ORIGINAL ARTICLE

Social and Communication Development in Toddlers With Early and Later Diagnosis of Autism Spectrum Disorders

Rebecca J. Landa, PhD; Katherine C. Holman, PhD; Elizabeth Garrett-Mayer, PhD

Context: To our knowledge, no prospective studies of the developmental course of early and later diagnosis of autism spectrum disorders from 14 months of age exist.

Objective: To examine patterns of development from 14 to 24 months in children with early and later diagnosis of autism spectrum disorders.

Design: Prospective, longitudinal design in which 125 infants at high and low risk for autism were tested from age 14 to 36 months. Comprehensive standardized assessments included measures of social, communication, and play behavior.

Setting: Testing occurred at a major medical and research institution as part of a large, ongoing longitudinal study.

Participants: Low-risk controls (n=18) and siblings of children with autism, grouped on the basis of outcome diagnostic classification at 30 or 36 months: autism spectrum disorders (early diagnosis, n=16; later diagnosis, n=14), broader autism phenotype (n=19), and non–broader autism phenotype (n=58).

Main Outcome Measures: Social, communication, and symbolic abilities were assessed.

Results: Social, communication, and play behavior in the early-diagnosis group differed from that in all other groups by 14 months of age. By 24 months, the later-diagnosis group differed from the non–autism spectrum disorder groups in social and communication behavior, but not from the early-diagnosis group. Examination of growth trajectories suggests that autism may involve developmental arrest, slowing, or even regression.

Conclusion: This study provides insight into different patterns of development of children with early vs later diagnosis of autism spectrum disorders.

Arch Gen Psychiatry. 2007;64(7):853-864

Author Affiliations: Kennedy Krieger Institute, Center for Autism and Related Disorders, The Johns Hopkins School of Medicine (Drs Landa and Holman), and Division of Biostatistics, Sidney Kimmel Comprehensive Cancer Center, The Johns Hopkins University (Dr Garrett-Mayer), Baltimore, Maryland.

AUTISM SPECTRUM DISORders (ASDs) represent one or more neurodevelopmental disorders in which aspects of social and communication impairment are distinguishing features. Despite the evidence of abnormality in neurobiological processes beginning as early as prenatal life,[1] ASD is rarely diagnosed before age 3 years.[2] To advance the earlier detection of ASD, and thereby promote earlier intervention, we report on a prospective, longitudinal study of social and communication development in ASD from 14 to 24 months of age. Understanding the nature and trajectory of change in these aspects of development may reveal clues about the neurobiological basis for ASD.[3]

The retrospective literature, based on parent report or analysis of home videotapes, indicates that abnormalities are present as early as the first year of life in ASD, affecting social, communication, and motor development.[4-10] By the first birthday, social and communication features that distinguish autism from typical development include decreased frequency of orientation to social stimuli (including joint attention, social interaction, social anticipation, eye contact, and response to name); complex babbling, gesture, and word production; and imitation.[7,11-13] Attenuation in social orienting reportedly distinguishes 12-month-olds with autism from those with developmental delay.[14,15] Despite these reports of social and communication abnormalities in infants with autism, some forms of social responsivity and engagement (eg, sequences of protoconversation) may not be obviously affected in toddlers with ASD.[16] Onset of linguistic development is delayed, as indicated by a prospective study of ASD from infancy.[17] By 24 months of age, children with ASD are distinguished from those with de-

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

velopmental delay or language delay in social functioning (eg, joint attention, affective expressiveness, and imitation),[17-20] and parents are clearly aware of their child's developmental disruption.[21,22]

Not all children with ASD clearly exhibit abnormalities early in life, according to retrospective studies. Up to 50% may display typical development or only mild delays until 15 to 24 months of age, followed by loss of language, communication, and/or social skills.[23-28] In a retrospective study of regression in autism, Werner and Dawson[23] compared 12- and 24-month videotapes of children with nonregressive early onset of autism, regressed autism, and typical development. The authors reported that levels of complex babbling, word production, and declarative pointing produced by the early-onset ASD group were lower than those produced by other groups at 14 months of age. At 24 months, both autism groups performed worse than the typical development group in language and social orienting behaviors. The present study aims to add to this literature by further differentiating the social communication behaviors of children with either early or later diagnosis of ASDs.

In this sample of children with ASDs studied prospectively from 14 to 36 months of age, we examined patterns of social and communication developmental trajectory from 14 to 24 months of age. Infant siblings of children diagnosed as having autism were selected because they are at increased genetic risk for ASD and milder variants, often referred to as the *broader autism phenotype* (BAP).[17,29-32] The prospective study of these infants enables us to examine the emergence of ASD without the inherent limitations imposed by retrospective research designs such as parental recall bias[33] and inability to manipulate the testing context and behavioral measures.

METHODS

This study was approved by The Johns Hopkins Medical Institutional Review Board before the collection of data, and all families gave written informed consent for the participation of their infant.

PARTICIPANTS

Infants at high and low risk for ASD participated, including siblings of children with idiopathic autism (AU sibs) (n=107; 59 boys and 48 girls) and low-risk (LR) controls having no family history of ASD (n=18; 11 boys and 7 girls). Low-risk controls had no known family history of ASD and were included in this report if they did not meet our criteria for ASD. Two LR controls, included in this report, were impaired: 1 with language delay and 1 with social delay. In addition, 1 LR control had a sibling with fragile X syndrome but was herself fragile X negative. Participants were recruited through a large federally funded research project focusing on early markers for ASD and early patterns of development in ASD. Recruitment sources included ASD advocacy groups, ASD conferences, schools with classes for children with ASD, the Kennedy Krieger Institute, local physicians' offices, caregiver-child play groups, and word of mouth.

Ten children had preterm births (1 at 34 weeks of gestation, 6 at 35 weeks, and 3 at 36 weeks). The numbers of children having preterm births in each of the groups described in the "Diagnostic Classification Procedures" section were as follows: early ASD diagnosis group, n=2; later ASD diagnosis group, n=0; BAP group, n=1; non-BAP group, n=6; and LR control group, n=1. Only participants with 14-month data who also completed 30- or 36-month assessments were included in this report. This sample did not completely overlap with that presented in Landa and Garrett-Mayer's report,[17] which included some children who entered under funding constraints permitting testing only through 24 months of age. The sample included 111 white participants, 1 African American, 9 multiracial, and 4 of unknown or unreported race, by parent report.

Participants in either group were ineligible if they met any of the following criteria: family's first language being other than English (because language measures are normed on English speakers, putting non-English speakers at a disadvantage), low birth weight (<1500 g), severe birth trauma, head injury, prenatal illicit drug or excessive alcohol exposure, or severe birth defects.

Participants were tested at 6, 14, 24, and 30 or 36 months of age, with study entry permitted until 14 months. Participants entering the study since 2003 were also invited to have assessments at 18 months of age, and those data are presented for analysis of developmental trajectory. Thirty-nine children in this sample had completed the Communication and Symbolic Behavior Scales Developmental Profile (CSBS DP) at 18 months of age. Outcome diagnosis of ASD was made at 30 or 36 months because diagnosis at that age is reliable.[1-5] Only the 4 measures relevant to this report are described.

MEASURES

Primary dependent variables were from the CSBS DP[34] (given at 14-24 months). It evaluated communicative, social-affective, and symbolic abilities, with norms established on children 8 to 24 months of age. Children were presented with communication temptations (eg, the adult opens a bubble jar, blows bubbles, tightly replaces the lid, then sets the jar in front of the child), probes for response to joint attention, receptive language, and an opportunity to play with a standardized set of toys. Social, communication, and play-dependent variables analyzed in this report are defined in **Table 1**.

Interrater reliability was tested on dependent variables from the CSBS DP in which 20% of the videotape segments were double coded. Intraclass correlation coefficients were computed for all frequency codes (range, 0.710-1.000 for 14-month videotapes; 0.700-0.945 for 18-month videotapes; and 0.705-0.990 for 24-month videotapes). The CSBS DP was administered to only a few children at 30 months of age, so those data are not presented herein. Data from the CSBS DP were available at both 14 and 24 months of age for 12 children in the early-diagnosis group, 12 in the later-diagnosis group, 16 in the BAP group, 45 in the non-BAP group, and 16 in the LR control group.

Additional measures, described as follows, were used to determine diagnostic impressions and outcome clinical judgments.

The Autism Diagnostic Observation Schedule (ADOS)[35] is a semistructured, play-based assessment with standardized administration and scoring schema without age norms (given at 14-36 months). It provides systematic probes for autism symptoms in social interaction, communication, play, and repetitive behaviors/interests. Module 1 (minimal to no language) or 2 (nonechoed phrase speech) was given. The ADOS provides algorithm criteria for classification of "ASD" or "autism." Since the ADOS was not designed for children younger than 18 months, our use of it at 14 months was experimental. All 14-month-olds and most 24-month-olds completed module 1. The ADOS scores were used, in conjunction with clinical judgment, to classify children with ASD or BAP. Meeting algorithm criteria for ASD or autism did not automatically result in ASD or BAP classification.

