied behavioral analysis, or ABA) suggested that, with intensive intervention, children with ASD could show vast improvement, with some even appearing to have recovered [4,15]. In contrast, early longitudinal studies and investigations of preschoolers with ASD have indicated that children with ASD do not usually recover from the disorder [16,17]. Certain impairments (e.g., response to and initiation of joint attention, looking at faces, eye contact, response to name and pretend play) are pervasive across children and across time [18–21]. These conflicting portrayals result in strikingly different impressions of early trajectories in ASD according to non-overlapping bodies of literature [22]. Whereas the models presented in the treatment literature suggest discontinuity in development, characterized by a transition from ASD to “normality” – or at least a considerable reduction of impairment in a sizeable proportion of children initially diagnosed with autism – early longitudinal studies of young children with ASD suggested strong continuity in symptoms and overall level of impairment [18].

This review presents findings from two prospective longitudinal studies: (1) a one year follow up of 30 two year-old children referred to a developmental pediatric clinic because of concerns about autism and (2) a longitudinal study of two cohorts of children, consecutive referrals of all children under age 3 for autism, to 4 state-funded autism clinics in North Carolina and to a private university-based child psychiatry clinic in Chicago, who were followed up to age 9. The primary questions addressed are: Can autism and ASD be reliably diagnosed at age two? Is there a reason to distinguish narrowly defined autism from more broadly defined ASD in young children? And what are the trajectories associated with early development in ASD?

1.1. First early diagnosis study

The first prospective study on early diagnosis in ASD followed 30 children who were referred for autism at age 2 [20]. A full assessment, including direct assessment as well as parent interview, was done at entry to the study (when children were approximately age 2) and again 12–15 months later (when children were approximately age 3). Formal diagnoses, blind to earlier information, were made when the children were 3 years old, and group comparisons

were based on these follow up diagnoses. In an analysis of parent report data from the Autism Diagnostic Interview – Revised [23] collected at age 2, Lord found that the two best discriminators of diagnosis at age 2 were the child's attention to voice and the child's spontaneous direction of other's attention (through pointing, other gestures, language and/or shift in gaze). Using the same dataset, Lord, Risi and Pickles found that groups were also discriminated based on an inability to understand words out of context [7]. Similar analyses were conducted using ADI-R data collected when the children were 3 years old. The best discriminators of autism at age 3 were the child's attention to voice, pointing to express interest, hand and finger mannerisms and using another person's body as a tool [20]. Lord and colleagues also reported that diagnostic groups at age 3 were discriminated by a lack of spontaneous meaningful words [7]. Thus, though there were children with autism who spoke, children at age 3 who had *no* meaningful spoken words and who did not have multiple disabilities (e.g., cerebral palsy, hearing problems, known genetic syndromes) were likely to have autism.

1.2. Second early diagnosis study

A second prospective study was conducted with two cohorts of children, one from North Carolina ($n = 214$) and one from Chicago ($n = 83$). In an effort to expand upon the earlier study described above, multiple measures were used for diagnosis (including both parent report and direct observations), and the sample size and diversity was increased.

In addition, a nonspectrum comparison group was recruited that included children with a number of nonASD conditions, including language delay and mental retardation. Children entered the study at age 2 and were given a “best estimate” diagnosis, based on the results of the ADI-R, an early version of the Autism Diagnostic Observation Schedule (Pre-Linguistic ADOS, or PL-ADOS) [24] and clinical impression. Children were seen at age 3 and most were also seen at age 5. A follow up evaluation was conducted at age 9, and an age 9 “best estimate” diagnosis was made using similar procedures. Stability of diagnosis [autism, Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS) or nonspectrum] from age 2 to age 9 was explored, and diagnoses of ASD were very stable overall [25]. As shown in Fig. 1, a diagnosis of autism was the most stable of the three diagnostic categories. Of those children with an autism diagnosis at age 2, almost all retained an autism diagnosis at age 9, with a small minority receiving a PDD-NOS diagnosis at age 9 and only 1 child moving completely out of the autism spectrum at follow up.

