American Psychological Association

Emotion

1528-3542/20/$12.00

2020, Vol. 20, No. 6, 980–992
http://dx.doi.org/10.1037/emo0000628

Attentional Bias to Fearful Faces in Infants at High Risk for Autism Spectrum Disorder

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Individuals with autism spectrum disorder (ASD) and their first-degree relatives show differences from neurotypical individuals in emotional face processing. Prospective studies of infant siblings of children with ASD, a group at high risk for autism (HRA), allow researchers to examine the early emergence of these differences. This study used eye tracking to examine disengagement of attention from emotional faces (fearful, happy, neutral) at 6, 9, and 12 months in low-risk control infants (LRC) and HRA infants who received a subsequent clinical judgment of ASD (HRA+) or non-ASD (HRA−). Infants saw centrally presented faces followed by a peripheral distractor (with face remaining present). For each emotion, latency to shift to the distractor and percentage of trials with no shift were calculated. Results showed increased saccadic latency and a greater percentage of no-shift trials for fearful faces. No between-group differences were present for emotion; however, there was an interaction between age and group for disengagement latency, with HRA+ infants slower to shift at 12 months compared with the other 2 groups. Exploratory correlational analyses looking at shift biases to fearful faces alongside measures of social behavior at 12 and 18 months (from the Communication and Symbolic Behavior Scales) revealed that for HRA+ infants, 9- and 12-month fear biases were significantly related to 12- and 18-month social abilities, respectively. This work suggests that both low- and high-risk infants show biases to threat-relevant faces, and that for HRA+, differences in attention shifting emerge with age, and a stronger fear bias could potentially relate to less social difficulty.

Keywords: attention disengagement, emotion processing, infancy, autism spectrum disorder, eye tracking

The ability to interpret the emotional expressions of others is a key aspect of successful development, as facial affect may convey internal feelings that otherwise might not be accessible. Adeptly reading another's emotional expression can have a variety of positive consequences. For example, from an evolutionarily perspective, recognizing threat-relevant affect could provide important cues for avoiding danger.

From birth, infants show preferential attention to facelike stimuli (e.g., Johnson, Dziurawiec, Ellis, & Morton, 1991; Valenza, Simion, Cassia, & Umiltà, 1996), and over the first few months of life, infants show an increasing interest in core features of the face such as eyes and mouth (e.g., Hunnius & Geuze, 2004; Maurer & Salapatek, 1976), areas that are consistently used to glean information about identity and emotional expression in studies with older children and adults (e.g., Ewing, Karmiloff-Smith, Farran, & Smith, 2017; Gosselin & Schyns, 2001; Guarnera, Hichy, Cascio, & Carrubba, 2015; Schurgin et al., 2014).

Over the first year of life, infants show rapid growth in processing facial expressions of emotion. Seminal studies showed that between 3 and 6 months, infants are able to discriminate positive and negative facial expressions (e.g., Barrera & Maurer, 1981; LaBarbera, Izard, Vietze, & Parisi, 1976; for a review, see de Haan and Nelson, 1998). More recently, work by Farroni and colleagues (Farroni, Menon, Rigato, & Johnson, 2007) showed that the ability to discriminate between emotional expressions is evident within a few days of birth, with newborns showing increased attention to happy faces as compared with fearful faces, illustrating a prefer-

This article was published Online First July 29, 2019.

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This research was made possible, in part, by grants from the Autism Speaks Pilot Grants Program, the Simons Foundation (Grant 137186), and the National Institute on Deafness and Other Communication Disorders (Grants R21 DC 08637 and R01 DC 10290 to Charles A. Nelson and Helen Tager-Flusberg), as well as the National Institute of Mental Health-funded Stuart T. Hauser Research Training Program in Biological and Social Psychiatry (to Jennifer B. Wagner).

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ence for positive affect in early infancy. By 5 to 8 months, studies have shown that infants have increased preferences and attentional biases for threat-relevant faces (e.g., Kotsoni, de Haan, & Johnson, 2001; LoBue & DeLoache, 2010; Nelson & Dolgin, 1985; Peltola, Leppänen, Mäki, & Hietanen, 2009; Peltola, Leppänen, Palokangas, & Hietanen, 2008; for reviews, see Leppänen and Nelson, 2009, 2012). For example, Peltola, Leppänen, Vogel-Farley, Hietanen, and Nelson (2009) used an adapted version of the gap/overlap paradigm used by Aslin and Salapatek (1975) to examine attention disengagement from emotional faces. Infants were presented with emotional faces (i.e., fearful, happy, neutral), followed by a distractor to the left or right of the screen while the face remained present (i.e., "overlap" trials). Peltola, Leppänen, Vogel-Farley, et al. (2009) showed that when infants were looking at a fearful face, they took more time to disengage and shift from the face to the distractor as compared with when looking at happy or neutral faces. This threat-relevant bias reflects successful attunement to signals of danger, which could have important consequences for survival (Leppänen and Nelson, 2012).

Children and adults with autism spectrum disorder (ASD) differ from neurotypical individuals in their visual attention to emotionally salient faces, and in many studies, these individuals have shown impairments in their recognition, discrimination, and processing of these stimuli (e.g., Bal et al., 2010; Clark, Winkielman, & McIntosh, 2008; Corden, Chilvers, & Skuse, 2008; de Wit, Falck-Ytter, & von Hofsten, 2008; Frank, Schulze, Hellweg, Koehne, & Roepke, 2018; Krebs et al., 2011; Pelphrey et al., 2002; see also Black et al., 2017). This includes differences in attention to core features during face scanning (e.g., Pelphrey et al., 2002), and poorer accuracy in differentiating between emotions (e.g., Clark et al., 2008; Frank et al., 2018). Some studies have found that negative emotions, in general, and threat-relevant emotions (i.e., angry and fearful), specifically, present greater difficulty for individuals with ASD (e.g., Farran, Branson, & King, 2011). For example, work by Ashwin, Chapman, Colle, and Baron-Cohen (2006) tested recognition of emotions from photographs and found that the basic negative emotions presented the biggest challenge to individuals with ASD relative to neurotypical controls, and this was most pronounced for fearful faces. Corden et al. (2008) tested emotion recognition across two study sessions and found impairments at recognizing fearful faces across both phases of testing (see also Pelphrey et al., 2002), while work by Bal et al. (2010) found impaired recognition for angry faces.

