Prospective Examination of Visual Attention during Play in Infants at High-Risk for Autism Spectrum Disorder: A Longitudinal Study from 6 to 36 Months of Age.

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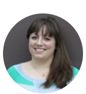

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Research report

Prospective examination of visual attention during play in infants at high-risk for autism spectrum disorder: A longitudinal study from 6 to 36 months of age

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HIGHLIGHTS

- We examine visual disengagement in infants at risk for autism using toy-based play.
- Infants were filmed at 6, 9, 12, 15, 18, 24, and 36 months of age as they play with toys.
- Infants who receive a diagnosis of autism at 36 months show delay in disengaging at 12 months.
- The delay in disengagement continues at 15, 18, 24 for infants who get a autism diagnosis.

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ABSTRACT

Regulation of visual attention is essential to learning about one's environment. Children with autism spectrum disorder (ASD) exhibit impairments in regulating their visual attention, but little is known about how such impairments develop over time. This prospective longitudinal study is the first to describe the development of components of visual attention, including engaging, sustaining, and disengaging attention, in infants at high-risk of developing ASD (each with an older sibling with ASD). Non-sibling controls and high-risk infant siblings were filmed at 6, 9, 12, 15, 18, 24, and 36 months of age as they engaged in play with small, easily graspable toys. Duration of time spent looking at toy targets before moving the hand toward the target and the duration of time spent looking at the target after grasp were measured. At 36 months of age, an independent, gold standard diagnostic assessment for ASD was conducted for all participants. As predicted, infant siblings subsequently diagnosed with ASD were distinguished by prolonged latency to disengage ('sticky attention') by 12 months of age, and continued to show this characteristic at 15, 18, and 24 months of age. The results are discussed in relation to how the development of visual attention may impact later cognitive outcomes of children diagnosed with ASD.

1. Background

Mature goal-directed reaching for objects is associated with restricted visual attention, that is, the eyes orient toward the object just before the hand moves to begin the reach and the eyes look away from the object as it is grasped [1–8]. There is progressive restriction of visual attention during the first year of life. Six-month-old infants visually engage a target for an extended duration prior to hand movement onset and continue to engage the target after it is grasped and is being manipulated. Prolonged visual attention may be associated with learning about objects and monitoring the objects, to ensure proper finger placement, and to learn about the association of the grasped object and the grasping hand [9]. Twelve-month-old infants display restricted visual attention during reaching; that is, they visually engage a target just before hand movement onset and disengage from the target as it is being grasped. This pattern of movement results in a brief period of visual attention to the target that is temporally coupled with advance of the hand to the target and then a redirection of visual attention away from the target as the target is grasped. Visual disengagement at the grasp may re-prioritize attention from vision to tactile feedback, enhance somatosensory awareness of the item for

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appropriate grasping [2,10–12], provide a visual anchor to stabilize posture for the grasp [13,14], and allows a visual search for the next item to be grasped [9]. Thus, the developmental restriction of visual attention allows us to explore our environment using both visual and tactile attention with increased efficiency.

Autism spectrum disorder (ASD) is a developmental disorder characterized by impairments in social communication and the presence of repetitive or restricted behaviors [15]. ASD is generally diagnosed at age 36 months or later [16] although evidence from retrospective studies of parental concerns and early home videos suggests a much earlier onset [17–27]. Recent prospective studies of 'high-risk' infants (infant siblings of children diagnosed with ASD [28–31]) have provided a window into the emergence of ASD early in life. Indeed, prospective longitudinal designs provide a unique opportunity to test specific hypotheses about early developmental mechanisms underlying the expression of subsequent symptoms [32,33]. Converging evidence suggests that impairments in visual attention may play a critical role in the development of ASD [34–41]. Landry and Bryson [39] compared three- to five-year-old typically developing children, children with ASD, and children with Down Syndrome on their ability to disengage using a visual orienting paradigm, the gap-overlap task. The task measures the latency to orient toward a peripheral target from a central fixation target using two stimulus conditions (central stimulus disappears before peripheral stimulus appears or central stimulus remains on throughout entire trial). Children with ASD were shown to display 'sticky attention', in that they took longer to disengage their attention from the central stimulus and orient their visual attention toward a second, peripheral target. 'Sticky attention' (or staring) for both engaging and disengaging attention is present in typically developing children at early ages and disappears by the first year [1,42–44]. Using the same task, Elsabbagh et al. [34] report that an impairment in disengaging attention at 14 months of age in high-risk infant siblings was associated with a diagnostic outcome of ASD at 36 months of age (see also [45]). Bryson et al. [46] also report than an impairment in disengaging attention at 12 months of age in high-risk infants was associated with a diagnosis of ASD at 36 months of age.

Although prolonged latencies to disengage visual attention have been reported in infants later diagnosed with ASD, little is known about the onset and developmental trajectory of this phenomenon. The purpose of the present study was to examine the development of visual attention in their first three years of life in high-risk infants during a naturalistic play task, in which visual attention was measured during reaching and grasping for toys. We hypothesized that high-risk infants would display a disengage deficit by 12 months of age and that this alteration in visual attention would be associated with later social communication and behavioral outcomes at 36 months of age.

2. Materials and methods

2.1. Participants

Thirty infants from a longitudinal study of infant siblings of children with ASD (see [29]) participated in the current study. The parent study tracks high-risk infant siblings (each with an older biological sibling diagnosed with ASD) and low-risk controls (no family history of ASD) to document any impairments or abnormalities in early development associated with ASD. All infants were enrolled at approximately 6 months of age and underwent comprehensive behavioral and cognitive assessment of their communication, social, and motor abilities at 6, 9, 12, 15, 18, 24, and 36 months of age. The infants in the present study were drawn from a subsample of participants from the Autism Research Centre in the Glenrose Rehabilitation Hospital (GRH), Edmonton, Alberta.

