Original Investigation

Developmental Trajectories of Symptom Severity and Adaptive Functioning in an Inception Cohort of Preschool Children With Autism Spectrum Disorder

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IMPORTANCE Symptom severity and adaptive functioning are fundamental domains of the autism spectrum disorder (ASD) phenotype. To date, the longitudinal association between these 2 domains has not been examined.

OBJECTIVE To describe the developmental trajectories of autistic symptom severity and adaptive functioning in a large inception cohort of preschool children with ASD.

DESIGN, SETTING, AND PARTICIPANTS The sample consisted of 421 newly diagnosed preschool children with ASD 2 to 4 years old (355 boys; mean age at study enrollment, 39.87 months) participating in a large Canadian multisite longitudinal study (Pathways in ASD Study). Prospective data collected at 4 points from time of diagnosis to age 6 years were used to track the developmental trajectories of children.

MAIN OUTCOMES AND MEASURES Autistic symptom severity was indexed using the Autism Diagnostic Observation Schedule. Adaptive functioning was indexed using the Vineland Adaptive Behavior Scales, Second Edition.

RESULTS Two distinct trajectory groups provided the best fit to the autistic symptom severity data. Group 1 (11.4% of the sample) had less severe symptoms and an improving trajectory ($P < .05$), whereas group 2 (88.6% of the sample) had more severe symptoms and a stable trajectory. Three distinct trajectory groups provided the best fit to the adaptive functioning data. Group 1 (29.2% of the sample) showed lower functioning and a worsening trajectory, group 2 (49.9% of the sample) had moderate functioning and a stable trajectory, and group 3 (20.9% of the sample) had higher functioning and an improving trajectory ($P < .05$). Cross-trajectory overlap between the autistic symptom severity and adaptive functioning groups was low ($\varphi = 0.13$, $P < .05$). Sex was a significant predictor of autistic symptom severity group membership and age at diagnosis, and language and cognitive scores at baseline predicted membership in adaptive functioning trajectories. Trajectories of both symptom severity and adaptive functioning predicted several different outcomes at age 6 years.

CONCLUSIONS AND RELEVANCE Findings confirm the heterogeneous nature of developmental trajectories in ASD. Change in adaptive functioning suggests that improvement is possible in roughly 20% of the sample. Autistic symptom severity appears to be more stable, with roughly 11% of the sample showing a marked decrease in symptom severity. During the preschool years, there appears to be only a small amount of "yoking" of developmental trajectories in autistic symptom severity and adaptive functioning. It is imperative that a flexible suite of interventions that target both autistic symptom severity and adaptive functioning should be implemented and tailored to each child's strengths and difficulties.

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Although a small proportion of children with autism spectrum disorder (ASD) will go on to lose the diagnosis at some point during their life,[1] the limited but informative body of literature on adult outcomes suggests that ASD is a lifelong condition that involves persisting and stable impairments in language, social skills, educational attainment, and activities of daily living.[2-4] A recent comprehensive review[5] concluded that the long-term outcome in ASD is mixed, including for individuals with typical IQ, and that most persons diagnosed as having ASD as children are unable to live and function as independent adults.[6,7] These findings highlight the heterogeneity in developmental outcomes in ASD. A common pattern in outcome studies using data at 2 time points is the identification of a lower-functioning group with persisting autistic symptoms that tends to be stable and a higher-functioning group that starts with fewer symptoms and has better adaptive functioning over time.[8,9] Cross-sectional analyses demonstrate a high inverse correlation between autistic symptom severity and adaptive functioning, reinforcing the clinical impression that autism represents a single spectrum encompassing these 2 phenotypic domains.[10,11] In these follow-up investigations, IQ and language skills appear to be the strongest predictors of outcome.[12] However, little is known about variables other than IQ and language that account for variability in outcomes for children with ASD.