Difficulties processing emotional faces also extend to family members of individuals with ASD, particularly first-degree relatives (e.g., Baron-Cohen & Hammer, 1997; Dorris, Espie, Knott, & Salt, 2004; Oerlemans et al., 2014; for reviews, see Cruz, Camargos-Júnior, & Rocha, 2013 and Pisula & Ziegart-Sadowska, 2015), and emotion recognition impairments are thought to reflect a broader endophenotype, or set of traits, relating to ASD (Oerlemans et al., 2014). To gain a better understanding of difficulties seen in individuals with ASD and their first-degree relatives, researchers have undertaken a prospective approach by studying infant siblings of children with ASD, a group with a 1 in 5 incidence of developing ASD (e.g., Elsabbagh & Johnson, 2010; Ozonoff et al., 2011), as compared with 1 in 59 in the general population (Baio et al., 2018). This population is an important group to study in order to identify early markers of ASD as well as other developmental difficulties that are found in unaffected siblings (e.g., Messinger et al., 2013; Ozonoff et al., 2014; Zwaigenbaum et al., 2005; for recent reviews, see Jones, Gliga, Bedford, Charman, & Johnson, 2014, and Szatmari et al., 2016). Because difficulties reading the emotions of others can play an important role in the social impairments found in ASD, research aimed at understanding when and how emotional processing difficulties develop could have important implications for supporting individuals who might struggle in this key area.

To date, many studies with infant siblings of children with ASD have focused on early attention to faces, in general (e.g., Chawarska, Macari, & Shic, 2013; Jones & Klin, 2013; Merin, Young, Ozonoff, & Rogers, 2007; Wagner, Luyster, Moustapha, Tager-Flusberg, & Nelson, 2018), but few of these studies examined emotional face processing. One study by Cornew and colleagues (Cornew, Dobkins, Akshoomoff, McCleery, & Carver, 2012) examined 18-month-old high-risk infants in a social referencing paradigm. Parents were taught to model facial expressions and vocalizations corresponding to happy, disgusted, and calm responses when their child approached a novel toy. Findings showed that high-risk infants who later developed ASD showed difficulty utilizing information from their parent's emotional cues, taking significantly longer to look toward the parent following their prompt as compared with both low-risk infants and high-risk infants without a subsequent ASD diagnosis. However, this pattern was unrelated to emotional content. In a study with younger infants, Wagner, Luyster, Tager-Flusberg, and Nelson (2016) presented happy, fearful, and neutral faces to 9-month-old infants with and without an older sibling with ASD, none of whom received a subsequent diagnosis of ASD. No group differences were found in overall attention to the three emotional faces, though the high-risk infants did show larger pupil size while viewing the emotional faces overall, indicative of elevated sympathetic arousal. To date, no other published studies of high-risk infants have focused on visual attention to faces varying in emotional expression.

The present study employed the infant attention disengagement paradigm designed by Peltola and colleagues (Peltola et al., 2008; Peltola, Leppänen, Vogel-Farley, et al., 2009) to study emotion processing in high-risk infants using a paradigm that examined emotion-modulated differences in attention during infancy. Past work using this method has identified threat-relevant biases to fearful faces during the first year of life, and with older individuals with ASD showing difficulties in emotion recognition, most pronounced with threat-relevant faces, this paradigm is ideal for examining early emotion processing in infants at family risk for ASD. Infants at high and low risk for ASD were presented with fearful, happy, and neutral faces, and a peripheral distractor in order to examine the ease of attention disengagement as a function of emotion. Based on past work (e.g., Peltola et al. (2008; Peltola, Leppänen, Vogel-Farley, et al., 2009), if processing of threat-relevant faces is enhanced in infant attention, they should show slower and less frequent attention shifting from fearful faces as compared with happy and neutral faces (non-threat-relevant). Further, because the development of an attentional bias to threat-relevant expressions is seen as a normative change during typical infant development (Leppänen & Nelson, 2012), and because successful emotional face recognition is key for social functioning, we sought to examine whether these early emotional biases might be related to later social-communicative development. Given that prior research with older ASD individuals suggests differential attention and impaired recognition of threat-relevant faces, we hypothesized that high-risk infants would show little or no differentiation between attention shifting for threat-relevant faces (i.e., fearful) versus non-threat-relevant faces (i.e., happy, neutral) as compared with low-risk infants, and this would be most pronounced for infants with a later ASD diagnosis. Further, if biased attention to threat-relevant faces is a sign of successful emotion processing, we also hypothesize that across all groups, biases in attention shifting to fearful faces could be predictive of later social functioning.

Method

Participants

The initial sample consisted of 161 infants who were tested on the attention disengagement task at one or more visits at 6, 9, and 12 months: a group of low-risk control infants (LRC) with a typically developing older sibling and no family history of ASD ($n = 70$) and a group of infants at high risk for ASD (HRA) with an older sibling with ASD ($n = 91$). Diagnosis of ASD in the HRA proband (and confirmation that the LRC proband did not have ASD) was corroborated via parent report using an age-appropriate screener prior to enrollment: for probands over 4 years old, the Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003) was used; for probands under 4 years old, the Pervasive Developmental Disorders Screening Test-II (Siegel, 2004) was used.

After this initial screening, participants were enrolled in a longitudinal infant sibling project and asked to participate regularly until 36 months of age in various tasks, with data collected using parent report, behavioral, eye tracking, electrophysiological, functional near-infrared spectroscopy, and genetic measures (please see prior work for further discussion, e.g., Keehn, Wagner, Tager-Flusberg, & Nelson, 2013; Luyster, Powell, Tager-Flusberg, & Nelson, 2014; Nelson, Varcin, Coman, DeVivo, & Tager-Flusberg, 2015; Talbott, Nelson, & Tager-Flusberg, 2015; Wagner et al., 2016). To be considered in the final sample for the present study, infants needed sufficient eye-tracking data (three valid trials with a shift for each emotion, see the Data Processing and Analysis subsection for more information) for at least one age point tested. With this criterion in place, an additional set of infants was excluded from the LRC and HRA samples: 17 out of 70 total LRC: 24% exclusion; 18 out of 91 total HRA: 20% exclusion. This data loss rate is comparable to prior infant eye-tracking studies in this age range (e.g., 32% in Chawarska et al., 2013; 16% in Elsabbagh et al., 2009; 40% in Peltola, Leppänen, Mäki, et al., 2009).

Lastly, to be included in subsequent analyses, HRA infants were required to be followed longitudinally in order to determine ASD outcome. As a result, an additional 12 HRA infants were excluded for not completing a visit at 24 or 36 months. An additional three LRC were excluded for receiving a positive clinical judgment for ASD or a non-ASD-related disorder (e.g., language impairment, anxiety). Given current research that has found both similarities and differences between individuals affected with ASD who come from multiple-incidence versus single-incidence families (e.g., Dissanayake, Searles, Barbaro, Sadka, & Lawson, 2019), a conservative approach was taken to exclude LRC with a positive ASD diagnosis in order to ensure that outcome groups were as homogenous as possible with respect to potential ASD etiology.

