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Associations between attentional biases to fearful faces and social-emotional development in infants with and without an older sibling with autism

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ABSTRACT

During the first year of life, infants become increasingly attuned to facial emotion, with heightened sensitivity to faces conveying threat observed by age seven months as illustrated through attentional biases (e.g., slower shifting away from fearful faces). Individual differences in these cognitive attentional biases have been discussed in relation to broader social-emotional functioning, and the current study examines these associations in infants with an older sibling with autism spectrum disorder (ASD), a group with an elevated likelihood of a subsequent ASD diagnosis (ELA; $n = 33$), and a group of infants with no family history of ASD who are at low likelihood of ASD (LLA; $n = 24$). All infants completed a task measuring disengagement of attention from faces at 12 months (fearful, happy, neutral), and caregivers completed the Infant-Toddler Social and Emotional Assessment at 12, 18, and/or 24 months. For the full sample, greater fear bias in attention disengagement at 12 months related to more internalizing behaviors at 18 months, and this was driven by the LLA infants. When examining groups separately, findings revealed that LLA with a greater fear bias had more difficult behaviors at 12, 18, and 24 months; in contrast, ELA showed the opposite pattern, and this was most pronounced for ELA who later received an ASD diagnosis. These preliminary group-level findings suggest that heightened sensitivity to fearful faces might serve an adaptive function in children who later receive an ASD diagnosis, but in infants with no family history of ASD, increased biases might reflect a marker of social-emotional difficulties.

Understanding the emotions of others is an essential part of successful social interactions, and precursors to emotion processing have been studied from attentional patterns in infancy. In the first year of life, infants show differential attention to faces based on the emotion conveyed, including an early preference for happy faces at birth (Farroni et al., 2007) that then becomes a preference for threat-relevant faces, most consistently fearful faces, by the second half of the first year of life (for reviews, see Bayet & Nelson, 2019,

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and Leppänen & Nelson, 2012). Various paradigms have been used to examine emotional face processing and attentional biases in infancy, including visual paired comparison (VPC; e.g., LoBue & DeLoache, 2010; Nelson & Dolgin, 1985; Safar & Moulson, 2020) and the modified dot probe task (e.g., Pérez-Edgar et al., 2017; Sareen et al., 2022), but one task that has consistently demonstrated biased attention to threat-relevant faces involves the attentional disengagement task, first utilized with infants by Peltola et al. (2008).

In their initial study, Peltola et al. (2008) examined emotion processing and attention shifting in 7-month-old infants with an adapted gap/overlap task. Trials began with emotional faces presented centrally, then the face remained present while a peripheral target (i.e., a checkerboard pattern) appeared on the left or right side of the screen, and attention shifting to the peripheral target was measured. Across multiple studies using this paradigm, Peltola et al. (2008, 2009a, 2009b) found that by 7 months, infants show slower attentional disengagement from fearful faces relative to happy faces, neutral faces, and/or other control stimuli, as illustrated by slower shifting and more no-shift trials to the target when a fearful face is present.

These findings are in line with a large literature that has explored attention to threat-relevant faces (i.e., angry, fearful) in adulthood, with many studies showing evidence of heightened attention to and superior detection of these faces as compared to happy, sad, or neutral ones (e.g., Fox et al., 2000; Georgiou et al., 2005; Holmes et al., 2005; Yang et al., 2007). This literature points to an evolutionarily important mechanism for maintaining safety from threat, and neural systems that include the amygdala are known to support this enhanced processing of threat-relevant information (for reviews, see Leppänen & Nelson, 2009, 2012). However, despite evidence from infancy through adulthood illustrating these normative biases to attend to threat-relevant faces, numerous studies also suggest that individual differences in these biases in children and adults might relate to clinical and non-clinical levels of anxiety, with anxious individuals showing heightened threat-relevant biases (e.g., Abend et al., 2018; Fox et al., 2001; Mogg et al., 2000; Taghavi et al. 1999; for a review, see Bar-Haim et al., 2007).

With threat-relevant biases appearing in the first year, developmental researchers have begun to ask how these biases in infancy might also be related to social and emotional development (see Fu & Pérez-Edgar, 2019). Two studies by Peltola et al. (2015, 2018) investigated how responses during the attentional disengagement task at 7 months were related to later outcomes. First, Peltola et al. (2015) found that infants with secure attachment at 14 months showed slower shifting of attention from fearful faces at 7 months as compared to insecurely attached infants. Second, Peltola et al. (2018) found that slower shifting from faces overall at 7 months predicted higher levels of helping behavior at 24 months and fewer callous-unemotional traits at 48 months, though these associations were not related to fearful face responses specifically. Taken together, these studies suggest that attention shifting from emotional faces in infancy could be a marker of later social-emotional characteristics.

Autism spectrum disorder (ASD) is a neurodevelopmental condition with an incidence of 1 in 44 (Autism and Developmental Disabilities Monitoring Network, 2021) and a typical age of diagnosis in the preschool years (van 't Hof et al., 2021). A growing area of research is aimed at identifying early markers of ASD in order to give children an opportunity to receive intervention at an earlier age, and these studies have focused on prospectively following infants with an older sibling diagnosed with ASD, a group with a 1 in 5 chance of also receiving an ASD diagnosis (e.g., Messinger et al., 2015; Ozonoff et al., 2011), meaning they are at elevated likelihood of ASD (ELA). Further, of the ELA infants who do not receive an ASD diagnosis, 1 in 3 show increased ASD-related symptoms and/or reduced language/cognitive ability (e.g., Messinger et al., 2013; Ozonoff et al., 2014). Several recent studies have identified elevated social-emotional difficulties at 18 months in ELA who later receive an ASD diagnosis (ELA+) as compared to both ELA who do not receive a diagnosis (ELA-) and a comparison group of infant siblings with no family history of ASD who are at low likelihood for ASD (LLA; Raza et al., 2020; Reid et al., 2020). While these studies highlight social-emotional development in toddlerhood as a marker of later ASD, questions remain about how early attentional biases to emotion might lay the groundwork for social-emotional development in these groups.