Table 1
Participant characteristics.

	Non-sib controls	Non-ASD sibling	ASD sibling
N	10	10	10
Age first visit (months)	6.94 (+1.82)	7.06 (±1.29)	8.56 (±2.14)
Age diagnostic visit (months)	36.84 (+1.13)	37.23 (±1.81)	37.66 (±1.98)
Sex	7 Males	3 Males*	6 Males#
ADOS			
18 months	7.7 (5.29)	9.2 (5.4)	14.8 (5.9)*
24 months	5.5 (3.03)	6.7 (4.9)	14.9 (6.1)*,#
36 months	4.2 (4.94)	5.0 (3.5)	17.3 (4.1)*,#
ADI			
Total Scon-	6.6 (2.76)	9.1 (2.28)	19.8 (10.8)*,#
Social Score	3.1 (1.37)	3.6 (1.17)	8.4 (4.9)*,#
Comm. Score	2.6 (1.90)	4.4 (1.90)	8.5 (3.98)*,#
AOSI			
6 months	11.11 (4.13)	10.38 (3.58)	14.75 (2.5)
9 months	6.89 (1.83)	8.89 (3.55)	7.22 (2.77)
12 months	5.0 (2.05)	7.6 (3.41)	9.7 (5.21)*
15 months	4.5 (3.72)	8.4 (4.86)	10.0 (5.16)*
18 months	5.13 (3.22)	7.8 (2.44)	9.8 (4.37)*
MSEL			
6 months	94.22 (7.28)	93.13 (9.89)	92.8 (11.95)
12 months	96.7 (10.03)	96.1 (17.03)	91.6 (18.84)
24 months	119.4 (17.84)	101.5 (14.86)	82.9 (17.61)*
36 months	123.6 (15.71)	106.6 (11.31)	96.44 (21.18)*
VABS			
12 months	105.0 (6.72)	102.4 (5.25)	96.5 (7.03)*
18 months	94.8 (2.30)	93.7 (3.27)	83.2 (7.56)*,#
24 months	99.4 (7.89)	93.1 (3.84)	80.9 (12.4)*,#
36 months	102.2 (7.12)	89.88 (12.03)	75.83 (11.94)*

Values reported are mean ± standard deviation
Mullen scores reported are the early learning composites
Statistically different from * control, # nonASD sib. $ps < 0.0167$.

The infants were selected at random to comprise three groups of equal size; (1) 10 non-sibling controls (control; 7 males); (2) 10 high-risk siblings without an ASD diagnosis (have an older sibling with ASD but they did not receive an ASD diagnosis at 36 months of age; non-ASD sibling; 3 males); and (3) 10 high-risk siblings with an ASD diagnosis (have an older sibling with ASD and they also received an ASD diagnosis at 36 months of age; ASD sibling; 6 males). The high-risk siblings were recruited from families following assessment of the older sibling with ASD at the GRH. The diagnosis of the older sibling (or 'proband') was based on evaluation by a multi-disciplinary team and expert clinical review using DSM-IV-TR criteria, supported by a comprehensive developmental history and the Autism Diagnostic Observation Schedule (ADOS). The non-sibling controls were included on the basis of having no first or second degree relatives with an ASD diagnosis and were recruited from the local community. All participants were born at 36–42 weeks gestation, had a birth weight greater than 2500 g, and had no known genetic or neurological disorders. Table 1 presents detailed participant characteristics. The local institutional review board approved the research protocol and parents provided written informed consent after receiving a detailed description of the longitudinal study.

2.2. Assessments administered

Several assessments were administered to track cognitive and ASD-specific characteristics over-time. A summary of these characteristics is presented in Table 1. For a complete description of the following assessments, see Zwaigenbaum et al. [47].

2.2.1. Mullen scales of early learning (MSEL [48])

The MSEL consists of four scales that, together, form the early learning composite (ELC). The MSEL was administered at 6, 12, 24, and 36 months of age.

2.2.2. Vineland adaptive behavior scales (VABS [49])

The VABS is a semi-structured parent interview designed to assess adaptive behavior, notably, communication, daily living, socialization, and motor skills. The VABS was administered at 12, 18, 24, and 36 months of age.

2.2.3. Autism observation scale for infants (AOSI [50])

The AOSI is a semi-structured, observational measure designed to detect and monitor early signs of ASD in infants aged 6–18 months. The AOSI uses 'presses' to elicit various target behaviors, including visual tracking and attentional disengagement, coordination of eye gaze and action, imitation, affective responses, early social-communicative behaviors, and behavioral reactivity. A 'press' is either a verbal or non-verbal request with the goal of eliciting a behavior in the child. For example, a press for a 'social smile' would involve the assessor looking at the child and smiling, with the goal of eliciting a reciprocal smile from the child. The AOSI was administered at 6, 9, 12, 15, and 18 months of age.

2.2.4. Autism diagnostic observation schedule (ADOS [51])

The ADOS uses standardized activities and 'presses' to elicit communication, social interaction, imaginative use of play materials, and repetitive behaviors, allowing the examiner to observe the occurrence or non-occurrence of behaviors important to the diagnosis of ASD. The ADOS was administered at 18, 24, and 36 months of age.

2.2.5. Autism diagnostic interview-revised (ADI-R; [52])

The ADI-R is an investigator-directed interview used to elicit information about social development, verbal and non-verbal communication skills and repetitive, stereotyped interests and behaviors required to make an ICD-10 or DSM-IV diagnosis of autism. The ADI-R was administered at 36 months.

