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Development of attention from birth to 5 months in infants at risk for autism spectrum disorder

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Abstract

Social-communication skills emerge within the context of rich social interactions, facilitated by an infant's capacity to attend to people and objects in the environment. Disruption in this early neurobehavioral process may decrease the frequency and quality of social interactions and learning opportunities, potentially leading to downstream deleterious effects on social development. This study examined early attention in infant siblings of children with autism spectrum disorder (ASD) who are at risk for social and communication delays. Visual and auditory attention was mapped from age 1 week to 5 months in infants at familial risk for ASD (high risk; $N = 41$) and low-risk typically developing infants (low risk; $N = 39$). At 12 months, a subset of participants ($N = 40$) was administered assessments of social communication and nonverbal cognitive skills. Results revealed that high-risk infants performed lower on attention tasks at 2 and 3 months of age compared to low-risk infants. A significant association between overall attention at 3 months and developmental outcome at 12 months was observed for both groups. These results provide evidence for early vulnerabilities in visual attention for infants at risk for ASD during a period of important neurodevelopmental transition (between 2 and 3 months) when attention has significant implications for social communication and cognitive development.

Keywords: visual attention, autism spectrum disorder, infancy, social communication, neonate

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social interaction and communication as well as the presence of restricted interests and repetitive behaviors (American Psychiatric Association, 2013). While a stable and reliable diagnosis of ASD is possible in infants as young as 18–24 months of age (Chawarska, Klin, Paul, & Volkmar, 2007; Guthrie, Swineford, Nottke, & Wetherby, 2013), the pathogenesis of ASD and its course across the first 2 years of life is largely unknown. In an attempt to identify the earliest markers of ASD, several studies have focused on developmental trajectories of infant siblings of children with ASD (Jones, Gliga, Bedford, Charman, & Johnson, 2014). Infant siblings are at a greater risk for developing ASD, with approximately 20% of siblings being diagnosed with ASD by the age of 3 years and an additional 30% exhibiting atypical development (Messinger et al., 2013; Ozonoff et al., 2011, 2014). Research with infant siblings has helped to identify early biomarkers of ASD and ASD risk in infants as young as 6 months of age; many of these biomarkers are related to disrupted patterns of social orienting and attention (Elsabbagh et al., 2011).

Social attention plays a key role in infant social, cognitive, and motor development. From the first days of life, social orienting and attention are critical for facilitating attuned responsiveness to the environment and providing a stable landscape of recurrent experiences that are themselves learning opportunities (Shultz, Klin, & Jones, 2018). Orienting to faces increases opportunities for dyadic interaction with a caregiver and helps shape the later emergence of reciprocal social interactions (Senju & Johnson, 2009). Orienting to objects creates opportunities for reaching, manipulation, and exploration, which lay a critical foundation for social and cognitive development (Hunnius & Bekkering, 2014). Studies have found that compared to typically developing infants, 6-month-old infants later diagnosed with ASD show decreased attention to social scenes and faces (Chawarska, Macari, & Shic, 2013; Shic, Macari, & Chawarska, 2014). Deeper levels of attention, such as sustained attention and sensitization to social stimuli, have also been found to be reduced in 6-month-olds later diagnosed with ASD (Jones et al., 2016). While there is substantial evidence that social attention is already disrupted in 6-month-old infants who are later diagnosed with ASD, less is known about the precise timing of this divergence prior to 6 months. In light of such uncertainty, here we report on a longitudinal

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examination of early visual and auditory attention to animate (faces and voices) and inanimate (objects) stimuli from 1 week to 5 months of age in infants at familial risk for ASD and low-risk typically developing infants.

Visual Attention in Early Infancy

Maturation of the visual attention system in infancy can be viewed as a series of key brain–behavior transitions. At birth, attention is predicated on the infant's ability to stabilize the nervous system and effectively regulate arousal (Brazelton & Nugent, 2011). Consequently, the infant's capacity for attention in the first 1–2 months of life is perhaps most strongly impacted by the infant's state of alertness, which can be compromised by immature neurological development, as is often seen in very low birthweight infants (Ross-Sheehy, Perone, Macek, & Eschman, 2017; Wolf et al., 2007). Once in a calm, alert state, newborn visual tracking is accomplished with a series of reflexive saccades and head turns, mediated by mature subcortical structures, primarily the superior colliculus and the retinocollicular pathway (Atkinson & Braddick, 2012; Johnson, 2005; Johnson et al., 2005).

Endogenous, or voluntary, control of attention comes online at around 3 months as a result of the maturing corticocortical pathway, allowing for gradually increasing cortical influence over visual attention (Halit, de Haan, & Johnson, 2003; Hunnius, Geuze, & van Geert, 2006; Johnson et al., 2005; Nakano & Nakatani, 2014). Behavioral evidence for this neurodevelopmental transition is robust. Infants show voluntary disengagement and attention shifting by 3 months (Hunnius et al., 2006), voluntary shifting between familiar and novel stimuli by 4 months (Colombo, Mitchell, Coldren, & Freeseman, 1991; Frick, Colombo, & Allen, 2000), and sustained attention, a function of voluntary attentional engagement and information processing, by 3–6 months (Richards, Reynolds, & Courage, 2010). It is also worth noting here the intrinsic link between perceptual and motor development (e.g., Kanakogi & Itakura, 2011; Lloyd-Fox, Wu, Richards, Elwell, & Johnson, 2015). Early transitions in visual attention are observed to coincide with motoric achievements that facilitate object exploration, including reaching (Rochat, 1993) and bimanual exploration coordinated with visual regard (Rochat, 1989; Ruff, Saltarelli, Capozzoli, & Dubiner, 1992). In turn, experience with reaching and grasping enhances visual attention to objects (Needham, Barrett, & Peterman, 2002).