More recent longitudinal investigations with multiple data points and longer follow-up periods show that the degree of heterogeneity in ASD outcome is even more striking than previously believed, as reviewed by Waterhouse.[13] Studies carried out by Lord and colleagues[14] on language, autism severity scores, and cognition, as well as investigations performed by Fountain et al[15] on social and communication skills and repetitive behaviors, illustrate the remarkable diversity in levels of these developmental domains and rates of change among children with ASD. In the most recent study to date by Gotham and colleagues,[16] four different trajectories for autistic symptom severity were identified in a sample followed up from age 2 to 15 years. Meanwhile, Fountain et al[15] described 6 different trajectories across the same age range using social and communication skills and repetitive behaviors as outcomes.

Modeling change over several points in time needs to take into account the multifaceted nature of ASD to truly characterize variation in the natural history of ASD. There is not only potential heterogeneity among a population of children with ASD within a single domain but also potential heterogeneity across different domains over time. These findings are consistent with recent investigations emphasizing the phenotypic independence of different dimensions that make up the ASD construct.[17] Three key methodological issues limit the generalization of findings from many of the available outcome studies in ASD, namely, sampling frame, sample size, and methods of assessment. Most previous studies have recruited participants at different points in the natural history of their disorder. Without sampling an inception cohort (a group assembled at a common time point early in the development of the disorder), there is no way of ensuring that specific subgroups of children with ASD are included in the sampling frame. For example, some very young children with ASD may make such rapid progress that they fall off the spectrum early on and so would not be picked up if sampling was to occur later in childhood. Second, convenience sampling is often used to recruit participants from highly specialized diagnostic or clinical centers or in nonsystematic ways. Both of these design features may select cases that are biased in important ways. Limits are thereby placed on the ability to generalize from the sample to the population. Small sample sizes (ie, often <50 children) in many previous studies place additional limits on the precision of estimates of change and make it difficult to use multivariable techniques to identify multiple predictors and moderators of outcome. Finally, many published outcome studies in ASD have relied on limited methods of assessment when looking at associations across domains. It is imperative to use a multimethod, multi-informant approach to minimize measurement error and to capture different perspectives on associations between predictors and outcomes and between different outcomes in ASD.

The ASD phenotype is multivariable, comprising several developmental domains. Among the 2 most common domains used to characterize children with ASD are adaptive functioning and autistic symptom severity.[18] Adaptive functioning refers to the attainment of developmentally appropriate skills and abilities in various areas, including socialization, communication, and activities of daily living. Conversely, autistic symptoms include deficits in social communication and a pattern of repetitive stereotyped behaviors. Previous factor analytic investigations have pointed out the independence of functioning and symptoms.[18] However, admittedly there is much overlap, and the true underlying associations among developmental domains in ASD are not well understood from a longitudinal perspective.

The objective of this study was to describe the developmental trajectories of autistic symptom severity and adaptive functioning in a large inception cohort of preschool children with ASD sampled in a systematic fashion. We are not aware of any studies that have explored the potential associations over time between these 2 fundamental phenotypic domains in ASD. A secondary objective was to understand potential predictors and outcomes associated with those trajectories.

Methods

Participants and Procedure

The study was approved by the local research ethics boards at all participating sites, and written consent was obtained from the caregivers for their children to participate. Our sample consisted of 421 newly diagnosed preschool children with ASD (355 boys; mean age at study enrollment, 39.87 months) who were participating in a large Canadian multisite longitudinal study (http://www.asdpathways.ca). Descriptive statistics for the combined sample are listed in **Table 1**. The sites in Canada were Halifax, Nova Scotia; Montreal, Quebec; Hamilton, Ontario; Edmonton, Alberta; and Vancouver, British Columbia. There were no substantive differences across the sites in terms of clinical characteristics of the children with ASD. However, the timing and type of interventions provided (once a diagnosis was given)

