Archival Report

Joint Attention in Infancy and the Emergence of Autism

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ABSTRACT

BACKGROUND: In typical infant development, parents and their children jointly contribute to establishing frequent episodes of joint attention that boost language acquisition and shape social cognition. Here we used novel live eyetracking technology to evaluate the degree to which autism spectrum disorder (ASD) is related to reduced responding to others' joint attention bids in infancy (RJA) and to a reduced tendency to initiate joint attention episodes (IJA). Because young infants use their gaze for both RJA and IJA, this approach allowed us to quantify these elusive processes early in life.

METHODS: The final sample consisted of 112 infants (54 boys and 58 girls), of whom 81 were at familial risk for ASD and 31 were typically developing low-risk infants. At follow-up (36 months of age), 22 children in the high-risk group were diagnosed with ASD.

RESULTS: At 10 months of age, rates of IJA were lower in infants later diagnosed with ASD than in the comparison groups (effect sizes d = 0.78-0.95) and followed an atypical developmental trajectory from 10 to 18 months (p < .002). RJA distinguished infants based on familial ASD risk, albeit not ASD diagnosis. The differences in IJA could not be explained by overall looking time, social preference, eye movement latencies, or number of fixations.

CONCLUSIONS: This live eye-tracking study suggests that during an important period for the development of social cognition (10-18 months of age), infants later diagnosed with ASD show marked atypicalities in IJA but not in RJA. The results indicate that IJA is an important target for future prodromal intervention trials.

Keywords: Biomarker, Neurodevelopmental disorders, Parent-child interaction, Prodromal intervention, Reward processing, Social cognition

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The term joint attention refers to the triadic sharing of attention between two individuals and an object or event [(1,2); for an overview of different theoretical perspectives of the concept of joint attention, see (3)]. In typical development, both infants and their parents flexibly use verbal and nonverbal behaviors to establish frequent episodes of joint attention. When the parent initiates, the child is said to be responding to joint attention (RJA) such as when he or she follows the gaze of the parent to look at an object. When the child initiates, it is referred to as initiation of joint attention (IJA). For example, by pointing or vocalizing, young children can guide an adult's attention and shape their own immediate social environment to fit their needs and interests. Importantly, already before infants can point or speak, they may use their eye movements to influence the parent by alternating gaze between the face of the parent and objects that have caught their attention (alternating gaze behavior). Engaging in RJA and IJA in infancy facilitates the development of core social cognition skills [e.g., (4,5)] and language [e.g., (6,7)]. Furthermore, a lower tendency to engage in joint attention is considered one of the most prominent features of autism spectrum disorder (ASD) in young children (8–12).

Joint attention is a heterogeneous construct, and therefore it is important to study the development of its subcomponents

[e.g., (13)]. The distinction between RJA and IJA is particularly crucial. In typical development, RJA and IJA differ in terms of onset and early trajectories (14-16) and contribute differently to language development in childhood (17) as well as to adult cognition and information processing (18). Furthermore, the brain networks supporting RJA and IJA are partially dissociable (13,19,20). Specifically, in adults, IJA is associated with greater activation of areas associated with reward processing, such as the ventral striatum (20,21), suggesting that IJA may be more related to social motivation (22) compared with the more automatically triggered RJA.

A few studies have used manual coding of video recordings to investigate RJA and IJA in infants with later ASD [using a so-called high-risk infant sibling design, about 20% of infant siblings in these studies are later diagnosed with ASD (23)]. Although findings are somewhat mixed, ASD has been associated with lower levels of both RJA and IJA in infancy (24,25). Some previous work suggests that IJA impairments in ASD may be more chronic than impairments in RJA (12,26,27). Our current approach builds on these important previous findings but differs in several key aspects. First, the infants' gaze during the interaction with the experimenter was recorded with an eye tracker. Eye tracking entails potential gains in terms of accuracy of the measurement, the types of measures one can produce, and automatization of data analysis (28). However, it is also associated with drawbacks such as losing trials owing to low tracking quality in some infants. Because no previous study has used eye tracking during live interaction in the context of early markers of ASD, it is important to assess its value empirically. Second, we included in the experimental sessions two clearly operationalized and specific measures of RJA and IJA (Figure 1). Finally, we repeated the eye-tracking assessment at 10, 14, and 18 months of age, allowing us to fine map the developmental trajectories of RJA and IJA during an important time period for the development of joint attention and for processes linked to ASD more generally (29–31).