2.3. Diagnostic procedure

At 3 years of age, each participant underwent an independent diagnostic evaluation, conducted by an expert clinician blind to assessments from previous study visits. ASD diagnoses were assigned using DSM-IV-TR criteria, based on the best judgment of the clinician (developmental pediatrician, child psychiatrist or clinical psychologist, all with at least 10 years of diagnostic experience), taking into account information from the concurrent ADI-R and ADOS and assessments of cognitive, language and adaptive skills. Some children with a clinical diagnosis of ASD had sub-threshold algorithm scores on the ADOS and/or ADI-R, but met DSM-IV-TR criteria based on expert review of all available 36-month data.

2.4. Assessments scored for visual attention

Visual attention measures were coded from the video-recordings of two assessments, the Autism Observation Scale for Infants and the Autism Diagnostic Observation Schedule. The individual who administered the assessments was different from the individual who coded the off-line data.

(1) *Autism Observation Scale for Infants* (*AOSI* [50]): Visual attention measures were coded from the AOSI at 6, 9, 12, and 15 months of age using the two *Free Play* sections. The free play sections together are approximately 10 min in length, with the first section occurring at the beginning of the AOSI and the second one occurring at the end of the AOSI. The two sections are separated by two tasks (peek-a-boo and imitation), lasting approximately 5 min. During the free play sessions, the child sits at a table across from the examiner, while seated in her/his parent's lap or alone in a posture supportive chair, with her/his hands and arms free to grasp and manipulate objects. Briefly, the examiner places a variety of graspable items on the table in front of the infant and encourages the child to reach and grasp for the items. The *Free Play* sections of the AOSI were chosen because (1) the child is encouraged to pick up small items (blocks, rings) for manipulation; (2) there is minimal interruption from the examiner; and (3) both sections make up the largest portion of the AOSI, allowing ample opportunity to gather a sufficient sampling of grasps (see below). All infants reached for the same toys at each age assessed (see Fig. 1A for objects used in the *Free Play* sections).

Fig. 1. Reach-to-grasp targets. Target toys that served as the grasping targets during the (A) AOSI and (B) ADOS. All infants reached for the same targets.

(2) *Autism Diagnostic Observation Schedule* (*ADOS* [51]): Visual attention measures were coded from the ADOS at 18, 24, and 36 months of age using the *Birthday Party* routine. The *Birthday Party* routine occurs at the end of the ADOS (followed only by 'snack') and is approximately 10 min in length. During this routine, the child sits at a table across from the examiner, while

Table 2
Number of reaches scored.

N	Non-sib controls	Non-ASD sibling	ASD sibling	Total
6 months	40	40	20	100
9 months	40	40	45	125
12 months	45	50	50	145
15 months	45	45	45	135
18 months	42	50	50	142
24 months	47	46	43	136
36 months	37	49	38	124
Total	296	320	291	907

seated in her/his parent's lap or alone in a posture supportive chair, with her/his hands and arms free to grasp and manipulate objects. Briefly, during the *Birthday Party*, the examiner "makes" a birthday cake from play-doh and encourages the child to grasp and place candles in the cake. After singing "Happy Birthday", the child is then encouraged to cut and feed cake and drinks to the birthday baby (i.e., the examiner says, "the baby is hungry" and the child is supposed to respond by feeding the baby cake). The *Birthday Party* routine of the ADOS was chosen for scoring because (1) the child is encouraged to pick up small items (candles, fork, knife) for manipulation; (2) the *Birthday Party* routine is one of the longer manipulation sections of the ADOS and thus there is ample opportunity to gather a minimum number of grasps; and (3) the *Birthday Party* routine is included in the two modules of the ADOS used to assess 18- to 36-month-olds in this study (see Fig. 1B for objects used in the *Birthday Party* routine).

2.5. Reaches sampled

The first five successful reach-to-grasp movements were sampled for each infant at each time-point. To be included as a sampled reach, the infant had to make an overt eye movement toward the target, reach his/her hand toward the target, grasp the target, lift the target from the substrate, and make an overt eye movement to disengage from the target. There were occasions in which an infant did not perform five successful reaches in a session (e.g., did not lift or manipulate an object). Table 2 displays the total number of reaches scored at each time-point and for each infant.

2.6. Visual attention measures

A digital video camera was positioned in front of the infant to record a frontal view of the participant from tabletop to head for video recording at 30 frames/s, with a shutter speed of 500 frames/s (a high shutter speed produces blur-free images and can capture rapidly occurring movements of the eyes and hands). The sampled reaches were scored off-line, by frame-by-frame analysis of the video record. For the purposes of this study, duration of movement was determined by counting the number of frames from movement onset to movement offset, as per previous work by our group [39].

2.6.1. Onset and offsets

The onset and offset of the movement phases were identified from the video record. Trial onset was defined as an overt eye movement directed toward the target, or (rarely) the first hand movement toward the target, if occurring before an eye movement toward the target. Trial offset was defined as either (1) an overt eye movement directed away from the target after target grasp or (2) grasp of the target if the eye disengages the target before it is grasped. Grasp is defined as the frame before the target is lifted from the substrate, suggesting a stable hold of the target (as per [1]).

Visual engagements and visual disengagements were inferred from gaze direction toward and away from the target, respectively. Visual fixation on the target was defined as an overt eye movement directed toward the target, with continuous visual fixation of the target as the hand transported toward the target and the target was grasped. Visual disengagement was defined as an overt eye movement away from the target or a blink accompanied with a redirection of gaze away from the target. The number of frames was recorded to determine the time spent looking at the target both before hand movement onset toward the target and after the target is grasped. Only those visual fixations on the target that were maintained prior to hand movement onset were included in analysis; however, multiple fixations prior to movement onset were rare.