Together this evidence suggests a time of transition, and perhaps several transitions, around 2–3 months when infant visual attention shifts from being arousal dependent and reflexive to cortically mediated and voluntary. This neurodevelopmental shift, from reflexive to voluntary behavior, is well aligned with observed developmental changes in infant social behavior. By 2–3 months of age, infants are able to sustain engagement in contingent, active, dyadic interaction with a caregiver (Emde & Harmon, 1972; Lavelli & Fogel, 2005; Rochat, 2001). There is evidence for sensitivity to caregiver bids for triadic attention as early as 6 weeks of age (Striano, Stahl, Cleveland, & Hoehl, 2007) and overt attention following as early as 3 months (Gredeback, Fikke, & Melinder, 2010; Perra & Gattis, 2010). Perra and Gattis (2010, 2012) observed a major transition in attentional engagement at 3 months of age, at which time infants increased time spent jointly engaged in object play with a caregiver, followed the attentional focus of a caregiver, and shifted attention between a caregiver and an object, all of which could be argued are foundational skills for the emergence of joint attention. In a recent study, attention skills at a much earlier age, 1 month, were associated with joint attention skills at 1 year of age (Salley et al., 2016).

The literature presented here suggests that early neurodevelopmental transitions in attention may be instrumental to an infant's social and communication development. While research suggests that infants later diagnosed with ASD exhibit altered patterns of social attention at 6 months (Chawarska et al., 2013; Jones et al., 2016; Shic et al., 2014), few studies have explored how trajectories of early visual attention, prior to 6 months, may be associated with the emergence of social communication in infants at risk for ASD. Disrupted neurodevelopment of attention systems in the first months of life could alter the infant's early social experiences, potentially diminishing the frequency and quality of contingent social interactions, and ultimately reducing opportunities for social and language learning. In the case of ASD, there are several possibilities for how early attention and later social communication deficits could be linked.

Attention and ASD in Early Infancy

The social orienting hypothesis describes ASD as the result of impaired social orienting and attention from birth, leading to atypical specialization of the cortical social brain network (Johnson, 2014). Very few studies have directly tested this hypothesis, but two recent studies offer evidence alongside conflicting interpretations that support and refute this theory. In a longitudinal study of looking to the eyes of a caregiver, Jones and Klin (2013) observed distinct trajectories of eye looking for infants later diagnosed with ASD: these infants showed normative eye looking at 2 months, followed by a significant decline from 2 to 24 months of age compared to typically developing infants. The authors concluded that for infants with ASD, reflexive social visual engagement is intact at birth, but that the onset of experience-dependent, cortically mediated, volitional attention results in a steady decline in social visual engagement (Klin, Shultz, & Jones, 2015). This hypothesis is in line with other research (Senju & Tomalski, 2015). In contrast, a recent study (Di Giorgio et al., 2016) reported on a lack of preference for social stimuli in 1-week-old high-risk infant siblings of children with ASD, suggesting that impaired exogenous social orienting at birth is an indicator of ASD risk. These studies frame their work in the context of key differences in the neurodevelopmental shift in visual attention, from subcortically mediated, reflexive orienting to cortically mediated, volitional orienting, that occurs around 2–3 months of age (Morton & Johnson, 1991; Senju & Tomalski, 2015; Shultz et al., 2018). Altered social communication development in ASD could be the result of disrupted subcortical visual attention mechanisms at birth, as suggested by Di Giorgio et al. (2016). However, it may be the case that initial social orienting is intact, but cortical specialization for faces and social information fails to emerge, leading to reduced social orienting after 2 months of age, as suggested by Jones and Klin (2013). Of course, it could also be a combination of decreased activation of subcortical *and* cortical social attention pathways, or even reduced emerging connectivity across cortical-to-subcortical structures subserving social attention. In light of the well-documented, specifically timed neurodevelopmental transitions that drive behavioral changes in visual attention across the first months of life, a greater understanding of the timing of attention differences in infants at risk for ASD can shed light on these hypotheses.

The current study aims to pinpoint the timing of divergence in early attention for infants at risk for ASD and identify how early attention is associated with later social communication skills for both high- and low-risk infants. We examine the early development of attention during a time of significant neurobehavioral maturation, from 1 week to 5 months of age, in infants at high and low risk for ASD. Using a behavioral task that requires orienting to and tracking visual and auditory animate (faces and voices) and inanimate (objects) stimuli, we first compare change in attention over time between high-risk and low-risk infants, and then test whether early attention is associated with 12-month social communication and/or nonverbal cognitive skills. Consistent with previous studies, we hypothesize that high-risk infants will exhibit early differences in attention, and that these cross-group differences will appear within a time window delineated by substantial neurodevelopmental shifts in attention that occur, specifically, between 2 and 4 months of postnatal life. We also hypothesize that attention during this time plays a specific facilitative role in *social* development, but not necessarily overall developmental skills. Thus, we predict that early attention will be associated with 12-month social communication skills, but not 12-month nonverbal cognitive skills. Because ASD is primarily a social disability, we expect that these differences will be most pronounced for animate (faces and voices) rather than inanimate (objects) stimuli.

Method

Participants

Participants included 41 infants at high risk for ASD and 39 low-risk infants. High-risk participants had an older full-biological sibling with ASD whose diagnostic status was ascertained via diagnostic evaluation by a licensed clinical or school psychologist or a medical doctor. ASD diagnoses were confirmed via clinical review of the evaluation reports, together with scores within the ASD range on the Social Responsiveness Scale (Constantino, 2012) and on the Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003). When diagnostic confirmation of the older sibling could not be sufficiently ascertained with these criteria (i.e., when Social Responsiveness Scale/Social Communication Questionnaire scores fell below cutoffs and/or when community-based diagnoses were made in the absence of documented testing), a direct assessment was conducted using the first or second edition of the Autism Diagnostic Observation Schedule (Lord et al., 2000, 2012) by a licensed and research reliable psychologist with expertise in diagnosis of ASD. In these cases, the psychologist administering the Autism Diagnostic Observation Schedule made an overall diagnostic judgment using DSM-5 criteria. This process was necessary for $N = 3$ high-risk participants whose community-based diagnoses were made in the absence of documented testing; sibling diagnoses were confirmed in these cases. This method of diagnostic confirmation is consistent with previous research (e.g., Chawarska et al., 2013; Ozonoff et al., 2015), but is less stringent than other siblings studies that confirm diagnoses for all participants using a diagnostic interview (e.g., Hazlett et al., 2017).