Table 1. Sample Descriptive Statistics at Baseline

Variable	Value (N = 421)
Sex, No. (%)	
Male	355 (84.3)
Female	66 (15.7)
Canadian site, No. (%)	
Halifax, Nova Scotia	56 (13.3)
Montreal, Quebec	134 (31.8)
Hamilton, Ontario	68 (16.2)
Vancouver, British Columbia	93 (22.1)
Edmonton, Alberta	70 (16.6)
Age, mean (SD), y	
At diagnosis	38.23 (8.75)
At study enrollment	39.87 (9.00)
Group 1	39.49 (8.95)
Group 2	40.27 (9.06)
M-P-R developmental index standard score, mean (SD)	57.23 (26.20)
PLS-4 total language standard score, mean (SD)	65.25 (19.21)

Abbreviations: M-P-R, Merrill-Palmer–Revised Scales of Development; PLS-4, Preschool Language Scale–Fourth Edition.

could differ by site. An intervention such as "More Than Words" (http://www.hanen.org/Programs/For-Parents/More-Than-Words.aspx) was offered soon after the diagnosis was given at one site (Montreal). In addition, children were diagnosed at a somewhat older age at one site compared with the others.[19] Children from these 2 sites did not have different outcomes than children from other sites. Finally, there was variation in the types of services offered in each province[20]; for these reasons, site was used as a covariate in the analysis.

To participate in the study, children had to meet the following inclusion criteria: (1) be between age 2 years and age 4 years 11 months, (2) have a recent (within 4 months) clinical diagnosis of ASD confirmed by the Autism Diagnostic Observation Schedule[21] (ADOS) and the Autism Diagnostic Interview-Revised,[22] and (3) have a clinical diagnosis assigned by a clinician using *DSM-IV* criteria.[23] More detail on the inclusion and exclusion criteria is available in a study by Georgiades et al.[17]

We used an accelerated longitudinal design with 2 waves of children sampled 1 year apart. There were 4 data collection points, namely, at baseline, at 6 months and 12 months after baseline, and at age 6 years (at the end of the first year of primary school). The measure of adaptive functioning was administered at all 4 points. The measure of autistic symptom severity was obtained at 3 data points, namely, at baseline, 6 months later, and at age 6 years.

Instruments

Trajectory Indicators

The ADOS[21] is a semistructured direct assessment of communication, social interaction, and play or imaginative use of materials for individuals suspected of having autism or other pervasive developmental disorders. The ADOS calibrated severity score[24] was used to index the developmental trajectories of autistic symptom severity. The development of a psychometrically reliable and valid measure of autism symptom severity that was developed to be independent from a measurement point of view from the level of functioning provides an important opportunity to test the association between symptom severity and adaptive functioning prospectively.[24]

The Vineland Adaptive Behavior Scales, Second Edition[25] assesses child adaptive behavior in the communication, socialization, daily living skills, and motor domains. It is administered to a parent or caregiver using a semistructured interview format. The standard composite score was used to index the developmental trajectories of adaptive functioning.

Trajectory Predictors and Outcomes

The Autism Diagnostic Interview-Revised[22] is a standardized semistructured interview used in the diagnosis of ASD. It is designed for use with a parent or caregiver who is familiar with the developmental history and current behavior of individuals older than 2 years. The diagnostic algorithms developed by Risi et al[26] were used in the inclusion criteria at baseline. At age 6 years, total scores (current) from the following 3 major domains were used in the analysis: (1) language and communication, (2) reciprocal social interaction, and (3) restricted, repetitive, and stereotyped behaviors and interests.

The 99-item Child Behavior Checklist[27] 1.5-5 norm-referenced instrument is widely used and evaluates a wide range of internalizing and externalizing problems. The Child Behavior Checklist is completed by parents based on observations of the child's behavior in the previous 2 months. The total *t* scores for the internalizing and externalizing scales were used in the analysis as outcome measures at age 6 years.

The Preschool Language Scale-Fourth Edition[28] is a comprehensive language test for identifying children with a language disorder or delay. It is administered individually to children between birth and age 6 years 11 months or to older children who function developmentally within this age range. The Preschool Language Scale-Fourth Edition, indexed by the total language standard score, was used to obtain an index of early syntax and semantic skill in this sample of preschool children with ASD[29] and was assessed at baseline and as an outcome measure at age 6 years.

