The Broader Autism Phenotype in Infancy: When Does It Emerge?

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Objective: This study had 3 goals, which were to examine the following: the frequency of atypical development, consistent with the broader autism phenotype, in high-risk infant siblings of children with autism spectrum disorder (ASD); the age at which atypical development is first evident; and which developmental domains are affected. **Method:** A prospective longitudinal design was used to compare 294 high-risk infants and 116 low-risk infants. Participants were tested at 6, 12, 18, 24, and 36 months of age. At the final visit, outcome was classified as ASD, Typical Development (TD), or Non-TD (defined as elevated Autism Diagnostic Observation Schedule [ADOS] score, low Mullen Scale scores, or both). **Results:** Of the high-risk group, 28% were classified as Non-TD at 36 months of age. Growth curve models demonstrated that the Non-TD group could not be distinguished from the other groups at 6 months of age, but differed significantly from the Low-Risk TD group by 12 months on multiple measures. The Non-TD group demonstrated atypical development in cognitive, motor, language, and social domains, with differences particularly prominent in the social-communication domain. **Conclusions:** These results demonstrate that features of atypical development, consistent with the broader autism phenotype, are detectable by the first birthday and affect development in multiple domains. This highlights the necessity for close developmental surveillance of infant siblings of children with ASD, along with implementation of appropriate interventions as needed. J. Am. Acad. Child Adolesc. Psychiatry, 2014;53(4):398–407. **Key Words:** autism spectrum disorder, broader autism phenotype, siblings, social-communication, infancy

The broader autism phenotype (BAP) is a constellation of subclinical characteristics that are seen at elevated rates in family members of children with autism spectrum disorder (ASD).[1] It is generally agreed that the BAP encompasses features related to the core diagnostic domains of ASD, such as language delays and deficits, social difficulties, and rigidity of personality or behavior.[2,3] Most previous studies have examined the BAP in parents and school-age siblings of children with ASD[2,3]; few have investigated BAP features in infancy and toddlerhood, so it is not clear when these differences in behavior first develop and can be detected.

For questions that require precise timing of onset, prospective studies provide an optimal experimental design, because they do not rely solely on parent report, which can be subject to recall errors and other biases. In the past decade, prospective studies of high-risk infants have proliferated. Most commonly, the individuals at increased risk for ASD studied thus far are later-born siblings of children with ASD. Such infant sibling study designs often compare high-risk samples to low-risk infants with no family history of ASD. Although several dozen such studies have been published, most focus on describing the early development and predictive early risk signs of infants who ultimately develop ASD.[4,5] Other infant sibling studies have reported differences between high- and low-risk groups in a variety of domains, including eye contact, joint

This article is discussed in an editorial by Dr. John R. Pruett, Jr. on page 392.

Clinical guidance is available at the end of this article.

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attention, and nonverbal reasoning, but did not follow the infants long enough to know whether these differences were early signs of ASD or might instead index other types of atypical outcomes, including the BAP.[6-9]

Only a few infant sibling studies have specifically focused on describing early signs of the BAP.[10-15] These investigations follow participants until age 3 years, determine which children develop ASD, and remove them from the larger high-risk group before analyses (because, by definition, the BAP and ASD are mutually exclusive). Several studies, most involving small samples, have found significant differences between high-risk non-ASD groups and low-risk control individuals early in life, on tasks of response to joint attention at 14 months (n = 8)[10] and social referencing at 18 months (n = 30),[11] as well as on parent report measures of temperament as early as 7 months (n = 12).[12] Early differences in parent-reported temperament in high-risk siblings without ASD have also been reported in a much larger sample at 24 months of age (n = 104).[13] In a comprehensive study examining multiple domains of development, 40 high-risk siblings without ASD outcomes were, as a group, below average in expressive and receptive language, overall IQ, adaptive behavior, and social communication skills at 18 to 27 months.[14] In addition, parents reported social impairments on a questionnaire by 13 months of age. A recent large study followed 170 high-risk children, none of whom were diagnosed as having ASD at age 3 years.[15] A cluster analysis identified a subgroup (19% of the high-risk sample) that had elevated scores on the Autism Observation Scale for Infants at 12 months of age. At age 3, this cluster demonstrated lower scores than low-risk controls on independent social-communication and cognitive measures. Taken together, these and other studies strongly suggest that behavioral and developmental features consistent with the BAP emerge early in life.

Most published sibling studies have been cross-sectional and/or focused on whether group differences are evident at a single age. Only 1 study thus far has examined longitudinal trajectories of development, following a cohort of 37 high-risk children from 4 months to 7 years of age.[16] At 7 years, the researchers split their high-risk group into 2 subgroups, 1 group with BAP features (40%) and 1 group without, and then examined their cognitive and language trajectories in the preschool years (4–54 months) using growth curve analysis. They found that language scores were different for the BAP group as early as 14 months, but that cognitive scores did not differentiate the group from the low-risk controls at any age. The current study took a similar approach, examining development longitudinally from 6 to 36 months in high- and low-risk infants (n = 294 and n = 116, respectively) and looking for the earliest inflection point at which the trajectories diverge from one of typical to atypical development. The current study is the largest sample to date that examines BAP features longitudinally. We focus on several domains of early development: social-communication, language, nonverbal cognitive, and fine motor abilities.

The studies reviewed above have taken 1 of 2 approaches when studying the BAP. Some have studied all children in the high-risk group, after excluding those with an ASD outcome, looking for differences from low-risk infants.[14] Others have classified an "atypical" outcome group, using varying criteria at varying outcome ages, and then examined whether this "atypical" subgroup differs from low-risk controls at earlier ages than when the groups were defined.[10,12,16] This latter approach is the one used in the current study. It is clear that there is substantial heterogeneity within the high-risk group; virtually all previous studies find that atypical development or BAP-like features are present in only a subset of siblings of children with ASD.[2,3,17] Therefore, studying all high-risk siblings without ASD outcomes risks the possibility of obscuring potential differences that may be evident in a subgroup. Using a definition similar to other recent investigations,[10,12] we identified a group of high-risk children with non-typical developmental outcomes at 36 months of age. We then used growth curve analysis to examine when non-typical development could first be detected. We studied multiple areas of development, extending more broadly than the BAP (e.g., social-communication, but also cognition and motor skills), to examine in which domains non-typical development was evident.

METHOD

Participants

The sample reported in this article was drawn from a larger longitudinal study of infant siblings of children with ASD (High-Risk group) or children with typical development (Low-Risk group), recruited at 2 sites (University of California, Davis [UC Davis] and University of California, Los Angeles [UCLA]) during 2 phases of grant funding (2003–2008 and 2008–2013).