We have previously published on both RJA and IJA using live eye-tracking technology in infants at risk for ASD (32,33), but neither of these reports included diagnostic outcome of ASD. We generally expected reduced rates of both RJA and IJA in the first year of life (10 months) to be associated with later ASD (24,32–34). However, while problems with RJA might decrease over time, we expected decreased IJA to be more constant over the age period studied (12,26,27). For RJA, we also tested the more specific hypothesis that atypicalities in gaze following could be specifically linked to a failure to use information from eye movements of other people (33).

METHODS AND MATERIALS

Participants

In line with previous studies (31), we divided our sample into three groups: typically developing (TD) low-risk infants, infants at high risk but without ASD at follow-up (HR-no-ASD), and infants at high risk with ASD at follow-up (HR-ASD) (see Table 1 for details about the final sample after exclusions). Families with infants in the HR groups were recruited through the project's website, through advertisements, and from clinical units. Infants in the TD group were recruited from live birth records and had at least one TD older full sibling and no first-or second-degree relatives with ASD. The infants at risk had at least one older full sibling with a community ASD diagnosis (verified via inspection of medical records). Infants with visual or auditory impairments or with known medical conditions or genetic syndromes were excluded, as were infants born before gestational week 36. There was no difference in birth weight

among the three groups (mean = 3682 g, SD = 463, p > .250). One TD infant received an ASD diagnosis and was excluded, and another TD infant and two HR-no-ASD infants were excluded owing to poor data quality (see criteria below).

Written informed consent was collected from parents. The study was approved by the Ethics Board in Stockholm and was conducted in accordance with the 1964 Declaration of Helsinki.

The 36-month assessment was carried out by experienced clinicians and was based on a comprehensive assessment that included the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2) (35) and Autism Diagnostic Interview-Revised (ADI-R) (36) supervised by an international ADOS-2/ADI-R trainer (the third author). Diagnostic decisions were made based on DSM-5 criteria.

Eye Tracking

The infant was seated on the lap of the parent approximately 200 cm from an adult experimenter who was seated at a low table (see Figure 1). The session started with a calibration procedure in which the experimenter moved a squeaky toy across predefined calibration points to attract the attention of the infant. Calibration was validated via online inspection of gaze replay on a monitor in the background of the room and was repeated if necessary. On each side of the table was a transparent oblong lamp (IJA task), and removable wooden screens could be placed on the table by the experimenter (RJA task). A Tobii TX300 eye tracker (Tobii, Danderyd, Sweden) was placed at a table between the scene area and the infant, and it recorded the gaze of the infant with a sample rate of 120 Hz. Two video cameras recorded the behavior of the infant and experimenter. The eye-tracking session comprised a number of tasks and lasted approximately 10 minutes in total. The RJA experiment was carried out first and consisted of four blocks interleaved by other short tasks to avoid habituation [see (37) for details]. The IJA experiment was then performed before ending the session. The parent was carefully instructed to sit still and not talk in order not to influence the child, apart from giving general postural support for optimal recording of eye movements.

RJA Task. Two screens, each with a hole in it, were placed on the sides of the experimenter on top of the table (Figure 1). The experiment consisted of four blocks, each containing four

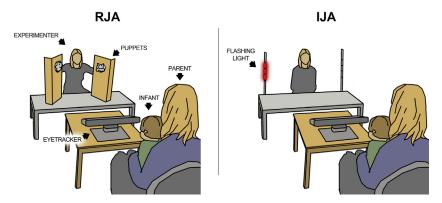


Figure 1. Experimental setup for responding to joint attention (RJA) and initiation of joint attention (IJA). RJA was operationalized as gaze following accuracy, while IJA was operationalized as alternating gaze between the flashing light and the experimenter (see Methods and Materials for details).