The Merrill-Palmer-Revised Scales of Development[30] is a revised and recently standardized measure of intellectual ability that is appropriate for children 2 to 78 months old. The developmental index standard score used in the analysis comprises cognitive, receptive language, and fine motor subscales and was administered at baseline and at age 6 years.

Data Analysis

Children with missing data on at least 1 outcome measure at age 6 years had a higher Vineland Adaptive Behavior Scales, Second Edition score only at that time point (but no difference on any ADOS score) compared with children with complete data, providing reasonable evidence that data were missing at random. Our main analytic plan encompassed the following 4 stages: (1) the identification of distinct trajectories in autistic symptom severity and adaptive functioning, (2) the examination of overlap of trajectories in symptoms and functioning, (3) the prediction of group trajectory mem-

bership using variables obtained at baseline, and (4) the association of group trajectory membership with outcomes of interest at age 6 years.

Based on the literature review, we assumed that the development of symptom severity and adaptive functioning over time would be extremely heterogeneous, so we needed a method that could capture that complexity. A semiparametric and group-based approach[31] was used with the ADOS severity metric scores and the Vineland Adaptive Behavior Scales, Second Edition composite (standard) scores to identify different developmental trajectories in these domains. This specific modeling approach was chosen because it identifies distinct mixtures of trajectories within the population (as opposed to latent growth curve analysis, which assumes a homogeneous pattern of development).[32] Furthermore, because the method assumes that data are missing at random, the retention of individuals with incomplete data in the analyses is possible, making full use of the available information. Multiple models were tested, and the Bayesian information criterion and average group posterior probability greater than 0.7 were used to determine the most parsimonious and best-fitting model to the data with the specified number of trajectory groups.[31] After identifying trajectories in adaptive functioning and symptom severity, the overlap between trajectories in the 2 domains was assessed using a χ^2 test of independence. The strength of association in overlap was estimated using the φ coefficient. A coefficient greater than 0.4 suggests moderate to strong "yoking" of developmental trajectories.[33]

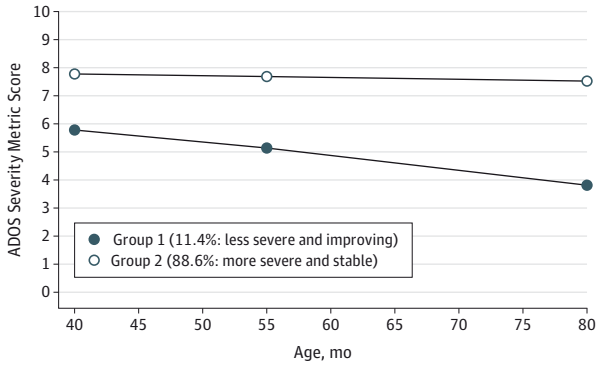
Several child-specific variables at baseline were examined to see to what extent they predicted trajectory group membership. Age at diagnosis, sex, baseline IQ, and language scores were directly included in the derived trajectory models as risk factors to predict trajectory group membership. The association between trajectory group membership and outcome measures at age 6 years was then examined using analysis of variance. Outcome measures included internalizing and externalizing problems on the Child Behavior Checklist, Autism Diagnostic Interview-Revised domain scores (to look at current autistic symptoms from the parent's perspective), IQ scores from the Merrill-Palmer-Revised Scales of Development, and language competence as measured by the Preschool Language Scale-Fourth Edition. Site was used as a covariate in these last 2 analyses to adjust for possible ascertainment or service differences across the data collection sites.

Results

Cross-sectional correlations between autistic symptom severity and adaptive functioning were of similar magnitude at each time point of data collection (range, $r = -0.11$ to $r = -0.25$). The wave-to-wave correlations for autistic symptom severity and adaptive functioning stayed stable over time: correlations between successive time points for autistic symptom severity and for adaptive functioning varied from 0.35 to 0.44 and from 0.77 to 0.84, respectively.

