Published in final edited form as:

J Am Acad Child Adolesc Psychiatry. 2016 March ; 55(3): 188–95.e1. doi:10.1016/j.jaac.2015.11.016.

Enhanced Social Attention in Female Infant Siblings at Risk for Autism

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Abstract

Objective—Sexual dimorphism in autism spectrum disorders (ASD) is a well-recognized but poorly understood phenomenon. Females are four times less likely to be diagnosed with ASD than males and, when diagnosed, are more likely to exhibit comorbid anxiety symptoms. One of the key phenotypic features of ASD is atypical attention to socially relevant stimuli. Eye-tracking studies indicate atypical patterns of spontaneous social orienting during the prodromal and early syndromic stages of ASD. However, there have been no studies evaluating sex differences in early social orienting and their potential contribution to later outcomes.

Method—We examined sex differences in social orienting in 6-, 9-, and 12-month-old infants at high genetic risk for ASD ($n = 101$) and in low-risk controls ($n = 61$), focusing on neurobehavioral measures of function across a spectrum of autism risk.

Results—Results suggest that, between 6 and 12 months of age, a period highly consequential for the development of nonverbal social engagement competencies, high-risk females show enhanced attention to social targets, including faces, compared to both high-risk males and low-risk males and females. Greater attention to social targets in high-risk infants was associated with less severe social impairments, but not with higher levels of social competence at 2 years.

Conclusion—The results suggest an alternate expression of autism risk in females, which manifests in infancy as increased attention toward socially relevant stimuli. This increased attention may serve as a cognitive female protective factor against ASD by providing increased access to social experiences in early development.

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Drs. Chawarska and Shic served as the statistical experts for this research.

K.C., S.M., and F.S. developed the initial idea and design of the study. K.C. and F.S. had full access to the data and take responsibility for the integrity of the data. K.C. performed statistical analysis and takes responsibility for the accuracy of the data analysis. S.M. and K.P. conducted and supervised participant characterization. F.S. supervised technological development and technical aspects of experimental procedure, data acquisition, and processing. L.D. contributed to eye tracking data collection and manuscript preparation. K.C. wrote the manuscript.

Supplemental material cited in this article is available online.

Disclosure: Dr. Shic has received research funding from Hoffmann-La Roche Ltd and Janssen Research and Development, LLC. Drs. Chawarska, Macari, Powell, and Ms. DiNicola report no biomedical financial interests or potential conflicts of interest.

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Keywords

infancy; autism; attention; sex differences; protective factors

INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social interactions and the presence of repetitive behaviors.¹ Females are four times less likely to be diagnosed with ASD than males² and, when diagnosed, display less severe repetitive and restricted behaviors³⁻⁶ and are more likely to exhibit co-occurring anxiety and other internalizing symptoms than males with ASD.^{4,6} These phenotypic sex differences are apparent already in preschoolers with ASD.^{4,5} The mechanisms underlying sexual dimorphism in ASD are not well understood.^{7,8} It has been suggested that the syndrome conceptualization may be biased toward the “male autism phenotype”; thus, our knowledge about sex differences in ASD may be influenced by ascertainment biases associated with current diagnostic criteria and referral practices.^{9,10} Biological factors, however, are also likely to play a role. One of the prominent hypotheses in the field, the genetic heterogeneity hypothesis, suggests that ASD in females may arise from a set of different etiologic, genetic, and epigenetic factors than in males resulting in differences in prevalence and phenotypic expression.¹¹ In contrast, the multiple threshold hypothesis suggests the presence of a female protective effect according to which females may have a higher threshold for reaching affectation status than males: i.e., in the face of a similar genetic liability, females may withstand more significant genetic risk factors than males before reaching criteria for ASD.^{10,12,13} The exact nature of the hypothesized protective or risk factors remains to be elucidated, although both hormonal and sex chromosome dosage mechanisms have been proposed⁸.