2.6.2. Measures

Visual attention was coded using the following measures:

(1) *Engaging Attention*: The duration of time between an overt eye movement toward a target and first movement of the hand toward the target. Engaging attention was divided into sub-categories based on eye movement: (i) 'Appropriate' is defined as an overt eye movement away from the target within 1 s before or after it was grasped; (ii) 'Stare' is defined as looking at the target for longer than 1 s before hand movement onset; and (iii) 'Late' is defined as the eyes oriented toward the target after hand movement *if* the hand was already moving for longer than 1 s.

(2) *Disengaging Attention*: The duration of time between grasp of the target and an overt eye movement away from the target. Disengaging attention was divided into sub-categories based on eye movement: (i) 'Appropriate' is defined as the eyes overtly oriented away from the target within 1 s before or after it was grasped; (ii) 'Early' is defined as the eyes looking away from the target *if* it occurs earlier than 1 s before it was grasped; and (iii) 'Stare' is defined as looking at the target for longer than 1 s after it was grasped.

(3) *Sustaining Attention*: The eyes remained fixated on the target throughout the reach and grasp. 'Fixation' is defined as a continual visual engagement of the target from movement onset until the target has been grasped. Sustaining attention was divided into two sub-categories based on eye movement: (i) 'Appropriate' is defined as the eyes remaining on the target until it is grasped, and (ii) 'Break' is defined as the eye disengages and reengages the target before it is grasped.

Appropriate eye movements were defined as 1 s before or after hand movement onset and offset. Sacrey et al. [1] reported that visual attention in typically developing infants decreased from approximately 1 s to less than 1 s for engaging, and from over 1 s to less than 1 s for disengaging between 6 and 12 months of age. Setting the "appropriate" marker for visual attention as 1 s allows for 'sticky attention' to be captured, even in the typically developing controls. In addition, any changes to the typical age-related decrease from 'sticky attention' to 'appropriate attention' in the high-risk infant siblings will also be detected.

2.7. Procedure

Video-recordings of administration of the Autism Observation Scale for Infants (AOSI) at 6, 9, 12, and 15 months of age and the Autism Diagnostic Observation Schedule (ADOS) at 18, 24, and 36 months of age were collected and given to the blind coder (LRS). The infants were given a four-digit ID number, without reference to sibling status or diagnostic outcomes.

The children were scored for visual attention measures at each time-point in chronological order; that is, one child was scored at a time until all infants were scored, and each infant was first scored at 6 months, and then at 9 months, through to 36 months. The scores from each time-point were stored in a binder and were not referenced during the following scoring in an attempt to minimize the influence of previous scoring on subsequent time-points. After all the infants were scored at each of the seven time-points, they were identified and placed into groups based on their sibling status and diagnostic outcomes at the 36-month assessment.

2.8. Statistical analysis

The first five successful reaches (i.e. overt eye movement toward target, target is grasped, and eyes disengage the target) per infant per time-point were included in the analysis. Because there was occasion in which an infant would have less than 5 successful reach and grasp movements, the eye movements of each infant were transformed into percentages of total trials to standardize the data for each participant. For example, for measures of disengaging attention, each infant would have a percentage value for 'appropriate', 'stare', and 'early' out of a total of 100% for each time-point measured.

The Statistical Package for the Social Sciences (SPSS) v. 19 was used to run a Repeated Measures Analysis of Variance (ANOVA). Group (non-sibling control, non-ASD sibling, ASD sibling) was identified as the between subjects variable and Age (6, 9, 12, 15, 18, 24, and 36 months of age) and Attention measures were identified as the within subjects measures. Greenhouse–Geisser corrections were applied where sphericity was violated (reflected by the adjusted degrees of freedom). Sex was included as a covariate in all analyses. Bonferroni corrections were applied to all post hoc comparisons.

The data are presented graphically using the Age × Group interactions. The results of the contrast analyses determined how the data were to be presented (i.e. linear, quadratic etc. relationship between the two variables). The contrast used is noted in the caption of each figure.

3. Results

3.1. Participant characteristics

3.1.1. Age at study onset and offset

To ensure that the three groups did not differ by age at study onset and completion, age at first visit and diagnostic visit were compared. As shown in Table 1, there were no Group differences in age at initial assessment ($F(2,27) = 2.43$, $p > 0.05$) or diagnostic assessment ($F(2,27) = 0.59$, $p > 0.05$).

3.1.2. Sex

There were more males in the low-risk control group and the ASD sibling group in comparison to the non-ASD sibling group, as shown in Table 1. To ensure Sex was not influencing the results of our statistical analysis, a repeated ANOVA compared males and females on the main visual attention measures. Sex did not have an effect on the Engage ($F(1,26) = 0.58$, $p > 0.05$), Disengage ($F(1,26) = 1.67$, $p > 0.05$), or Fixation ($F(1,26) = 0.64$, $p > 0.05$) measures.

3.2. Engaging attention

The means and standard errors for the three measures of Engaging Attention, 'Appropriate,' 'Stare,' and 'Late,' are reported in Table 3.

Table 3
Mean and standard error for engaging attention for each Group at each Age.