Goodness-of-fit statistics for all tested trajectory models for autistic symptom severity and adaptive functioning are listed in eTable 1 and eTable 2 in the Supplement. **Figure 1** shows the results for the trajectory analysis of autistic symptom severity. Two distinct trajectory groups provided the best fit to the data. The Bayesian information criterion was −2111.23, and the average group posterior probabilities were 0.80 for group 1 and 0.92 for group 2. Group 1 (11.4% of the sample) had less severe symptoms and a statistically significant improving trajectory ($P < .05$), whereas group 2 (88.6% of the sample) had more severe symptoms and a stable trajectory, suggesting little change in symptom severity over the period assessed. Descriptive statistics for autistic symptom severity by trajectory group and time of assessment are listed in **Table 2**.

Figure 1. Developmental Trajectories of Autistic Symptom Severity



ADOS indicates Autism Diagnostic Observation Schedule.

Figure 2 shows the results of the trajectory analysis for adaptive functioning (using standard scores). Three distinct quadratic trajectory groups provided the best fit to the data. The Bayesian information criterion was −5063.22, and the average group posterior probabilities were 0.93 for group 1, 0.86 for group 2, and 0.93 for group 3. Group 1 (29.2% of the sample) had lower functioning at baseline and a statistically significant worsening trajectory. Group 2 (49.9% of the sample) had moderate functioning at baseline and a stable trajectory. Group 3 (20.9% of the sample) had higher functioning at baseline and a statistically significant improving trajectory ($P < .05$). Descriptive statistics for adaptive functioning by trajectory group and time of assessment are listed in Table 2.

Figure 3 shows the cross-trajectory membership between the autistic symptom severity and adaptive functioning groups ($\chi^2_2 = 7.35$, $P < .05$). The φ coefficient of 0.13 ($P < .05$) indicates a small but statistically significant amount of overlap across the trajectory groups. For example, 20.4% of the more severe and stable symptom group were in the group with higher functioning and improving adaptive functioning; 12.5% of the group with less severe and improving symptoms were in the group with lower functioning and worsening adaptive functioning. There was no one-to-one correspondence between symptom severity and adaptive functioning trajectories.

The results of the analyses of risk factors showed that sex was the only significant predictor of autistic symptom group trajectory membership ($P = .03$) (eTable 3 in the Supplement). Boys were more likely to be in the group with more severe symptoms and a stable trajectory than girls, who were more likely to be in the group with less severe symptoms and

Table 2. Descriptive Statistics by Trajectory Group and Time of Assessment

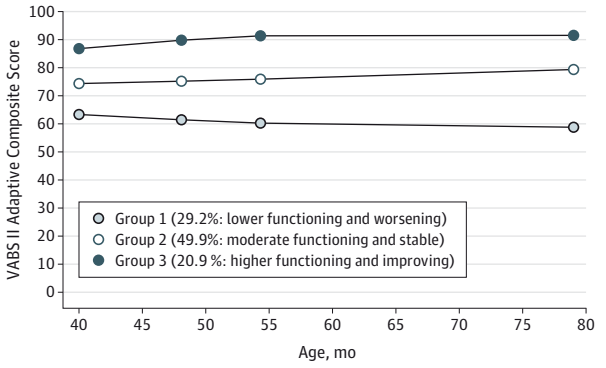
Variable	No.	Mean (SD)
ADOS Severity Metric Score[a]		
Baseline		
Entire sample	**406**	7.57 (1.70)
Group 1	48	5.73 (1.50)
Group 2	358	7.82 (1.57)
12 mo After baseline		
Entire sample	**342**	7.06 (1.95)
Group 1	43	4.19 (1.93)
Group 2	299	7.47 (1.58)
Age 6 y		
Entire sample	**285**	6.99 (2.23)
Group 1	37	3.35 (1.58)
Group 2	248	7.54 (2.23)
VABS II Adaptive Composite Score[b]		
Baseline		
Entire sample	**399**	72.75 (10.13)
Group 1	123	62.98 (5.80)
Group 2	189	73.48 (6.10)
Group 3	87	85.01 (7.49)
6 mo After baseline		
Entire sample	**361**	74.52 (13.00)
Group 1	105	60.45 (6.89)
Group 2	176	75.22 (6.48)
Group 3	80	91.44 (7.74)
12 mo After baseline		
Entire sample	**345**	76.21 (13.77)
Group 1	104	60.76 (5.51)
Group 2	162	77.46 (6.59)
Group 3	79	93.97 (8.09)
Age 6 y		
Entire sample	**285**	76.55 (13.96)
Group 1	74	58.66 (7.53)
Group 2	144	79.12 (7.70)
Group 3	67	90.81 (8.22)