Low-risk participants had no familial history of ASD in first-, second- or third-degree relatives. Exclusion criteria for both high-risk and low-risk infants included gestational age below 37 weeks, major hearing and/or visual impairment, nonfebrile seizure disorders, known genetic syndrome, and clinically significant pre- or perinatal complications. Complications included significant, persistent medical conditions (e.g., respiratory or temperature regulation problems) that prevented the neonate from safely tolerating the NICU Network Neurobehavioral Scale (NNNS) procedures by 1 month of age. Families were recruited through local pediatric practices, hospitals, OB/GYN offices, radio and media ads, and state and local autism organizations. Written, informed consent was obtained from a parent or guardian of each child before any assessment or data collection. All procedures involving human subjects in this study were approved by the institutional review board of Emory University.

Procedures

The data reported here are a subset of a large longitudinal study in which infant siblings of children with ASD and infant siblings of typically developing children were recruited from birth and followed prospectively. The aims of the current study were to map trajectories of early visual attention prior to 6 months of age and associations thereof with social communication and cognitive skills measured at 12 months. Therefore, the data presented here include only visits that occurred between 1 week and 5 months of age, as well as the 12-month developmental measures. At each monthly visit from 1 week to 5 months, infants were administered the NNNS (Lester, Andreozzi-Fontaine, Tronick, & Bigsby, 2014; Noble & Boyd, 2012; Tronick & Lester, 2013), which includes an attention task that is the focus of the current study and described in detail below. The full NNNS was administered to all infants, with the exception of the incurvation item, which was not administered to infants older than 2 months. The NNNS was administered by licensed clinical psychologists or doctoral students in clinical psychology who were certified NNNS examiners or supervised by certified NNNS examiners. All examiners were trained to 80% reliability in administration and scoring of the task prior to independent administration. Ten percent of administrations per examiner were then selected at random for reliability, resulting in an average of 84% interrater agreement. All examiners were masked to risk status of the participant.

At 12 months, infants were seen again for a 1-day evaluation of social communication, cognitive, motor, and language skills. The visit window for the 12-month visit was 1 week before or 2 weeks after the 12-month birthday. This evaluation consisted of the Communication and Symbolic Behavior Scales (CSBS; Wetherby & Prizant, 2002) and the Mullen Scales of Early Learning (Mullen, 1995). All 12-month study visits began with the CSBS, which takes approximately 30 min to complete, followed by an approximate 20- to 30-min break. The Mullen Scales of Early Learning was then administered and lasted for 20–30 min. Infants were seated in a hook-on high chair attached to a full-sized table with a parent seated next to them for the duration of both assessments. The CSBS was administered by licensed speech–language pathologists with expertise in infant development and ASD. All speech–language pathologists were trained by an author of the CSBS (A. Wetherby) to 90% reliability in administration and scoring. Training and reliability monitoring occurred through biweekly meetings for 2 years that involved review of videos and discussion of administration and scoring issues. The Mullen Scales of Early Learning was administered by licensed psychologists with expertise in infant development and ASD, or a doctoral psychology trainee supervised by a licensed psychologist. Psychologists and trainees were masked to risk status of the participant and to the aims of the present study. The clinical evaluations conducted at 12 months were fully independent from the aims, hypotheses, and results of the experimental attention task.

Measures

Attention

The attention task was modified from the "Orientation" items of the NNNS. This task tests the infant's ability to orient to animate and inanimate visual and auditory stimuli. It consists of six items that involve animate (examiner's face and voice) and inanimate (examiner's presentation of ball and rattle) stimuli. Stimuli are presented visually, auditorily, and visual-auditorily as follows: inanimate visual (ball only), inanimate auditory (sound of rattle only), inanimate visual/auditory (rattle with sound of rattle), animate visual (face only), animate auditory (sound of voice only), and animate visual/auditory (face with sound of voice).

Items are presented with the infant in the examiner's lap for infants aged 1 week to 2 months and with the infant lying supine on a padded table for infants aged 3 to 5 months. Each item is administered per instructions provided in the NNNS manual (Lester & Tronick, 2005); items are presented in a flexible order designed to engage and optimize infants' performance. All visual and visual/auditory items begin with the stimulus (face, ball, or rattle) presented in the infant's midline. Once the infant focuses on the stimulus, the stimulus is moved horizontally to one side and back to center, horizontally to the opposite side and back to center, up and down on a vertical plane, and finally up and around in a circular path for a 180-degree arc. Auditory items consist of presenting an auditory stimulus (examiner's voice or a shaking rattle) approximately 6–12 inches from the infant's ear and out of sight; a total of four trials are presented, two trials on each side.

All six attention items are scored according to the definitions in the NNNS manual. Scores range from 1 to 9, with higher scores indicating better performance. For example, a score of 1 on the inanimate and animate visual tasks indicates that the infant did not focus on or follow the stimulus, a score of 6 indicates that the infant followed the stimulus for two 30-degree arcs with eyes and head, and a score of 9 indicates that the infant followed with smooth and continuous eye and head movement horizontally, vertically, and in a circular 180-degree arc. Infant performance was scored in real time and subsequently confirmed by the examiner via review of video. An overall attention score is calculated by averaging the scores across all six tasks.

The infant is required to be in a quiet or active awake state for administration of the attention items. If the infant becomes fussy during the task, handling strategies are used to soothe the infant and facilitate reengagement. In accordance with the NNNS manual, possible handling strategies include repeated breaks, hand holding/ventral pressure, auditory stimulation, jiggling/vertical rocking, covering/wrapping, swaddling, rocking while walking, pacifier, or taking a break for feeding/diaper change. The type and number of handling strategies used for each infant were recorded. If the infant was not able to sustain a quiet or active awake state, the task was discontinued.