	Appropriate	Stare	Late	Total
6 months				
Non-sib control	60 (7.3)	40 (7.3)	0 (0)	100
Non-ASD sib	55 (5.7)	45 (5.7)	0 (0)	100
ASD sib	70 (2.1)	30 (2.1)	0 (0)	100
9 months				
Non-sib control	62.5 (4.6)	35 (5.7)	2.5 (1.9)	100
Non-ASD sib	60 (7.8)	37.5 (7.5)	2.5 (1.9)	100
ASD sib	60 (10.3)	37.8 (10.5)	2.2 (1.9)	100
12 months				
Non-sib control	68.9 (7.3)	28.9 (7.9)	2.2 (1.9)	100
Non-ASD sib	58 (11.3)	30 (10.4)	12 (9.9)	100
ASD sib	68 (9.5)	28 (8.5)	4 (2.6)	100
15 months				
Non-sib control	80 (6.6)	2.2 (1.9)	17.8 (6.9)	100
Non-ASD sib	62.2 (8.1)	22.2 (7.5)	15.6 (6.5)	100
ASD sib	71.1 (5.2)	26.7 (4.2)	2.2 (1.9)	100
18 months				
Non-sib control	76.7 (6.6)	16.6 (7.6)	6.6 (2.9)	100
Non-ASD sib	62 (7.5)	14 (4.2)	24 (7.1)	100
ASD sib	76 (6.5)	24 (6.5)	0 (0)	100
24 months				
Non-sib control	84.2 (14.9)	7.3 (4.8)	8.5 (3.5)	100
Non-ASD sib	74.7 (5.8)	19.3 (6.4)	6 (3.0)	100
ASD sib	82.2 (3.5)	17.8 (3.5)	0 (0)	100
36 months				
Non-sib control	84.5 (7.0)	0 (0)	15.5 (7.0)	100
Non-ASD sib	85.5 (5.2)	12 (5.3)	2.5 (2.5)	100
ASD sib	80 (5.1)	20 (5.1)	0 (0)	100

Standard error reported in brackets.

3.2.1. 'Stare'—before hand movement

Repeated Measures ANOVA was used to assess for age-related changes and Group differences in the engagement measure of 'Stare', with Age as the within subjects factor and Group as the between subjects factor. There were no significant differences for Group ($F(2,26) = 1.27$, $p > 0.05$, $\eta^2 = 0.085$), Age ($F(4.41,114.78) = 1.36$, $p > 0.05$, $\eta^2 = 0.042$), or an Age × Group interaction ($F(4.41,114.78) = 1.64$, $p > 0.05$, $\eta^2 = 0.010$) (see Fig. 2A).

3.2.2. 'Late'—after hand movement

A Repeated Measures ANOVA was used to assess for age-related changes and Group differences in the engagement measure of 'after', with Age as the within subjects factor and Group as the between subjects factor. There was a significant difference for Age ($F(3.83,99.67) = 2.76$, $p < 0.05$, $\eta^2 = 0.080$) and Group ($F(2,26) = 4.20$, $p < 0.05$, $\eta^2 = 0.073$), but not an Age × Group interaction ($F(3.83, 99.67) = 1.63$, $p > 0.05$, $\eta^2 = 0.13$). As shown in Fig. 2B, post hoc tests revealed that the non-sibling controls and the non-ASD siblings were more likely to move their hand toward a target prior to visually engaging the target than were the ASD siblings ($ps < 0.0167$).

3.3. Disengaging attention

The means and standard errors for the three measures of Disengaging Attention, 'Appropriate', 'Early', and 'Stare,' are reported in Table 4.

3.3.1. 'Early'—before grasp

A Repeated Measures ANOVA was used to assess age-related changes and group differences for the disengagement measure of 'Early', with Age as the within subjects factor and Group as the between subjects factor. There was a significant difference for Group ($F(2,26) = 19.79$, $p < 0.001$, $\eta^2 = 0.54$), Age ($F(4.105,106.72) = 2.37$, $p < 0.05$, $\eta^2 = 0.067$) and an Age × Group interaction ($F(8.21,106.72) = 2.89$, $p < 0.001$, $\eta^2 = 0.16$). As shown in Fig. 3B, post hoc tests revealed that both the non-sibling controls and the non-ASD siblings were more likely to look away from the

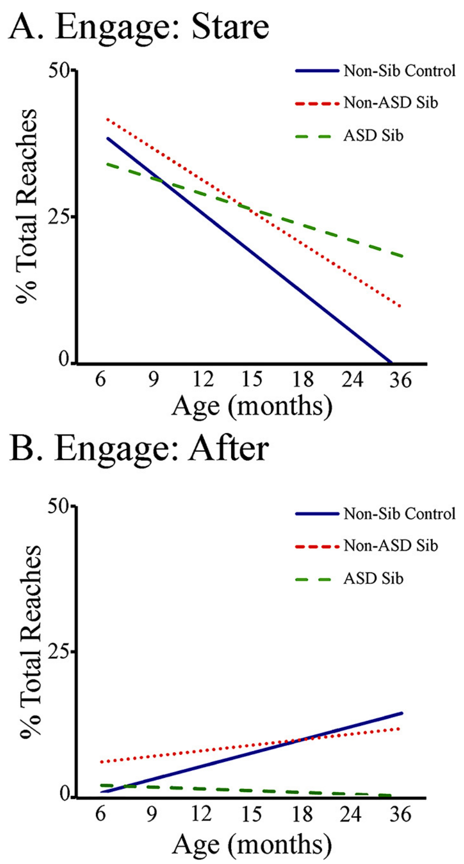

Fig. 2. Engaging attention. The percentage of total reaches associated with (A) staring at the target for a prolonged period to hand movement onset, and (B) engagement of the target following hand movement onset for each age measured. Curves presented are based on linear contrasts (Age × Group interaction for (A) $F(2,26) = 1.097$, $p = 0.022$ and (B) $F(2,26) = 6.26$, $p = 0.006$).