Of the remaining 111 infants who made up the final sample (50 LRC and 61 HRA), HRA infants were divided into positive (HRA+) and negative (HRA−) ASD outcome, with all infants in the HRA+ group receiving a final clinical judgment of ASD by a licensed clinical psychologist on staff with expertise in the area of autism and neurodevelopmental disorders after review of all information, including videos and scores from the Autism Diagnostic Observation Schedule (Lord et al., 2000) from all available lab visits. Following these criteria, the final groups consisted of 50 LRC (20 female), 39 HRA− (16 female), and 22 HRA+ (7 female) who had valid data at one or more time points, with just over half of infants (59 of 111) with data from only one time point (Table 1 displays more details on longitudinal data available for each group). Broken down further into 6-, 9-, and 12-month data, the sample included 56 total 6-month-old data points (31 LRC, 15 HRA−, 10 HRA+), 62 total 9-month-old data points (24 LRC, 25 HRA−, 13 HRA+), and 62 total 12-month-old data points (27 LRC, 19 HRA−, 16 HRA+). The current sample size was justified based on past work by Peltola and colleagues (Peltola, Hietanen, Forssman, & Leppänen, 2013; Peltola, Leppänen, Maki, et al., 2009) identifying significant effects using a similar paradigm in similar age groups. Demographic characteristics of the final groups, including ethnicity, race, paternal and maternal educational levels, and household income, can be found in Table 2. Project approval was obtained from the Institutional Review Boards of Boston Children's Hospital and Boston University and informed consent was obtained from the parent(s) of each infant participant.

Stimuli

The paradigm and stimuli were adapted from Peltola, Leppänen, Vogel-Farley, et al. (2009). Infants were presented with color images of one female face expressing three different emotions: fearful (open mouth), happy (open mouth), and neutral (closed mouth). Face stimuli were taken from four female faces in the NimStim library (Tottenham et al., 2009). Faces subtended a visual angle of roughly 15.4° vertically and 10.8° horizontally and the distractor in the periphery measured 15.4° of visual angle vertically and 4.3° of visual angle horizontally (for sample stimuli, see Peltola, Leppänen, Vogel-Farley, et al., 2009). All stimuli were used in overlap trials, where the centrally presented female face expressing one of the three emo-

Table 1
Number of Participants Contributing One, Two, or Three Time Points

Number of time points	LRC	HRA−	HRA+
Three time points	9	5	3
Two time points	14 (5, 4, 5)	10 (4, 2, 4)	11 (3, 1, 7)
One time point	27 (13, 5, 9)	24 (4, 12, 8)	8 (3, 0, 5)

Note. For two time points, numbers in parentheses reflect participant that contributed combinations of 6 and 9, 6 and 12, and 9 and 12; for one time point, numbers in parentheses reflect participants contributing only 6-, only 9-, or only 12-month data.

Table 2
Demographic Characteristics

Demographic category	LRC, % (*n*)	HRA−, % (*n*)	HRA+, % (*n*)
Infant ethnicity			
Hispanic	2.0 (1)	5.1 (2)	22.7 (5)
Non-Hispanic	96.0 (48)	94.9 (37)	77.3 (17)
(Not reported)	2.0 (1)		
Infant race			
White	84.0 (42)	94.9 (37)	77.3 (17)
Asian	2.0 (1)		4.5 (1)
Black or African American	4.0 (2)	2.6 (1)	
More than one race	8.0 (4)	2.6 (1)	18.2 (4)
Unknown	2.0 (1)		
Highest completed education: Father			
Before high school			13.6 (3)
High school degree	6.0 (3)	7.7 (3)	9.1 (2)
2-year college degree		2.6 (1)	
4-year college degree	32.0 (16)	41.0 (16)	36.4 (8)
Master's degree	26.0 (13)	23.1 (9)	18.2 (4)
Doctoral or professional degree	20.0 (10)	15.4 (6)	9.1 (2)
(Not reported)	16.0 (8)	10.3 (4)	13.6 (3)
Highest completed education: Mother			
Before high school			
High school degree	2.0 (1)	18.0 (7)	9.1 (2)
2-year college degree	2.0 (1)	7.7 (3)	9.1 (2)
4-year college degree	26.0 (13)	10.3 (4)	45.4 (10)
Master's degree	40.0 (20)	38.5 (15)	18.2 (4)
Doctoral or professional degree	16.0 (8)	15.4 (6)	4.5 (1)
(Not reported)	14.0 (7)	10.3 (4)	13.6 (3)
Household income			
Less than $15,000	4.0 (2)		
$15,000–$35,000			
$35,000–$55,000	2.0 (1)	5.1 (2)	
$55,000–$75,000	6.0 (3)	10.3 (4)	4.5 (1)
More than $75,000	74.0 (37)	74.4 (29)	77.3 (17)
(Not reported)	14.0 (7)	10.3 (4)	18.2 (4)

Note. All percentages rounded to the nearest tenth of a percent and therefore the sum of group percentages within a given category does not always total exactly 100%. LRC = low-risk controls; HRA− = high-risk autism with no autism spectrum disorder (ASD) diagnosis; HRA+ = high-risk autism with ASD diagnosis.

tions was presented for 1,000 ms (e.g., Peltola et al., 2008). Next, with the face remaining on the screen, a black-and-white flickering distractor pattern was shown in the periphery on the right or left side of the face. This peripheral distractor pattern was designed by Peltola, Leppänen, Vogel-Farley, et al. (2009) to attract attention from the central stimulus and the black and white areas alternated their colors at 10 Hz for the first 1,000 ms of the distractor presentation and then remained static for the remaining 2,000 ms (distractor remained on the screen for 3,000 ms in total).

Apparatus

Infants were seated on a caregiver's lap and presented with face images on a 17-in. TFT Tobii T60 monitor using Clearview software (Tobii Technology AB; www.tobii.com). The Tobii monitor recorded gaze for both eyes at 60 Hz based on the reflection of near-infrared light from the cornea and pupil. The monitor specifications include accuracy of 0.5° of the visual angle, and a tolerance of head movements within the range of 44 × 22 × 30 cm.

Procedure

Infants were brought into a dimly lit testing room and seated on their caregiver's lap approximately 60 cm from the Tobii T60 monitor. A calibration procedure was used to confirm that the infant and monitor positions allowed for satisfactory gaze tracking. During calibration, a blue-and-white checkered sphere appeared in the four corners of the monitor and the center of the screen. Following the five-location calibration procedure, the Clearview program reported whether the eye tracker successfully tracked eye gaze in these five locations. If successful, the testing session began. If unsuccessful, infant position and monitor position were adjusted and calibration was repeated until successful calibration was achieved.