Several studies have focused on attentional disengagement as a potential marker of ASD diagnosis and/or symptomology in ELA (e.g., Baranek et al., 2018; Bryson et al., 2018; Elsabbagh et al., 2013; Zwaigenbaum et al., 2005; see also Sacrey et al., 2014, for a review) and our group was the first to examine disengagement in the context of emotion processing (Wagner et al., 2020). Utilizing the paradigm of Peltola et al. (2008, 2009b), we studied 6-, 9-, and 12-month-old infants with or without an older sibling with ASD. For fearful face trials, we found increased reaction time (RT) and an increased proportion of no-shift trials, consistent with previous work; however, there were no differences between the infant groups, pointing to emotion-modulated attentional biases across infants regardless of family history of ASD. A second set of analyses examined fear bias (calculated as RT to shift from fearful faces minus the average RT for happy and neutral faces) alongside social functioning, as measured by the Communication and Symbolic Behavior Scales (CSBS; Wetherby et al., 2002), and our findings suggested that increased fear biases in ELA+ at 9 and 12 months predicted better social abilities at 12 and 18 months, respectively (Wagner et al., 2020).

The current study extends our past work to ask whether fear biases at 12 months in infants with and without a family history of ASD might be related to concurrent and predictive levels of social-emotional difficulties and competencies as measured by the Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006), a caregiver questionnaire that assesses several domains that indicate elevated likelihood for later psychopathology (e.g., anxiety, depression) and developmental disorders (e.g., ASD). The ITSEA was administered at 12, 18, and 24 months in the current longitudinal sample of ELA and LLA, and we analyzed 12-month fear biases as they were associated with all three time points based on prior studies that have found significant associations between infant social attention and both concurrent measures of social development (e.g., Pons et al., 2019) and predictive measures of social development 6 months later (e.g., Wagner et al., 2020) and 12 months later (e.g., Wagner et al., 2018).

This study examined how these ITSEA associations with fear biases might differ by group based on ASD family history and subsequent diagnosis. Following from our prior work, we hypothesized that increased fear biases in ELA+ would be related to better social-emotional abilities (e.g., Wagner et al., 2020). For LLA, because a large number of studies with older children and adults have pointed to relations between heightened attentional biases to emotional faces and increased clinical symptoms, such as anxiety (e.g.,

Fox et al., 2001; for a review, see Bar-Haim et al., 2007), we hypothesized that, in contrast to ELA+, increased fear biases in infancy might be associated with increased socio-emotional difficulties for LLA. Finally, because past findings have been mixed as far as whether ELA– more closely resemble ELA+ or LLA (e.g., see Pisula & Ziegart-Sadowska, 2015), we predicted that no significant associations would be found in this intermediate group. We explored these questions across the seven different ITSEA scores relating to social-emotional competence.

1. Method

1.1. Participants

All infants were part of a longitudinal study examining infants with an older sibling with or without autism spectrum disorder (ASD). The initial sample for the current study included 124 12-month-old infants who participated in the attentional disengagement task, 69 with an older sibling with ASD who are therefore at elevated likelihood of a subsequent ASD diagnosis (ELA) and 55 with a typically developing older sibling and no family history of ASD who are at low likelihood of ASD (LLA). To be included in the current analyses, infants were required to contribute sufficient eye-tracking data (see Data Processing and Analysis for more information), and for ELA, to be followed to 24 months or older in order to determine ASD outcome. Insufficient eye-tracking data led to the exclusion of 58 infants (47% of infants initially tested; see Peltola et al., 2009b, for comparable attrition in a disengagement paradigm with 7-month-olds). The rate of exclusion for insufficient eye-tracking data was similar across groups (31 of 69 excluded for ELA, 27 of 55 excluded for LLA). Of the remaining 66 infants, three ELA were excluded for not being followed to 24 or 36 months when an ASD outcome could be determined, and one LLA was excluded for receiving a positive clinical judgment for ASD. Finally, for the current analyses, infants were also required to have parents complete the ITSEA questionnaire measure to assess socio-emotional development at 12, 18, and/or 24 months, resulting in the exclusion of an additional five infants (3 LLA, 2 ELA) who were included in the original study utilizing this eye-tracking paradigm (Wagner et al., 2020).

The final sample therefore included 57 12-month-old infants ($M_{\text{age}} = 379.1$ days, $SD = 11.3$), 33 ELA and 24 LLA. The 33 ELA infants were divided into positive (ELA+) and negative (ELA–) ASD outcome, with all infants in the ELA+ group receiving a final clinical judgment of ASD by a licensed clinical psychologist with expertise in the area of autism and neurodevelopmental disorders after reviewing all information, including videos and scores from the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) from all available lab visits. Following these criteria, the final groups consisted of 24 LLA (7 female; $M_{\text{age}} = 378.6$ days, $SD = 9.3$), 19 ELA– (6 female; $M_{\text{age}} = 379.3$ days, $SD = 12.8$), and 14 ELA+ (4 female; $M_{\text{age}} = 379.8$ days, $SD = 12.9$).

As has been reported in prior publications from this longitudinal dataset (e.g., Edwards et al., 2017; Wagner et al., 2020), demographic patterns show that participants were largely non-Hispanic (91.2%) and White (84.2%), with a small subset of participants reporting race as Asian (3.5%), Black or African American (1.8%), more than one race (8.8%), or unknown (1.8%). For parental education, 77.2% of both maternal and paternal education was reported at the level of a 4-year college degree or higher, and family income was reported as \$75,000 or higher for 80.7% of participating families.

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.