Abbreviations: ADOS, Autism Diagnostic Observation Schedule; VABS II, Vineland Adaptive Behavior Scales, Second Edition.

[a] Trajectory groups are group 1 (less severe and improving) and group 2 (more severe and stable).

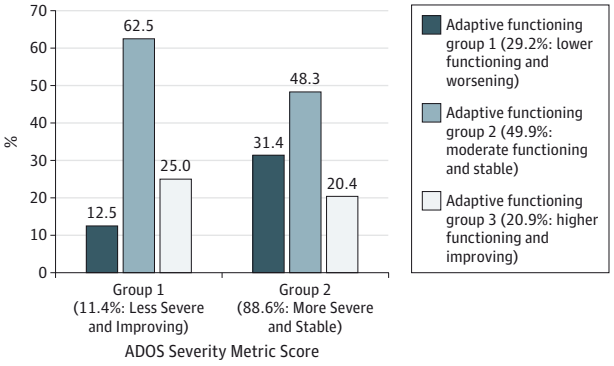
[b] Trajectory groups are group 1 (lower functioning and worsening), group 2 (moderate functioning and stable), and group 3 (higher functioning and improving).

Figure 2. Developmental Trajectories of Adaptive Functioning



VABS II indicates Vineland Adaptive Behavior Scales, Second Edition.

Figure 3. Cross-Trajectory Group Membership for Autistic Symptom Severity and Adaptive Functioning



ADOS indicates Autism Diagnostic Observation Schedule.

an improving trajectory (controlling for age at diagnosis, cognitive and language scores, and site). In contrast, the results of the analysis of the adaptive functioning trajectories showed that age at diagnosis ($P = .02$), language competence ($P < .001$, indexed by the Preschool Language Scale-Fourth Edition), and IQ ($P < .001$, indexed by the Merrill-Palmer-Revised Scales of Development) at baseline predicted adaptive functioning trajectory group membership (eTable 4 in the Supplement) (controlling for site and sex). In other words, earlier age at diagnosis was more likely associated with membership in a group with higher functioning and improving. Higher baseline IQ or higher baseline language scores were associated with a greater likelihood of being in the trajectory groups with moderate functioning and a stable trajectory and with higher functioning and an improving trajectory.

The analysis of variance results (**Table 3**) show that the 2 autistic symptom severity trajectory groups differed significantly on all outcome measures at age 6 years with the exception of externalizing problems (indexed by the Child Behavior Checklist). For the 3 adaptive functioning trajectory groups, there were significant differences on all outcome measures at age 6 years.

Discussion

To our knowledge, the present study represents the largest investigation to date of the developmental trajectories of autistic symptom severity and adaptive functioning in an inception cohort of preschool children with ASD. Study findings confirm that the heterogeneity within this sample of children with ASD seen at the point of ASD diagnosis appears to persist and in some cases increase from baseline to age 6 years. This outcome is particularly evident in the adaptive

Table 3. Correlates of Autistic Symptom Severity Trajectory Groups and Adaptive Functioning Trajectory Groups at Age 6 Years