During testing, infants saw only overlap trials, with the face remaining present during the appearance of the distractor. The three emotions were presented in a semirandomized order with the same expression appearing no more than two times in a row. The distractor in the periphery was also semirandomized, not appearing more than three times in a row on the same side. Between each trial, a static color image of an underwater scene was presented, and trials were initiated by the experimenter when the infant's attention was directed toward this image. Trials were presented until the infant became too fussy or until a total of 75 trials had been reached (25 of each emotion).

Social Communication Measure at 12 and 18 Months

At 12 and 18 months parents completed the Communication and Symbolic Behavior Scales Developmental Profile (CSBS-DP, Wetherby, Allen, Cleary, Kublin, & Goldstein, 2002). The CSBS-DP is a norm-referenced measure used to capture the early social-communicative competence of young children. The questionnaire includes 45 items covering seven domains of social communication and symbolic development: emotion and eye gaze, communication, gestures, sounds, words, understanding, and object use. Scoring of the CSBS-DP yields three composite scores: Social (comprised of the Emotion and Eye Gaze, Communication, and Gestures clusters), Speech (comprised of the Sounds and Words clusters) and Symbolic (comprised of the Understanding and Object Use clusters). A total score, which captures performance across the three composites, is also obtained. Each raw score is assigned a standard score and percentile rank according to previously established norms (Wetherby et al., 2002).

Cognitive Assessment at 12 and 18 Months

The Mullen Scales of Early Learning (MSEL; Mullen, 1995) was administered by an experimenter during the lab visits at 12 and 18 months. The MSEL evaluates cognitive functioning for children from birth to 68 months of age. Standardized domain scores (*T* scores: $M = 50$, $SD = 10$) are calculated for five subtests (Gross Motor, Fine Motor, Visual Reception, Receptive Language, and Expressive Language), and these domain scores (excluding the Gross Motor subtest) are used to generate one overall composite score, termed the Early Learning Composite (ELC; $M = 100$, $SD = 15$).

Data Processing and Analysis

Eye tracking. Gaze data was collected for overlap trials from the onset of the face until the start of the interstimulus interval. Data were exported and analyzed in Matlab (MathWorks, Natick, MA) using a series of criteria to identify valid trials for subsequent analysis. First, for both shift (i.e., trials with a saccade to the distractor) and no-shift (i.e., trials with no distractor-related saccade) trials, infants were required to be looking at the face at least 50% of the time during the 400 ms prior to the onset of the peripheral distractor. Second, for shift trials, a saccade had to be made toward the distractor after distractor onset but before 1,500 ms had elapsed (anticipatory saccades [<100 ms] were removed), and additionally, no more than 25% of gaze data could be missing between distractor onset and saccadic eye movement. No-shift trials required that no saccade was made within 1,500 ms after distractor onset and no more than 25% of the gaze data was missing for the duration of the trial. A cutoff of 1,500 ms, or 50% of the elapsed time with the face and distractor present, was used as a conservative cutpoint between shift and no-shift trials to ensure that long fixations did not unduly influence the averages calculated for shift latency (as might have happened in some past studies using a similar paradigm and weighting all shift trials equally, e.g., Peltola, Leppänen, Vogel-Farley, et al., 2009). Related work by Elsabbagh et al. (2013) utilized a similar cutoff (i.e., failure to disengage after 1,200 ms of a 2,500 ms time window) to categorize no-shift trials. To be included in the present analyses, infants were required to have at least three valid shift trials for each emotional expression for at least one time point (6, 9, or 12 months). Based on past work (Peltola et al., 2008, Peltola, Leppänen, Vogel-Farley, et al., 2009), the present study examined two variables of interest: (a) latency to disengage attention from the central stimulus, and (b) percentage of trials where no shift of attention occurred out of total valid trials. For trials with a saccade latency under 1,500 ms, latencies were averaged for each emotional expression for each child at each age. On average, infants contributed 16.84 valid trials ($SD = 4.67$), with 5.73 valid trials for fearful faces ($SD = 1.91$), 5.56 for happy faces ($SD = 1.83$), and 5.56 for neutral faces ($SD = 1.91$). The number of valid trials did not significantly differ across the three groups, $F(2, 179) = 2.191$, $p = .12$, with LRC averaging 16.06 valid trails ($SD = 3.88$), HRA− averaging 17.61 valid trials ($SD = 5.65$), and HRA+ averaging 17.33 valid trials ($SD = 4.40$).

CSBS-DP at 12 and 18 months. The present analyses examined social and communicative development at 12 and 18 months using the CSBS-DP percentile ranks for the Social Composite score (Table 3 displays group means). CSBS-DP scores were unavailable for a subset of children due to failure of parents to return the completed questionnaire (12 months: 6 LRC, 7 HRA−, 4 HRA+; 18 months: 8 LRC, 8 HRA−, 8 HRA+). Additionally, four LRC discontinued before their 12-month visit and therefore did not have CSBS data at 12 or 18 months, and another four LRC discontinued before their 18-month visit and therefore did not have CSBS data at 18 months.

MSEL at 12 and 18 months. The present analyses examined cognitive ability with the MSEL ELC score at 12 and 18 months (see Table 3 for group means). MSEL ELC scores were unavailable for two LRC and two HRA− at 12 months and for one LRC, one HRA−, and three HRA+ at 18 months as a result of no lab visit at that time point. One additional HRA− infant did not complete the MSEL at 18 months due to fatigue at the end of the 18-month lab visit. Two additional LRC infants discontinued in the study before turning 12 months and therefore did not have 12- or 18-month MSEL data, and another seven LRC discontinued before turning 18 months and did not have 18-month MSEL data.

Results

Eye Tracking

Linear mixed modeling using maximum likelihood estimation in SPSS (Version 23) was used to examine the data longitudinally. This method was used to examine (a) shift latency, and (b) percentage of no-shift trials, and in both cases, the model included the within-subjects variables of emotion (fearful, happy, neutral) and age (6 months, 9 months, 12 months) and the between-subjects variable of group (LRC, HRA−, HRA+), and all two-way and three-way interactions were included as fixed factors and intercept as a random effect and fitted with an unstructured covariance matrix. Cohen's f^2 was used as a measure of effect size (Selya, Rose, Dierker, Hedeker, & Mermelstein, 2012).