Social communication skills

The CSBS—Developmental Profile, Behavior Sample (Wetherby & Prizant, 2002) is a standardized early childhood play-based assessment of communication designed for infants and toddlers. The assessment includes 20 individual items that make up seven clusters in three composite domains ("social," "speech," and "symbolic"), all of which yield a "total" score. The social composite assesses infants' use of emotion expression and eye gaze, frequency and function of communication, initiation and response to joint attention, and use of gestures. The speech composite measures directed vocalizations and word approximations, and includes sounds and words clusters. The symbolic composite measures language comprehension and symbolic play skills. In the current study, the CSBS total score (standard score with a mean of 100 and standard deviation of 15) is used as a measure of overall social communication skills.

Nonverbal cognitive skills

The Mullen Scales of Early Learning (Mullen; Mullen, 1995) is a standardized developmental measure designed for children from birth to 68 months. It provides *t* scores (mean of 50, standard deviation of 10) and age equivalences for five domains of development: visual reception (nonverbal cognition), gross motor, fine motor, receptive language, and expressive language. Scores from the Mullen visual reception domain were used in this study as a proxy for nonverbal cognitive development.

Statistical methods

Descriptive statistics were calculated for all variables of interest and include means and standard deviations for continuous variables or counts and percentages for categorical variables. Differences in demographic variables between risk groups were evaluated using *t* tests for continuous variables and chi-square tests for categorical variables.

Prior to statistical modeling of our longitudinal measure of attention, scatter plots were examined to assess the functional form of change in attention over time. Given the nonlinear nature of the relationship between age and attention, a basis spline function was used to model the effect of age in subsequent analyses. In addition, to account for subject-specific effects and differential trajectories, we utilized mixed-effects models to compare the effect of age on attention from 1 week to 5 months between high-risk and low-risk infants. For each mixed model, the fixed effects included risk status (two levels) and the interaction between risk with the splined effect of age at each visit. For the splined age effect, we used a third-degree polynomial with three equally spaced internal knots focused around 45, 95, and 145 days. Subject-specific intercepts and b-spline functions for age were fit as random effects and an autoregressive variance–covariance matrix was utilized. The autoregressive covariance matrix assumes homogeneous variances and correlations that decline exponentially over time such that measurements closest in time have the highest degree of correlation. Differences between risk groups are presented as model-based least-square mean differences with associated 95% confidence intervals (CIs). To control for Type I error, a multiplicity correction was used and simulation-based step-down-adjusted *p* values are reported. In addition, potential confounding effects of demographic characteristics on the outcome were tested in the model. This same model was used to evaluate each of the six attention items that make up the total attention score. Model fit was gauged using residual plots and model fit statistics.

Linear models were used to evaluate associations between early attention and 12-month social communication and nonverbal cognitive outcome. Associations with each of the six monthly time points (from 1 week to 5 months) and social communication outcome at 12 months were modeled separately. For this analysis, participant visits were binned into age windows, such that each monthly time point (30, 60, 90, 120, and 150 days) included participants seen +/−14 days of that time point. The 1-week time point included participants who were younger than 20 days.

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Results were corrected for multiple comparisons using a Bonferroni correction, setting the critical value to 0.008 (0.05/6). Initially, models included the main effect of risk group, time-specific attention score, and the interaction between group and attention. If the interaction was significant, this indicated that the relationship between attention and social communication differed by risk group at a specific time point. In these instances, a stratified model was run for each risk group. If the interaction was nonsignificant, a single slope was fit to model the relationship between attention and CSBS scores. Similar analyses were used to examine the relationship between early attention and 12-month nonverbal cognitive outcome. Analyses were conducted using SAS v. 9.4 (Cary, NC), and statistical significance was assessed at the .05 level unless otherwise noted.

Results

Sample characteristics for high-risk and low-risk infants are presented in Table 1. Demographic characteristics, including sex, gestational age, and household income, were comparable across high-risk and low-risk infants; however, there were significant differences in maternal education and race. The low-risk group reported higher maternal education and was made up of a greater proportion of White families compared to high-risk infants. The mean number of study visits per participant did not differ across groups. The proportion of infants in each group who were unable to complete the attention task at any time point due to fussiness was minimal and comparable across groups (high risk, $n = 6$; low risk, $n = 6$), χ^2 (1) = 0.003, $p = .96$. As expected, performance on the CSBS at 12 months was significantly lower for high-risk infants compared to low-risk infants, especially in regard to the social and speech composites.

Developmental change in attention

Change in overall attention for high-risk and low-risk infants from 1 week to 5 months of age is displayed in Figure 1. Both high-risk and low-risk infants exhibited an increase in overall attention from a mean score between 5 and 6 at 7 days to a mean score between 8 and 9 at 150 days. While low-risk infants exhibited a relatively linear increase from 60 to 120–150 days, high-risk infants showed very little change from 30 to 60 days, followed by a steep increase from about 75 to 120 days. Model-based estimates at each monthly time point, selected a priori and adjusted for multiple comparisons (see Table 2), revealed that high-risk infants scored nearly 1 point lower than low-risk infants at 60 days, t (245) = −3.26, $p < .01$, and a little more than half a point lower at 90 days, t (245) = −2.43, $p = .07$. There were no subsequent differences between the groups at 120 or 150 days.

To test for possible confounding variables, we ran this same model including demographic variables that were significantly different between the groups (race and maternal education) as covariates. Between-group comparison of the resulting model-based estimates at each monthly time point, adjusting for multiple comparisons, retained significance at 60 days across the models. The difference at 90 days became significant when controlling for race, t (222) = −2.74, $p = .03$, and maternal education, t (222) = −2.77, $p = .03$. Differences at all other time points remained nonsignificant across models. Because the inclusion of these covariates did not significantly affect the results of the initial model, the initial model was retained and covariates were not included in subsequent analyses.