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

The Mullen Scales of Early Learning[36] is a standardized developmental test for children between 3 and 69 months of age, with 5 subscales: gross motor, fine motor, visual reception, receptive language, and expressive language. The Mullen Scales of Early Learning was given from 6 through 36 months of age. Receptive and expressive language scales were used to identify children with language delays at the outcome assessment.

The Preschool Language Scale 3 or 4[37,38] is a normed and standardized test yielding receptive and expressive standard scores and age equivalencies (given at 14-36 months) that were used to identify children with language delays at the outcome assessment.

DIAGNOSTIC CLASSIFICATION PROCEDURES

Master's- or doctoral-level clinical research examiners who had experience with young children with autism assigned diagnostic impressions at every age, indicating whether there were clinically significant signs of delay or impairment. Concerns about developmental disruption in speech, language, social communication, social, temperament, behavior, sensory, motor, or other domains were noted. Examiners also indicated their impression about whether the child exhibited ASD. In the absence of guidelines for diagnosing ASD at 14 months, we followed, as closely as possible, the *DSM-IV*[39] criteria for autism and pervasive developmental disorder not otherwise specified. Some were not applicable for 14-month-olds (eg, reciprocal friendships), so diagnostic impressions were based on impairments in social interaction (affective reciprocity, eye contact, sustaining social responsivity to adults' bids for social interaction, spontaneous imitation, communicative/vocal responsivity, or object-oriented behavior to the near exclusion of social attention), with additional consideration given to the presence of stereotypic behavior. A language delay was not required for a diagnostic impression of ASD. A precedent for provisional "diagnosis" of ASD as early as 20 months of age has been established in previously published prospective work.[13,18,20] Examiners were blind to the child's diagnosis from the previous assessment about 50% of the time, mainly owing to the probability of 1 examiner administering 2 consecutive assessments for that child.

In addition, one evaluator (R.J.L.) assigned outcome clinical judgments based on a chart review sometimes supplemented by a video review of data collected at the child's outcome visit. For the 19 children who had not reached 36 months of age, the 30-month visit provided the "outcome" data. These outcome clinical judgments fell into 3 categories: (1) ASD, (2) non-ASD impairment, and (3) no social, language, or behavioral impairment. This evaluator was blind to recruitment group membership for 107 (86%) of the participants as clinical judgments were being assigned. In the cases where the evaluator assigned a clinical judgment of ASD without being blind to recruitment group membership, the clinical judgment was supported by (1) a blind clinical research examiner's diagnostic classification (one of the staff who tested the children), (2) a blind video review by other master's- or doctoral-level clinical researchers from our laboratory (when the tester and the evaluator were not blind), or (3) a diagnosis of ASD made by an independent clinician outside of our research program, to which the evaluator was blind at the time of her chart and video review.

With the use of these outcome clinical judgments, the AU sibs were classified into 1 of the following groups.

ASD Group

The AU sibs were given this classification (n=30; 25 boys and 5 girls) if they had an outcome clinical judgment of ASD (autism or pervasive developmental disorder not otherwise specified) and also met ADOS algorithm criteria for autism or ASD. Clinical judgments of ASD were based on social and communication behavior, as well as the presence of repetitive and stereotyped patterns of behavior and interests. The diagnostic criteria for autism or pervasive developmental disorder not otherwise specified as defined in *DSM-IV*[39] were used in this

Table 1. Definitions of CSBS DP Dependent Variables Examined Longitudinally

Variable Name	Domain Assessed	Definition
Shared positive affect	Social affect	Frequency of looking at another person while smiling (coded once in each temptation)
Gaze shifts	Social cognition: joint attention	Frequency with which child shifted gaze from object to person's eyes and back to object or the reverse (every occurrence was coded in 2 of 6 temptations, then once in remaining 4 temptations)
Response to joint attention bids	Social cognition: joint attention	Looking toward targets placed (1) on wall 90° to one side and (2) 180° away from front midline of child in response to examiner's point paired with gaze toward object while saying "Look" (given once attempts have been made to establish eye contact with child) (score = total correct looks toward target)
Initiation of joint attention	Social cognition: joint attention	Frequency of initiation of communication bids for purposes of sharing attention with another person around object or event (every occurrence coded)
Initiation of behavior regulation	Communication: regulatory intentionality	Frequency of initiation of communication bids for purposes of requesting assistance in obtaining desired action or object, but not social interaction (every occurrence counted)
Inventory of gestures, consonants in syllables, words, and word combinations	Communication form (nonvocal, nonlinguistic vocal, and linguistic)	Total variety of gestures, consonants in syllables, words, and word combinations produced in intentional communicative acts of any kind that were clearly directed to caregiver or examiner
Action schema inventory	Play	Total variety of action schema displayed during play sample
Action schema sequences	Play	Total variety of ≥2 action schema of functional or symbolic use of objects combined in immediately adjacent temporal sequence (eg, putting spoon in cup and stirring)
Action schema toward others	Play: social engagement	Frequency with which children directed play actions toward another, representing social engagement in play (every occurrence coded)

Abbreviation: CSBS DP, Communication and Symbolic Behavior Scales Developmental Profile.

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

process. Clinical judgment has been shown to be a valid basis on which to determine diagnostic classification.[40] The number of AU sibs with ASD was higher than expected given the literature on recurrence risk in autism, which is between 4.5% and 8% according to statistical estimates.[41,42] Sampling bias is likely in our study because, of the parents who completed the intake questionnaire, 14 (44%) and 25 (76%) parents of 6- and 14-month-olds, respectively, reported concerns about their children on entry to the study.

The ASD group was further divided into 2 groups on the basis of whether they were given a diagnosis of ASD at the 14-month visit. The *early ASD diagnosis group* (n=16; 14 boys and 2 girls) received a diagnostic impression of ASD at 14 months and a clinical judgment of ASD at the outcome visit. In addition, ADOS criteria for ASD or autism were met at both ages. The *later ASD diagnosis group* (n=14; 11 boys and 3 girls) did not have a diagnostic impression of ASD at 14 months but received outcome clinical judgments of ASD. All but one of the children in the later-diagnosis group had received diagnostic impressions of at least mild "impairment" at 14 months of age.

BAP Group

The AU sibs in this group (n=19; 13 boys and 6 girls) exhibited language and/or social delays but did not have an outcome clinical judgment of ASD. They met 1 or both of the following criteria: (1) score on the Mullen Scales of Early Learning or Preschool Language Scale receptive and/or expressive language subtests was at least 1.25 SDs below the mean or (2) score on the ADOS Reciprocal Social Interaction algorithm met criteria for ASD or autism *and* the child received a diagnostic impression of impairment from the research examiner. The diagnostic impression of impairment indicated that there was significant evidence of social, behavioral, and/or communication impairment during the testing session based on disruption in social initiation and/or reciprocity, linguistic behavior (eg, grammatical errors, reduced inventory of words, difficulty expressing ideas, and pragmatic language errors), or, for example, highly uncooperative behavior.

Non-BAP Group

This group of AU sibs (n=58; 21 boys and 37 girls) did not meet the criteria specified for the ASD and BAP groups, but could have articulation or motor impairments. They might also have had a diagnostic impression of at least mild impairment, but standardized test scores fell within normal limits. The nature of the outcome diagnostic impression of impairment was language delay in 2 children, articulation impairment in 2 children, motor delay in 1 child, and impairment in multiple developmental domains in 8 children.

ANALYSES

To evaluate between-group comparisons for scores at 14 months of age (**Table 2**), we compared scores across groups by means of the Wilcoxon rank sum test (aka Mann-Whitney test), which is a nonparametric test for assessing differences in distributions. We used the same approach for assessing differences at 24 months (**Table 3**). However, the variable "response to joint attention," which had possible scores of 0, 1, and 2, was compared across groups by means of a 2-tailed Fisher exact test (all other variables were assumed to be continuous and evaluated by the Wilcoxon rank sum test).

To evaluate scores over time, we used a random effects linear regression model including data from ages 14, 18, and 24 months. Random intercepts were included for each child, main effects of age and group, and the interaction between age and group. We also considered more flexible models (eg, quadratic), but there was no evidence in the data that any additional flexibility was warranted beyond the linear assumption between age and scores for each score considered (based on Akaike Information Criterion and Bayesian Information Criterion). From these models, we estimated slopes for each group for each score and summarized these in **Table 4** with their 95% confidence intervals. Slopes of zero indicate no change over time, positive slopes indicate a positive association between age and score, and negative slopes indicate a negative association between age and score within a group. Differences in slopes were also estimated, along with 95% confidence intervals and their *P* values.