Table 3
CSBS and MSEL Means (SDs) for LRC, HRA−, and HRA +

Measure	LRC	HRA−	HRA+	Group differences*
CSBS-DP (12 months)	n = 40	n = 32	n = 18	
Social percentile	56.15 (26.86)	42.59 (32.32)	32.06 (28.02)	LRC > (HRA− = HRA+)
Range	2–98	2–99	1–84	
CSBS-DP (18 months)	n = 34	n = 31	n = 14	
Social percentile	66.79 (24.16)	51.51 (27.79)	49.71 (34.82)	LRC > HRA−
Range	16–99	2–99	2–98	
MSEL (12 months)	n = 46	n = 37	n = 22	
ELC	106.28 (12.22)	102.59 (15.54)	98.00 (15.90)	LRC > HRA+
Range	77–134	70–138	72–131	
MSEL (18 months)	n = 40	n = 37	n = 19	
ELC	107.28 (14.83)	99.30 (16.76)	91.58 (19.39)	LRC > (HRA− = HRA+)
Range	76–133	72–131	63–132	

Note. Communication and Symbolic Behavior Scales—Developmental Profile (CSBS-DP) at 12 months missing for 10 low-risk controls (LRC), seven high-risk autism with no autism spectrum disorder (ASD) diagnosis (HRA−), and four high-risk autism with ASD diagnosis (HRA+). CSBS-DP at 18 months missing for 16 LRC, eight HRA−, and eight HRA+; Mullen Scales of Early Learning (MSEL) at 12 months missing for four LRC and two HRA−; MSEL at 18 months missing for 10 LRC, two HRA−, and three HRA+ (see the Method section for more detail). ELC = Early Learning Composite score.
* $p < .05$.

Latency to shift attention. For latency to shift attention, a main effect of emotional expression was found, $F(2, 420.8) = 3.035$, $p = .049$, $f^2 = .05$ (Figure 1A), with infants showing the slowest latency to disengage from fearful faces (M = 483 ms, SD = 145) as compared with both happy faces (M = 457 ms, SD = 131; $t(179) = 2.864$, $p = .005$, $d = .19$) and neutral faces (M = 463 ms, SD = 152; $t(179) = 2.134$, $p = .034$, $d = .14$). No difference in latency to shift was found between happy and neutral faces ($p = .53$). There was also a significant interaction between group and age, $F(4, 519.7) = 6.573$, $p < .001$ (Figure 2A) Follow-up tests showed that at 12 months, HRA+ (M = 523 ms, SD = 160) took longer to disengage their attention than HRA− infants (M = 433 ms, SD = 91; $t(33) = 2.079$, $p = .045$, $d = .73$); for LRC (M = 445 ms, SD = 142), while the shift difference with HRA+ was in the same direction, it was not significant, $t(41) = 1.646$, $p = .11$, $d = .53$; no other tests were significant. There were no other significant main effects or interactions in this analysis (see Table 4 for mean shift latencies for each group, separated by age and emotion).

Percentage of no-shift trials. Analysis of the percentage of no-shift trials revealed a main effect of emotion, $F(2, 415.4) = 9.835$, $p < .001$, $f^2 = .07$ (see Figure 1B), whereby infants showed the highest percentage of no-shift trials for fearful faces (M = 13.8%, SD = 16.4) as compared with happy faces (M = 10.6%, SD = 15.1, $t(179) = 2.802$, $p = .006$, $d = .20$) and neutral faces (M = 8.1%, SD = 13.1, $t(179) = 5.311$, $p < .001$, $d = .39$). Percentage of no-shift trials was also greater for happy faces than for neutral faces, $t(179) = 2.324$, $p = .021$, $d = .18$. There was also a significant interaction between group and age, $F(4, 527.4) = 4.101$, $p = .003$ (see Figure 2B). Follow-up tests revealed that this was driven by a significant increase in no-shift percentage in HRA− between 6 months (M = 4.5%, SD = 6.9) and 9 months (M = 12.6%, SD = 11.6; $t(38) = 2.438$, $p = .020$, $d = .82$), and a marginal increase between 6 months and 12 months (M = 10.0%, SD = 10.6; $t(32) = 1.732$, $p = .093$, $d = .62$); no other tests were significant. The overall analysis showed no other significant main effects or interactions (Table 4 displays mean percentage of no-shift trials for each group, separated by age and emotion).

Associations Between Eye Tracking and CSBS-DP

A series of correlational analyses were conducted to examine relations between attentional biases at 6, 9, and 12 months and social-communicative outcomes at 12 and 18 months. Emotion effects were consistent with biases to fearful faces, and these effects were independent of group and independent of age. The eye-tracking measure used in this analysis therefore focused on a "fear bias" score, calculated as the difference in latency to shift from fearful faces as compared with the average of happy and neutral faces. Because the range of responses in no-shift percentage was restricted (e.g., all usable trials contained shift behavior for 38% of 6-month-olds, 32% of 9-month-olds, and 29% of 12-month-olds), these responses were not included in the present correlational analyses. The CSBS-DP measures included percentile rank for (a) the Social Composite score at 12 months, and (b) the Social Composite score at 18 months. Partial correlations, controlling for developmental level using the MSEL ELC, were run between eye-tracking measures and CSBS-DP measures at each age. The first wave of analyses looked at all infants together, the second wave of analyses combined HRA− and HRA+ into a single at-risk (HRA) group and looked at HRA and LRC separately, and the final exploratory wave of analyses examined the HRA groups separately based on outcome status.

For the full group of infants, there were no significant associations between fearful face bias at 6, 9, or 12 months and CSBS social scores at 12 or 18 months after controlling for MSEL ELC. When separating groups into LRC and HRA, the LRC infants showed no significant associations, but the HRA group showed a positive association between the fearful face bias at 12 months and CSBS social scores at 18 months ($r(21) = .41$, $p = .050$). This suggests that HRA infants who were slower to shift from fearful