Conversely, of those children who had an autism diagnosis at age 9, about three-quarters had an autism diagnosis at age 2 and one-quarter had a PDD-NOS diagnosis at age 2. Two children had received a nonspectrum diagnosis at age 2 (see Fig. 2).

PDD-NOS was significantly less stable as a diagnosis. Of those children who had a PDD-NOS diagnosis at age 2, more than half had shifted to a diagnosis of autism at age 9. Only one-quarter maintained their PDD-NOS diagnosis and a small minority received a nonspectrum diagnosis at follow up (see Fig. 1). Of those children diagnosed with PDD-NOS at age 9, nearly half had been diagnosed with autism at age 2, a third had been diagnosed with PDD-NOS at age 2 and about a quarter had initially been diagnosed as nonspectrum (see Fig. 2).

Based on the diagnostic data collected via parent report (i.e., ADI-R), structured observations (i.e., ADOS [26]) and clinician’s “best estimate,” it was possible to investigate the contribution of multiple sources of information to the initial diagnoses. Whereas both standardized instruments classified a fair number of children as having autism when neither of the other 2 sources did (8% of children by only the ADI-R, and 15% of children by only the ADOS/PL-ADOS), clinicians did this only 1% of the time (2 children out of 214). Not surprisingly, diagnoses which were confirmed across multiple sources were more reliable than those confirmed by only one or two. Furthermore, clinician’s judgment was the strongest contributor to a reliable diagnosis.

Because of the strong association between age 2 “best estimate” diagnosis and follow up diagnosis, analyses were conducted to explore the best age 2 predictors of an age 9 diagnosis of ASD if age 2 diagnosis was excluded. The predictors that emerged were the repetitive behaviors score

from the parent interview (i.e., the ADI-R) and social-communication and repetitive behaviors scores from the structured observation (i.e., the PL-ADOS, scored as Module 1 of the ADOS). Common examples in such young children included behaviors like hand mannerisms and repetitive object play. Though several studies have indicated that repetitive behaviors at age 2 are not universal in children who will later receive diagnoses of ASD [20,27,28], in fact, the presence of repetitive behaviors at 2 (either from parent report or direct observation) was clearly associated with a diagnosis of ASD at age 9.

Stability was also explored in terms of general severity of impairment (i.e., the distinction between autism and PDD-NOS). Data from an interim assessment at age 5 were used in these analyses. Results suggested greater instability from 2 to 5 than from 5 to 9. Between the ages of 2 and 5, 21% of children showed worsening in their symptoms of ASD, 13% appeared to improve, and the majority (65%) stayed the same. In contrast, between the ages of 5 and 9, 11% of children worsened, 8% improved and 81% stayed the same [25].

Similar variability was observed in verbal and nonverbal IQ, as well as PL-ADOS (analyzed as Module 1 of the ADOS) subtotals, another proxy for severity of social-communication symptoms [29]. Individuals were placed into groups based on patterns of change in verbal IQ – intercepts and slopes – from ages 2 to 9. Results of latent growth curves (SAS: PROC TRAJ) suggested diversity in profiles of change over time in all three areas of

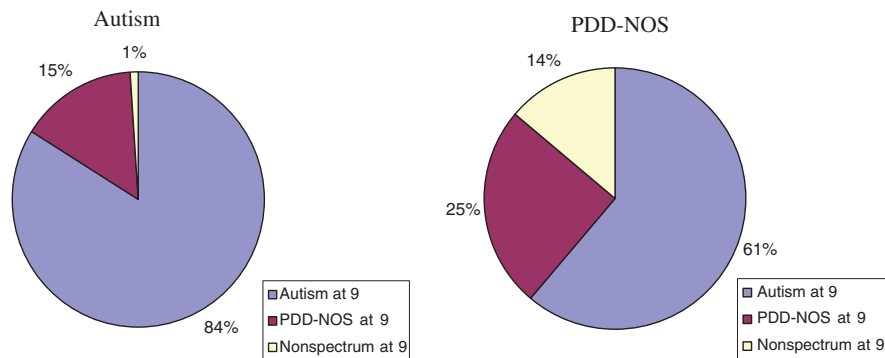


Fig. 1. Follow up (age 9) diagnoses of all children with age 2 diagnosis of autism and PDD-NOS.