One of the early prototypical symptoms of ASD is a limited ability to attend spontaneously to socially relevant stimuli in the context of real-life interactions.¹⁴ Eye-tracking methods have been used to help deconstruct these complex deficits into more elementary processes. Studies typically suggest that some of the reflexive or exogenous facets of social orienting involved, e.g., in detection of faces¹⁵ or gaze cues,¹⁶ appear intact in young children with ASD. However, facets of social attention that are driven endogenously and are concerned with spontaneous selection of processing of social stimuli within complex social contexts (e.g., a face within a complex visual scene or a mouth within an expressively moving and speaking face) are impaired. Compared to chronological and mental age-matched controls, toddlers with ASD look less at the faces of interactive partners,^{17,18,19} at objects attended to by others,²⁰ and at activities performed by others.¹⁹ Individual differences in specific facets of social attention in the second year are associated with severity of impairment 1-2 years later.^{18,19,21,22} Moreover, different facets of social attention to complex social scenes appear to be driven by different latent constructs potentially linked to the limited behavioral relevance of social targets to toddlers with autism and the limited knowledge about these targets.²³ Importantly, as indexed by studies of infants at risk for ASD due to genetic factors, some of the social attention deficits observed in ASD predate the onset of behavioral symptoms.²⁴⁻²⁶ Considering that attention enables learning by channeling limited cognitive

resources toward specific task-relevant targets and contingencies, individual differences in social attention may play a large role in shaping the social cognitive system and its neural substrates in an experience-dependent manner.²⁷ Consequently, the presence of sex-linked attentional biases early in life may channel developmental trajectories toward greater pathology or health.^{21,28}

Prospective longitudinal studies of younger siblings of children with ASD, who are at increased risk for developing the disorder due to familial factors, offer a unique opportunity for examining sex differences in ASD in the first years of life and for advancing the search for protective cognitive and biological factors.²⁹ Approximately 18% of high-risk siblings are eventually diagnosed with ASD,^{29,30} and an additional 25% exhibit a broader autism phenotype (BAP).³⁰⁻³² The major advantage of the infant sibling design relevant to the current study is that it diminishes potential ascertainment biases inherent in studies relying on clinic-referred samples both with regard to severity of impairments and diagnostic ratios, particularly when infants are enrolled in the studies in the first months of life before behavioral symptoms of ASD become apparent.⁵ Here, we prospectively examined sex differences in the development of social attention in infants carrying genetic risk for autism. We focused our investigation on the critical period between 6 and 12 months when social-cognitive skills known to be impaired in toddlers with ASD, such as dyadic engagement and joint attention, begin to develop. This period is considered prodromal in ASD as it precedes the emergence of behavioral symptoms occurring typically during the second year.¹⁴ Based on extant evidence from high-risk infant research,³³ we hypothesized that both high- and low-risk females would show greater attention to socially relevant stimuli as compared to their male counterparts, suggesting the presence of sexual dimorphism across study populations.³⁴ Relatedly, we also hypothesized that high-risk infants would exhibit diminished attention to social targets compared to low-risk infants, reflecting their genetic vulnerability to ASD.^{35,36} Consistent with earlier work on affected toddlers,²¹ we hypothesized that better social attention in HR infants will be associated prospectively with lesser severity of autism symptoms. Considering that the dimension of social disability as measured by the Autism Diagnostic Schedule (ADOS) is distinct from the dimension of social ability as measured by the Vineland Adaptive Behaviors Schedule (VABS),³⁷ we also examined if better social attention in infancy was associated prospectively with higher level of adaptive social functioning. The latter reflects the ability to translate cognitive potential in real-life social interaction skills.³⁸ To decrease the impact of potential diagnostic biases toward a male ASD phenotype,^{7,39} instead of categorical outcomes (e.g., ASD versus non-ASD), we treated autistic traits as continuous,^{10,40} adopting a dimensional approach across a spectrum of autism risk, an approach consistent with the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) recommendations.⁴¹

METHOD

The study was approved by the Human Investigations Committee of Yale University School of Medicine, and written informed consent was obtained from all parents prior to testing. Diagnosis and assessment were conducted at the Yale Child Study Center Toddler Developmental Disabilities Clinic. The eye-tracking procedures and clinical phenotyping were conducted by research staff blind to the participants' risk status.