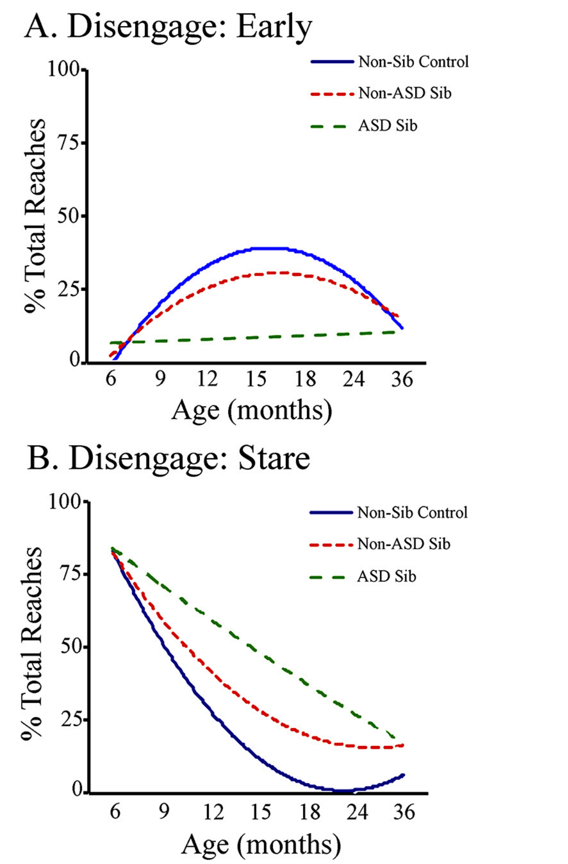

Fig. 3. Disengaging attention. The percentage of total reaches associated with (A) disengagement of the target prior to grasp, and (B) staring at the target for a prolonged period following grasp of the target for each age measured. Curves presented are based on quadratic contrasts (Age × Group interactions for (A) $F(2,26) = 8.35$, $p = 0.008$ (B) $F(2,26) = 11.84$, $p = 0.002$).

Table 4
Mean and standard error for disengaging attention for each Group at each Age.

	Appropriate	Early	Stare	Total
6 months				
Non-sib control	20 (5.9)	0 (0)	80 (5.9)	100
Non-ASD sib	20 (5.9)	5 (3.9)	75 (9.3)	100
ASD sib	15 (1.8)	0 (0)	85 (1.8)	100
9 months				
Non-sib control	27.5 (4.1)	12.5 (5.9)	60 (7.8)	100
Non-ASD sib	10 (5.9)	10 (7.8)	80 (8.9)	100
ASD sib	20 (5.9)	8.9 (6.0)	71.1 (9.48)	100
12 months				
Non-sib control	26.7 (7.3)	51.1 (8.9)	22.2 (7.5)	100
Non-ASD sib	46 (9.4)	26 (6.6)	28 (7.4)	100
ASD sib	30 (9.5)	12 (6.1)	58 (9.6)	100
15 months				
Non-sib control	66.7 (7.3)	22.2 (5.5)	11.1 (7.9)	100
Non-ASD sib	35.5 (6.5)	40 (6.7)	24.5 (9.3)	100
ASD sib	40 (6.6)	13.3 (2.9)	46.7 (6.6)	100
18 months				
Non-sib control	71 (8.1)	24 (6.7)	5 (2.5)	100
Non-ASD sib	46 (6.6)	28 (8)	26 (8.9)	100
ASD sib	50 (6.8)	14 (5.2)	36 (7.1)	100
24 months				
Non-sib control	85 (4.4)	15 (4.4)	0 (0)	100
Non-ASD sib	67.3 (7.7)	16.7 (7.6)	16 (6.5)	100
ASD sib	57.8 (8.6)	6.6 (2.9)	35.6 (9.7)	100
36 months				
Non-sib control	89 (4.0)	11 (4.0)	0 (0)	100
Non-ASD sib	65 (10.8)	19 (7.3)	16 (6.5)	100
ASD sib	80.8 (4.9)	6.6 (3.5)	12.6 (5.1)	100

Standard error reported in brackets.

target before the grasp was complete than were the ASD siblings ($ps < 0.001$).

3.3.2. 'Stare'—after grasp

A Repeated Measures ANOVA was used to assess age-related changes and group differences to the disengagement measure of 'Stare', with Age as the within subjects factor and Group as the between subjects factor. There was a significant difference for Age ($F(6,156) = 5.90$, $p < 0.001$, $\eta^2 = 0.16$) and Group ($F(2,26) = 19.14$, $p < 0.001$, $\eta^2 = 0.53$), but not an Age × Group interaction ($F(12,156) = 1.46$, $p > 0.05$, $\eta^2 = 0.081$). As shown in Fig. 3A, post hoc tests revealed that the non-sibling controls and the non-ASD siblings were more likely to look away from the target at the grasp, whereas the ASD siblings were more likely to continue staring at the target after it was grasped ($ps < 0.001$).

3.3.3. Cross-sectional analysis of disengage—'Stare'

To determine when the differences for 'staring' emerged between the ASD siblings in relation to the non-sibling controls and non-ASD siblings, data at each age were compared. A series of Univariate ANOVAs, with Group as the between subjects factor were performed at 6, 9, 12, 15, 18, 24, and 36 months of age, with Bonferroni corrected follow-up tests. There were no Group differences at either 6 ($F(2,26) = 0.48$, $p > 0.05$) or 9 months of age ($F(2,26) = 0.69$, $p > 0.05$). Group differences began to emerge at 12 months of age ($F(2,26) = 6.14$, $p < 0.01$), and continued at 15 months ($F(2,26) = 7.20$, $p < 0.01$), 18 months ($F(2,26) = 5.31$, $p < 0.01$), and 24 months of age ($F(2,26) = 8.01$, $p < 0.01$), with ASD siblings 'staring' more than non-sibling controls and non-ASD siblings at ages 12, 15,

Table 5
Mean and standard error for sustaining attention for each Group at each Age.