Variable	Trajectory Group	No.	Mean (SD)	*P* Value
Autistic Symptom Severity				
ADI-R social domain total score, current	Less severe and improving	38	6.84 (5.49)	<.001
	More severe and stable	269	12.16 (7.32)	
ADI-R communication domain nonverbal/verbal total score, current	Less severe and improving	38	6.53 (5.68)	<.001
	More severe and stable	270	10.15 (4.68)	
ADI-R repetitive behaviors domain total score, current	Less severe and improving	38	3.05 (2.16)	.001
	More severe and stable	269	4.53 (2.61)	
PLS-4 total language standard score	Less severe and improving	28	85.46 (22.53)	<.001
	More severe and stable	197	67.65 (21.63)	
M-P-R developmental index standard score	Less severe and improving	34	91.18 (19.15)	.02
	More severe and stable	203	79.67 (28.09)	
CBCL internalizing problems total *t* score	Less severe and improving	21	48.43 (13.79)	.007
	More severe and stable	203	55.66 (11.35)	
CBCL externalizing problems total *t* score	Less severe and improving	21	46.24 (12.93)	.06
	More severe and stable	203	51.31 (11.73)	
Adaptive Functioning				
ADI-R social domain total score, current	Lower functioning and worsening	81	19.15 (5.14)	<.001
	Moderate functioning and stable	152	10.07 (6.02)	
	Higher functioning and improving	74	6.09 (4.67)	
ADI-R communication domain nonverbal/verbal total score, current	Lower functioning and worsening	81	12.41 (3.59)	<.001
	Moderate functioning and stable	153	9.65 (5.04)	
	Higher functioning and improving	74	6.84 (4.42)	
ADI-R repetitive behaviors domain total score, current	Lower functioning and worsening	81	5.07 (2.07)	<.001
	Moderate functioning and stable	152	4.49 (2.65)	
	Higher functioning and improving	74	3.24 (2.71)	
PLS-4 total language standard score	Lower functioning and worsening	73	52.79 (9.35)	<.001
	Moderate functioning and stable	116	74.39 (22.17)	
	Higher functioning and improving	36	89.92 (18.68)	
M-P-R developmental index standard score	Lower functioning and worsening	31	48.61 (29.25)	<.001
	Moderate functioning and stable	139	79.22 (24.31)	
	Higher functioning and improving	67	100.82 (11.58)	
CBCL internalizing problems total *t* score	Lower functioning and worsening	56	61.98 (9.44)	<.001
	Moderate functioning and stable	111	54.22 (10.93)	
	Higher functioning and improving	57	49.58 (12.16)	
CBCL externalizing problems total *t* score	Lower functioning and worsening	56	57.55 (9.80)	<.001
	Moderate functioning and stable	111	50.21 (11.45)	
	Higher functioning and improving	57	45.46 (11.71)	

Abbreviations: ADI-R, Autism Diagnostic Interview–Revised; CBCL, Child Behavior Checklist; M-P-R, Merrill-Palmer–Revised Scales of Development; PLS-4, Preschool Language Scale–Fourth Edition.

functioning trajectories, in which the possibility of improvement in the first few years after diagnosis is seen in roughly 20% of the sample. Autistic symptom severity appears to be more stable, but here again roughly 11% of the children in our sample show a decrease in symptom severity from baseline to age 6 years. The patterns of substantial stability of symptom severity in most children and a decrease in symptom severity in a smaller subgroup of children with ASD are consistent with the findings by Gotham et al[16] and by Venker et al.[34]

The developmental trajectories identified in the present study appear to be clinically meaningful in terms of variables that predict trajectory membership and in terms of outcomes. The different trajectories in both domains (symptom severity and adaptive functioning) are associated with differences in terms of variables that predict group membership and in terms of outcomes. It was intriguing that female sex was more commonly associated with the group with less severe and improving symptoms (controlling for the other variables) and that age at diagnosis was more commonly associated with the group with higher functioning and improving (again controlling for the covariates). These findings have important implications for surveillance and early identification efforts.