1.2. Stimuli

The emotional disengagement task was adapted from Peltola et al. (2009b). Four female faces from the NimStim library (Tottenham et al., 2009) were utilized, and infants were presented with one of the four faces expressing three different emotions throughout the task: fearful, happy, and neutral. Faces subtended a visual angle of approximately 15.4 degrees vertically and 10.8 degrees horizontally, and the distractor in the periphery measured 15.4 degrees of visual angle vertically and 4.3 degrees of visual angle horizontally (for sample stimuli, see Peltola et al., 2009b). Trials began with a centrally-presented female face for 1000 ms, then with the face remaining present, a black and white flickering distractor pattern was shown in the periphery on the right or left side of the face. For the first 1000 ms of the distractor, the black and white areas alternated their colors at 10 Hz to attract attention, and then the pattern remained static for the remaining 2000 ms of the trial.

1.3. Apparatus

Infants were seated on a caregiver's lap and presented with face images on a 17" TFT Tobii T60 monitor using Clearview software (Tobii Technology AB; www.tobii.com). Gaze was recorded 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 degrees of the visual angle, and a tolerance of head movements within the range of $44 \times 22 \times 30$ cm.

1.4. Procedure

Infants were seated on their caregiver's lap approximately 60 cm from the Tobii T60 monitor in a dimly lit testing room. Caregivers were told to look down at their infant throughout the eye-tracking task to prevent them from influencing their infant's looking behavior and also to ensure that the eye-tracker did not attempt to track the wrong set of eyes. Calibration was completed before the emotional disengagement task to ensure satisfactory gaze tracking, using a 5-location procedure presenting a blue and white checkered

sphere in the four corners of the monitor and the center of the screen. Calibration was repeated until successful, with adjustments made to infant position and monitor position as needed.

The emotional disengagement task was then presented with up to 75 trials (25 of each emotion), and all trials were ‘overlap’ trials, with the central face remaining present during the appearance of the distractor. The three emotions and the side of the distractor (left vs. right) were semi-randomized, and between trials, a colorful image of an underwater scene was presented. Trials were initiated by the experimenter when the infant was attending to this inter-trial image.

1.5. Social-emotional development measure at 12, 18, and 24 months

At 12, 18, and/or 24 months, caregivers completed the Infant-Toddler Social and Emotional Assessment (ITSEA, [Carter & Briggs-Gowan, 2006](#)). The questionnaire items assess a range of socio-emotional behavioral competencies and problems in 1- to 3-year-old children, and the measure shows acceptable test-retest reliability and construct validity (e.g., [Carter et al., 2003](#)). Scoring of the ITSEA yields four primary domain scores: Internalizing (e.g., general anxiety, separation distress), Externalizing (e.g., activity/impulsivity, aggression/defiance), Dysregulation (e.g., negative emotionality, sensory sensitivity), and Competence (e.g., imitation/play, prosocial peer relations). Additionally, the ITSEA includes three item clusters assessing problem behaviors that can be used to assess red flags for clinically-relevant behaviors (e.g., see [Thurm et al., 2018](#)): Social Relatedness, Atypical, and Maladaptive. The Social Relatedness and Atypical clusters were designed to assess behaviors associated with ASD and related developmental difficulties ([Carter et al., 2003](#)).

1.6. Eye-tracking data processing

For each trial, gaze data were collected from the onset of the face until the start of the inter-stimulus interval, and data were analyzed to determine shift trials (i.e., trials with a saccade to the distractor) and no-shift trials (i.e., trials with no distractor-related saccade). Data were exported and analyzed in Matlab using a series of criteria to identify valid trials for subsequent analysis. For both shift and no-shift trials, sufficient attention to the face before the onset of the distractor was required (50% of the time during the 400 ms prior to the onset of the distractor). Additionally, for shift trials, saccades to the distractor were only included if they occurred 100 ms or more after the appearance of the distractor (to avoid anticipatory saccades), but also within 1500 ms, and 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 1500 ms of the appearance of the distractor, and no more than 25% of gaze data was missing for the duration of the trial (see also [Wagner et al., 2020](#)).

To be included in the present analyses, infants were required to have at least three valid shift trials for each emotional expression. On average, infants contributed 17.33 valid trials ($SD = 4.36$), with 6.05 valid trials for fearful faces ($SD = 2.01$), 5.63 valid trials for happy faces ($SD = 1.59$), and 5.65 for neutral faces ($SD = 2.00$). The number of valid trials did not significantly differ across the three groups, $F(2, 54) = 0.44, p = .65$, with LLA averaging 16.92 valid trials ($SD = 3.20$), ELA– averaging 18.11 valid trials ($SD = 5.08$), and ELA+ averaging 17.00 valid trials ($SD = 5.19$).

Two metrics were then calculated to estimate individual differences in biases towards fearful faces (see also [Peltola et al., 2015](#)): 1) reaction time (RT) fear bias, calculated as RT to shift from fearful faces minus the average RT to shift from happy and neutral faces (RT fear bias), and 2) no-shift (NS) percentage fear bias, calculated as the percentage of no-shift trials for fearful faces minus the average percentage of no-shift trials for happy and neutral faces (NS fear bias). Larger values for RT and NS fear bias reflect greater differences in shifting from fearful faces relative to happy and neutral faces. One-way ANOVAs revealed no group differences between LLA, ELA–, and ELA+ for RT fear bias ($F(2, 54) = 0.55, p = .58$) nor for NS fear bias ($F(2, 54) = 0.01, p = .99$). [Table 1](#) presents descriptive statistics of RT and NS fear bias scores.

1.7. Statistical analysis

All statistical analyses were conducted using IBM SPSS software (version 27). Analyses began with an examination of skew and kurtosis for the two disengagement variables (RT fear bias, NS fear bias) and the seven ITSEA variables at each of the three ages (Internalizing, Externalizing, Dysregulation, Social Competence, Social Relatedness, Atypical, Maladaptive). Three variables showing

Table 1
Means (SDs), range, skewness, and kurtosis for RT and NS fearful face bias for LLA, ELA–, and ELA+.