To be conservative and to account partially for multiple comparisons, the stringent threshold for significance was set at an α of .01. Trends toward differences were defined as having *P* values of .011 through .050. The only trends toward significance discussed in the "Results" section pertain to the within-group improvements from 14 to 24 months of age, which are not presented within the tables.

RESULTS

SOCIAL, COMMUNICATION, AND PLAY: EARLY- AND LATER-DIAGNOSIS GROUPS

We compared communication, social, and play behavior of the early and later ASD diagnosis groups, as well as the behavior of these ASD groups with the non-ASD groups (BAP, non-BAP, and LR controls at 14 and 24 months of age) (Table 2).

Early vs Later ASD Diagnosis Groups

Compared with the later-diagnosis group at 14 months of age, the early-diagnosis group produced significantly less frequent shared positive affect ($P=.002$), initiation of behavior regulatory bids ($P=.001$), and initiation of joint attention bids ($P=.009$), as well as a smaller inventory of gestures and consonants (all $P=.001$) (Table 2). By 24 months, these ASD groups exhibited similar frequency and diversity of social, communication, and play behaviors.

Early ASD Diagnosis vs Non-ASD Groups

At 14 months of age, the early-diagnosis group performed significantly worse than the non-BAP group on all variables (all $P\leq.01$). They performed worse than all non-ASD groups on gaze shifts and number of different action schema sequences ($P\leq.01$), initiation of joint attention, behavior regulatory bids, and inventory of gestures and consonants in syllables ($P\leq.001$). In addition, they performed worse than the LR controls in play behavior, producing a smaller inventory of action schema ($P\leq.01$). They also produced fewer instances of shared positive affect than the BAP group ($P=.009$) (Table 2).

At 24 months of age, the early-diagnosis group continued to perform worse than all of the non-ASD groups on all but 4 variables ($P<.009$). On 2 of these 4 variables (response to joint attention bids of others and directing play acts to others), they performed worse than the BAP and non-BAP groups ($P\leq.01$). They produced fewer

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

Table 2. Differences on CSBS DP Variables Between Early ASD Diagnosis, Later ASD Diagnosis, and Other Groups at 14 Months

Variable	Group[a]				
	ED (n = 15)	LD (n = 13)	BAP (n = 19)	Non-BAP (n = 51)	Control (n = 17)
Gaze shifts	5.67 (3.36 to 7.98)	8.46 (6.02 to 10.90)	10.58 (7.93 to 13.23)	12.53 (10.97 to 14.09)	14.18 (9.63 to 18.72)
Wilcoxon test *P* value					
ED vs other	. . .	.09	.01[b]	<.001[c]	.002[c]
LD vs other	.09	. . .	.34	.01[c]	.07
Shared positive affect	1.60 (0.60 to 2.60)	3.62 (2.85 to 4.38)	3.26 (2.48 to 4.05)	3.14 (2.65 to 3.62)	2.71 (1.88 to 3.53)
Wilcoxon test *P* value					
ED vs other	. . .	.002[c]	.009[c]	.005[c]	.06
LD vs other	.002[c]	. . .	.65	.43	.17
Response to joint attention bids	0.86 (0.47 to 1.24)	0.92 (0.40 to 1.44)	1.06 (0.62 to 1.49)	1.37 (1.15 to 1.60)	1.38 (0.95 to 1.80)
Wilcoxon test *P* value					
ED vs other	. . .	.37	.22	.01[c]	.07
LD vs other	.37	. . .	.99	.19	.41
Initiation of joint attention	0.60 (0.25 to 0.95)	5.08 (1.58 to 8.58)	4.53 (2.91 to 6.14)	7.04 (5.71 to 8.36)	4.41 (2.36 to 6.46)
Wilcoxon test *P* value					
ED vs other	. . .	.009[c]	<.001[c]	<.001[c]	<.001[c]
LD vs other	.009[c]	. . .	.64	.08	.78
Initiation of behavior regulation	4.07 (2.15 to 5.98)	10.00 (7.41 to 12.59)	9.95 (7.72 to 12.18)	11.08 (9.41 to 12.75)	13.24 (10.26 to 16.21)
Wilcoxon test *P* value					
ED vs other	. . .	.001[c]	<.001[c]	<.001[c]	<.001[c]
LD vs other	.001[c]	. . .	.98	.71	.12
Gesture inventory	1.60 (0.98 to 2.22)	3.62 (2.71 to 4.52)	3.05 (2.53 to 3.57)	3.90 (3.52 to 4.28)	3.71 (2.94 to 4.47)
Wilcoxon test *P* value					
ED vs other	. . .	.001[c]	.001[c]	<.001[c]	<.001[c]
LD vs other	.001[c]	. . .	.25	.64	.83
Consonant inventory	0.47 (0.06 to 0.88)	2.23 (1.30 to 3.16)	2.32 (1.58 to 3.05)	2.80 (2.32 to 3.29)	1.82 (1.19 to 2.46)
Wilcoxon test *P* value					
ED vs other	. . .	.001[c]	<.001[c]	<.001[c]	.001[c]
LD vs other	.001[c]	. . .	.95	.31	.43
Word inventory	0.20 (−0.03 to 0.43)	1.77 (0.27 to 3.27)	1.05 (0.12 to 1.98)	1.33 (0.88 to 1.79)	0.53 (0.21 to 0.85)
Wilcoxon test *P* value					
ED vs other	. . .	.06	.17	.002[c]	.12
LD vs other	.06	. . .	.55	.99	.41
Action schema inventory	3.20 (2.13 to 4.27)	5.15 (3.68 to 6.63)	4.95 (4.03 to 5.86)	5.25 (4.75 to 5.76)	5.18 (4.32 to 6.03)
Wilcoxon test *P* value					
ED vs other	. . .	.03[b]	.02[b]	.002[c]	.01[c]
LD vs other	.03[b]	. . .	.98	.77	.86
Action schema sequences	0.13 (−0.15 to 0.42)	0.46 (−0.07 to 0.99)	0.63 (0.26 to 1.00)	0.75 (0.49 to 1.00)	0.94 (0.44 to 1.44)
Wilcoxon test *P* value					
ED vs other	. . .	.23	.01[c]	.004[c]	.008[c]
LD vs other	.23	. . .	.25	.53	.23
Action schema toward others	0.73 (0.02 to 1.44)	1.69 (0.79 to 2.59)	1.53 (0.98 to 2.07)	1.71 (1.30 to 2.11)	1.35 (0.70 to 2.01)
Wilcoxon test *P* value					
ED vs other	. . .	.02[b]	.02[b]	.009[c]	.09
LD vs other	.02[b]	. . .	.98	.90	.54

Abbreviations: ASD, autism spectrum disorder; BAP, broader autism phenotype; CSBS DP, Communication and Symbolic Behavior Scales Developmental Profile; ED, early diagnosis; LD, later diagnosis; ellipses, not applicable.

[a] Unless otherwise indicated, data are given as mean score (95% confidence interval).

[b] Significant at $P \leq .050$ to .011, which indicates a trend for significance.

[c] Significant at $P \leq .010$, the standard used in this report.

types of action schema sequences than the non-BAP and LR control groups ($P \leq .01$). They did not differ from any group on inventory of action schema (Table 3).

Later ASD Diagnosis vs Non-ASD Groups

At 14 months of age, the later-diagnosis group differed from the non-ASD groups on only 1 variable, where they produced fewer gaze shifts than the non-BAP group ($P = .01$). However, by 24 months of age, the later-diagnosis group exhibited less frequent and diverse social and communication behavior than the non-ASD groups. Specifically, they exhibited less frequent shared positive affect ($P \leq .007$) and reduced inventory of gestures ($P \leq .008$) compared with all non-ASD groups. In comparison with the non-BAP group,

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

Table 3. Differences on CSBS DP Variables Between Early ASD Diagnosis, Later ASD Diagnosis, and Other Groups at 24 Months