Table 1. Participant Characteristics by Group

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	TD (n = 31; 17 Boys)	HR-no-ASD ($n = 59; 25 \text{ Boys}$)	HR-ASD (n = 22; 12 Boys)	ANOVA
RJA, 10 Months, n (n Boys)	27 (15)	50 (20)	11 (4)	
RJA, 14 Months, n (n Boys)	25 (13)	48 (19)	18 (10)	
RJA, 18 Months, n (n Boys)	25 (13)	49 (21)	20 (11)	
IJA, 10 Months, n (n Boys)	26 (14)	51 (23)	15 (7)	
IJA, 14 Months, n (n Boys)	27 (15)	50 (19)	17 (9)	
IJA, 18 Months, n (n Boys)	26 (14)	50 (21)	20 (11)	
Age 10 Months, Mean (SD)	10.4 (0.5)	10.4 (0.6)	10.4 (0.5)	n.s. (p = .991)
Age 14 Months, Mean (SD)	14.4 (0.7)	14.4 (0.6)	14.5 (0.4)	n.s. (p = .631)
Age 18 Months, Mean (SD)	18.7 (1.0)	18.5 (0.5)	18.6 (0.5)	n.s. (p = .438)
MSEL ^a , Mean (SD), n	103.6 (11.9), <i>n</i> = 31	100.6 (12.9), <i>n</i> = 58	98.5 (14.4), <i>n</i> = 22	n.s. (p = .352)
SES ^b , Education, Mean (SD), n	0.3 (0.8), n = 31	0.0 (1.0), n = 58	-0.3 (1.2), $n = 22$	n.s. (p = .105)
SES ^b , Salary, Mean (SD), n	0.1 (0.9), n = 30	0.1 (1.1), <i>n</i> = 54	-0.3 (1.0), $n = 22$	n.s. (p = .377
Parents' Origin ^c				
Sweden, n	28	46	20	
Europe, n	1	5	2	
North America, n	0	2	0	
South America, n	0	0	0	
Asia, n	1	3	0	
Africa, n	0	1	0	

ANOVA, analysis of variance; HR-ASD, high risk with autism spectrum disorder at follow-up; HR-no-ASD, high risk but without autism spectrum disorder at follow-up; IJA, initiation of joint attention; n.s., not significant; RJA, responding to joint attention; TD, typically developing.

trials belonging to two conditions (Eyes and Head condition vs. Eyes Only condition, counterbalanced between blocks). Occasionally a few more trials were administered in each category; all administered trials were analyzed. In both conditions, the experimenter first made pairs of puppets appear through the holes with his or her hands/arms hidden behind the screen, out of sight of the infant. Then, the experimenter called the infant's name to elicit eye contact. If necessary, the name was called a second time, and if the infant still did not respond, the experimenter made a funny face and a sound. In the Eyes and Head condition, the experimenter then turned his or her head toward one of the puppets while making an excited sound ("Oj!", a Swedish interjection expressing surprise and excitement). The experimenter kept looking at the puppet for 4 seconds before turning back and looking at the infant. The 4second interval was an a priori decision based on previous research on gaze following in infancy (15). The Eyes Only condition was identical to the Eyes and Head condition, but instead of moving his or her head, the experimenter kept the head still, facing forward, while moving only the eyes in the direction of the puppet. Using this experiment, we have previously found that 10-month-old infant siblings of children with ASD are able to follow gaze but may rely more on the head movement when following gaze compared with low-risk infants (33).

The dependent measure in this task, gaze following accuracy, was a difference score in which the number of trials in which the infant did not follow gaze (i.e., looked at the unattended target first) was subtracted from the number of trials in which the infant did follow gaze (i.e., looked at the attended target first).

IJA Task. In this task, the experimenter started by attracting the infant's attention before activating a lamp on his or her left side by the use of a remote control hidden under the table, out of sight for the infant (Figure 1). Lights began to flash, changing color approximately every second. The lights flashed for 10 seconds, during which the experimenter remained still, facing the infant, intermittently speaking softly (not about the lights) without vivid communicative cues to provide the infant with an opportunity to initiate joint attention. If the infant made an explicit attempt at directing the experimenter's attention toward the lights, such as by pointing or vocalizing (e.g., saying "there" or "look"), the experimenter responded by turning toward the lights and commenting on them, and the trial was then interrupted. This was done to prevent extinguishing joint attention behaviors by being unresponsive (see Data Analysis section below for further details). The procedure was repeated four times (i.e., 4×10 seconds in total for uninterrupted trials). These four trials were identical except for the fact that the lights on the experimenter's left side were activated on the first and third trials and the lights on the right side were activated on the second and fourth trials. Using this task, we have previously shown that HR infants produce less alternating gaze shifts between the experimenter and an unexpected event (flashing lights) appearing in the periphery compared with lowrisk infants (32).