	LLA	ELA–	ELA+
RT Fear Bias	10.30 (93.46)	37.04 (83.22)	41.53 (135.54)
Range	–120.30 to 287.21	–80.08 to 217.17	–174.67 to 340.87
Skew, Kurtosis	1.16, 2.00	0.76, 0.33	0.42, 0.75
NS Fear Bias	0.05 (0.16)	0.05 (0.12)	0.05 (0.13)
Range	–0.20 to 0.49	–0.12 to 0.33	–0.19 to 0.36
Skew, Kurtosis	1.32, 2.20	0.69, 0.13	0.82, 2.64

Note: RT: Reaction Time; NS: No shift percentage; LLA: Infants with no family history of ASD who are at low likelihood of a subsequent ASD diagnosis; ELA: Infants who have an older sibling diagnosed with ASD who are at elevated likelihood of a subsequent ASD diagnosis (ELA– infants did not receive a subsequent ASD diagnosis; ELA+ infants did receive a subsequent ASD diagnosis).

skewness above $|2|$ and/or excess kurtosis of $|4|$ across the full sample were classified as non-normal (Kim, 2013): 18-mo Maladaptive, 24-mo Maladaptive, and 24-mo Atypical. After examining skew and kurtosis in each group individually, 12-mo Maladaptive was also classified as non-normal (see Tables 1, 2, and 3 for mean, SD, range, skewness, and kurtosis for disengagement variables, ITSEA Domain scores, and ITSEA Cluster scores, respectively).

Associations between fear biases and ITSEA subdomains were examined using correlational analyses, with Spearman's rank-order correlation used as a non-parametric measure for the four variables showing elevated skew and/or kurtosis, and Pearson correlation used as a parametric measure for the remaining analyses. With seven ITSEA subdomains examined in each analysis, a Bonferroni correction was used to conservatively account for inflated Type I errors, with an alpha of .05 divided by 7, resulting in an adjusted p value of .0071. Correlations were first examined for the full group of children, then a second set compared LLA and ELA, and finally, a third set examined ELA+ and ELA- separately.

To further examine the influence of group on relations between fear bias at 12 months and ITSEA subdomains at 12, 18, and/or 24 months, all Pearson correlations reaching the corrected $p < .0071$ level were followed up with a set of univariate ANOVAs that included the relevant ITSEA subdomain as the dependent variable and looked at fear bias as it interacted with group. (e.g., see Wagner et al., 2016). This follow-up therefore examined how the relations between fear biases and ITSEA domains might differ by group.

2. Results

An initial set of analyses used a series of one-way ANOVAs to look for effects of group (LLA, ELA-, ELA+) on the seven ITSEA domain and cluster scores at 12, 18, and 24 months, and results showed no significant group effects for any age (all p -values $> .075$).

2.1. Fear bias and ITSEA domain scores

Across the full sample, a series of Pearson correlations examined associations between RT and NS fear bias measures and the four primary ITSEA domains: Internalizing, Externalizing, Dysregulation, and Competence. Results showed no significant associations

Table 2

ITSEA Domain score means (SDs), range, skewness, and kurtosis for LLA, ELA-, and ELA+.

	LLA	ELA-	ELA+
Internalizing			
12 month	0.31 (0.15); 0.04 to 0.60	0.35 (0.22); 0.11 to 0.95	0.29 (0.18); 0.08 to 0.60
Skew, Kurtosis	0.31, -0.31	1.35, 2.12	0.71, -0.73
18 month	0.41 (0.19); 0.04 to 0.78	0.49 (0.25); 0.18 to 1.00	0.34 (0.14); 0.18 to 0.57
Skew, Kurtosis	-0.38, -0.15	0.26, -0.83	0.37, -1.43
24 month	0.40 (0.19); 0.04 to 0.80	0.58 (0.27); 0.13 to 1.14	0.45 (0.21); 0.15 to 0.95
Skew, Kurtosis	0.53, 1.02	0.65, 0.56	1.37, 2.47
Externalizing			
12 month	0.22 (0.15); 0 to 0.55	0.29 (0.22); 0 to 0.78	0.19 (0.13); 0 to 0.43
Skew, Kurtosis	0.58, -0.46	0.82, 0.11	0.76, 0.16
18 month	0.36 (0.15); 0.08 to 0.75	0.37 (0.31); 0.03 to 1.00	0.32 (0.23); 0.08 to 0.89
Skew, Kurtosis	0.25, 1.31	0.31, -0.63	1.69, 3.66
24 month	0.48 (0.19); 0.11 to 0.81	0.38 (0.32); 0.06 to 1.16	0.36 (0.22); 0.14 to 0.80
Skew, Kurtosis	0.14, -0.05	1.27, 1.53	0.87, 0.03
Dysregulation			
12 month	0.32 (0.22); 0.06 to 1.03	0.34 (0.28); 0.05 to 1.03	0.42 (0.30); 0.10 to 0.98
Skew, Kurtosis	1.55, 3.25	1.31, 1.21	0.94, 0.12
18 month	0.31 (0.16); 0.06 to 0.71	0.42 (0.25); 0.05 to 0.89	0.32 (0.23); 0.09 to 0.63
Skew, Kurtosis	0.87, 0.30	0.64, -0.74	0.32, -1.95
24 month	0.26 (0.18); 0.02 to 0.73	0.35 (0.28); 0.07 to 0.85	0.44 (0.33); 0.06 to 1.21
Skew, Kurtosis	1.03, 2.18	1.00, -0.52	1.25, 2.05
Competence			
12 month	0.76 (0.33); 0.15 to 1.66	0.79 (0.36); 0.27 to 1.41	0.67 (0.26); 0.26 to 0.98
Skew, Kurtosis	0.71, 1.28	0.45, -1.04	-0.51, -1.18
18 month	1.21 (0.23); 0.75 to 1.52	1.06 (0.30); 0.51 to 1.70	1.00 (0.35); 0.55 to 1.53
Skew, Kurtosis	-0.62, -0.44	0.45, 0.38	0.07, -1.56
24 month	1.36 (0.24); 0.81 to 1.64	1.35 (0.30); 0.88 to 1.87	1.24 (0.22); 0.89 to 1.57
Skew, Kurtosis	-1.12, 0.68	0.21, 0.04	-0.12, -0.50