Variable	Group[a]				
	ED (n = 13)	LD (n = 13)	BAP (n = 16)	Non-BAP (n = 52)	Control (n = 17)
Gaze shifts	3.54 (1.49 to 5.58)	7.08 (4.30 to 9.85)	8.75 (6.56 to 10.94)	11.81 (10.02 to 13.60)	11.76 (8.81 to 14.72)
Wilcoxon test *P* value					
ED vs other	. . .	.03[b]	.001[c]	<.001[c]	<.001[c]
LD vs other	.03[b]	. . .	.34	.02[b]	.03[b]
Shared positive affect	1.00 (0.15 to 1.85)	1.62 (0.85 to 2.38)	3.19 (2.43 to 3.95)	3.46 (3.04 to 3.88)	3.41 (2.45 to 4.37)
Wilcoxon test *P* value					
ED vs other	. . .	.13	.001[c]	<.001[c]	<.001[c]
LD vs other	.13	. . .	.006[c]	<.001[c]	.007[c]
Response to joint attention bids	0.92 (0.40 to 1.44)	1.00 (0.51 to 1.49)	1.69 (1.43 to 1.94)	1.71 (1.56 to 1.86)	1.76 (1.48 to 2.05)
Wilcoxon test *P* value					
ED vs other	. . .	.99	.01[c]	.001[c]	.02[b]
LD vs other	.99	. . .	.03[b]	.002[c]	.02[b]
Initiation of joint attention	3.31 (0.27 to 6.34)	5.23 (2.13 to 8.33)	9.81 (5.75 to 13.87)	14.37 (11.02 to 17.71)	12.71 (8.98 to 16.43)
Wilcoxon test *P* value					
ED vs other	. . .	.18	.005[c]	<.001[c]	<.001[c]
LD vs other	.18	. . .	.05[b]	.002[c]	.003[c]
Initiation of behavior regulation	7.00 (4.97 to 9.03)	10.00 (7.53 to 12.47)	13.50 (10.83 to 16.17)	13.87 (12.45 to 15.28)	14.59 (11.56 to 17.61)
Wilcoxon test *P* value					
ED vs other	. . .	.07	<.001[c]	<.001[c]	<.001[c]
LD vs other	.07	. . .	.06	.01[c]	.04[b]
Gesture inventory	2.62 (1.71 to 3.52)	3.08 (2.32 to 3.84)	4.50 (3.67 to 5.33)	4.60 (4.16 to 5.03)	4.82 (4.16 to 5.48)
Wilcoxon test *P* value					
ED vs other	. . .	.41	.004[c]	<.001[c]	<.001[c]
LD vs other	.41	. . .	.008[c]	.001[c]	.001[c]
Consonant inventory	2.46 (0.83 to 4.09)	4.69 (2.96 to 6.43)	6.44 (5.03 to 7.84)	7.21 (6.70 to 7.72)	6.59 (5.73 to 7.44)
Wilcoxon test *P* value					
ED vs other	. . .	.05[b]	.001[c]	<.001[c]	<.001[c]
LD vs other	.05[b]	. . .	.10	.003[c]	.04[b]
Word inventory	3.62 (1.17 to 6.06)	7.23 (3.42 to 11.04)	10.69 (7.67 to 13.71)	13.35 (12.17 to 14.53)	13.06 (11.07 to 15.05)
Wilcoxon test *P* value					
ED vs other	. . .	.13	.001[c]	<.001[c]	<.001[c]
LD vs other	.13	. . .	.10	.001[c]	.01[c]
Word combination inventory	0.46 (−0.12 to 1.05)	2.31 (0.68 to 3.93)	3.75 (1.80 to 5.70)	5.37 (4.53 to 6.20)	4.24 (2.43 to 6.04)
Wilcoxon test *P* value					
ED vs other	. . .	.04[b]	.01[c]	<.001[c]	.002[c]
LD vs other	.04[b]	. . .	.43	.003[c]	.24
Action schema inventory	4.92 (3.66 to 6.17)	5.23 (3.83 to 6.63)	6.19 (4.97 to 7.41)	6.35 (5.76 to 6.93)	5.76 (4.86 to 6.67)
Wilcoxon test *P* value					
ED vs other	. . .	.68	.11	.03[b]	.21
LD vs other	.68	. . .	.23	.09	.57
Action schema sequences	0.50 (0.07 to 0.93)	1.00 (0.45 to 1.55)	1.19 (0.60 to 1.78)	1.48 (1.18 to 1.78)	1.53 (0.80 to 2.26)
Wilcoxon test *P* value					
ED vs other	. . .	.21	.10	.003[c]	.01[c]
LD vs other	.21	. . .	.73	.19	.39
Action schema toward others	1.33 (0.60 to 2.07)	2.85 (1.52 to 4.17)	2.81 (2.01 to 3.62)	3.35 (2.89 to 3.80)	2.71 (1.80 to 3.61)
Wilcoxon test *P* value					
ED vs other	. . .	.09	.01[c]	<.001[c]	.04[b]
LD vs other	.09	. . .	.93	.39	.89

Abbreviations: ASD, autism spectrum disorder; BAP, broader autism phenotype; CSBS DP, Communication and Symbolic Behavior Scales Developmental Profile; ED, early diagnosis; LD, later diagnosis; ellipses, not applicable.

[a] Unless otherwise indicated, data are given as mean score (95% confidence interval).

[b] Significant at $P \leq .050$ to .011, which indicates a trend for significance.

[c] Significant at $P \leq .010$, the standard used in this report.

they responded less often to others' joint attention bids ($P = .002$), produced less frequent behavior regulatory bids ($P = .01$), and produced a smaller inventory of consonants ($P = .003$) and word combinations ($P < .001$). In addition, they initiated joint attention with others less often ($P \leq .003$) and produced a reduced inventory of words ($P \leq .01$) compared with the LR control and non-BAP groups.

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

Table 4. Average Changes From 14 to 24 Months (With Confidence Intervals)

Variable	Group[a] ED (n = 12)	LD (n = 12)	BAP (n = 16)	Non-BAP (n = 45)	Control (n = 16)
Gaze shifts	−2.37 (−5.65 to 0.92)	−1.50 (−4.87 to 1.88)	−1.88 (−4.81 to 1.04)	−0.82 (−2.53 to 0.89)	−2.49 (−5.43 to 0.46)
P value					
ED vs other	. . .	.72	.83	.41	.96
LD vs other	.72	. . .	.86	.73	.66
Shared positive affect	−0.67 (−1.70 to 0.36)	−2.14 (−3.20 to −1.08)	−0.20 (−1.11 to 0.72)	0.29 (−0.24 to 0.83)	0.68 (−0.25 to 1.60)
P value					
ED vs other	. . .	.05[b]	.50	.10	.06
LD vs other	.05[c]	. . .	.007[c]	<.001[c]	<.001[c]
Response to joint attention bids	0.02 (−0.45 to 0.50)	0.11 (−0.37 to 0.59)	0.60 (0.18 to 1.03)	0.33 (0.09 to 0.57)	0.38 (−0.06 to 0.81)
P value					
ED vs other	. . .	.80	.08	.27	.28
LD vs other	.80	. . .	.13	.43	.42
Initiation of joint attention	2.82 (−1.78 to 7.42)	−0.09 (−4.82 to 4.64)	5.30 (1.20 to 9.40)	7.33 (4.94 to 9.71)	8.08 (3.95 to 12.22)
P value					
ED vs other	. . .	.39	.43	.09	.10
LD vs other	.39	. . .	.09	.006[c]	.011[b]
Initiation of behavior regulation	2.70 (−1.11 to 6.50)	−0.18 (−4.11 to 3.75)	3.49 (0.08 to 6.89)	2.65 (0.67 to 4.62)	1.31 (−2.13 to 4.75)
P value					
ED vs other	. . .	.30	.76	.98	.60
LD vs other	.30	. . .	.17	.21	.58
Gesture inventory	1.07 (0.21 to 1.93)	−0.62 (−1.50 to 0.26)	1.46 (0.70 to 2.22)	0.73 (0.29 to 1.18)	1.03 (0.26 to 1.80)
P value					
ED vs other	. . .	.007[c]	.51	.49	.95
LD vs other	.007[c]	. . .	<.001[c]	.007[c]	.006[c]
Consonant inventory	1.92 (0.77 to 3.08)	2.40 (1.21 to 3.59)	4.16 (3.13 to 5.19)	4.43 (3.83 to 5.03)	4.66 (3.62 to 5.69)
P value					
ED vs other	. . .	.58	.005[c]	<.001[c]	<.001[c]
LD vs other	.58	. . .	.03[b]	.003[c]	.005[c]
Word inventory	3.42 (0.99 to 5.84)	5.56 (3.06 to 8.06)	9.73 (7.57 to 11.90)	12.00 (10.74 to 13.26)	12.45 (10.27 to 14.64)
P value					
ED vs other	. . .	.23	<.001[c]	<.001[c]	<.001[c]
LD vs other	.23	. . .	.01[c]	<.001[c]	<.001[c]
Word combination inventory	0.47 (−1.06 to 2.00)	2.29 (0.71 to 3.87)	3.78 (2.41 to 5.15)	5.45 (4.66 to 6.25)	4.25 (2.87 to 5.64)
P value					
ED vs other	. . .	.10	.001[c]	<.001[c]	<.001[c]
LD vs other	.10	. . .	.16	<.001[c]	.06
Action schema inventory	1.60 (0.25 to 2.95)	0.09 (−1.27 to 1.45)	1.20 (0.02 to 2.37)	1.10 (0.42 to 1.78)	0.57 (−0.62 to 1.75)
P value					
ED vs other	. . .	.12	.66	.52	.26
LD vs other	.12	. . .	.23	.19	.60
Action schema sequences	0.29 (−0.36 to 0.94)	0.54 (−0.10 to 1.19)	0.54 (−0.02 to 1.10)	0.75 (0.42 to 1.07)	0.59 (0.02 to 1.15)
P value					
ED vs other	. . .	.59	.57	.22	.50
LD vs other	.59	. . .	.99	.59	.92
Action schema toward others	0.55 (−0.58 to 1.67)	1.18 (0.05 to 2.31)	1.23 (0.25 to 2.20)	1.60 (1.03 to 2.17)	1.32 (0.33 to 2.31)
P value					
ED vs other	. . .	.44	.37	.10	.31
LD vs other	.44	. . .	.95	.51	.86

Abbreviations: BAP, broader autism phenotype; ED, early diagnosis; LD, later diagnosis; ellipses, not applicable.