In a secondary analysis, a set of similar mixed models were run for the six attention items that make up the overall attention score: inanimate visual, inanimate visual/auditory, inanimate auditory, animate visual, animate visual/auditory, and animate auditory (see Figure 2). Again, all comparisons were corrected for multiplicity, and presented p values reflect this adjustment (see Table 3). For the inanimate visual task, high-risk infants scored about 1 point lower at 60 days, t (240) = −2.35, p =.09, and 1.3 points lower at 90 days, t (240) = −3.09, $p < .05$, but scored similarly to low-risk infants at 120 and 150 days. For the animate visual task, high-risk infants scored nearly 1.5 points lower at 60 days, t (237) = −2.82, $p < .05$, but did not differ from low-risk infants at 90 days or at any time points thereafter. A similar, though statistically nonsignificant, trend was observed for the animate and inanimate visual/auditory tasks in which high-risk infants scored about 1 point lower at 60 and 90 days, but caught up to the low-risk infants by 120 days. There were no differences between high-risk and low-risk infants at any time point for either the inanimate or the animate auditory tasks.

Association of early attention and 12-month outcome

A total of 40 infants (22 high risk and 18 low risk) were administered the CSBS and Mullen at 12 months. When assessing the relationship between early attention at each time point (1 week through 5 months) and 12-month outcome, each model included only participants who had both the early time point being evaluated and the 12-month outcome assessment. Initial models of the relationship between attention and outcome included a Risk Group × Attention interaction term; however, our models did not demonstrate a significant interaction between risk group and attention score at any time point, thus indicating that the relationship between attention and social communication did not differ by risk group. Accordingly, the risk groups were combined for all models to increase statistical power and provide more precise estimates of the association between social communication and early attention. There was a significant association between 3-month attention and the 12-month CSBS Total score, F (1, 36) = 12.50, $p < .01$; b_1 = 3.79, 95% CI [1.62, 5.96] (see Figure 3). Attention at 3 months accounted for 26% of the variance in the CSBS total score at 12 months, $R^2 = .26$. This model included 19 high-risk infants and 18 low-risk infants who had both the 3-month attention and 12-month CSBS scores. Attention at all other time points was not significantly associated with the 12-month CSBS total score.

The same strategy was used to test for associations between early attention and nonverbal cognitive skills at 12 months. Linear models showed no significant interaction between risk group and attention at any time point, and so risk groups were combined for all models. Using a Bonferroni correction for multiple comparisons, 12-month Mullen visual reception was significantly associated with attention at 3 months, F (1, 37) = 8.01, $p = .008$ $b_1 = 2.91$, 95% CI [0.83, 5.00], but not at any other time point. Attention at 3 months accounted for 18% of the variance in Mullen visual reception at 12 months, $R^2 = .18$. While 3-month attention was significantly associated with social communication and nonverbal cognitive skills at 12 months, it was more strongly associated with social communication skills, explaining about 8% more of the variance compared to nonverbal cognitive skills.

Discussion

The current study sought to characterize the development of attention in very young infants and identify points of departure

Table 1. Participants characteristics

	High risk ($n = 41$)	Low risk ($n = 39$)	Test statistic
Sex			χ^2 (1) = 0.07, p = .79
Male	21 (56%)	23 (59%)	
Female	18 (44%)	16 (41%)	
Race			χ^2 (4) = 8.8, p = .04
White	25 (61%)	32 (82%)	
Black	10 (24%)	2 (5%)	
Asian	1 (3%)	0 (0%)	
Mixed	3 (7%)	1 (3%)	
Not reported	2 (5%)	4 (10%)	
Maternal education[a]			χ^2 (2) = 12.5, p = .002
Some college	9 (23%)	1 (3%)	
College degree	21 (54%)	14 (39%)	
Postgraduate degree	9 (23%)	21 (58%)	
Household income[b]			χ^2 (2) = 3.03, p = .26
Less than \$60,000	8 (22%)	4 (11%)	
\$60,000–\$100,000	11 (30%)	7 (20%)	
Above \$100,000	18 (48%)	24 (69%)	
Gestational age[c]	39.0 (1.5)	39.2 (1.4)	t (75) = −0.59, p = .56
Number of visits per participant	4.2 (1.1)	4.5 (1.3)	t (78) = −1.29, p = .20
12-month outcome			
Communication and Symbolic Behavior Scales—Behavior Sample[d]			
Social composite	8.1 (2.5)	9.3 (1.4)	t (48) = −2.09, p = .04
Speech composite	8.4 (1.6)	9.6 (2.0)	t (48) = −2.30, p = .03
Symbolic composite	7.3 (2.1)	8.0 (2.2)	t (48) = −1.20, p = .23
Total score	85.2 (9.6)	92.0 (8.2)	t (48) = −2.66, p = .01

Note: Values represent the mean (standard deviation) for continuous variables or n (% within risk group) for categorical variables. [a]High risk $n = 39$, low risk $n = 36$. [b]High risk $n = 37$, low risk $n = 35$. [c]High risk $n = 38$, low risk $n = 39$. [d]High risk $n = 26$, low risk $n = 24$.

for infants at risk for ASD. For low-risk infants, we observed relatively steady improvements in attention from 1 to 5 months of age. In comparison, infants at heightened risk for ASD performed similarly to low-risk infants at 1 month, but failed to show substantial improvements in attention until the end of the third month of life. Following Month 3, high-risk infants showed a steep incline and were no longer distinguishable from their low-risk peers at 4 and 5 months. When the six attention items were individually explored, between-group differences were especially robust for the animate visual task at 2 months and inanimate visual task at 3 months. Marginal differences were observed for the animate and inanimate visual/auditory tasks at 2 and 3 months. Auditory attention was not different between risk groups at any time point, indicating that differences in attention were primarily driven by visual engagement (fixating and tracking visual stimuli), rather than auditory engagement (orienting toward and locating auditory stimuli). In contrast to our hypothesis, these results point to differences that are not specific to animate stimuli. High-risk infants showed vulnerabilities in visual attention to both faces and objects during this early period. In a subset of infants who also received a developmental evaluation at 12 months, we found that 3-month attention was associated with both social communication and, to a lesser extent, nonverbal cognitive development. This is somewhat inconsistent with a study by Salley et al. (2016) that identified an association earlier in development between 1-month attention and 12-month social communication abilities in a non-ASD sample. It is possible that the present study was simply underpowered to detect this association at this early age. In addition, the outcome measure used in Salley et al. (2016) reflects a frequency count of joint attention behavior, while our outcome measure, the CSBS total score, is a standardized score based on several categories of social, speech, and symbolic behavior skills. Joint attention skills constitute only a small fraction of the behaviors that go into the CSBS total score. If 1-month attention predicts the frequency of joint attention behaviors, it is reasonable to expect that the CSBS total score may not reflect this specific ability.