Participants

The sample consisted of 101 (71 males) younger siblings of children with ASD (high-risk, HR) and 61 (32 males) infants with no familial history of ASD considering 1st or 2nd degree relatives (low-risk, LR) (Table 1). All infants were enrolled in the study by 6 months. Exclusionary criteria were gestational age below 34 weeks, hearing or visual impairment, non-febrile seizure disorders, or known genetic syndrome. Although the prospective high-risk sibling design remains susceptible to gender biases potentially inherent in diagnostic practices,⁹ compared to clinic-referred samples, the design is significantly less prone to ascertainment biases, as infants are enrolled prior to the emergence of behavioral symptoms of ASD.⁵

All infants participated in an experimental study of social attention at 6, 9, and 12 months. The HR infants underwent direct behavioral assessments using the Mullen Scales of Early Learning (MSEL) at 6, 12, 24, and 36 months, ADOS-Toddler (ADOS-T) at 12 and 24 months, and ADOS-G at 3 years. All LR infants were assessed with the same battery at 6, 12, and 24 months. The LR infants with reported or documented delays in the first two years were evaluated directly again at 3 years. Those with no history of developmental concerns were screened for the presence of ASD and other disorders at 3 years, and if they failed the screening, they were assessed directly by the clinical team. Clinical best estimate (CBE) diagnosis was assigned by an interdisciplinary clinical team based on the MSEL and ADOS-G scores and medical/developmental history review. Consistent with earlier reports,^{29,42} 18.8% ($n = 19$) of HR infants were diagnosed with ASD, with female and male recurrence rates of 10% and 22.5%, respectively. The HR non-ASD sample included 82 infants either developing typically ($n = 44$) or exhibiting various developmental delays or the BAP ($n = 38$). In the LR non-ASD group, 8 had atypical and 53 had typical outcomes (global or language delay, subthreshold motor or behavioral issues). An additional 3 LR children were diagnosed with ASD, but they were excluded a priori from the analysis due to the small sample size. Thus, full characterization data were available on all participating infants at 2 years and for HR infants at 3 years. In the HR group, 92% of parents identified their child's race as Caucasian as compared to 87% in the LR group, and the distribution did not differ by group ($X^2[4] = 4.65, p = .32$). There was a significant difference between HR and LR groups in gender distribution, with males more represented in the HR (70%) than in the LR (52%) group ($X^2[1] = 5.22, p = .022$). There were no differences between the risk groups and genders with regard to age at the assessments at 6, 9, 12, and 24 months (Table 1).

Stimuli

Previous work has shown that bids for social engagement consisting of gaze cues and child-directed speech are particularly effective in eliciting ASD-specific attentional response patterns both during prodromal^{24,30} and early syndromal¹⁷ stages of the disorder, and individual differences in response to such cues are related to long-term outcomes with regard to severity of impairment.²¹ The stimulus video was designed to capture the top-down control of visual attention in response to the ebbs and flows of social events. The video contained 15 episodes during which a woman tried to engage the viewer using facial, verbal, and affective cues for social engagement (e.g., by looking at the camera and using child-directed speech or redirecting the viewer's attention to one of the toys using gaze shifts and

child-directed speech; Figure 1a, see¹⁷ for detailed description). There were no artificial breaks in the video to re-engage or re-center the viewer's attention, thus requiring the infants to adjust their gaze patterns depending on context as they would in real life. The scene subtended 27×21 degrees of visual angle, the face 3.9×5.6 , mouth 3.5×2.0 , and each of the toys, 5.8×6.4 .

Apparatus

Gaze trajectories were recorded at a sampling rate of 60Hz using a SensoMotoric Instruments IView X™ RED eye-tracking system. Eye-tracking data were processed using custom software written in MATLAB. The software accommodated standard techniques for processing eye-tracking data, including blink detection, data calibration, recalibration, and region of interest (ROI) analysis.

Procedure

Infants were seated in a car seat in a dark and soundproof room 75cm in front of a 24" widescreen liquid crystal display (LCD) monitor. Each session began with a cartoon video to help the infant get settled. A five-point calibration procedure was then initiated with calibration points consisting of dynamic targets (e.g., a meowing, walking cartoon tiger). Subsequently, each participant was presented with the video described in the Stimulus section.