[a] Unless otherwise indicated, data are given as mean change in score (95% confidence interval) from 14 to 24 months of age and are based on slopes in a random effects linear regression model including data on the 5 diagnostic groups at 14, 18, and 24 months of age.

[b] Significant at $P \leq .050$ to .011, which indicates a trend for significance.

[c] Significant at $P \leq .010$, the standard used in this report.

WITHIN-GROUP IMPROVEMENT IN SOCIAL, COMMUNICATION, AND PLAY DOMAINS

To determine whether the amount of change occurring within a group was significant, we tested whether the change between 14 and 24 months differed from zero. The early-diagnosis group made significant improvement in inventory of consonants and words produced ($P = .001$ and .006, respectively). A trend toward improvement was noted for inventory of gestures ($P = .01$) and action schema ($P = .02$).

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

The later-diagnosis group showed statistically significant improvement in inventory of consonants in syllables ($P < .001$), inventory of words ($P < .001$), and inventory of word combinations ($P = .004$), with significant decrease in frequency of shared positive affect ($P < .001$). A trend toward improvement was noted for frequency of action schema directed toward others ($P = .04$).

In stark contrast to the developmental pattern seen in ASD was the robust developmental gain made in communication, social, and play domains within the non-ASD groups. In the communication domain, all non-ASD groups exhibited significant gain in variety of gestures, consonants, words, and word combinations between 14 and 24 months of age (all $P < .008$). Socially, gains in joint attention were noted in increasing accuracy of response to others' joint attention bids in the BAP and non-BAP groups ($P \leq .008$) and in frequency of initiation of joint attention in the non-BAP and LR control groups ($P < .001$). The non-BAP group also exhibited significant gain in initiation of behavior regulatory acts ($P = .008$), inventory of action schema ($P = .002$), and inventory of action schema sequences ($P < .001$). Increase in the frequency of directing action schema to others was noted in the non-BAP and LR control groups ($P < .001$ and $P = .009$, respectively). There was a trend for an increase in frequency of initiation of behavior regulatory acts ($P = .04$), inventory of action schema ($P = .046$), and frequency with which action schema were directed to others in the BAP group ($P = .01$).

BETWEEN-GROUP COMPARISON OF DEVELOPMENTAL TRAJECTORY FROM 14 TO 24 MONTHS

The groups' change in frequency of production of shared positive affect, frequency of initiation of joint attention, inventory of gestures, and inventory of words are displayed in the **Figure**. The later-diagnosis group differed from the early-diagnosis group in trajectory of change in gesture inventory (decreasing slope for the later-diagnosis group with slightly increasing slope for the early-diagnosis group [Figure, C]; $P = .007$). In addition, the early-diagnosis group's developmental trajectory differed from that of the non-ASD groups in inventory of consonants in syllables ($P < .004$), words ($P < .001$), and word combinations ($P \leq .001$ compared with all non-ASD groups).

The change between 14 months and 24 months of age in the later ASD diagnosis group differed from that of all non-ASD groups for declining frequency of shared positive affect and inventory of gestures, while the non-ASD groups maintained a steady rate or inventory of these behaviors (all $P < .007$). The later-diagnosis group showed slower gains in rate of initiation of joint attention ($P \leq .01$), inventory of consonants ($P \leq .005$), and inventory of words ($P < .001$ compared with the non-BAP and LR control groups), as well as word combinations ($P < .001$ compared with the non-BAP group). The Figure displays the developmental trajectory in the 5 groups and illustrates that the children with ASD tended to show decreases (shared positive affect for both ASD groups; gesture inventory for later-diagnosis group) or arrest (initiation of joint attention for the later-diagnosis group) or make very slow gains compared with other groups (eg, in word inventory) from 14 to 24 months of age.

COMMENT

This is, to our knowledge, the first prospective study of ASD from 14 to 36 months of age to document distinct patterns of social, communication, and play development associated with early and later diagnoses of ASD; these findings support the retrospective findings of significantly disrupted development by the first birthday in some children with autism,[4-15] but not others. Indeed, some children in this study showed sufficient social and communication variation from typical development by 14 months of age to justify a diagnostic impression of ASD. The toddlers with an early diagnosis of ASD were clearly differentiated at 14 months of age from all other groups, even from those with a later diagnosis of ASD, in social and communication domains. Their social, communication, and play behavior also differed from that of the non-ASD groups at 24 months of age. In contrast, toddlers having a later diagnosis of ASD exhibited a progressive shift away from typical social and communication development between 14 and 24 months of age. At 14 months, they were essentially indistinguishable from those without ASD on the social and communication variables examined. By 24 months, however, they exhibited less frequent and diverse social and communication behavior than the non-ASD groups. Of note is the continuum of scores for particular variables, such as gaze shifts and initiation of joint attention at 14 and 24 months, for the siblings of children with autism: the early-diagnosis group produced the fewest, followed by the later-diagnosis and BAP groups, followed by the non-BAP group. Our data may suggest the presence of some continuously, rather than discretely, distributed traits in families with genetic risk for autism.

Gains in toddlers with ASD outcomes were minimal, in stark contrast to toddlers without ASD outcomes. Examination of growth trajectories indicated that social gains were even more negligible than gains in play and communication. In fact, a statistically significant decrease in shared positive affect was noted in the later-diagnosis group. Our data suggest that, in many cases, ASD has a progressive phase involving developmental arrest, slowing, or even regression in social and/or language systems. This phenomenon has been indicated by retrospective reports of autistic regression[23-28] and in one prospective report.[32] In a prospective study of infant AU sibs, Zwaigenbaum and colleagues[32] noted an atypical trajectory of development of attention disengagement. That is, some infant AU sibs showed increasing latencies to disengage attention between 6 and 12 months of age, which contrasts with the pattern seen in typically developing infants, where latency to disengage attention decreases within that time frame.[43]

CHARACTERISTICS OF CHILDREN IN THE EARLY-DIAGNOSIS GROUP

Children classified as having an early ASD diagnosis showed abnormalities in all aspects of joint attention, in initiation of communication with others, and in the variety of vocal and nonvocal forms used to express com-