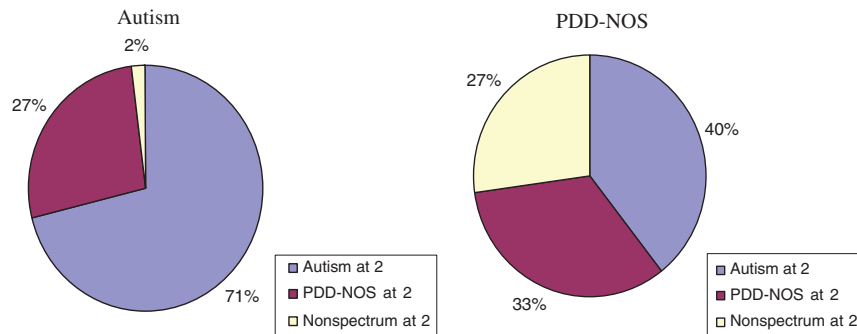


Fig. 2. Initial (age 2) diagnosis of all children with age 9 diagnosis of autism and PDD-NOS.

functioning. In verbal IQ (see Fig. 3), two parallel groups of children at different age 2 levels showed relatively rapid and parallel gains before the age of 5 and then slower but steady improvement up to age 9. A third group showed little change from 2 to 9, with a parallel but more delayed group showing consistent and profound impairment.

In nonverbal IQ, a more limited range of trajectories was observed (see Fig. 4). One group showed a marked increase in nonverbal IQ between the ages of 3 and 5 and then stayed fairly stable until age 9. Two other groups showed steady but nonsignificant decreases between age 2 and age 9.

Patterns of change in symptom severity as measured on the PL-ADOS/ADOS (with scores pro-rated because of differences in possible totals) during structured observa-

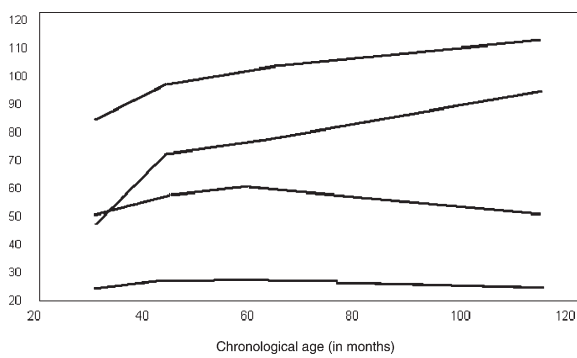


Fig. 3. Verbal IQ by chronological age (in months).

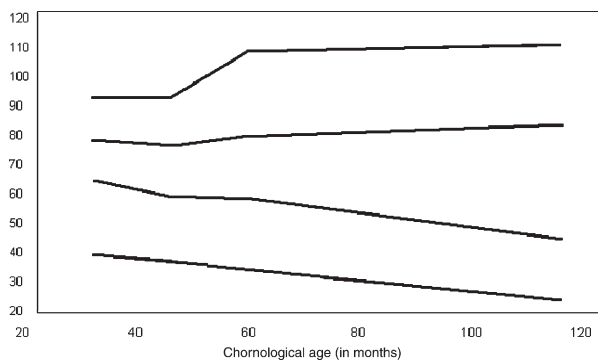


Fig. 4. Nonverbal IQ by chronological age (in months).