Perhaps the main message of this study is that, during the preschool years, there appears to be only a small amount of yoking of the developmental trajectories in autistic symptom severity and adaptive functioning. For example, it is possible for some children with more severe and stable autistic symptoms to show notable improvement in adaptive functioning, underscoring their capacity to learn (Figure 3). This finding highlights the importance of close surveillance of these 2 domains independently over

time. The commonly held notion of higher-functioning and lower-functioning types of ASD being congruent with less and more severe autistic symptoms, respectively, might be too simplistic and is not supported by the trajectory data presented herein. Although there is certainly a link (based on cross-sectional correlations) between a child's autistic symptom severity and adaptive functioning at any given point, longitudinal data presented herein suggest that this association is much more complex over time. The *DSM-5* has recently replaced the different pervasive developmental disorder subtypes (autism, Asperger, and pervasive developmental disorder–not otherwise specified) with a single diagnostic category of ASD.[35] Although this change may be justified by a lack of reliable differentiation and stability of subtypes and by a lack of evidence supporting differences in etiological markers, it should not obscure the fact that ASD is a remarkably heterogeneous disorder.[36,37] Fortunately, the *DSM-5* includes several ways of dealing with this heterogeneity by using a dimensional approach and by adding specifiers of language, cognitive ability, and other markers (adaptive functioning, however, not being one of them). We would argue that specifiers of the developmental trajectories (up to at least age 6 years) could prove useful in capturing diversity and could contribute to the identification of more meaningful and relevant subgroups to be the focus of future research in etiology and treatment response. The inclusion of such developmental specifiers (including adaptive functioning) might expand the capability of the *DSM-5* from a static diagnostic to a dynamic prognostic classification framework for ASD.

The strengths of the study include the large sample size, the ascertainment of an inception cohort, and the use of multimethod, multi-informant instruments, as well as the inclusion of carefully selected predictor and outcome variables that are conceptually distinct (from a measurement point of view) from the indicators used in the trajectory analysis. To our knowledge, this is the largest prospective outcome study of children with ASD published and is only the second ascertaining an inception cohort, following the study by Lord et al.[14] Both of these design features should ensure the precision of our estimates, allow the detection of small but possibly important effects, and assure the representativeness of our findings.

Despite its strengths, the present study has several limitations. First, we cannot be certain that the children and families who agreed to participate in our study (58.2% of those approached) are similar to those who declined regarding variables that potentially influence the trajectories under investigation. Second, within the children and families enrolled in our study, we cannot be certain that those who did not participate at all data points are similar to those who did on key predictor or confounding variables. Third, we only had 3 data points for the ADOS symptom severity measure (compared with 4 for the Vineland Adaptive Behavior Scales, Second Edition adaptive functioning measure), so the difference in trajectory variability or pattern may be at least in part a function of the number of data points. Limited data points also make it difficult to estimate the shape of the trajectory curve to see if the rate of change varies over time. Additional follow-up assessments are under way and will allow us to address this issue in more detail. Fourth, the present analysis did not investigate the possible effect of services or opportunities to learn adaptive functioning skills on the developmental trajectories of children with ASD. This is a complex issue because services can vary by age at onset and by length, intensity, type, and quality of intervention; any of these factors could have a major role in outcomes and might account for significant variability in the developmental trajectories. Fifth, the trajectories of preschool children described in the present study reflect only the heterogeneity in adaptive functioning and symptom severity and do not capture the entire ASD phenotype that comprises additional developmental domains.

Conclusions

Individual children with ASD differ from each other in terms of autistic symptom severity and adaptive functioning from the time of diagnosis in the preschool years, and some of these differences appear to increase by age 6 years. Moreover, change in one domain is not necessarily associated with change in another. Children with ASD appear to start their course with important baseline differences. Therefore an important key to improving trajectories may occur before the diagnosis is officially given when children manifest behavioral or functional concerns during an at-risk or prodromal phase.[38] Once children with ASD are given a diagnosis and are enrolled in treatment programs, it is imperative that a flexible suite of interventions should then be implemented and tailored to each child's strengths and difficulties. Individualized interventions need to focus on both adaptive functioning and autistic symptom severity because improvement in one domain does not ensure improvement in the other.

ARTICLE INFORMATION

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