The dependent measure in this task, alternating gaze, was defined as the number of gaze shifts made by the infant between the experimenter's face and the flashing lights (any direction) during the time period the lights were flashing divided by the number of seconds the lights were flashing. As in our previous study (32), we analyzed the first 9 seconds of

^aMullen Scales of Early Learning, total composite score, measured at 10 months of age.

^bSocioeconomic status (SES) expressed as a Z score based on total sample.

 $^{^{}c}n$ differs from global n in some cases due to missing data.

the trial (because several trials were found to be slightly shorter than 10 seconds) but occasionally less when the trial was interrupted by the infant's pointing or vocalizing. Interruptions occurred in only $\sim\!4.6\%$ of the trials (42 of 919 trials in total). In $\sim\!5.9\%$ of the recording sessions (19 of 322 sessions in total), the experimenter needed to perform five or six trials to compensate for infant's inattention or movement.

Data Analysis

In designing the experiment, we made sure that the scene included just a few and spatially clearly separated areas of interest (AOIs; one or two objects plus the experimenter). This allowed us to use the spatial distribution of the gaze data from individual children to optimize the specific boundaries for AOIs (see Supplement for illustrations and further information). This maximizes the chances that data could be analyzed even in cases with low spatial accuracy.

Trials with less than 50% gaze data were excluded automatically, and the remaining trials were visually inspected to remove trials with dubious data. This was done by plotting the gaze coordinates (x, y) over time together with AOI positions (see Supplement), which two independent eye-tracking experts (blinded to group) then rated as valid or invalid (Cohen's kappa = .85). In the final sample, the trial exclusion procedure resulted in 36.0% excluded trials in the RJA experiment (1726 of 4800 trials) and 23.1% in the IJA experiment (273 of 1180 trials) (no group differences; see Supplement). To be included in the analysis, each infant needed to contribute at least 25% valid trials, that is, at least four valid RJA trials (and at least one trial in each condition) and at least one valid IJA trial.

Linear mixed models were fitted with the restricted maximum likelihood method using the MATLAB fitlme function (MATLAB; The MathWorks, Inc., Natick, MA) for the main statistical analyses, which entails that each individual does not need to contribute data to all three measurement points in order to be included in the analysis (Table 1). The number of data points (i.e., degrees of freedom) in the analyses varies slightly between analyses. Fixed factors were group, outcome (TD, HR-no-ASD, or HR-ASD), and age in months nested within subject. For the RJA analyses, we also included condition (Eyes Only or Eyes and Head) as a fixed factor. Subject was used as a random factor in all analyses and was fitted with random intercept and slope (for further details, see the Supplement).

Adding the number of valid trials, overall looking time, and gender as covariates in the main analyses of RJA and IJA did not change the pattern of significant results. Furthermore, these covariates did not contribute significantly to the model and thus were not included.

To assess continuous relations between our dependent measures and ASD symptoms in the whole HR sample, we performed Pearson correlations against the ADOS-2 and ADI-R (ADI-R raw score based on the algorithm items). To further investigate the relation between our variables and the Social Affect (SA) and Repetitive and Restricted Behaviors (RRB) domains, we performed correlations with the SA and RRB subscales of the ADOS-2. Most infants were assessed using ADOS-2 module 2 at 36 months of age, but because some

infants were assessed using module 1 of the ADOS-2, we transformed the ADOS total score and the SA subscale to comparison scores (CS) (31). Similar to Nyström *et al.* (31), the RRB subscale was not transformed to CS because this 10-point scale does not use the interval 2 to 4 and distorts the correlation analysis. These analyses were conducted only for measures where the ASD group performed differently from the other groups.

