Decreased Spontaneous Attention to Social Scenes in 6-Month-Old Infants Later Diagnosed with Autism Spectrum Disorders

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Background: The ability to spontaneously attend to the social overtures and activities of others is essential for the development of social cognition and communication. This ability is critically impaired in toddlers with autism spectrum disorders (ASD); however, it is not clear if prodromal symptoms in this area are already present in the first year of life of those affected by the disorder.

Methods: To examine whether 6-month-old infants later diagnosed with ASD exhibit atypical spontaneous social monitoring skills, visual responses of 67 infants at high-risk and 50 at low-risk for ASD were studied using an eye-tracking task. Based on their clinical presentation in the third year, infants were divided into those with ASD, those exhibiting atypical development, and those developing typically.

Results: Compared with the control groups, 6-month-old infants later diagnosed with ASD attended less to the social scene, and when they did look at the scene, they spent less time monitoring the actress in general and her face in particular. Limited attention to the actress and her activities was not accompanied by enhanced attention to objects.

Conclusions: Prodromal symptoms of ASD at 6 months include a diminished ability to attend spontaneously to people and their activities. A limited attentional bias toward people early in development is likely to have a detrimental impact on the specialization of social brain networks and the emergence of social interaction patterns. Further investigation into its underlying mechanisms and role in psychopathology of ASD in the first year is warranted.

Key Words: Autism, eye-tracking, infants at risk, social development, spontaneous monitoring, visual attention

Identification of prodromal symptoms of autism spectrum disorder (ASD) in the first year of life is one of the key priorities in the field of autism research (1). Discovery of such behavioral or biological features would advance the understanding of which symptoms are primary and, consequently, facilitate the identification of underlying genetic and neurobiological mechanisms, improve early screening and diagnostic instruments, and inform about novel behavioral or biological treatment targets (2–6). Considering that ASD is usually not diagnosed until the early preschool age, work on identifying prodromal symptoms has historically taken the form of retrospective studies. In recent years, however, studies leveraging the increased risk in younger siblings of children with ASD due to genetic associations (7) have offered a powerful avenue for studying the emergence of ASD in statu nascendi.

Although prevalence estimates of ASD in the general population range from .07% to 1.8% (8–12), conversion rates in prospective studies of high-risk (HR) infants average around 19% (13). In addition, up to 30% of HR siblings exhibit broader autism phenotype features, which include social difficulties, rigidities, and language delays (5,14–17). At 12 months, those later diagnosed with ASD exhibit delays and atypical characteristics in several domains, including eye contact, social smiling, and vocalizations (18–22); initiation of joint attention and requesting (20); object exploration (23); response to name (24); and responses to distress of others (21,25). The delays and abnormal features are often pronounced, as a large proportion of infants later diagnosed with ASD exhibit clinically relevant levels of symptoms by the age of 12 months (26).

Yet, identification of prodromal symptoms of ASD in the first months of life has proven more complex. Global behavioral measures that were once considered optimal candidates as early markers, including eye contact, social smiling, and frequency of socially directed vocalizations observed in a context of parent-infant or examiner-infant interactions, have shown limited predictive value when measured at 6 months (15,18–20,27). Investigations into development of working memory (28) or vocalizations (22) have also yielded negative results at 6 months. Similarly, interpretation of negative findings in studies comparing only HR and low-risk (LR) infants is complicated by the fact that HR samples include infants with a broad range of outcomes. Despite these largely negative behavioral findings, a recent study suggests that atypicalities in development of white matter might be detectable as early as 6 months (29). Other positive findings include the presence of physical overgrowth (including head circumference, height, and weight) (30), as well as atypical event-related potential responses to gaze shifts in 6- to 10-month-olds later diagnosed with ASD (31).

Taken together, the extant, albeit still limited, evidence suggests that more readily measurable global behavioral symptoms associated with ASD begin to emerge between 6 and 12 months and further intensify in the second year of life (5,18,19,32). It is plausible that differences in structural brain organization early in development may restrict the experience-dependent specialization of neural systems involved in social cognition and, in this sense, precede the emergence of behavioral symptoms of ASD. However, the developmental mechanisms that link atypical neural development and its consequent impact on social cognition skills

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remain to be identified. An alternative possibility is that prodromal vulnerabilities in elementary aspects of attention and perception emerging in the first months of life may, by limiting access to critical social experiences, have a detrimental effect on specialization of neural networks involved in social cognition.

The present article examines the spontaneous monitoring of complex dynamic social scenes in 6-month-old infants at high risk and low risk for ASD. Similar research efforts targeting toddlers with ASD have uncovered pronounced deficits in this domain (33–35). In one such study, spontaneous monitoring of an actress engaged in several kinds of activities (e.g., making a sandwich, speaking to the camera, shifting attention to various objects) was tested in 14- to 24-month-old clinic-referred toddlers with autism using eye tracking. Compared with developmentally delayed and typical control subjects, toddlers with autism showed particularly atypical visual responses when the actress tried to engage their attention using dyadic cues (i.e., eye contact and child-directed speech). In such a context, they showed diminished attention to the scene in general, and when they looked at the scene, they showed deficits in monitoring the actress' face and mouth (33). In typical development, the ability to orient preferentially to direct eye contact and child-directed speech are present in a rudimentary form from the first few days of life (36–38). Given that learning about people is a highly experience-dependent process (39,40), the presence of abnormal attention to these essential social cues in early infancy is likely to detrimentally impact the development of social cognition and communication, as well as developmentally appropriate specialization of the neural networks involved in processing social stimuli. Thus, the ability to spontaneously regulate attention to social cues of others represents a highly promising area of inquiry for studying prodromal symptoms of ASD in high-risk infants.