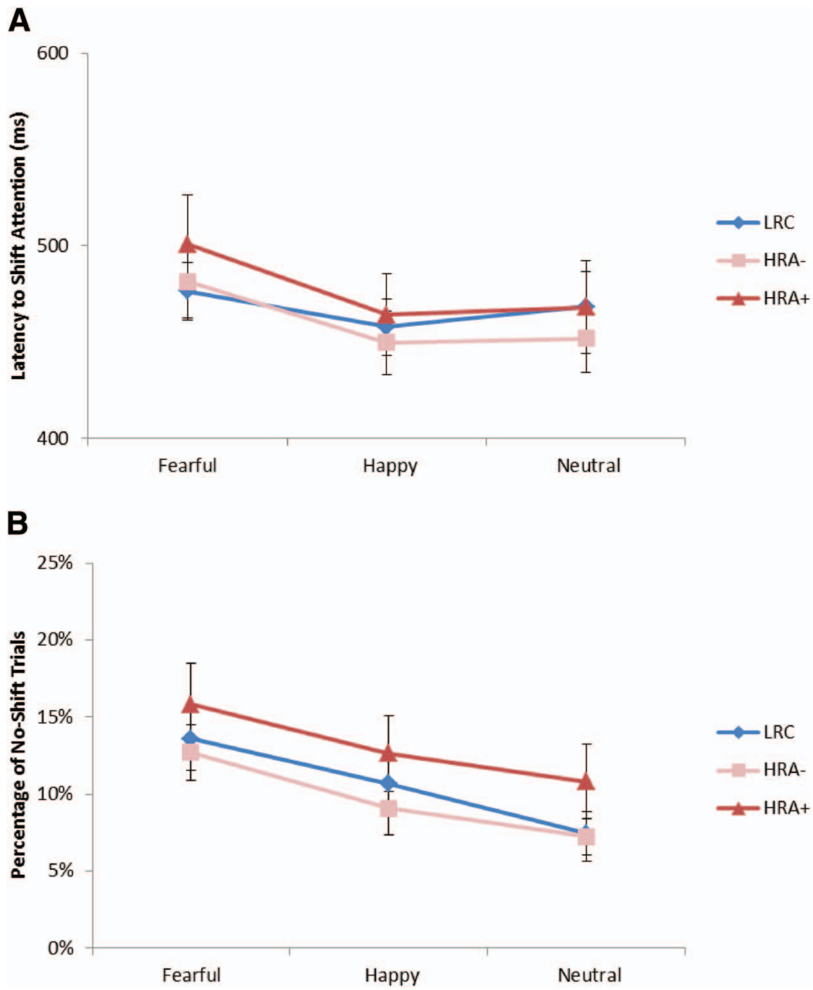

Figure 1. Emotion-based attentional responses in low-risk control infants (LRC), high risk for autism (HRA) infants who received a subsequent clinical judgment of autism spectrum disorder (ASD; HRA+), or non-ASD (HRA−). (A) Latency to shift attention showed a main effect of emotion (p = .049), with fearful > happy = neutral. (B) Percentage of no-shift trials showed a main effect of emotion (p < .001), with fearful > happy > neutral. Neither analysis revealed an interaction between group and emotion. Error bars represent ±*SEM*. See the online article for the color version of this figure.

faces relative to happy and neutral faces at 12 months showed better social ability at 18 months.

For the final set of analyses, HRA− and HRA+ infants were examined separately. Analyses showed no significant relations for HRA− between fearful face bias at any age and social outcomes at 12 or 18 months after controlling for MSEL ELC. In contrast, several significant findings were seen with HRA+ infants. At 9 months, the fearful face bias in HRA+ was positively correlated with CSBS social scores at 12 months (n = 11, $r(8)$ = .69, p = .029; see Figure 3A), and this was also true for the 12-month fearful face bias as it related to CSBS social scores at 18 months (n = 9, $r(6)$ = .72, p = .045; see Figure 3B). Though exploratory due to the limited sample size, these associations suggest that in HRA+, the fear bias at 9 and 12 months could possibly relate to social outcomes at 12 and 18 months, with a more pronounced bias to fearful faces predicting better social functioning in these children.

Discussion

The present study examined attentional biases to emotional faces at 6, 9, and 12 months in infants at high and low risk for autism and asked whether these early biases relate to later social-communicative development. Analyses focused on three groups: LRC, HRA−, and HRA+. Contrary to our hypothesis, infants in all three groups showed a similar attentional bias for fearful faces as compared with happy and neutral faces, with a longer latency to shift away from fearful faces and a higher percentage of fearful face trials with no shift away from the face. Interactions between group and age pointed to similar shifting behavior across the three groups at 6 and 9 months, but slower shifting in HRA+ compared with the other groups at 12 months. Additionally, exploratory correlational analyses showed that for HRA+ infants, associations between fearful face biases and social functioning were found, suggesting that biases to fearful faces at 9 and 12 months in this

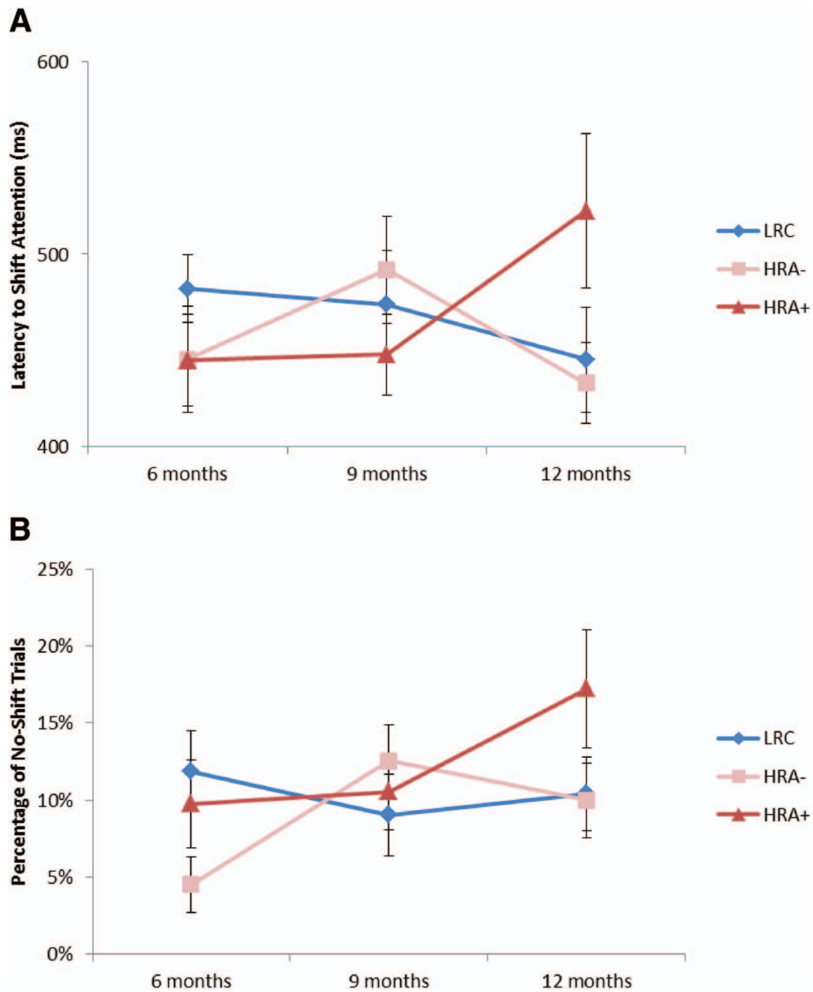

Figure 2. Attentional responses at 6, 9, and 12 months for low-risk control infants (LRC), high risk for autism (HRA) infants who received a subsequent clinical judgment of autism spectrum disorder (ASD; HRA+), or non-ASD (HRA−). (A) Latency to shift attention showed a significant interaction between age and group ($p <$ .001), and follow-up tests revealed significantly slower shifting at 12 months in HRA+ as compared with HRA− (p = .045). (B) Percentage of no-shift trials also showed a significant interaction between age and group (p = .003), and follow-up tests showed a significantly smaller percentage of no-shift trials in HRA− at 6 months as compared with 9 months (p = .020) and marginally less than at 12 months (p = .093). Error bars represent ±*SEM*. See the online article for the color version of this figure.

outcome group might be predictive of social functioning at 12 and 18 months, respectively.