Data Reduction

The visual scene was divided into several ROIs (see Figure 1b). Variables of interest were proportions of total looking (dwell) time on the entire scene (%Scene) and the proportion of looking time on the person's face (%Face) and on toys (%Toys). The proportion of the looking time (%Scene) was standardized by the total duration of the video displayed; the remaining variables were standardized by the total looking time at the scene. Sessions were excluded if the computed calibration error was equal to or greater than 2 degrees. Moreover, sessions in which infants contributed less than 15% of valid eye-tracking data were excluded from the analysis of %Face and %Toys. In the retained sample, a comparison of the quality of eye-tracking data indicated only a significant effect of age ($F[2, 163] = 6.11, p = .003$), with the calibration error remaining stable between 6 and 9 months ($p = .141$) and decreasing from 9 to 12 months ($p = .002$). There were no effects of gender ($F[1, 158] = .37, p = .546$) or risk status ($F[1, 163] = .11, p = .997$). None of the second- or third-order interactions were significant (all p -values $> .366$). The average calibration error at 6, 9, and 12 months was 0.87, 0.76, and 0.67 degrees, respectively. At 6, 9, and 12 months, data from 37%, 25%, and 14% infants, respectively, were excluded from analysis due to motion- or inattention-related eye-tracker calibration failure. There was no differential dropout by risk status at 6, 9, or 12 months ($X^2[1] = .47, p = .495$; $X^2[1] = 1.31, p = .252$; $X^2[1] = .04, p = .839$, respectively). After these initial exclusions, eye-tracking data from 94 (59 HR, 20 females, and 35 LR, 15 females) 6-month-olds, 107 (68 HR, 22 females, and 39 LR, 14 females) 9-month-olds, and 132 (81 HR, 23 females, and 51 LR, 22 females) 12-month-olds were analyzed.

Statistical Analysis

Primary hypotheses were tested with age (3) x risk status (2) x sex (2) linear mixed models. Severity of ASD symptoms—ADOS Social Affect (SA) and ADOS Restricted, Repetitive Behaviors (RRB) scores—were included into the models as continuous measures of autism symptom severity at 24 months. Planned contrasts were conducted between HR males and females, LR males and females, HR and LR males, and HR and LR females. The magnitude of effects was quantified with Cohen's *d*. Given detected risk group and sex differences in Verbal (V) and nonverbal (NV) developmental quotients (DQ), these measures were included in the models as covariates. All planned contrasts are reported with a Tukey-Kramer correction for multiple comparisons. In alternative analyses, we applied arcsine followed by Box-Cox transforms to data and verified linearity, homogeneity, and residual normality via diagnostic plots and Lilliefors test. Patterns of significance were almost identical. This was expected due to the robustness of linear mixed models.⁴³⁻⁴⁵ For this reason, and to maintain comparability to prior work^{17,23-25} and to aid reproducibility, no transformations on data were used in analyses presented here. Associations between eye-tracking measures and phenotypic characteristics were evaluated using Pearson's *r* correlation coefficient analysis. Data analyses were implemented in SAS 9.3.

RESULTS

Preliminary Analyses

Analysis of developmental skills and severity of autism symptoms revealed an expected pattern of results. An age x risk status x gender analysis of verbal developmental quotient (VDQ) indicated significant effects of age ($F[2, 184] = 131.35, p < .001$) and risk status ($F[1, 168] = 7.41, p = .007 [d = -.30]$), and an age x gender interaction ($F[2, 184] = 4.64, p = .01$). VDQ scores increased significantly between 6 and 12 ($p < .001$) and 12 and 24 ($p < .001$) months. High-risk infants performed more poorly than low-risk infants. Females outperformed males at 12 ($p = .026, d = .56$) and 24 months ($p = .011, d = .45$), but not at 6 months ($p = .257$). No other simple or interaction effects were significant. For nonverbal DQ (NVDQ), there were significant effects of age ($F[2, 184] = 61.25, p < .001$), gender ($F[1, 168] = 8.11, p = .005 [d = .38]$), and risk status ($F[1, 186] = .629, p = .013 [d = -.40]$). The scores increased from 6 to 12 months ($p < .001$) and from 12 to 24 months ($p = .002$). High-risk infants performed more poorly than low-risk infants, and females outperformed males. No other simple or interaction effects were significant. With regard to severity of autism symptoms, analysis of the ADOS-T total algorithm scores indicated a significant effect of age ($F[1, 99] = 26.64, p < .001$), with the ADOS total scores declining from 12 to 24 months. The ADOS-T total scores were significantly higher in HR than LR infants ($F[1, 161] = 8.62, p = .004 [d = .50]$), and females had lower scores than males ($F[1, 161] = .471, p = .031 [d = .62]$). No other simple or interaction effects were significant. Given the observed group differences in verbal and nonverbal outcomes at 24 months, ADOS SA and RRB as well as Mullen VDQ and NVDQ were included in the models as covariates.