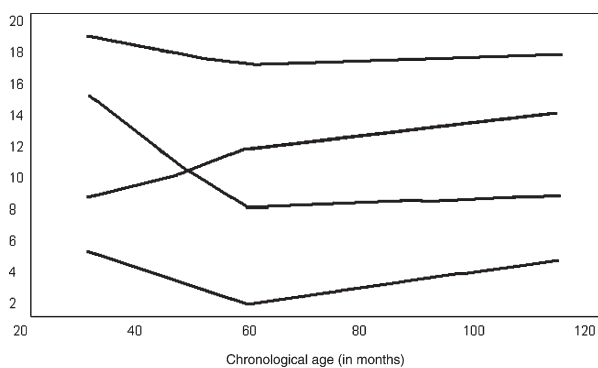


Fig. 5. ADOS subtotals by chronological age (in months).

tions were quite diverse, showing four distinct profiles (see Fig. 5). One group showed quite elevated (indicating a high level of abnormality) scores at age 2, which stayed fairly steady to age 9. A second group showed a striking drop between age 2 and 5 (suggesting a considerable lessening of symptoms), and then stability between the ages of 5 and 9. The social-communication symptoms of a third group appeared to worsen steadily between the initial and final assessment, with a more pronounced change between 2 and 5. A final group (who did not meet cut-offs for ASD) showed no significant change from 2 to 9.

A similar set of analyses used growth curve analyses to evaluate predicted and individual trajectories in language development [30]. Although the autism, PDD-NOS and nonspectrum groups started at similar language levels (measured in terms of age equivalent scores) at age 2, considerable group differences were observed in predicted language trajectories. The autism group showed a much slower rate of change and remained below the other two groups across all ages. The other two groups had similar profiles of language development, with the children with PDD-NOS showing a steeper slope until after age 5, resulting in them appearing to move slightly in advance of the nonspectrum group by age 9.

The individual language trajectories across diagnostic groups revealed the diversity and range of development. For the group with autism at 9, the majority of participants showed slow or no change over time and remained far below the expected path of development. However, some children with autism were not considerably behind the norm; there were even a few who were in advance of their age expectations. The children with PDD-NOS were more evenly distributed and did not fall as far behind as the children with age 9 autism diagnoses. Children with PDD-NOS were more often closer to the expected path of development, and fewer showed the flat trajectory of development observed in the children with autism. Individual trajectories in the heterogeneous group of children with nonspectrum disorders looked much like those observed in the PDD-NOS group, with a substantial number of children approximating age appropriate skills.

2. Conclusion

Prospective longitudinal studies yield valuable information about autism- and ASD-specific behaviors and trajectories that contribute to our ability to make early diagnoses and to our understanding of developmental pathways in ASD. Conclusions are organized in terms of the initial inquiries presented above.

2.1. Can autism and ASD be reliably diagnosed at age two?

The answer is “Autism and ASD can be diagnosed reliably at age 2, with some important caveats.” In the larger prospective study, the stability of age 2 diagnoses of autism was quite high (84%). Only 1% of children diagnosed with

autism at age 2 in this sample had a nonspectrum diagnosis at age 9. Similarly, the most common age 9 diagnostic outcome for children classified at age 2 with PDD-NOS was autism, though 14% received a nonspectrum diagnosis at age 9. An important caveat is that all of the children studied were identified as having some sort of developmental delay at age 2, and this study was begun over 10 years ago. It is impossible to know if children with symptoms of autism but who were not referred, or if children with milder difficulties who were referred in recent years, would show the same stability. Furthermore, many (but not all) of these children received early intervention, but few had intensive therapy. Most of those who did receive intensive intervention had more severe impairments even at age 2. Thus, the generalizability of these findings to children in 2006, especially those who have had high quality interventions, is not known. Nevertheless, the present results indicate that diagnoses of autism and PDD-NOS by experienced clinicians on the basis of multiple measures were valid and reliable over time. Overall, it appears that autism diagnoses made at age 2 are somewhat more reliable than PDD-NOS diagnoses. However, if a child is given an ASD diagnosis (either autism or PDD-NOS) at age 2, it is overwhelmingly likely to still apply at age 9, although there may be some shifting within the range of ASD diagnostic categories.