Note: LLA: Infants with no family history of ASD who are at low likelihood of a subsequent ASD diagnosis; ELA: Infants who have an older sibling diagnosed with ASD who are at elevated likelihood of a subsequent ASD diagnosis (ELA- infants did not receive a subsequent ASD diagnosis; ELA+ infants did receive a subsequent ASD diagnosis).

Table 3

ITSEA Cluster score means (SDs), range, skewness, and kurtosis for LLA, ELA–, and ELA+.

	LLA	ELA–	ELA+
Social Relatedness			
12 month	1.61 (0.24); 1.10 to 1.90	1.63 (0.30); 1.00 to 2.00	1.46 (0.45); 0.70 to 2.00
Skew, Kurtosis	–0.62, –0.60	–0.69, –0.12	–0.48, –0.95
18 month	1.74 (0.18); 1.30 to 2.00	1.69 (0.21); 1.20 to 2.00	1.53 (0.40); 0.90 to 2.00
Skew, Kurtosis	–0.76, 0.15	–0.71, 0.98	–0.52, –1.40
24 month	1.76 (0.14); 1.50 to 2.00	1.69 (0.22); 1.30 to 2.00	1.73 (0.11); 1.60 to 1.90
Skew, Kurtosis	0.02, –0.24	–0.23, –0.69	0.44, –0.92
Atypical			
12 month	0.23 (0.15); 0 to 0.50	0.31 (0.27); 0 to 0.88	0.35 (0.30); 0 to 1.00
Skew, Kurtosis	0.33, –0.77	0.42, –0.76	0.81, 0.38
18 month	0.10 (0.11); 0 to 0.38	0.21 (0.23); 0 to 0.75	0.26 (0.29); 0 to 0.88
Skew, Kurtosis	0.99, 0.23	0.89, 0.21	1.41, 1.18
24 month	0.09 (0.13); 0 to 0.38	0.16 (0.27); 0 to 1.00	0.19 (0.26); 0 to 0.75
Skew, Kurtosis	1.20, 0.51	2.89, 9.25	1.43, 0.98
Maladaptive			
12 month	0.06 (0.07); 0 to 0.23	0.04 (0.06); 0 to 0.23	0.07 (0.09); 0 to 0.31
Skew, Kurtosis	0.80, –0.08	1.86, 4.31	1.83, 4.15
18 month	0.05 (0.06); 0 to 0.15	0.09 (0.08); 0 to 0.23	0.11 (0.17); 0 to 0.54
Skew, Kurtosis	0.76, –0.86	0.35, –1.18	1.96, 3.57
24 month	0.02 (0.05); 0 to 0.15	0.05 (0.09); 0 to 0.23	0.06 (0.09); 0 to 0.31
Skew, Kurtosis	2.07, 3.64	1.42, 0.45	2.32, 6.20

Note: LLA: Infants with no family history of ASD who are at low likelihood of a subsequent ASD diagnosis; ELA: Infants who have an older sibling diagnosed with ASD who are at elevated likelihood of a subsequent ASD diagnosis (ELA– infants did not receive a subsequent ASD diagnosis; ELA+ infants did receive a subsequent ASD diagnosis).

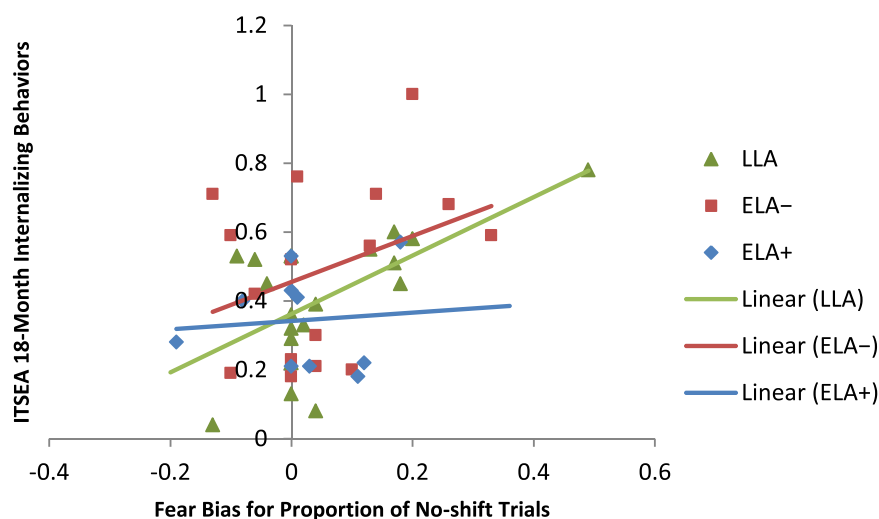


Fig. 1. Association between 12-month no-shift fear bias and 18-month ITSEA Internalizing domain for LLA, ELA+, and ELA–. Across all infants, a significant positive correlation was found ($p = .002$), but when looking at each group separately, the result held only for LLA infants ($p = .004$).

between 12-month fear bias and ITSEA subdomain scores at 12 or 24 months, but greater NS fear bias was associated with more Internalizing behaviors at 18 months ($r(44) = 0.44$, $p = .002$; see Fig. 1).