In this study, we employed the same experimental procedure in 6-month-old infants at risk for ASD as that used in a study of 14- to 24-month-old clinic-referred toddlers (33). We compared visual responses of infants later diagnosed with ASD with typically developing high-risk and low-risk infants, as well as high-risk infants who had a history of clinically relevant delays and abnormalities in the second year of life. We hypothesized that 6-month-old infants who later developed ASD would, in comparison with the other groups, show deficits in attending to complex social scenes in general and, in a manner similar to that observed in toddlers, would show difficulties attending to the speaker's face and mouth.

Methods and Materials

Participants

All infants ($n = 117$) participated in a prospective study of infants at risk for ASD due to genetic liability. The sample consisted of 67 high-risk and 50 low-risk infants. To be considered HR, an infant had to have an older sibling with a diagnosis of ASD. The older sibling's diagnostic status was ascertained based on a review of assessment records, including the Autism Diagnostic Observation Schedule-Generic (41) and/or the Autism Diagnostic Interview-Revised (42). Infants considered as LR had no history of ASD in first- or second-degree relatives. All infants were enrolled in the study by the age of 6 months. Exclusionary criteria were gestational age below 34 weeks, any hearing or visual impairment, nonfebrile seizure disorder, or known genetic syndrome. At 6 months, all infants underwent developmental assessment using the Mullen Scales of Early Learning (43) and completed the eye-tracking procedure. Clinical best estimate diagnosis was assigned by a team of expert clinicians based on the results of the Mullen Scales, Autism Diagnostic Observation Schedule-Generic (41), language assessments (either Communication and Symbolic Behavior Scales [44] or Reynell Developmental Language Scales III [45]), as well as medical and family history. The assessment instruments were administered by Ph.D.-level psychologists and licensed speech and language pathologists. In 68% of cases, the clinical best estimate diagnosis was based on a 36-month assessment; the remaining 32% of high-risk infants were diagnosed based on a 24-month assessment. Based on these outcomes, the infants were divided into three groups: 1) infants with frank symptoms of ASD ($n = 15$) (14 HR, 1 LR); 2) infants with no evidence for clinically significant symptoms in the second or third year (TYP) (HR-TYP, $n = 19$, LR-TYP, $n = 50$); and 3) high-risk infants with clinically significant symptoms (HR-ATYP) (e.g., language or other developmental delay or abnormal social-communication or repetitive behaviors) evident in the second or third year of life but who did not meet criteria for ASD (HR-ATYP, $n = 33$). Though developmental problems were transient in some HR-ATYP infants, for the purpose of this analysis they were included in this group in appreciation of their early atypical developmental course. Conversion rates to ASD among HR infants was 21%, well within the previously reported range (13). All parents signed an informed consent in adherence to the University Human Investigation Committee requirements.

Data from 38 (32%) of the 117 infants were not included in the analysis due to motion- or inattention-related eye-tracker calibration problems. There was no differential dropout by diagnosis in any of the four experimental conditions (see Procedure section): sandwich [$\chi^2(3) = 1.63$, $p = .653$]; dyadic bid [$\chi^2(3) = .97$, $p = .819$]; joint attention [$\chi^2(3) = 1.46$, $p = .693$]; and moving toys [$\chi^2(3) = 3.105$, $p = .376$]. Infants who were excluded due to calibration problems did not differ in chronological age [$F(1,115) = 1.42$, $p = .236$], Mullen Scale visual reception [$F(1,113) = 2.63$, $p = .108$], fine motor [$F(1,113) = 2.86$, $p = .093$], receptive language [$F(1,113) = .09$, $p = .766$], or expressive language [$F(1,113) = .88$, $p = .349$] age equivalent scores.

After the initial exclusions, a total of 84 infants were retained for analysis, including 12 (80%) infants with ASD, 22 (67%) HR-ATYP, 15 (79%) HR-TYP, and 35 (70%) LR-TYP. Ninety-two percent of parents identified their child's race as Caucasian and the distribution did not differ by group [$\chi^2(3) = 1.56$, $p = .667$]. The groups did not differ in terms of gender, chronological age, or age equivalent scores on the Mullen visual reception, fine motor, receptive language, and expressive language scales at 6 months (Table 1). At 24 months, the children did not differ in chronological age, though the clinically affected groups differed from nonaffected toddlers in a predictable manner on measures of developmental and social-communicative functioning (Table 1).

Stimuli. The stimuli were designed to capture, in a task-relevant fashion, the spontaneous regulation of visual attention in response to the ebbs and flows of social events. The stimulus consisted of a 3-minute video of an actress filmed in a setting containing four toys and a table with ingredients for making sandwiches (33) (Figure 1A). The video contained four types of activity (conditions) interspersed with one another, depicting a woman making a sandwich, occasionally looking at the camera and trying to engage the viewer using eye contact and child-directed speech, then going back to the sandwich, or looking at the toys positioned in the four corners of the screen, with toys sometimes remaining still and sometimes moving. The content of