Together, these findings highlight a critical window, between 2 and 3 months of age, when high-risk infants are showing vulnerabilities in their ability to fixate and track visual animate and

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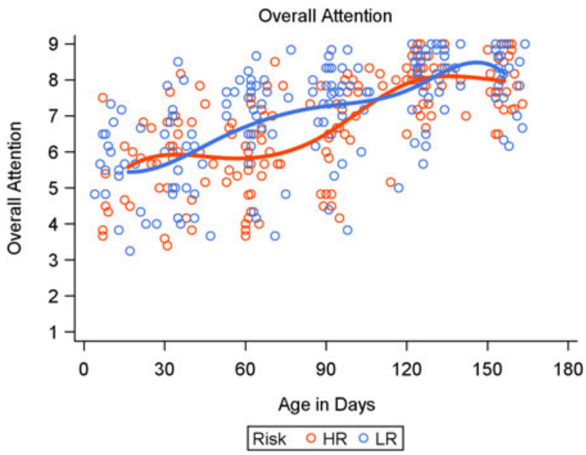

Figure 1. Attention from 1 week to 5 months of age for high-risk (HR) and low-risk (LR) infants.

Table 2. Model-based estimates of attention at each monthly time point

	Mean estimate (standard error)			
	High risk	Low risk	*t* (245)	*p*[a]
7 days	4.85 (0.44)	5.81 (0.34)	−1.71	.30
30 days	5.92 (0.23)	5.59 (0.22)	1.03	.65
60 days	5.82 (0.19)	6.71 (0.20)	−3.33	.006
90 days	6.54 (0.20)	7.19 (0.18)	−2.43	.07
120 days	7.82 (0.17)	7.85 (0.17)	−0.14	.89
150 days	8.10 (0.24)	8.29 (0.24)	−0.58	.81

[a]Simulation-based step-down-adjusted *p* values are reported to adjust for multiple comparisons.

inanimate stimuli. Moreover, attention skills at this time were significantly associated with social communication and nonverbal cognitive abilities at 12 months. While it is outside the scope of this study to make conclusions about visual preference for social stimuli over nonsocial stimuli (as in Di Giorgio, 2016), our data show interesting trends across the first month of life for both high- and low-risk infants that warrant further investigation. While high-risk infants scored an average of 1–2 points lower than low-risk infants on the animate attention tasks at 1 week, this difference was not statistically significant, and the standard errors were largest for both groups at this age. Our data set is limited by a relatively small sample size, and additional research with larger samples are needed in order to speculate further about these trends in the first month of life. After this time point, however, our evidence strongly suggests a divergence in visual engagement that emerges between 2 and 3 months of age and that exists for both faces and objects. There is evidence that during this time typically developing infants are in the midst of a critical transition from subcortically mediated, reflexive control of their behavior, including eye and head movements, to cortically mediated, voluntary control of behavior (Johnson, 1990). This early neurodevelopmental shift is thought to enable the emergence of intentional gaze shifting between a person and an object (i.e., joint attention), which is a core deficit of ASD (Mundy, Sullivan, & Mastergeorge, 2009). As suggested by Shultz et al. (2018), it is possible that lower performance on this attention task at 2 and 3 months reflects a neurodevelopmental divergence whereby processes and mechanisms related to the transition from reflexive to voluntary attention are different for high-risk infants. If the gradual improvement in attention observed in low-risk infants is attributed to the gradually increasing cortical influence on attention, resulting in improved voluntary control and attentional disengagement, it is possible that the emergence of cortically mediated attention is delayed or disrupted in high-risk infants.

In order to visually engage with people and objects in the environment, infants must flexibly select among, and shift between, the array of elements in the global visual field. Impaired disengagement of attention during this 2- to 3-month period would be in line with previous research documenting deficits in attentional disengagement for high-risk infants at older ages (Elsabbagh et al., 2013). An alternative explanation may be related to the link between motor and perceptual development (von Hofsten, 2004). Visual exploration of faces and objects is enabled and facilitated by increased postural control and more sophisticated fine motor skills (e.g., reaching and manual exploration; Iverson, 2010; Libertus & Needham, 2011; Soska, Adolph, & Johnson, 2010). This research, along with evidence for delayed fine motor development in high-risk infants (LeBarton & Iverson, 2013), points to the possibility that delayed fine motor skills in high-risk infants may be associated with observed differences in attention around 2–3 months of age. Relatedly, coordination of eye and head movement in visual tracking is a skill that improves with age (von Hofsten & Rosander, 1996). The attention task used in this study requires coordination of visual and motor systems, such that infants must coordinate visual fixation and saccades with motoric control of the head and neck. While comparable performance on the auditory orienting task does not suggest that high-risk infants experience a global deficit in motoric control of the head and neck, it is possible that coordination of eye and head movements during visual tracking is disrupted. Our preliminary data suggest that high-risk infants may experience difficulties with these types of visual tracking tasks on developmental assessments (Carpenter, Evans, Beacham, Klaiman, & Bradshaw, 2017). This hypothesis could be tested directly using a more precise coding system of attention that separates eye and head movement during visual tracking tasks. It would also be useful to investigate eye and head movement during visual tracking tasks that require varying levels of motoric control. For example, visual tracking in supine, prone, supported sitting, and independent sitting positions all place unique motoric demands on the infant. We are currently examining the effect of motor development on infant attention during this early age period.