Next, analyses examined these correlations separately for ELA and LLA. For ELA, no significant associations were found, but for LLA, NS fear bias at 12 months was positively associated with Internalizing at 12 months ($r(21) = 0.57$, $p = .004$). Similarly, for LLA, NS fear bias at 12 months was positively associated with Internalizing at 18 months ($r(18) = 0.61$, $p = .004$; see Fig. 1). A final set of correlations examined ELA– and ELA+ separately, and findings showed that for both groups, no relations reached significance after correction for multiple comparison (see Supplementary Table 1 for a full summary of correlational results with ITSEA domain scores).

Based on the significant findings between NS fear bias and 12- and 18-month Internalizing, follow-up univariate ANOVAs were conducted to further examine the influence of group on these relations. For each ANOVA, the ITSEA domain was treated as the dependent variable, with group, NS fear bias, and the interaction between group and NS fear bias examined; ANOVAs were examined twice, once with two levels for group (LLA, ELA) and once with three levels for group (LLA, ELA–, ELA+), in order to examine the effects of group membership.

The ANOVAs examining 12-month Internalizing as the dependent variable (both the 2-group and 3-group analyses) were non-significant, with no main effects of group, NS fear bias, or interaction between group and NS fear bias. For the ANOVA examining 18-month Internalizing, when including two levels of group, there was a significant effect of NS fear bias ($F(1, 42) = 10.22, p = .003, \eta_p^2 = .20$), but group did not interact with NS fear bias ($p = .61$). When including three levels of group, NS fear bias again had a main effect on 18-month Internalizing ($F(1, 40) = 4.42, p = .042, \eta_p^2 = .10$), but group did not interact with NS fear bias ($p = .57$). These findings suggest that the association between NS fear bias and 18-month Internalizing does not meaningfully differ based on group. Fig. 1 illustrates the relationship between 12-month NS fear bias and 18-month ITSEA Internalizing for the three groups.

2.2. Fear bias and ITSEA cluster scores

Using Spearman's rank-order correlation, analyses examined RT and NS fear bias measures as they related to 12-, 18-, and 24-month Maladaptive and 24-month Atypical cluster scores. Across the full sample, no associations were found. When examining ELA and LLA separately, no significant associations were found for ELA, but for LLA, RT fear bias was found to positively relate to 24-month Atypical behavior ($r_s(12) = 0.77, p = .001$). After further dividing ELA into ELA- and ELA+, findings showed no significant associations (see Supplementary Table 2).

For the remaining ITSEA clusters (12- and 18-month Atypical, and 12-, 18-, and 24-month Social Relatedness), Pearson correlations were used to examine associations with 12-month fear bias measures. Across the full sample, no significant correlations were found. Analyses of ELA and LLA separately found that in ELA, RT fear bias was negatively associated with 18-month Atypical behavior ($r(25) = -0.52, p = .005$). When looking at ELA- and ELA+ separately, no associations were significant (see Supplementary Table 3).

Following from the Pearson correlational findings, a univariate ANOVA was conducted to further examine the influence of group on the relation between RT fear bias and 18-month Atypical behavior. Parallel to the analyses above, the ITSEA cluster was treated as the dependent variable, with group, RT fear bias, and the interaction between group and RT fear bias examined; the ANOVA was again conducted twice, once with two levels for group and once with three levels for group to see if the influence of group would differ.

For 18-month Atypical behavior, when including two levels of group, main effects of group ($F(1, 43) = 12.24, p = .001, \eta_p^2 = .22$) and RT fear bias were found ($F(1, 43) = 4.51, p = .04, \eta_p^2 = .095$), and there was a significant interaction between group and RT fear bias ($F(1, 43) = 7.20, p = .01, \eta_p^2 = .14$). When including three levels of group, the same findings were seen, with main effects of group ($F(2, 41) = 6.14, p = .005, \eta_p^2 = .23$) and RT fear bias ($F(1, 41) = 8.62, p = .005, \eta_p^2 = .17$) that were qualified by the interaction between group and RT fear bias ($F(2, 41) = 3.71, p = .033, \eta_p^2 = .15$). This suggests that the relation between RT fear bias and 18-month Atypical behavior differs meaningfully based on group. Fig. 2 illustrates the relationship between 12-month RT fear bias and 18-month ITSEA Atypical behavior for the three groups.

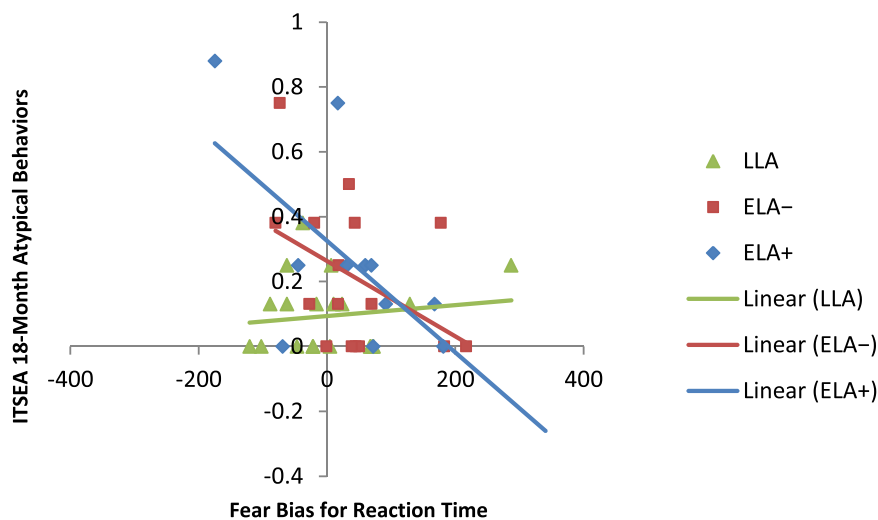


Fig. 2. Association between 12-month reaction time (RT) fear bias and 18-month ITSEA Atypical cluster for LLA, ELA+, and ELA-. Across all ELA, a significant negative association was found ($p = .005$), and a follow-up univariate ANOVA found an interaction between group and RT fear bias in predicting 18-month Atypical behaviors (2-group model: $p = .01$; 3-group model: $p = .033$). This suggests that the association between RT fear bias and 18-month Atypical behaviors differs as a function of group.