Social Attention

First we compared the amount of time the infants spent actively attending to the entire social scene (%Scene). For the full model, see tables S1–S3, available online. There were

significant effects of age ($F[2, 161] = 7.63, p < .001$), gender ($F[1, 153] = 5.27, p = .023$), and risk status ($F[1, 153] = 4.47, p = .036$), and a gender x risk status interaction ($F[1, 153] = 5.42, p = .021$) on %Scene, as well as a significant effect of ADOS SA score ($F[1, 153] = 6.64, p = .011$). No other effects were significant, and the proportion of time spent engaged with the complex visual scene in the first year of life was not related to ADOS RRB ($p = .129$), VDQ ($p = .939$), or NVDQ ($p = .299$) at 24 months. Attention to the scene increased from 6 to 12 months ($p < .001$) across groups (Figure 2a). Planned contrasts indicated that HR females had higher %Scene than HR males ($p = .003, d = .60$) and LR females ($p = .026, d = .39$) (Table 2). HR and LR males did not differ ($p = .999$), nor did LR females and LR males ($p = 1.00$). Greater attention to the scene at 6 and 12 months was associated with lower 24-month ADOS SA scores in the HR group ($t[59] = -.43, p < .001$; $t[81] = -.22, p = .047$), but not in the LR group ($t[35] = .277, p = .107$, $t[51] = -.167, p = .241$). Next, we evaluated if %Scene was associated with the VABS Socialization Scale as an index of social ability. None of the effects at 6 ($r = .18, p > .17$ and $r = .12, p > .48$ in HR and LR groups) and 12 months ($r = .00, p > .96$ and $r = .12, p > .38$ in HR and LR groups) were significant.

An analysis of %Face indicated a significant effect of age ($F[1, 143] = 3.56, p = .031$), a sex x risk group interaction ($F[1, 151] = 4.74, p = .031$), and a significant effect of ADOS SA score ($F[1, 151] = 4.46, p = .036$) at 24 months (Figure 2b). No other effects were significant. There were no significant contributions of ADOS RRB ($p = .690$), VDQ ($p = .551$), or NVDQ ($p = .965$) to the model. Attention to the face increased marginally from 6 to 9 months ($p = .091$) and decreased from 9 to 12 months ($p = .034$), but overall, there were no significant changes in %Face from 6 to 12 months ($p = .989$). HR females exhibited greater attention to the speaker's face than HR males ($p = .048, d = .44$) and marginally higher face attention than LR females ($p = .057, d = .48$) (Table 2). HR and LR males did not differ ($p = .992$), nor did LR females and males ($p = .932$). Greater attention to the face was associated with lower 24-month ADOS SA scores in the HR sample, with the effect more pronounced at 6 months ($t[54] = -.382, p = .005$) than at 12 months ($t[80] = -.19, p = .084$). There were no significant associations between %Face and ADOS SA in the LR group at 6 or 12 months ($t[33] = .269, p = .129$, $t[50] = -.189, p = .189$), respectively. Analysis of associations between %Face and the VABS Socialization score revealed no significant effects at 6 ($r = .21, p > .13$ and $r = .02, p > .87$ in HR and LR groups) or 12 months ($r = .07, p > .52$ and $r = .12, p > .38$ in HR and LR groups).

Finally, an analysis of %Toys indicated a significant effect of age ($F[2, 144] = 8.92, p < .001$) and marginal effect of gender ($F[1, 151] = 3.50, p = .073$), with males looking slightly longer at the objects than females (Figure 2c). No other effects were significant, and there were no significant associations with autistic features or levels of functioning at 24 months. Attention to objects did not change between 6 and 9 months ($p = .955$) but increased between 9 and 12 months ($p = .002$).

DISCUSSION

To the best of our knowledge, this is the first study to prospectively examine sex-related differences in spontaneous social attention in 6-, 9-, and 12-month-old infants at high- and low-risk for ASD. No sex differences were found in the low-risk group on any of the social