In addition to the main results reported below, the Supplement contains several analyses conducted to examine potential confounders of diagnostic group-based differences as well as an analysis of the development of higher-level IJA.

RESULTS

RJA (Gaze Following)

We found no significant group differences at 10 months of age for Eyes Only, Eyes and Head, or combined conditions (statistics in the Supplement). In the longitudinal analysis (including the factors group, age, and condition), we found that a model with a quadratic age term provided the best fit and is reported here (for details, see the Supplement). We found no interaction effects. RJA generally increased with age ($F_{1.540} = 19.220$, p < .001, coefficient estimate = 1.467), but with a significant negative bend (quadratic age term, $F_{1.540} = 15.771$, p < .001, coefficient estimate = -0.045). Furthermore, infants generally followed gaze less in the Eyes Only condition than in the Eyes and Head condition ($F_{1.540} = 190.98$, p < .001, coefficient estimate = -1.255). We also found a main effect of group ($F_{2.540} = 5.660, p = .004$). The TD group had higher RJA scores compared with the other two groups (TD vs. HR-ASD: $t_{2.543} = -2.428$, p = .015, coefficient estimate = -0.933; TD vs. HR-no-ASD: $t_{2.543} = -2.375$, p = .018, coefficient estimate = -0.694) (Figure 2). The HR-ASD and HRno-ASD groups did not differ significantly (p > .250).

IJA (Alternating Gaze)

As hypothesized, at 10 months of age, the HR-ASD infants produced less alternating gaze than both other groups (TD vs. HR-ASD: $t_{39} = 2.870$, p = .007, Cohen's d = 0.951; HR-no-ASD vs. HR-ASD: $t_{64} = -2.611$, p = .011, Cohen's d = 0.778), whereas the TD group did not differ from the HR-no-ASD group ($t_{75} = 0.908$, p > .250, Cohen's d = 0.215) (Figure 3A).

In the longitudinal analysis, we found a significant interaction effect between group and age ($F_{2,276} = 6.158$, p = .002). To further understand and visualize this effect, we calculated the slope of a linear regression using the available data points (at 10, 14, and 18 months of age) for each individual. As expected, slopes differed between groups ($F_{2,100} = 6.543$, p = .002). We then compared this measure across groups using planned comparisons with independent t tests [see (31) for a similar approach]. These comparisons showed significant differences between HR-ASD group slopes and those of the other two groups (TD vs. HR-ASD: $t_{46} = -3.800$, p < .001, Cohen's d = 1.118; HR-no-ASD vs. HR-ASD: $t_{72} = -2.592$, p = .012, Cohen's d = 0.703; TD vs. HR-no-ASD: $t_{82} = -1.548$, p = .126, Cohen's d = 0.361) (Figure 3B).

TD

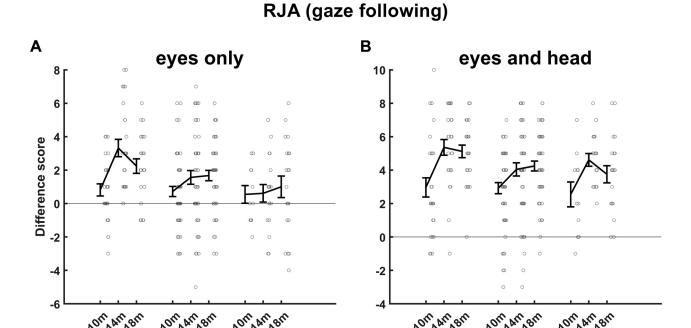


Figure 2. Gaze following in infants later diagnosed with autism spectrum disorder (ASD) and control subjects. The y-axis shows gaze following difference scores (number of congruent gaze shifts minus number of incongruent gaze shifts) when the model moves only her or his eyes toward the peripheral target while the head remains facing the child (A) or moves both the head and eyes toward the target (B). Error bars are SEM, and circles represent the mean value across trials for individual infants. HR-ASD, high risk with ASD at follow-up; HR-no-ASD, high risk but without ASD at follow-up; TD, typically developing.