Consistent with past work (e.g., Peltola et al., 2008, Peltola, Leppänen, Vogel-Farley, et al., 2009), the present study showed attentional biases to fearful faces in 6- to 12-month-olds, with infants taking longer to shift away from fearful faces than happy and neutral faces, and also showing a higher occurrence of sticky attention to fearful faces compared with the other emotions. Despite evidence that older individuals with ASD show impairments in the recognition of emotional faces, often with regard to threat-relevant faces (e.g., Ashwin et al., 2006; Corden et al., 2008), the current finding suggests that this might not be the case in the first year of life. In work by Pelphrey et al. (2002), adults with ASD showed disorganized scanning of emotional faces and worse recognition of fearful faces, and the authors suggest that attentional differences could underlie the social difficulties found in ASD. Relatedly, Corden et al. (2008) found that adults with ASD who spend less time scanning the eyes, a common finding across studies (Black et al., 2017), were worse at recognizing fearful faces, again suggesting a mechanism whereby patterns of attention to faces in ASD could lead to difficulties with emotion processing. The current infant work shows that infants at high and low risk for ASD show similar differences in attention to threat-relevant versus non-threat-relevant faces. With no evidence of diminished attention to core features of emotional faces in HRA infants (e.g., Wagner et al., 2016), it might then follow that infants who later develop ASD are able to modulate their attention based on emotion. At a later point in development, as attentional patterns to faces change in

Table 4
Mean Latency to Shift and No-Shift Percentage (and SD) for LRC, HRA−, and HRA+

Age	LRC			HRA−			HRA+		
	Fearful	Happy	Neutral	Fearful	Happy	Neutral	Fearful	Happy	Neutral
6 months									
Latency (ms)	487 (124)	480 (123)	480 (141)	450 (131)	445 (98)	442 (156)	437 (116)	416 (76)	482 (76)
No-shift %	16.3 (18.6)	10.0 (15.7)	9.3 (15.2)	8.0 (9.4)	3.9 (10.4)	1.7 (6.5)	14.4 (16.6)	9.1 (8.4)	5.8 (7.5)
9 months									
Latency (ms)	484 (144)	461 (143)	476 (169)	519 (174)	462 (158)	495 (141)	492 (134)	469 (133)	382 (85)
No-shift %	9.3 (17.1)	11.9 (17.4)	5.9 (11.0)	15.0 (14.9)	11.2 (13.8)	11.5 (14.1)	13.1 (13.9)	7.9 (13.2)	10.7 (12.7)
12 months									
Latency (ms)	458 (143)	430 (137)	448 (184)	458 (117)	437 (105)	404 (102)	548 (194)	491 (158)	529 (194)
No-shift %	14.2 (18.6)	10.4 (16.5)	6.6 (11.4)	13.5 (14.9)	10.3 (13.7)	6.1 (11.1)	18.9 (18.8)	18.7 (18.3)	14.0 (19.7)

Note. Latency is time (in ms) to shift attention from emotional face to peripheral distractor. No-shift % is percentage of valid trials on which no shift was made within 1,500 ms of distractor onset. LRC = low-risk controls; HRA− = high-risk autism with no autism spectrum disorder (ASD) diagnosis; HRA+ = high-risk autism with ASD diagnosis.

ASD and attention to core features decreases (e.g., Chawarska & Shic, 2009), difficulties in emotion recognition might then emerge.

Several previous studies with infants at high risk for ASD have examined patterns of attention disengagement from nonsocial stimuli and found that increasing latency to shift attention with increasing age was an early marker for which infants later developed ASD (e.g., Elsabbagh et al., 2013; Zwaigenbaum et al., 2005). For example, Zwaigenbaum et al. (2005) examined latency to disengage from a central target and look to a peripheral distractor in 6- and 12-month-old high-risk infants and found that those infants who showed slower shifting at 12 months as compared with 6 months received an autism classification at their 24-month visit. Researchers posit that difficulties in flexibly orienting attention can lead to a decrease in information gathering, and that this could lead to difficulties accurately orienting to and processing social information that can be characteristic of individuals with autism as they get older (e.g., Zwaigenbaum et al., 2005; for a review, see Keehn, Müller, & Townsend, 2013). The current study found a significant interaction between group and age, with similar shifting behavior across groups at 6 and 9 months, but slower shifting in HRA+ as compared with HRA− (and marginally for LRC), and this finding was independent of the emotional face presented. Although past findings have found slower shifting of attention by 12 to 14 months as a distinguishing characteristic of HRA infants who later develop ASD, the current study suggests that this pattern may be less pronounced when disengaging attention from emotionally salient faces.

A large body of work has shown attentional biases to fearful faces in infancy (for reviews, see Leppänen & Nelson, 2009, 2012) and some recent studies have found that early attention to faces can be predictive of later social and communicative outcome (e.g., Elsabbagh et al., 2014; Schietecatte, Roeyers, & Warreyn, 2012; Wagner, Luyster, Yim, Tager-Flusberg, & Nelson, 2013). Work by Peltola, Forssman, Puura, van Ijzendoorn, and Leppänen (2015) found that attention to fearful faces at 7 months predicted security of attachment at 14 months, with greater attention to fearful expressions related to more secure attachment. More recently, Peltola, Yrttiaho, and Leppänen (2018) used a similar paradigm and found that slower shifting behavior from faces overall at 7 months predicted more helping behavior at 24 months and fewer callous-unemotional traits at 48 months. The present study examined whether attentional biases to fearful faces in infancy could be predictive of later social behaviors, and although preliminary due to small sample sizes, the present findings showed that when looking at the three outcome groups separately, the only significant associations found were in HRA+, with a greater fearful face bias at 9 months predicting social functioning at 12 months, and a greater fearful face bias at 12 months predicting social functioning at 18 months. These exploratory analyses suggest that early attentional biases to threat-relevant faces could be a positive marker for development in HRA+, but continued work with larger samples is needed to better understand these findings. Related to the present findings, a study of adults with ASD by Corden et al. (2008) found that poor fear recognition was significantly associated with increased social anxiety, and this association was not found in a group of age- and IQ-matched controls. Our preliminary findings with HRA+ and the work of Corden et al. (2008) both point to recognition of fearful faces as a marker of better social development in individuals with ASD, and future studies should continue to explore these associations across development.