	Fixate	Break	Total
6 months			
Non-sib control	90 (4.2)	10 (4.2)	100
Non-ASD sib	87.5 (4.1)	12.5 (4.1)	100
ASD sib	85 (3.4)	15 (3.4)	100
9 months			
Non-sib control	97.5 (1.9)	2.5 (1.9)	100
Non-ASD sib	80 (6.6)	20 (6.6)	100
ASD sib	75.5 (5.7)	24.5 (5.7)	100
12 months			
Non-sib control	91.1 (3.1)	8.9 (3.1)	100
Non-ASD sib	92 (3.2)	8 (3.2)	100
ASD sib	86 (4.2)	14 (4.2)	100
15 months			
Non-sib control	100 (0)	0 (0)	100
Non-ASD sib	100 (0)	0 (0)	100
ASD sib	88.9 (4.3)	11.1 (4.3)	100
18 months			
Non-sib control	100 (0)	0 (0)	100
Non-ASD sib	94 (4.2)	6 (4.2)	100
ASD sib	92 (3.2)	8 (3.2)	100
24 months			
Non-sib control	100 (0)	0 (0)	100
Non-ASD sib	90 (2)	10 (2)	100
ASD sib	96.4 (3.2)	3.6 (3.2)	100
36 months			
Non-sib control	92.2 (5.1)	7.8 (5.1)	100
Non-ASD sib	98 (2)	2 (2)	100
ASD sib	100 (0)	0 (0)	100

Standard error reported in brackets.

18, and 24 months (all *ps* < 0.01). There were no Group differences at 36 months of age ($F(2,26) = 0.67$, $p > 0.05$).

3.4. Sustaining attention

The means and standard errors of the two measures of sustaining attention, 'Appropriate' and 'Break' are reported in Table 5.

3.4.1. 'Break'—in visual fixation

A Repeated Measures ANOVA was used to assess age-related changes and group differences for 'Break' in visual fixation, with Age as the within subjects factor and Group as the between subjects factor. There was a significant difference for Group ($F(2,26) = 4.61$, $p < 0.05$, $\eta^2 = 0.26$) and an Age × Group interaction ($F(7.29, 94.78) = 2.23$, $p < 0.01$, $\eta^2 = 0.13$), but no effect for Age ($F(3.65,94.78) = 1.60$, $p > 0.05$, $\eta^2 = 0.048$). As shown in Fig. 4, post hoc tests revealed that the ASD siblings were more likely to break visual fixation by disengaging from the target and then re-engaging the target prior to grasp than were the non-sibling controls ($p < 0.01$). Post hoc corrections on the Age × Group interaction did not result in significant effects.

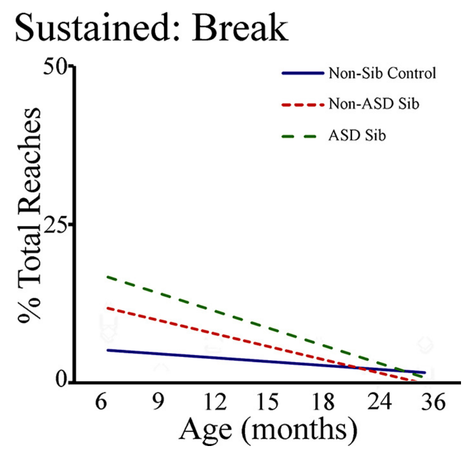

Fig. 4. Sustaining attention. The percentage of visual fixations associated with a break in fixation, associated with a disengagement and reengagement of the target prior to grasp for each age measured. Curves presented are based on order 4 contrasts ($F(2,26) = 3.59$, $p = 0.04$).

4. Discussion

This study provides the first description of the developmental trajectories of visual attention in infants at low-risk and high-risk for ASD using a naturalistic play task. The procedure of filming infants engaging in play behavior and examining the behavior frame-by-frame allowed for the capture of natural behavior as it unfolded as an act over time and avoided placing infants in a structured experiment. The large data sample was thus derived from an ethologically relevant play task [53] and was not experimentally driven using laboratory equipment [54]. Critically, all infants displayed "sticky attention" with the target at 6 and 9 months of age, in that they continued to stare at the target for at least 1 s following grasp. However, by 12 months of age, the groups began to diverge. Infants who were diagnosed with ASD at 36 months of age continued to stare at the target following grasp, whereas the non-sibling controls and non-ASD siblings began to disengage from the target as it was grasped. Group differences between ASD siblings and the other two groups were maintained at 15, 18, and 24 months, but no longer differed at 36 months of age. Thus, our study suggests that the development of visual attention is impaired in high-risk infants who later receive a diagnosis of ASD and that their impairments distinguish them from non-ASD siblings and non-sibling controls by 12 months of age.

Infants with ASD showed an impairment in engagement of visual attention, in that they were less likely to engage a target following hand movement onset than non-ASD siblings and non-sibling controls. Although this group difference was significant, such eye movements accounted for a small minority of all visual engagements for all groups at all the ages examined. The large majority of eye movements toward the target were appropriate. Although tangential, this finding does accord with the results of the gap-overlap task, in which high-risk infants do not show an impairment orienting toward a peripheral target if the central target is removed [34,45,46].

Disengaging attention from a target was also impaired in children who received a diagnosis of ASD. Impairments in disengagement of attention distinguished infants later diagnosed with ASD from non-ASD siblings and non-sibling controls by 12 months of age and continued to distinguish the ASD siblings from the other two groups at 15, 18, and 24 months of age. Impairments in disengaging visual attention have been previously reported in the literature [38,39,46; for related findings, also see 40,41,55]. For example, using the gap-overlap task, which measures the latency to orient toward a peripheral target from a central fixation point, Elsabbagh et al. [34] found that high-risk infants who received an ASD diagnosis at 36 months could be distinguished from high-risk non-ASD siblings and non-sibling controls by 14 months of age based on prolonged disengagement latencies.