TD

HR-no-ASD

HR-ASD

HR-ASD

HR-no-ASD

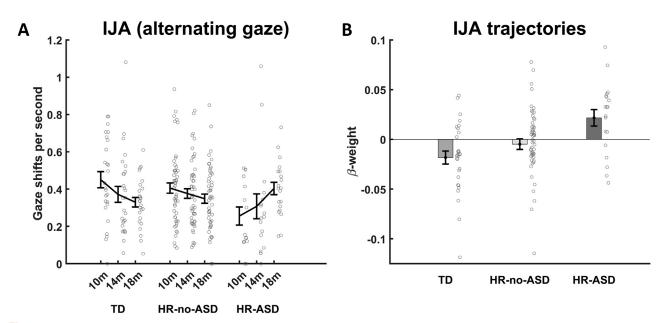


Figure 3. Initiating joint attention (IJA) in infants later diagnosed with autism spectrum disorder (ASD) and control subjects. (**A, B)** Infants with later ASD (HR-ASD) produced less alternating gaze shifts than both the typically developing (TD) group and the infants without later ASD (HR-no-ASD) at 10 months of age (**A**) and showed a different developmental trajectory of this behavior over time (10–18 months) (**B**). One-sample t tests showed that the HR-ASD group had a significantly positive developmental trajectory, whereas the TD group had a significantly negative trajectory (TD: n = 29, $t_{28} = -2.797$, p = .009, Cohen's d = 0.519; HR-no-ASD: n = 55, $t_{54} = -0.921$, p > .250, Cohen's d = 0.124; HR-ASD: n = 19, $t_{18} = 2.607$, p = .018, Cohen's d = 0.598). Error bars are SEM, and circles represent the mean value within individual infants.

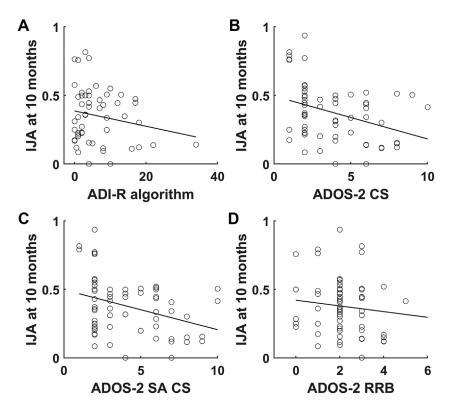


Figure 4. Correlations between autism spectrum disorder symptoms and 10-month initiating joint attention (IJA) (alternating gaze), high-risk sample only: (A) Autism Diagnostic Interview-Revised (ADI-R) algorithm scores; (B) Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2) comparison scores (CS); (C) ADOS-2 Social Affect (SA) CS; (D) ADOS-2 Repetitive and Restricted Behaviors (RRB). Inferential statistics are in the main text.

Correlations With ASD Symptoms

The analyses relating our IJA measure at 10 months of age (HR group only) to ADI-R score did not show a significant association (n=53, Pearson's r=-.192, p=.169). There were significant correlations for the ADOS-2 measures ADOS-Total CS (n=63, r=-.352, p=.005) and ADOS-SA CS (n=63, r=-.348, p=.005) but not ADOS-RRB (n=63, n=-.127, n=.320) (Figure 4).

Analysis of Potential Confounders of Diagnostic Group-Based Differences and Other Adjacent Measures

The atypicalities in IJA development in ASD (Figure 3) could potentially reflect alterations in more basic measures such as social viewing preference (face vs. nonsocial object) and general attention. However, as shown in the Supplement, a series of supplemental analyses of such measures failed to support such an explanation of the IJA results (Supplemental Figures S1–S3).

DISCUSSION

This live eye-tracking study provides support for the hypothesis that infants later diagnosed with ASD have reduced rates of IJA in the first year of life. Specifically, at 10 months of age, when observing an interesting novel event apparently out of sight of an interaction partner, the TD infants as well as the HR-no-ASD infants produced frequent gaze shifts between the lights and the adult's face. Because caregivers tend to follow the gaze direction of their children, this behavior is the most

efficient way for a preverbal infant to establish joint attention in everyday life.