3. Discussion

The present study examined the interaction between cognitive attentional biases and emotional development in the first two years of life, measuring the relations between fearful face biases at 12 months and social-emotional development at 12, 18, and 24 months in infants with an older sibling diagnosed with ASD who are at elevated likelihood of a subsequent ASD diagnosis (ELA) and a comparison group of infant siblings with no family history of ASD who are at low likelihood of ASD (LLA). Overall, results showed that greater fear biases at 12 months were differentially related to difficult behaviors in LLA and ELA, with greater biases associated with worse social-emotional outcomes in LLA and better social-emotional outcomes in ELA. Although these group-level findings are preliminary due to the small sample sizes, the current work suggests the importance of examining interactions between attentional biases and developmental outcomes in infants with and without a family history of ASD.

Early attentional biases to fearful faces in infants are in line with studies in adults that identify threat-relevant biases in attention (e.g., Fox et al., 2000; Georgieu et al., 2005; Yang et al., 2007), and numerous studies have found that individual differences in this normative response to threat are related to both clinical and non-clinical levels of anxiety in children and adults (e.g., Abend et al., 2018; Fox et al., 2001; Mogg et al., 2000; Taghavi et al. 1999; see also Bar-Haim et al., 2007, for a review). Related to this, the current study found that a greater proportion of no-shift trials for fearful faces relative to happy and neutral at 12 months predicted increased internalizing behaviors at 18 months across the full sample. On the ITSEA, the Internalizing domain is composed of Depression/Withdrawal, General Anxiety, Separation Distress, and Inhibition to Novelty scales (Carter et al., 2003), aligning the present finding with prior work relating to anxiety-related symptoms.

Exploring the infant groups separately revealed that the significant association found with internalizing behavior was driven by LLA infants with no family history of ASD who showed significant positive associations between no-shift fear bias at 12 months and internalizing behaviors at both 12 and 18 months. Additionally, slowed disengagement from fearful faces relative to happy and neutral (RT fear bias) at 12 months in LLA was associated with more atypical behaviors at 24 months. This suggests that greater bias in vigilance to threat-relevant faces in infants with no family history of ASD is related to concurrent and predictive measures of social-emotional difficulties. Further longitudinal work is needed to understand how these difficulties in 12- to 24-month-olds might relate to later childhood psychopathology, and based on studies with anxious adults, this could lead to discussion of how attention modification training could support later development (e.g., for reviews, see Hakamata et al., 2010, and Linetzký et al., 2015).

Past work in ASD has identified difficulties in attention shifting and disengagement (e.g., for reviews, see Keehn et al., 2013, and Sacrey et al., 2014), and prospective work with ELA infants has pointed to these difficulties as a potential early marker of autism (e.g., Elsabbagh et al., 2013). When threat-relevant emotional faces are used, however, children and adults with ASD (for a review, see Fan et al., 2020) and ELA (Wagner et al., 2020) show attentional biases that are comparable to individuals without ASD. However, the current study did show that, in contrast to LLA, greater biases to fearful faces relative to happy and neutral for ELA at 12 months were predictive of fewer atypical behaviors at 18 months, one of the two ITSEA scores most closely aligned with ASD. Follow-up analyses examining whether the relation between RT fear bias and 18-month Atypical behavior changed as a function of group were significant, and this further supports the present findings of group-specific differences in the relations between biases to fearful faces at 12 months and 18-month autism-related characteristics. Our prior work with the same group of infants looked at fear biases as predictors of social development, as measured by the CSBS (Wagner et al., 2020), and taken together, both sets of results point to increased attentional biases to fearful faces predicting better outcomes six months later in ELA overall. Wagner et al. (2020) found this relation to be driven by infants with a later ASD diagnosis (for related work in autistic adults, see Corden et al., 2008), but the association for ELA+ was not significant in the current analysis (see Supplementary Table 3). With the contrasts between LLA and ELA, and more specifically, ELA+ in some cases, further studies should continue to explore whether early threat-relevant biases could be a potential protective factor for infant siblings of children with autism.

The notion of threat-relevant biases as a marker of adaptive functioning was examined in a study by Price et al. (2016) with a sample of children clinically diagnosed with anxiety. Their work used a dot-probe task with fearful-neutral face pairs at an initial time point (mean sample age was 11 years), and then examined symptoms of depression two years later. Price et al. (2016) showed that anxious children with greater patterns of avoidance to threat had the highest levels of depressive symptoms at 2-year follow-up, pointing to an adaptive function for threat-relevant biases in clinically anxious children as is suggested in the current work in ELA. More work is needed though to better understand why threat-relevant biases vs. avoidance might be adaptive for different populations at different stages of development.

The current study found no significant associations for ELA-, and these findings might be related to the known phenotypic heterogeneity of ELA- as a group (e.g., Messinger et al., 2013; Ozonoff et al., 2014). Mixed findings with ELA- have been found across many prior studies (e.g., see Pisula & Ziegart-Sadowska, 2015), with some studies finding similarities between ELA- and ELA+ (e.g., Gammer et al., 2015) and others finding similarities between ELA- and LLA (e.g., Elsabbagh et al., 2013). Upon visual inspection, Figs. 1 and 2 point to a similar mix of findings, with Fig. 1 (18-month Internalizing) suggesting more similar trendlines for LLA and ELA- than for ELA- and ELA+, but Fig. 2 (18-month Atypical behaviors) suggesting more similar trendlines for ELA- and ELA+ than for LLA and ELA-. Further work with larger samples will allow for a better understanding of how ELA- might differentially align with ELA+ and LLA in terms of fear biases and social-emotional development.