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

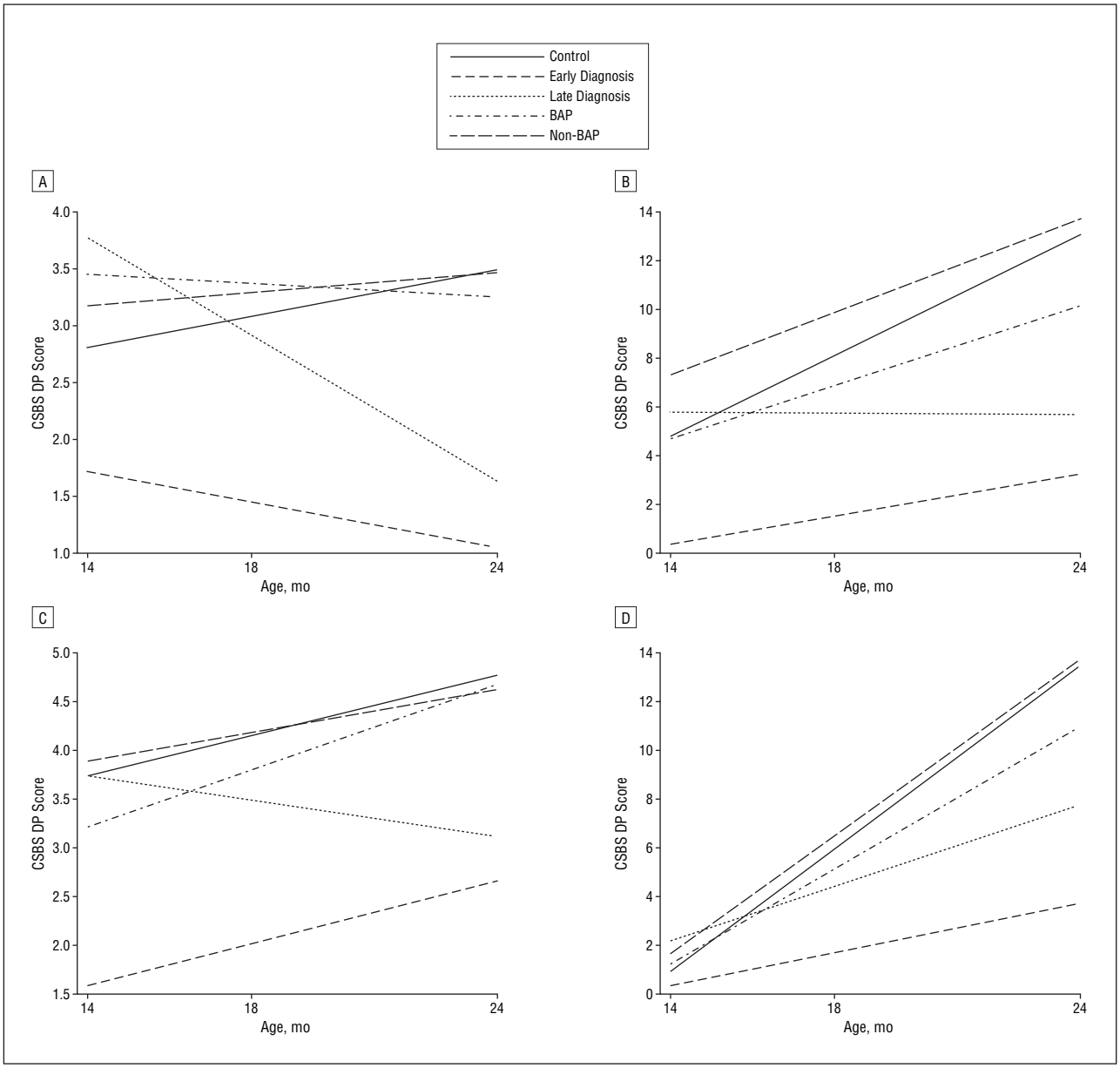

Figure. Developmental change of the 5 groups from 14 to 24 months of age on the Communication and Symbolic Behavior Scales Developmental Profile (CSBS DP) for frequency of shared positive affect (A), frequency of initiation of joint attention bids (B), inventory of gestures (C), and inventory of words (D). BAP indicates broader autism phenotype.

municative initiations by 14 months of age, and these persisted through 24 months of age. Furthermore, the deficits extended beyond the social-communication domain to include object play; toddlers with an early diagnosis were also less able to integrate play into social engagement. The deficits observed at 14 months of age involved skills that emerge in typically developing infants at 8 to 10 months. These deficits were greater than what would be expected given the level of development as indicated by the mean Mullen Scales of Early Learning early learning composite of 79.6 in this group. Of note were the unconventional forms of some communication behavior in the early-diagnosis group, which were sometimes so atypical that they were difficult to recognize as intentional attempts to direct a message to another. In addition, vocalizations were less often paired with eye contact or gesture and, thus, were not credited in the CSBS DP coding system as communicative initiations.

CHARACTERISTICS OF CHILDREN IN THE LATER-DIAGNOSIS GROUP

Children classified as having a later ASD diagnosis began to exhibit signs of ASD by the second birthday in most cases. All but 1 of these children had been rated by expert clinicians as having developmental disruption at 14 months (communication impairment for 6 children, motor impairment for 1 child, and multiple areas of concern involving some combination of motor, social, behavioral, and language difficulties for 6 children), but, overall, they were not judged to have an ASD at that age. By the second birthday, the course of development for a

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

child in the later ASD diagnosis group had shifted, differing from non-ASD groups in social and communication behavior, but not from children with an early ASD diagnosis. This developmental departure was accounted for by slowed growth (inventory of consonants in syllables, words, and word combinations), plateaus (initiation of joint attention and behavior regulatory bids), and even decreases (shared positive affect and inventory of gestures) in behaviors within social and communication systems. We identified this developmental change between 14 and 24 months of age, but it may begin before or continue after this age; we did not have sufficient numbers of children with CSBS DP data before 14 or after 24 months to examine this issue. Our data validate parents' reports that ASD may appear after a period of nonautistic development; such reports should not be attributed to recall bias. Thus, we propose a continuum of impairment, where children reach the threshold for diagnosis at different times in the first 3 years of life. We will examine this issue in future studies.

PATTERN OF SOCIAL AND COMMUNICATION GROWTH FROM 14 TO 24 MONTHS

For some aspects of development, no differences in pattern of growth were detected across ASD and non-ASD groups between 14 and 24 months of age. For example, none of the groups showed an increase in frequency of gaze shifts, and both the early-diagnosis and BAP groups made gains in frequency of initiation of behavior regulatory bids, although these gains were not statistically significant. In other aspects of development, the ASD and non-ASD groups differed in their pattern of growth from 14 to 24 months of age. In contrast to significant gains made by all or some non-ASD groups in verbal forms of communication, nonverbal communication (eg, gestures), initiation of communicative bids, response to others' joint attention bids, and play, the ASD groups showed significant gains only in variety of verbal forms of communication (consonants, words, and word combinations). These gains were smaller than in the non-ASD group. These findings are clinically relevant because this pattern of slowing, plateauing, and decline in development occurred within the same age period during which parents usually report their first concerns about their child later diagnosed as having ASD.[42,44] Important neurobiological processes that typically occur during this period of robust social and communication growth may be disrupted in autism. Those processes include selective neural pruning, rapid synaptogenesis, expansion of dendritic and axon arbors, shaping of neural architecture, and cortical connectivity.[45]

Our findings of slowed social and communication development between 14 and 24 months, paired with findings from Charman and colleagues[46,47] that nonverbal communication characteristics of autism are stable from 3 to 7 years of age, emphasize the urgency to determine whether very early interventions could alter the course of ASD. Given our finding that gains in variety of communicative forms (eg, consonants in syllables) are made, albeit slowly, by children with ASD between 14 and 24 months, we are hopeful that even greater gains would be possible through early intervention. Because early social and communication functioning in ASD plays a major role in prognosis[47,48] and community acceptance, efforts to alter the severity of these aspects of the disorder should be made as early in life as possible.

IMPLICATIONS OF THE SOCIAL AND COMMUNICATION BEHAVIOR IN TODDLERS WITH ASD

Early and persistent impairment in the ASD groups involved joint attention, including coordination of attention with another through triadic gaze shifting (from object/event to person and back to object/event), response to others' bids to share attention to an object, and initiation of bids for others to share attention with the child. An early impairment in joint attention has many implications for a child, including the ability to learn new words in incidental learning contexts (which constitute most of the lexical learning opportunities toddlers encounter),[49] development of understanding of others' intentions and internal states,[50] and severity of ASD symptoms in adolescence.[51,52]

Yet the deficits in the toddlers with ASD extended beyond just joint attention. Toddlers with ASD appeared to be quite compromised in the motivation and resources required to exchange communicative intentions by using conventional acts (eg, variety of gestures, consonants, and words) to share experience or to elicit assistance from someone. The aspects of impairment seen in the toddlers with ASD involved early-developing skills[53,54] that represent a critical milestone in early social learning.[55,56] Our data are consistent with proposals by others that an early deficit in ASD involves maldevelopment of motivation for social approach and social orienting,[57,58] which is reportedly mediated by frontal systems.[59] Such a disturbance in very early development, such as documented in this report, could interfere with infants' ability to co-create social learning opportunities in their engagement with others. This, in turn, could lead to considerable reductions in the diversity and amount of social input that contributes to experience-dependent neurodevelopmental processes.[60-62] Furthermore, the ASD groups' widespread attenuation of diversity in nonverbal and verbal communicative forms may reflect an overall inflexibility in communicative development. Nevertheless, at least for the later ASD diagnosis group, gains in new communicative forms (consonants, words) occurred at the same time that social functioning behaviors had plateaued or were even declining.