It is interesting that the difference observed at 2 and 3 months is no longer observable at 4 and 5 months. This alludes to the possibility that our attention task is picking up on important neurodevelopmental processes at an early age period, from birth to 3 months, but that our task may not be sensitive to later developing, more mature neurodevelopmental processes that are in place by 4 months. In other words, we may be observing a ceiling effect on this rather simple attention task by age 4–5 months. This would not be surprising given that the NNNS was developed for infants younger than 2 months of age. Similarly, it is possible that a floor effect is observed at the earlier time points and that attention differences would emerge even earlier using a measure designed to be even more sensitive to differences in social attention in neonates. Although our attention task was based on an established,

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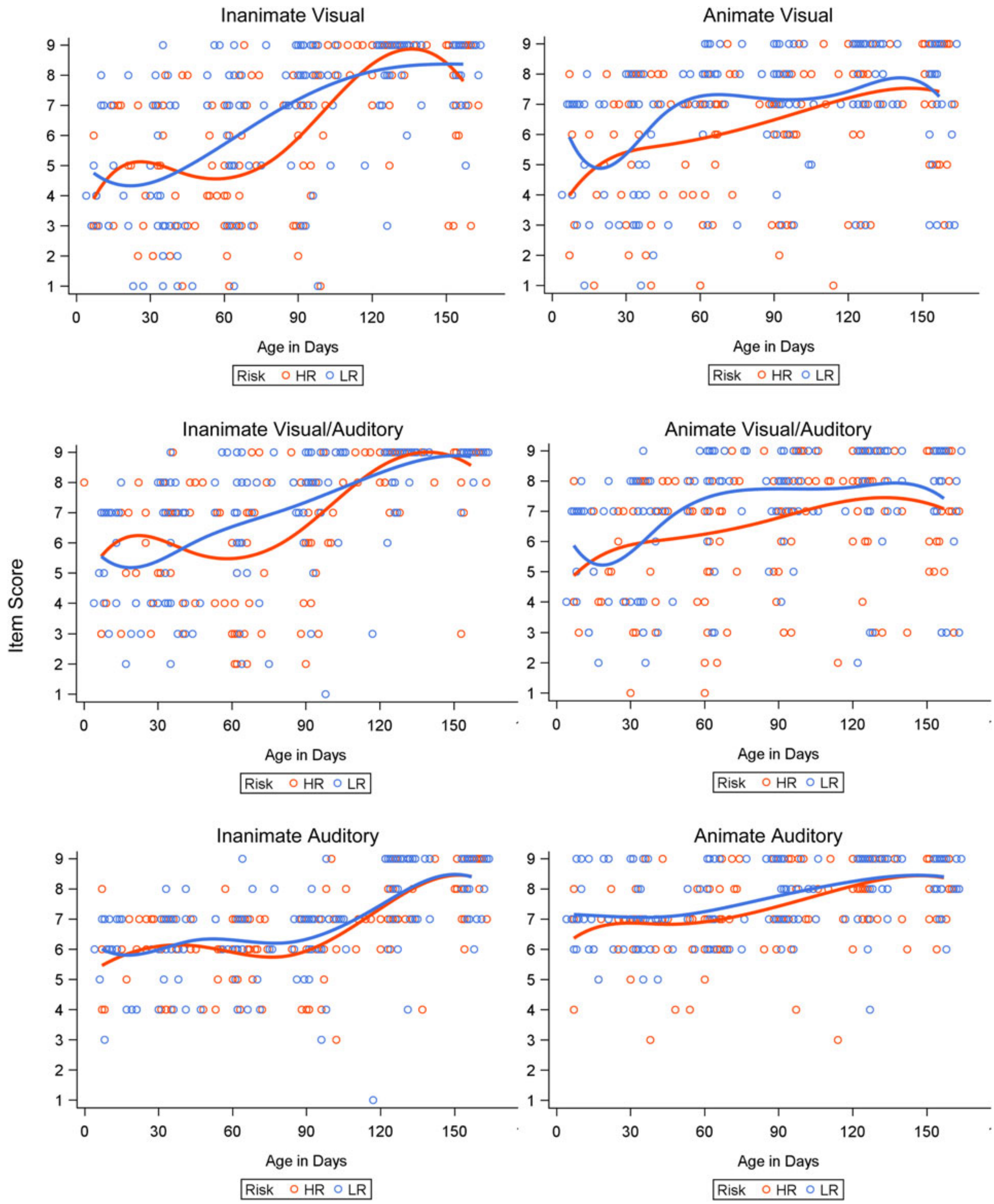

Figure 2. Inanimate (left) and animate (right) attention for high-risk (HR) and low-risk (LR) infants.

standardized measure and there was high interrater reliability in administration and scoring of the task among all examiners, it may be beneficial to address this limitation by replicating findings with more objective and quantifiable measurement of eye and head movement. While eye-tracking technology presents a challenge when applied to infants younger than 3 months of age, filming and frame-by-frame coding of behavior may be an alternative. Still, it remains unclear what benefits this type of behavioral coding may have above and beyond the already well-established NNNS scoring system.

This study also highlights the need to understand factors contributing to the observed developmental increase in attention for both high- and low-risk infants. Many developmental capacities, such as self-soothing/regulation, motor skills, and cognitive skills,

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Table 3. Model-based estimates of attention at each monthly time point