The current study had several limitations that will be important to consider in future research. First, the current paradigm saw the exclusion of roughly 20% of infants for not having a sufficient number of valid trials. While this is in line with infant eye-tracking studies (e.g., Chawarska et al., 2013), due to the unique population of infants tested in prospective infant sibling research, future work should consider ways to increase retention of infants in this paradigm, perhaps using videos instead of static images and/or varying the exemplars of the faces to maintain novelty for infants. If the present study had shown higher retention, more infants might have had data at multiple time points, allowing for correlational analyses using individual patterns of change in attention regulation, an approach that would expand on past work that focused on group-level differences in shift latency trajectories (e.g., Elsabbagh et al., 2013; Zwaigenbaum et al., 2005). The present study was also limited in not including a nonsocial control condition in addition to the three facial expressions to allow for direct comparison with past attention disengagement work in HRA (e.g., Elsabbagh et al., 2013). With some prior work showing that attention in ASD is enhanced to nonsocial stimuli (e.g., Pierce, Conant, Hazin, Stoner, & Desmond, 2011; Pierce et al., 2016), it would be interesting for

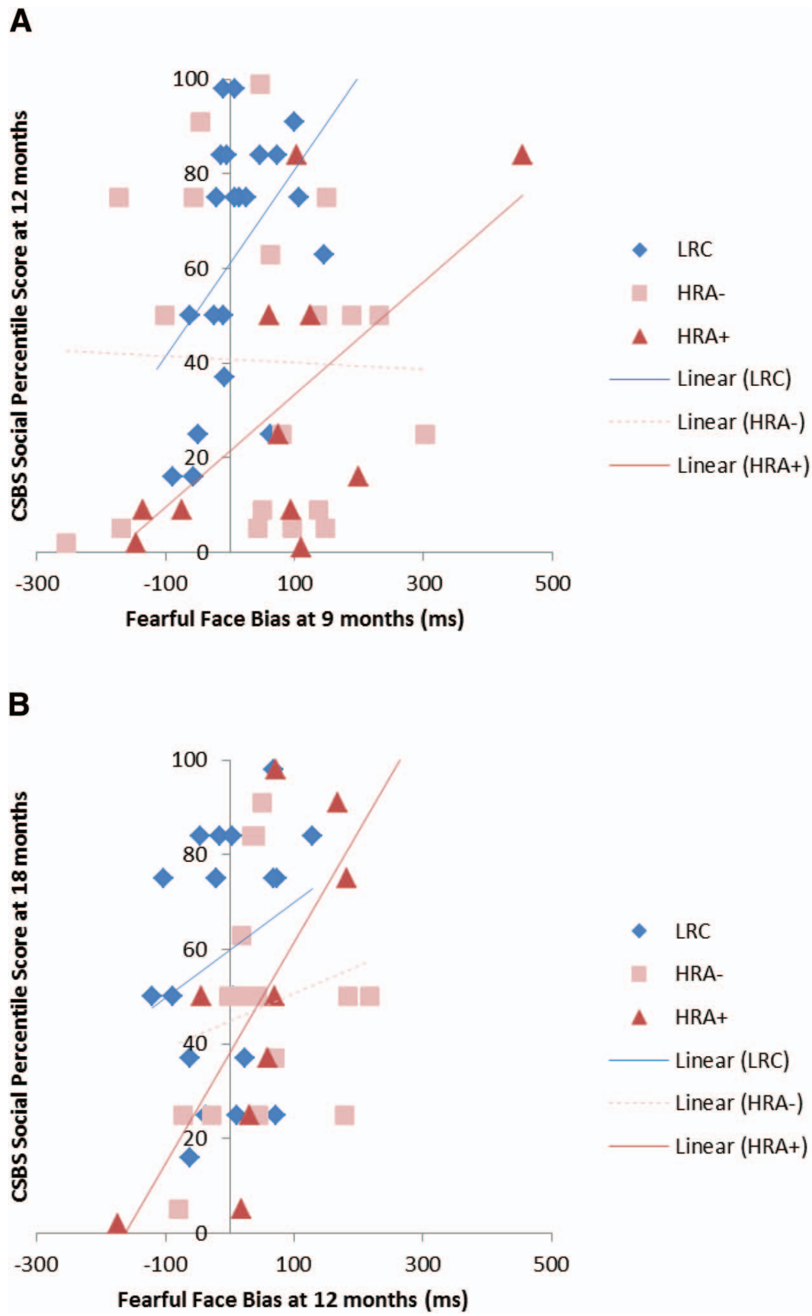

Figure 3. Associations between fearful face bias (latency to shift from fearful faces minus the average latency to shift from happy and neutral faces) and Communication and Symbolic Behavior Scales (CSBS) social percentile score. (A) An association between fearful face bias at 9 months and CSBS social percentile at 12 months was found after partialing out 12-month IQ for high risk for autism (HRA) infants who received a subsequent clinical judgment of autism spectrum disorder (ASD; HRA+; $p = .029$), and a marginal trend was found for low-risk control infants (LRC; $p = .061$), while non-ASD infants (HRA−) showed no relation ($p = .97$). (B) An association between fearful face bias at 12 months and CSBS social percentile at 18 months was found after partialing out 18-month IQ for HRA+ ($p = .045$), but not HRA− ($p = .56$) or LRC ($p = .49$). See the online article for the color version of this figure.

future work to more fully examine similarities and differences in attention disengagement from social and nonsocial stimuli in infants at high risk for ASD (see also Noland, Reznick, Stone, Walden, & Sheridan, 2010, for related work on differential memory for social and nonsocial stimuli in high-risk infants). An additional limitation was that calibration accuracy was checked only at the beginning of the session, so it is not known whether calibration drift may have occurred over the course of the task.

Finally, the current correlational analyses were not corrected for multiple comparisons. The present correlational findings should therefore be taken as exploratory and follow-up studies with larger samples will be needed to confirm and extend these results. When studying special populations like infants at high risk for ASD, it will be important for future work to focus on collaborative data collection across multiple labs. This approach will allow for larger samples, thereby increasing power and allowing for stronger analytic approaches with this important population (e.g., Nyström et al., 2018).

In summary, the present study found that infants at low and high risk for ASD show similar attentional biases to fearful faces from 6 to 12 months, and that infants who develop ASD show slower attention shifting at 12 months as compared with their same-age peers. Further, preliminary correlations showed that in the ASD group, attentional biases to fearful faces were related to better social outcomes. While findings from previous research have reported emotional face processing difficulties in older individuals with ASD, results from the present study indicate that low- and high-risk infants show similar responses to emotional faces, and for infants who later received an ASD diagnosis, the group showing slowest shifting at 12 months, their threat-relevant attentional biases could potentially serve as a protective factor during early development.

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Received September 21, 2018
Revision received April 22, 2019
Accepted April 23, 2019 ■