In contrast, the results did not support the hypothesis that low rates of gaze following (RJA) were associated with later diagnosis, although we found that the TD children engaged more in gaze following than the combined HR groups. This finding is in line with the view that although RJA alterations are often observed in infants at risk for ASD, RJA may play a less critical part in the development of the disorder compared with IJA (3). Considering that RJA represents a basic visual social attention skill, it is noteworthy that recent research suggests that even other skills of this sort, such as orienting to faces (38) and to biological motion (39), may be retained in infants later diagnosed with ASD. Future studies should attempt to replicate these negative findings in larger samples and include measures of auditory social attention as well.

We observed that seeing isolated eye movements produced less gaze following than seeing both the head and eyes turn but that this effect was similar in all groups (Figure 2). Thus, we did not find support for the more specific hypothesis that movement information from the eyes alone was too subtle to trigger gaze following in infants with later ASD (33).

Previous research has suggested that IJA impairments in ASD are enduring (3,27). Therefore, the finding that alternating gaze reached typical levels in the second year of life in infants with a later diagnosis was unexpected (Figure 3). It is important to note that while these children catch up in terms of this rather basic IJA behavior, they continue to have marked impairments with more advanced forms of IJA such as pointing

and showing (see analysis in the Supplement and Supplemental Figures S4 and S5). This pattern is consistent with a previous study (25) that found lower frequencies of more advanced IJA at 12 months of age in children later diagnosed with ASD but found only marginal differences in terms of lower-level IJA at this intermediate age point. Why infants with later ASD catch up in terms of alternating gaze but continue to use less advanced IJA behaviors is an intriguing question worth further study.

Previous studies of low-level IJA have used composite measures of alternating gaze and other measures such as eye contact [e.g., (24,25)]. However, the contrasting findings between IJA (Figure 3) and social preference (Supplemental Figure S1) in the current study suggest that these phenomena might not reflect a unitary underlying construct and that combining them may mask effects associated with one phenomenon but not the other. Previous studies using composite measures (16,24) have suggested curvilinear development of IJA over the late infancy and toddler period, but for the reasons just outlined, it is difficult to directly compare the patterns seen in this study with these previous data.

The social motivation theory of ASD states that early reductions in social motivation cause impoverished social experiences that in turn lead to later challenges with social thinking (22). While this fits with our results regarding IJA, the social motivation theory cannot account for the dissociation between IJA (alternating gaze) and social preference. Our results tentatively suggest that one should differentiate general viewing preferences from behaviors used to actively guide the behaviors of others [see also (40)].

In this study, the primary gain of eye tracking was the possibility to automatize data analysis (see the Supplement) and the fact that we could accurately quantify potential confounding variables such as the duration of looking time to social versus nonsocial aspects of the scene (social preference) and the latency of gaze shifts (Supplemental Figures S1–S3). Looking duration and the precise timing of gaze shifts are difficult to assess accurately with traditional video coding. Another general strength of eye tracking is that the data can easily be reanalyzed to focus on new aspects of gaze behavior [e.g., the duration of individual fixations (41)] or other measures such as pupillary responses (indicative of arousal).

The study has a few notable limitations. First, the sample size was modest, and independent replication is decisive. This is particularly true for RJA at 10 months of age, for which the ASD sample consisted of only 11 infants. Second, our conclusion concerns the 10- to 18-month period, and potential earlier differences (e.g., in RJA) are not captured. Third, we relied on community diagnosis in the probands, which means that the exact diagnostic procedures used for the older siblings may have varied (see Methods and Materials; see also discussion in the Supplement). However, more than 70% of the medical records specified use of either the ADOS-2 or ADI-R as part of the diagnostic assessment (the actual percentage is likely to be higher because the use of these instruments is quite standard in Sweden). Lastly, the eye tracker did not provide measures of accuracy or precision (but see the Supplement for how we handled these issues).

This study demonstrates that alternating gaze trajectories are not only different in ASD but also distinct from the trajectories of RJA and social preference. It highlights the potential of live eye tracking for quantifying early gaze atypicalities in ASD, some of which may go unnoticed by the naked eye. Finally, given that IJA and gaze alternation typically elicit communicative situations with caregivers, the observed atypicalities in ASD are likely to give rise to transactional processes (e.g., the parent responding less to a child who does not initiate joint attention). Such processes are likely to be important targets for future prodromal intervention trials (42).

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