Non-sibling controls and non-ASD siblings were more likely to disengage from the target prior to grasp than were the ASD siblings. In the present study, grasp was defined as 'one frame before lift of the target from the substrate', suggesting a secure grip on the target. This definition does not account for the duration of time the hand was in contact with the target prior to grasp. It has been previously reported that tactile contact with a target, using either the digits or palm, provides sufficient somatosensory feedback to finalize the grasp and lift of the target [56,57] and that mature sensory control of reaching behavior involves a shift from visual attention to somatosensory attention at tactile contact with the target [2]. Evidence that the non-sibling controls and non-ASD siblings were disengaging their visual attention at tactile contact and reorienting to somatosensory attention to finalize the grasp suggests that they are maximizing their attentional strategy when manipulating objects. Previous studies examining reaching and grasping in Huntington's disease [59] and Parkinson's disease [74,75] also demonstrate deficient visual attention (as described as staring at the target after grasp), which is compensated for by a reliance on proprioceptive feedback. If so, our disengagement findings suggests that the development of visual control of arm and hand movements is delayed in infants who later receive a diagnosis of ASD [40,58], and the reliance on proprioceptive feedback may be an adaptive response.

Another interesting finding in the present study was that children with ASD were more likely than non-sibling controls and non-ASD siblings to break visual fixation by disengaging and re-engaging the target prior to grasping. Disengaging and re-engaging a target prior to grasping has been reported for people with Huntington's disease. Klein et al. [59] had participants with Huntington's disease and age-matched controls reach toward small food targets that were grasped and placed in the mouth for eating. Twenty-five percent of participants with Huntington's disease, but none of the controls, disengaged and reengaged the food target prior to contact. Evidence of a disengage-reengage abnormality in high-risk infants later diagnosed with ASD suggests that similar circuitry underlying abnormal eye movements in Huntington's disease may also be affected by ASD [60]. Indeed, Huntington's disease and ASD participants perform similarly on an anti-saccade task [61,62].

Previous literature has indicated an association between visual attention and cognitive outcomes. Keehn et al. [35] report that impairments in visual attention are associated with poorer social and communication outcomes (as indexed by the ADOS). Work from our group has shown an association between deficient disengagement and later social-communication impairment (i.e., in using information from the environment to regulate arousal and affect [29,39], and emotional distress (i.e., less active, more irritable, and difficult to soothe [46]). Disengaging attention serves to free the visual system and allow it to reorient toward a salient target in the visual scene [2]. Thus, impairments in disengaging attention may prevent children with ASD from maximizing their use of visual attention to explore their environment or make eye contact with peers to share their attention [69].

It is interesting that infants diagnosed with ASD differed from non-diagnosed siblings and non-sibling control children from 12 months onward, until 36 months of age when the groups no longer differed. Infants in this study were required to orient toward a toy target, reach out to grasp the toy target, and disengage from the target as it was being manipulated. There are two possible reasons to explain the lack of group differences at 36 months of age. First, although not reported, manipulations at the earliest ages consisted of mouthing behavior, banging the toys, or showing the toy to the experimenter or parent. At the older ages, the manipulations often consisted of using the toys more functionally, i.e. placing candles in the cake, using the fork to pick up cake, etc. It is interesting that disengagements after 12 months of age for the non-sibling controls and non-ASD siblings were associated with a reorientation toward the next target for manipulation. For example, after grasping a block, the eyes disengaged the target and reoriented toward a second block, which was then used to build a tower. Rather than disengaging the target object and reorienting toward a secondary object for manipulation at the grasp, the ASD siblings continued to 'stare' at the object that was grasped and showed a delay in object manipulation. This finding supports the hypothesis that ASD is associated with impairments in global processing [63–65]. It may be that ASD siblings have trouble extracting the appropriate information from grasped objects, and thus 'stare' at the target for a longer duration in order to extract the relevant tactile information for processing [66]. Such impairments in global processing have been supported by behavioral evidence [67], as well as recent neuroimaging studies of visual attention [45,68]. Second, the percentage of time spent staring at the toys continually decreased in the second year of life, and by 36 months of age, repeated exposure to the toys may have allowed the infants with ASD to extract the relevant intrinsic features, and thus allowed for more age-appropriate interactions with the objects.

Our findings provide support for the hypothesis that impairments in visual attention may contribute to the abnormal social and communication development in ASD [39,46,70]. Indeed, early markers for ASD, including joint attention, spontaneous gaze to faces, orienting to name, and making eye contact, all involve orienting visual attention to biologically relevant information in the environment [29,39,71,72]. Our findings also extend previous research on visual attention in ASD using the gap-overlap task [34,39,46] by showing that the disengage impairment can be demonstrated in, and most likely interferes with, naturally occurring behaviors, such as toy play. It has been suggested that abnormal oculomotor functioning may be a familial risk marker for ASD [73]. In this respect, it is noteworthy that alterations in visual attention and oculomotor control have also been documented in adults with the neurological conditions of Parkinson's disease [74] and Huntington's disease [59]. Evidence that an impairment in disengaging attention (1) is apparent at 12 months of age [present study, 46], (2) can distinguish between high-risk siblings who will and will not go on to receive an ASD diagnosis [present study, 34,46], and (3) can distinguish between ASD and Down's syndrome [39] suggests that visual attention can be used as a marker for the early identification of children at risk for ASD.

Competing interests

The authors have no competing interests to declare.

Authors' contributions

LRS made substantial contributions to conception and design, collected and analyzed the data and prepared the first draft of the paper, and approved the final draft.

SEB contributed to the conception of the project, provided a critical review of the manuscript, and approved the final draft.

LZ contributed to the conception of the project, provided a critical review of the manuscript, and approved the final draft.

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