IMPLICATIONS FOR EARLY DETECTION OF ASD

Around the time of the first birthday, some toddlers later diagnosed as having ASD may produce near-typical or fully typical frequencies of social and communicative behaviors. That is, they may fail to show early markers of ASD involving joint attention, shared positive affect, or communicative initiations with others. These toddlers are likely to pass early ASD-specific screenings or assessments. Thus, if screening is implemented near the first birthday, it must be repeated near the second birthday to capture those who do not present with an ASD diag-

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

nosis until later. Siblings of children with autism require diligent developmental surveillance given their high risk for ASD and milder variants.[17,30,63] Continued work is needed for the development of reliable and valid diagnostic tools to make more accurate and earlier diagnoses in children 2 years and younger. Such work is currently under way at the University of Michigan, where Lord is preparing a version of the ADOS for use with children younger than 24 months and with very little or no spoken language (Catherine Lord, PhD, oral communication, June 2006). The existing version of the ADOS was not intended for use with children as young as 14 months, and our use of it in 14-month-olds was experimental. We found that some children (3 LR controls, 2 in the non-BAP group, and 2 in the BAP group) met ADOS algorithm criteria for ASD or autism at 14 months of age but did not have outcome diagnoses of ASD. At 24 months of age, the number of children from non-ASD groups who met ADOS criteria for ASD or autism remained the same as at 14 months, except for the BAP group, in which 6 children met these criteria. The diagnosis of ASD should not be made on the basis of ADOS scores alone; expert clinical judgment is required.

TREATMENT IMPLICATIONS

The developmental trends identified in children with ASD in this report highlight the need for early intervention and for these programs to robustly target social affective, social cognitive, and communication development in toddlers with ASD, in addition to the current emphasis on visual-spatial, vocabulary, receptive identification, and gross motor imitation skills. These skills can be taught[64-67] and may transform outcome. In addition, gestural aspects of communication, which were quite impaired in our sample of toddlers with ASD, should be emphasized in intervention, at least during the early stages of lexical and syntactic development, because early gesture may pave the way for future linguistic development.[68,69] In addition, longitudinal research indicates that failure to acquire gestural joint attention may be related to impaired language development.[50,70]

Caution should be taken with interpretation of our results until this study is replicated. The findings of this study may not be generalizable to the population at large because the toddlers with ASD in this study were at high genetic risk for ASD and the majority were white. More research is needed with larger samples to further explore the patterns of early and later diagnoses of ASD reported herein and to establish behavioral and biological markers for ASD in infants and toddlers.

Submitted for Publication: August 25, 2006; final revision received December 15, 2006; accepted December 15, 2006.
Correspondence: Rebecca J. Landa, PhD, Kennedy Krieger Institute, 3901 Greenspring Ave, Baltimore, MD 21211.
Author Contributions: Dr Landa had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Financial Disclosure: None reported.
Funding/Support: This study was funded by grants MH59630 and 154MH066417 (Studies to Advance Autism Research and Treatment) from the National Institute of Mental Health (R.J.L., principal investigator).
Additional Contributions: We thank the participants in this study. We also thank the superb staff who provided administrative support, videotaped test sessions, and processed data. We thank Dana Christina, BS, for data organization at the Boston site; Alison Marvin, MPhil, who assisted with data management for the overall study; Jim Mancini, MS, Ashley Edmunds, MEd, Sarah Beal, MEd, Cornelia Taylor, PhD, and Julie Cleary, PhD, for their assistance with data coding; and Laura Becker, PhD, Julie Cleary, PhD, Kelley Shaw, MS, Seton Lindsay, MS, Jim Mancini, MS, Allison Nelson, MS, and Audrey Thurm, PhD, for their assistance in data collection. Special appreciation is expressed to Margaret Bauman, MD, for her oversight of the Boston data collection process.

REFERENCES

1. Bauman ML, Kemper T. The neuropathology of the autism spectrum disorders: what have we learned? *Novartis Found Symp*. 2003;251:112-122.
2. Mandell DS, Walrath CM, Manteuffel B, Sgro G, Pinto-Martin J. Characteristics of children with autistic spectrum disorders served in comprehensive community-based mental health settings. *J Autism Dev Disord*. 2005;35(3):313-321.
3. Courchesne E, Carper R, Akshoomoff N. Evidence of brain overgrowth in the first year of life in autism. *JAMA*. 2003;290(3):337-344.
4. Adrien JL, Perrot A, Sauvage D, Leddet I, Larmande C, Hameury L, Barthelemy C. Early symptoms in autism from family home movies: evaluation and comparison between 1st and 2nd year of life using I.B.S.E. scale. *Acta Paedopsychiatr*. 1992;55(2):71-75.
5. Maestro S, Casella C, Milone A, Muratori F, Palacio-Espasa F. Study of the onset of autism through home movies. *Psychopathology*. 1999;32(6):292-300.
6. Mars AE, Mauk J, Dowrick P. Symptoms of pervasive developmental disorders as observed in prediagnostic home videos of infants and toddlers. *J Pediatr*. 1998; 132(3, pt 1):500-504.
7. Osterling J, Dawson G. Early recognition of children with autism: a study of first birthday home videotapes. *J Autism Dev Disord*. 1994;24(3):247-257.
8. Osterling J, Dawson G. Early identification of one-year-olds with autism versus mental retardation. Poster presented at: Society of Research in Child Development Meeting; April 15, 1999; Albuquerque, NM.
9. Werner E, Dawson G, Osterling J, Dinno N. Report of autism spectrum disorder before one year of age: a retrospective study based on home videotapes. *J Autism Dev Disord*. 2000;30(2):157-162.
10. Werner E, Dawson G, Munson J, Osterling J. Variation in early developmental course in autism and its relation with behavioral outcome at 3-4 years of age. *J Autism Dev Disord*. 2005;35(3):337-350.
11. Adrien JL, Lenior P, Martineau J, Perrot A, Hameury L, Larmande C, Sauvage D. Blind ratings of early symptoms of autism based upon family home movies. *J Am Acad Child Adolesc Psychiatry*. 1993;32(3):617-626.
12. Baranek GT. Autism during infancy: a retrospective video analysis of sensory-motor and social behaviors at 9-12 months of age. *J Autism Dev Disord*. 1999; 29(3):213-224.
13. Osterling JA, Dawson G, Munson J. Early recognition of 1-year-old infants with autism spectrum disorder versus mental retardation. *Dev Psychopathol*. 2002; 14(2):239-251.
14. Dawson G, Webb S, Carver L, Panagiotides H, McPartland J. Young children with autism show atypical brain responses to fearful versus neutral facial expressions of emotion. *Dev Sci*. 2004;7(3):340-359.
15. Maestro S, Muratori F, Cesari A, Pecini C, Apicella F, Stern D. A view to regressive autism through home movies: is early development really normal? *Acta Psychiatr Scand*. 2006;113(1):68-72.
16. Maestro S, Muratori F, Cesari A, Cavallaro MC, Paziente A, Pecini C, Grassi C, Manfredi A, Sommario C. Course of autism signs in the first year of life. *Psychopathology*. 2005;38(1):26-31.
17. Landa R, Garrett-Mayer E. Development in infants with autism spectrum disorders: a prospective study. *J Child Psychol Psychiatry*. 2006;47(6):629-638.
18. Charman T, Swettenham J, Baron-Cohen S, Cox A, Baird G, Drew A. Infants with autism: an investigation of empathy, pretend play, joint attention and imitation. *Dev Psychol*. 1997;33(5):781-789.