The overall pattern of findings from the current study points to increased fear biases associated with worse concurrent and predictive ITSEA measures in LLA (both 6 and 12 months later), and better scores on predictive ITSEA measures 6 months later in ELA. Our past work also found associations between greater 12-month fear bias and better 18-month social behaviors in ELA, but no concurrent associations (Wagner et al., 2020). Work in infancy more broadly, and past work with LLA, has identified both concurrent and predictive associations between social attention and social-communicative behaviors (e.g., Pons et al., 2019; Wagner et al., 2018). More

work is needed to better understand why groups might differ on these concurrent vs. predictive associations, and the differential predictive findings with 18-month outcomes and 24-month outcomes. This pattern is especially striking for Internalizing behaviors in LLA, as significant associations were found with this domain at both 12 months and 18 months, but not at 24 months.

Another question that arises from the current results is why the strongest associations found with ITSEA Domain scores were with the no-shift (NS) fear bias, while the strongest associations found with ITSEA Cluster scores were with the reaction time (RT) fear bias. Studies with younger infants have consistently found biases to fearful faces for both RT and NS measures, with slower latencies to disengage attention and a larger proportion of no-shift trials for fearful as compared to happy and neutral/control faces (e.g., [Peltola et al., 2008, 2009b](#)). In our prior work examining emotion disengagement effects on RT and NS trials in 6-, 9-, and 12-month-olds, we also found effects of emotion for both metrics and age did not interact with emotion ([Wagner et al., 2020](#)). We therefore expect that in this type of paradigm, the RT and NS fear bias scores are capturing overlapping phenomena with fear biases. The present results, however, may suggest that the more subtle slowing of attention to fearful faces relative to the other faces, as captured by RT fear bias, is more relevant in predicting ASD-related characteristics measured by the ITSEA. In contrast, differences in getting 'stuck' on fearful faces relative to the other faces might reflect a more heightened sense of vigilance related to social-emotional abilities more broadly, as captured by the ITSEA Domain scores. It is important to note that one key difference between our studies and the work of [Peltola et al. \(2009b\)](#) is that our current and prior studies classify long latency RT trials (1500 ms or more) as NS trials, in an effort to minimize long RTs from having undue influence on averages calculated for shift latency (for a similar approach, see [Elsabbagh et al., 2013](#)). It is possible that this classification of RT and NS trials might have also had an influence on how these fear biases interacted with ITSEA scores. Future work should continue to ask how RT and NS fear biases, across both methods of calculation, might differentially relate to social-emotional outcomes and how this might change based on attentional biases across the first year.

With preliminary findings supporting differential relations between biases to fearful faces and social-emotional development in infants with and without an older sibling with autism, several important limitations and outstanding questions are important to address. First, although steps were taken to strengthen the analyses conducted, including the use of Bonferroni correction for multiple comparisons and the use of follow-up analyses to comprehensively explore how relations between fear bias and ITSEA scores differed by group, the current group-specific findings should still be considered as preliminary due to small sample sizes.

A second limitation that should be noted relates to the group composition in the current study (which is highly similar to that found in our prior work using this attentional disengagement task, see [Wagner et al., 2020](#)). Across past work studying infants who have an older sibling with ASD, the likelihood of also receiving an ASD diagnosis is found to be near 20% (e.g., [Ozonoff et al., 2011](#)), but in the current sample of 12-month-olds, the percentage of ELA infants classified as having ASD is 42%. In other published work from our group on the same longitudinal dataset, we find recurrence likelihood closer to 20% for a task with less restrictive inclusion criteria (e.g., [Wagner et al., 2018](#)), but in both this sample and that of [Wagner et al. \(2020\)](#) looking at attentional disengagement, an elevated recurrence rate is found. Although it is not clear why the stricter inclusion criteria for valid attentional shift trials might have an influence on the ELA recurrence rate, this will be important for future work with larger samples to further explore.

With the focus of the current work on research questions related to fear biases as they relate to behavior, only infants who passed the strict inclusion criteria for sufficient attentional disengagement data were included. This led to an additional limitation, as the sample did not therefore allow for a systematic look at patterns of ITSEA scores across the full participant sample, as has been explored in work by other groups (e.g., [Raza et al., 2020](#)). Future work with the full participant sample is needed to explore questions of how the ITSEA differs for infants across likelihood group.

One final remaining question that comes from the current study is related to the many potential intrinsic and extrinsic factors that could influence attentional biases, and how these threat-relevant biases might act as a mediator between these factors and later social-emotional development in infants with and without a family history of autism. Prior work with community samples so far has focused on temperamental qualities of the infant, as well as characteristics of the mother, as contributors to attentional biases (e.g., [Fu et al., 2020](#); [Kataja et al., 2020](#); for a review, see [Fu & Pérez-Edgar, 2019](#)), and future work with ELA should incorporate these factors to more comprehensively understand the role of cognitive attentional factors in social-emotional functioning. With a better understanding of the long-term clinical consequences of individual differences in these biases in infancy, research can then explore questions of whether attention modification may provide a useful target to consider for supporting early development, as has begun with other populations, including anxious adults (e.g., [Linnetzky et al., 2015](#)) and older children with ASD (e.g., [Alvares et al., 2019](#); [Wieckowski & White, 2020](#)).

CRedit authorship contribution statement

Jennifer Wagner: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, Project administration. **Brandon Keehn:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – review & editing. **Helen Tager-Flusberg:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Funding acquisition. **Charles Nelson:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Funding acquisition.

Declaration of interest

None.

Data Availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.infbeh.2023.101811](https://doi.org/10.1016/j.infbeh.2023.101811).

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