Attention item	Mean estimate (standard error) High risk	Low risk	*t*	*p*
Inanimate visual[a]				
7 days	3.86 (0.76)	4.75 (0.62)	−0.91	.74
30 days	5.09 (0.40)	4.42 (0.38)	1.22	.63
60 days	4.58 (0.32)	5.70 (0.34)	−2.40	.08
90 days	5.89 (0.34)	7.20 (0.32)	−2.80	.03
120 days	8.39 (0.29)	8.11 (0.30)	0.65	.76
150 days	8.23 (0.42)	8.37 (0.41)	−0.22	.82
Inanimate visual/auditory[b]				
7 days	5.53 (0.55)	5.54 (0.52)	−0.01	.99
30 days	6.12 (0.33)	5.39 (0.33)	1.57	.39
60 days	5.48 (0.28)	6.53 (0.30)	−2.58	.06
90 days	6.53 (0.30)	7.33 (0.28)	−1.95	.23
120 days	8.52 (0.25)	8.32 (0.26)	0.55	.93
150 days	8.69 (0.37)	8.85 (0.36)	−0.31	.94
Inanimate auditory[c]				
7 days	5.43 (0.50)	5.98 (0.38)	−0.87	.85
30 days	6.10 (0.25)	5.98 (0.24)	0.33	.97
60 days	5.91 (0.21)	6.32 (0.22)	−1.36	.68
90 days	5.92 (0.22)	6.30 (0.20)	−1.31	.68
120 days	7.38 (0.19)	7.49 (0.19)	−0.43	.97
150 days	8.35 (0.27)	8.43 (0.27)	−0.21	.97
Animate visual[d]				
7 days	3.98 (0.82)	5.90 (0.66)	−1.92	.29
30 days	5.41 (0 .42)	5.34 (0.40)	0.11	.92
60 days	5.85 (0.33)	7.27 (0.36)	−2.91	.02
90 days	6.48 (0.35)	7.13 (0.34)	−1.34	.54
120 days	7.20 (0.30)	7.46 (0.33)	−0.58	.92
150 days	7.52 (0.44)	7.80 (0.44)	−0.44	.92
Animate visual/auditory[e]				
7 days	4.86 (0.77)	5.86 (0.59)	−1.03	.76
30 days	5.88 (0.40)	5.63 (0.37)	0.46	.76
60 days	6.24 (0.32)	7.43 (0.34)	−2.58	.06
90 days	6.78 (0.34)	7.72 (0.32)	−2.03	.20
120 days	7.37 (0.29)	7.81 (0.31)	−1.03	.76
150 days	7.24 (0.43)	7.85 (0.42)	−1.02	.76
Animate auditory[f]				
7 days	6.36 (0.50)	7.15 (0.36)	−1.28	.74
30 days	6.86 (0.24)	7.06 (0.22)	−0.60	.91
60 days	6.90 (0.19)	7.24 (0.21)	−1.19	.74
90 days	7.42 (0.21)	7.77 (0.19)	−1.21	.74
120 days	8.09 (0.17)	8.24 (0.19)	−0.58	.91
150 days	8.45 (0.25)	8.47 (0.25)	−0.05	.96

[a]*df* = 240. [b]*df* = 241. [c]*df* = 242. [d]*df* = 237. [e]*df* = 234. [f]*df* = 233.

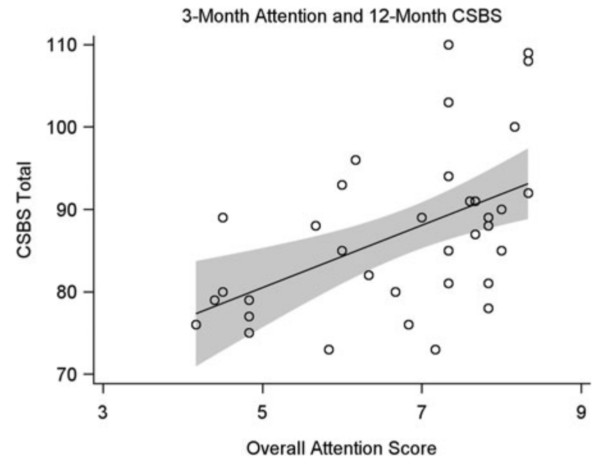

Figure 3. Association between 3-month attention score and 12-month Communication and Symbolic Behavior Scales score with 95% confidence interval.

are rapidly emerging during this early period, and it is outside the scope of the current study to examine how acquisition of these skills are facilitating attention task performance. Recent research has begun to consider how motor, attention, and ASD symptomology are interrelated in the ASD phenotype (e.g., Mous, Jiang, Agrawal, & Constantino, 2017), and it is up for debate whether weakness in one domain confers risk for ASD, is a core feature of ASD, or is an unrelated comorbid feature. Understanding the sequential unfolding of motor, attention, and social abilities in the first months of life is critical for creating mechanistic hypotheses for the emergence of social communication and the ASD phenotype.

In order to understand early trajectories of attention as a predictor of autism spectrum disorder, it will be necessary to compare trajectories of high-risk infants who are diagnosed with ASD to those who are typically developing at outcome. While high-risk infants, as a group, frequently experience significant developmental vulnerabilities in the first years of life, the majority of high-risk infants reach a typical outcome with no diagnosis by age 3. However, our evidence for a positive association between early attention and later social communication abilities, that predict later social communication deficits and ASD, suggests that attention during this early period, or mechanisms underlying attention during this period, may be critical for the emergence of social communication.

In addition to the limitations already mentioned, the present study is limited by the relatively small size of our sample, especially at the 12-month outcome assessment. Determining whether early attention is associated with developmental and diagnostic outcomes beyond 12 months, at ages 2 and 3 years, will be valuable. Finally, the low-risk families in this study were characterized by higher maternal education and significant racial/ethnic differences compared to high-risk participants. Our results suggest that this did not have a significant impact on our findings, but it is important to gather a more representative sample of low-risk typically developing infants in future work.

The current study is among very few behavioral research studies that have investigated the development of high-risk infants as young as 1 week of age. Using a densely sampled, longitudinal research design, we were able to uncover early differences in visual attention for high-risk infants that were associated with social communication and nonverbal cognitive skills at 12 months.

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Our data suggest that the transition from reflexive to voluntary control of visual attention occurring between 2 and 3 months of age may be disrupted. Following Month 3, however, it appears that either this process self-corrects and becomes fully functional, or performance is bolstered by the onset of compensatory mechanisms that support visual attention, resulting in comparable performance in the fourth and fifth months. Future research should investigate the precise brain–behavior transitions that occur during this time period across social, cognitive, and motor domains of development that may be related to the heterogeneity observed in early visual attention.

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