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016

19. Sullivan M, Finelli J, Marvin A, Garrett-Mayer E, Bauman M, Landa R. Response to joint attention in toddlers at risk for autism spectrum disorder: a prospective study. *J Autism Dev Disord*. 2007;37(1):37-48.
20. Wetherby AM, Woods J, Allen L, Cleary J, Dickinson H, Lord C. Early indicators of autism spectrum disorder in the second year of life. *J Autism Dev Disord*. 2004; 34(5):473-493.
21. Baghdadli A, Picot MC, Pascal C, Pry R, Aussiloux C. Relationship between age of recognition of first disturbances and severity in young children with autism. *Eur Child Adolesc Psychiatry*. 2003;12(3):122-127.
22. De Giacomo A, Fombonne E. Parental recognition of developmental abnormalities in autism. *Eur Child Adolesc Psychiatry*. 1998;7(3):131-136.
23. Werner E, Dawson G. Validation of the phenomenon of autistic regression using home videotapes. *Arch Gen Psychiatry*. 2005;62(8):889-895.
24. Hoshino Y, Kaneko M, Yashima Y, Kumashiro H, Volkmar FR, Cohen DJ. Clinical features of autistic children with setback course in their infancy. *Jpn J Psychiatry Neurol*. 1987;41(2):237-245.
25. Lord C, Shulman C, DiLavore P. Regression and word loss in autistic spectrum disorders. *J Child Psychol Psychiatry*. 2004;45(5):936-955.
26. Luyster R, Richler J, Risi S, Hsu W, Dawson G, Bernier R, Dunn M, Hepburn S, Hyman SL, McMahon WM, Goudie-Nice J, Minshew N, Rogers S, Sigman M, Spence MA, Goldberg WA, Tager-Flusberg H, Volkmar FR, Lord C. Early regression in social communication in autism spectrum disorders: a CPEA study. *Dev Neuropsychol*. 2005;27(3):311-336.
27. Ozonoff S, Williams B, Landa R. Parental report of the early development of children with regressive autism: the delays-plus-regression phenotype. *Autism*. 2005; 9(5):461-486.
28. Tuchman RF, Rapin I. Regression in pervasive developmental disorders: seizures and epileptiform electroencephalogram correlates. *Pediatrics*. 1997;99 (4):560-566.
29. Bailey A, Le Couteur A, Gottesman I, Bolton P, Simonoff E, Yuzda E, Rutter M. Autism as a strongly genetic disorder: evidence from a British twin study. *Psychol Med*. 1995;25(1):63-77.
30. Yirmiya N, Gamliel I, Pilowsky T, Feldman R, Baron-Cohen S, Sigman M. The development of siblings of children with autism at 4 and 14 months: social engagement, communication, and cognition. *J Child Psychol Psychiatry*. 2006; 47(5):511-523.
31. Folstein SE, Santangelo SL, Gilman SE, Piven J, Landa R, Lainhart J, Hein J, Wzorek M. Predictors of cognitive test patterns in autism families. *J Child Psychol Psychiatry*. 1999;40(7):1117-1128.
32. Zwaigenbaum L, Bryson S, Rogers T, Roberts W, Brian J, Szatmari P. Behavioral manifestations of autism in the first year of life. *Int J Dev Neurosci*. 2005; 23(2-3):143-152.
33. Fombonne E, Chakrabarti S. No evidence for a new variant of measles-mumps-rubella–induced autism. *Pediatrics*. 2001;108(4):e58.
34. Wetherby A, Prizant B. *CSBS DP Manual: Communication and Symbolic Behavior Scales Developmental Profile*. Baltimore, MD: Paul H Brookes Publishing Co; 2002.
35. Lord C, Rutter M, DiLavore P, Risi S. *Autism Diagnostic Observation Schedule*. Los Angeles, CA: Western Psychological Services; 1999.
36. Mullen EM. *Mullen: Scales of Early Learning (AGS Edition)*. Circle Pines, MN: American Guidance Service; 1995.
37. Zimmerman IL, Steiner VG, Pond RE. *Preschool Language Scale, Third Edition (PLS-3)*. San Antonio, TX: Psychological Corp; 1991.
38. Zimmerman IL, Steiner VG, Pond RE. *Preschool Language Scale, Fourth Edition (PLS-4)*. San Antonio, TX: Psychological Corp; 2002.
39. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
40. Klin A, Lang J, Cicchetti DV, Volkmar FR. Interrater reliability of clinical diagnosis and *DSM-IV* criteria for autistic disorder: results of the *DSM-IV* autism field trial. *J Autism Dev Disord*. 2000;30(2):163-167.
41. Volkmar FR, Cohen DJ. Disintegrative disorder or "late onset" autism. *J Child Psychol Psychiatry*. 1989;30(5):717-724.
42. Howlin P, Moore A. Diagnosis of autism: a survey of over 1200 patients in the UK. *Autism*. 1997;1:135-162.
43. Hood BM, Atkinson J. Disengaging visual attention in the infant and adult. *Infant Behav Dev*. 1993;16:405-422.
44. Siegel B, Pliner C, Eschler J, Elliott GR. How children with autism are diagnosed: difficulties in identification of children with multiple developmental delays. *J Dev Behav Pediatr*. 1988;9(4):199-204.
45. Retz W, Kornhuber J, Riederer P. Neurotransmission and the ontogeny of human brain. *J Neural Transm*. 1996;103(4):403-419.
46. Charman T, Baron-Cohen S, Swettenham J, Baird G, Drew A, Cox A. Predicting language outcome in infants with autism and pervasive developmental disorder. *Int J Lang Commun Disord*. 2003;38(3):265-285.
47. Charman T, Taylor E, Drew A, Cockerill H, Brown J, Baird G. Outcome at 7 years of children diagnosed with autism at age 2: predictive validity of assessments conducted at 2 and 3 years of age and pattern of symptom change over time. *J Child Psychol Psychiatry*. 2005;46(5):500-513.
48. Lord C, Schopler E. Stability of assessment results of autistic and non-autistic language-impaired children from preschool years to early school age. *J Child Psychol Psychiatry*. 1989;30(4):575-590.
49. Baron-Cohen S, Baldwin DA, Crowson M. Do children with autism use the speaker's direction of gaze strategy to crack the code of language? *Child Dev*. 1997; 68(1):48-57.
50. Tomasello M, Carpenter M, Call J, Behne T, Moll H. Understanding and sharing intentions: the origins of cultural cognition. *Behav Brain Sci*. 2005;28(5):675-735.
51. Mundy P, Sigman M, Kasari C. Joint attention, developmental level, and symptom presentation in autism. *Dev Psychopathol*. 1994;6:389-401.
52. Sigman M, Ruskin E, Arbeile S, Corona R, Dissanayake C, Espinosa M, Kim N, Lopez A, Zierhut C. Continuity and change in the social competence of children with autism, Down syndrome, and developmental delays. *Monogr Soc Res Child Dev*. 1999;64(1):1-114.
53. Scaife M, Bruner JS. The capacity for joint visual attention in the infant. *Nature*. 1975;253(5489):265-266.
54. Butterworth G, Jarrett N. What minds have in common is space: spatial mechanisms serving joint visual attention in infancy. *Br J Dev Psychol*. 1991;9:55-72.
55. Bakeman R, Adamson LB. Coordinating attention to people and objects in mother-infant and peer-infant interaction. *Child Dev*. 1984;55(4):1278-1289.
56. Baldwin D. Understanding the link between joint attention and language. In: Moore C, Dunhan PJ, eds. *Joint Attention: Its Origins and Role in Development*. Mahwah, NJ: Lawrence A Erlbaum Associates Inc; 1995:131-158.
57. Dawson G, Toth K, Abbott R, Osterling J, Munson J, Estes A, Liaw J. Early social attention impairments in autism: social orienting, joint attention and attention to distress. *Dev Psychol*. 2004;40(2):271-283.
58. Mundy P. Annotation: the neural basis of social impairments in autism: the role of the dorsal medial-frontal cortex and anterior cingulate system. *J Child Psychol Psychiatry*. 2003;44(6):793-809.
59. Panksepp J. A neurochemical theory of autism. *Trends Neurosci*. 1979;2:174-177.
60. Johnson MH, Munakata Y. Processes of change in brain and cognitive development. *Trends Cogn Sci*. 2005;9(3):152-158.
61. Klin A, Jones W, Schultz R, Volkmar F. The enactive mind, or from actions to cognition: lessons from autism. *Philos Trans R Soc Lond B Biol Sci*. 2003; 358(1430):345-360.
62. Mundy P, Neal AR. Neural plasticity, joint attention, and a transactional social-orienting model of autism. *Int Rev Res Ment Retard*. 2000;23:139-168.
63. Mitchell S, Brian J, Zwaigenbaum L, Roberts W, Szatmari P, Smith I, Bryson S. Early language and communication development of infants later diagnosed with autism spectrum disorder. *J Dev Behav Pediatr*. 2006;27(2)(suppl):S69-S78.
64. Kasari C, Freeman S, Paparella T. Joint attention and symbolic play in young children with autism: a randomized controlled intervention study. *J Child Psychol Psychiatry*. 2006;47(6):611-620.
65. Landa R, Holman KC. The effects of targeting interpersonal synchrony on social and communication development in toddlers with autism. Presented at: Annual Collaborative Programs Excellence in Autism/Studies to Advance Autism Research and Treatment Meeting; November 9, 2005; Washington, DC.
66. Whalen C, Schreibman L. Joint attention training for children with autism using behavior modification procedures. *J Child Psychol Psychiatry*. 2003;44(3): 456-468.
67. Whalen C, Schreibman L, Ingersoll B. The collateral effects of joint attention training on social initiations, positive affect, imitation, and spontaneous speech for young children with autism. *J Autism Dev Disord*. 2006;36(5):655-664.
68. Iverson JM, Goldin-Meadow S. Gesture paves the way for language development. *Psychol Sci*. 2005;16(5):367-371.
69. Ozçalişkan S, Goldin-Meadow S. Gesture is at the cutting edge of early language development. *Cognition*. 2005;96(3):B101-B113.
70. Mundy P, Sigman M, Kasari C. A longitudinal study of joint attention and language development in autistic children. *J Autism Dev Disord*. 1990;20(1):115-128.

©2007 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 02/14/2016