Although measures of repetitive behavior during structured observation (ADOS) and as reported in parent interviews (ADI-R) were not considered crucial for a diagnosis of autism at age 2, they were important predictors of diagnostic status at age 9. Restricted and repetitive behaviors (as measured by both instruments) emerged as two of the best predictors of an age 9 diagnosis of autism and of more broadly defined ASD. Early evidence of these repetitive behaviors contributes to diagnostic stability from early to middle childhood.

Furthermore, one of the most important elements of reliable early diagnosis was clinical judgment. It is worth noting, however, that the clinicians in the present investigations had considerable experience working with young children suspected of having ASD and had carried out evaluations lasting three to six hours using standardized measures. This finding may not be true for less experienced counterparts and/or less intensive, structured or standardized evaluations.

2.2. Is there a reason to distinguish narrowly defined autism from more broadly defined ASD in young children?

Children diagnosed with autism at 2 showed more stability in diagnosis, with the vast majority retaining an autism diagnosis at 9 and only 1 child receiving a follow up diagnosis of nonspectrum (in this case, the diagnosis changed between 2 and 3 from autism to PDD-NOS and from 3 to 5 from PDD-NOS to typical development). In contrast, children with PDD-NOS had a greater likelihood (1 in 6) of shifting into a nonspectrum diagnosis. In contrast though, the majority of children with PDD-NOS at 2 (61%) were

given an autism diagnosis at follow up, suggesting that development resulted in increasingly clear expression of autistic symptoms. Furthermore, there were differences in both predicted and observed language trajectories across the autism and PDD-NOS groups, with the PDD-NOS group showing more typical development, less likelihood of continued profound impairment and more children approximating or exceeding age expectations in language development and nonverbal problem solving.

Generally, then, it appears that the overall picture of development for the autism and PDD-NOS groups is similar, with most children experiencing continued impairment. The PDD-NOS group, however, had more children who were doing relatively better at age 9. Based on these two studies, there does not appear to be evidence for qualitatively discrete groups (i.e., autism versus PDD-NOS). In the studies described here, PDD-NOS was used to refer to a less-impaired group of children at age 2, particularly in social-communication and restricted and repetitive behaviors, but also in terms of verbal and nonverbal IQ. Early differences in severity had important implications for the likelihood of improvement. Clinical “best estimate” of PDD-NOS at age 2 was associated with a 1/6 chance of receiving a nonspectrum at age 9 and an additional 1/6 likelihood of having mild symptomatology, while the chances of a child with an age 2 autism diagnosis making such improvements by age 9 were much less.

2.3. What are the trajectories associated with early development in ASD?

The majority of children showed stability in the degree of impairment from 2 to 5 and from 5 to 9. Of those who showed pronounced change from one period to the next (both from 2 to 5, and from 5 to 9), the majority appeared to develop more recognizable symptoms. Trajectories of change in verbal and nonverbal IQ indicated that approximately one-third of children showed improvement from age 2 to age 9, with the other two-thirds evidencing steady patterns of impairment. Similarly, language ability showed continued impairment for the majority of children, although some did show steady improvement over time. It is worth noting that a significant minority of our sample had relatively mild or no symptoms at age 9.

There is tremendous heterogeneity in the development of children who receive an early diagnosis of ASD. It has become increasingly clear that an accurate diagnosis must be made on the basis of the three primary areas of impairment (rather than solely on the presence of social or communication deficits). Consideration must also be given to the degree of nonverbal impairment – which can range from none at all to profound – and the extent of language delay, since both of these developmental realms can influence the profile of skill and behavior. It is crucial that these domains, which require assessment beyond that which most physicians can provide, be adequately described and used in both research and treatment planning. The present

research suggests patterns of development in children with ASD which differ according to early mastery and severity of impairment. Some of these pathways can be predictably associated with slight or considerable improvement for certain groups of children. That we can expect gains for some children with ASD (particularly in a sample which was not characterized by intensive early intervention) is heartening; however, the next challenge for researchers and practitioners is to work towards interventions that can lead to greater improvement for more children.

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