attention measures. There was, however, strong evidence for sexual dimorphism in the high-risk group, with girls spending significantly more time attending to social scenes and to the face of an interactive partner than their male high-risk counterparts. Importantly, high-risk girls also displayed greater attention to social stimuli than low-risk girls. These effects were present after the verbal, nonverbal, and social outcomes in both risk groups were considered. In contrast, the verbal, nonverbal, and social impairment scores in our sample conformed to the model in which females generally outperform males, and performance levels were lower in the high-risk compared to the low-risk sample, which is consistent with the findings of a recent multi-site high-risk sibling study.³³ Greater attention to social targets in the first year of life was associated with less severe autism symptoms at 2 years in the high-risk but not in the low-risk group. However, better social attention did not necessarily translate into better social adaptive skills at the age of 2. Between 6 and 12 months, attention to dynamic social scenes and to toys increased with age, while attention to faces remained high and largely unchanged. This developmental pattern reflects, on one hand, consistently high interest in the faces of interactive partners and, on the other, increasing overall attentional capacity and interest in the exploration of complex visual scenes and objects. Taken together, our results suggest that during the highly formative period of early infancy, younger female siblings of children with ASD display a social orienting advantage, and this advantage is associated prospectively with decreased severity of social impairment at 2 years. Lack of association with increased social adaptation suggests that increased attention to interactive partners may predict lesser symptom severity, but not necessarily greater level of social competence among high-risk infants.

The period between 6 and 12 months is marked by the emergence of dyadic engagement, social referencing, and joint attention skills, the social–cognitive skills that are prototypically impaired in toddlers with ASD.¹⁴ This is also a period of rapid specialization in face⁴⁶ and voice⁴⁷ recognition along with development of audiovisual speech perception,⁴⁸ and, considering that learning is an experience-dependent process, even a small alteration in the type and availability of learning opportunities may have cascading developmental effects.^{49,50} Links between overall attention to a social scene in infancy and later developmental outcomes have been reported in typically developing children⁵¹ as well as amongst those with ASD. Specifically, limited orienting to social partners in infancy is associated with later ASD diagnoses amongst high-risk siblings^{24–26} and greater severity of autism symptoms amongst clinic-referred toddlers with ASD.²¹ We hypothesize that the enhanced orienting to social stimuli observed in high-risk females may serve as a protective factor by providing increased access to critical social experiences in early development. Although enhanced social orienting in females may not prevent ASD from emerging in some cases, it may mitigate the deleterious effects of the pathogenic factors associated with ASD, consequently placing high-risk female infants on a different developmental trajectory than high-risk males.

Our study suggests that the attentional system in high-risk female infants is tuned to favor faces and scenes containing people. What might be driving such behavior? A recent study aimed at decomposing the latent structure of gaze behaviors in toddlers with ASD or TD in response to a task identical to that used in the current study revealed that gaze is driven by two sets of orthogonal factors: (1) a non-specific factor related to attention to dynamic social

scenes in general (i.e., looking at or away from the scene), and (2) a set of context-specific factors facilitating selection for processing the most informative social features within the scene (e.g., selecting a face rather than toys when an actress is speaking, or selecting hands rather than face when she performs an action).²³ Compared to TD controls, toddlers with ASD exhibited multilevel differences involving both domain-general and domain-specific factors. Current models of gaze behavior in dynamic environments stress the roles of behavioral relevance (i.e., costs and benefits of gaze behaviors in acquisition of goal-relevant information, linked with the reward system) and prior knowledge (i.e., learned models of the environment) as forces driving attention in service of foraging for survival- or task-relevant information.⁵² In that study, we hypothesized that, while limited attention to social scenes may be due to a core disruption of reward circuitry, the difference in domain-specific factors may reflect limited social learning opportunities conferred by such a disruption. The observed in the current study enhanced performance of female infants at risk, even when compared to low-risk females, may represent early maturation of the system involved in evaluating the behavioral relevance of social stimuli or a compensatory process occurring in response to genetic risk factors related to ASD.^{52, 53} Alternatively, their attentional patterns might represent heightened vigilance toward novel stimuli sometimes observed in infants who later develop anxiety symptoms, relevant here given increased risk for anxiety reported in females with ASD and related disorders.^{4,6} Consistent with this view is the finding that the same genetic abnormality (*SHANK1* deletion) produces an autism phenotype in males but anxiety symptoms in females.¹³ The hypotheses evoking the protective effects of enhanced maturation, presence of compensatory strategies, and anxiety-related mechanisms as well as their role in development of high-risk male and female sibling phenotypes await empirical verification.

Findings from our study advance understanding of sexual dimorphism in the prevalence and expression of symptoms of ASD in high-risk populations. This study also provides new perspectives for genetic and neurobiological research focused on mechanisms underlying risk and protective factors involved in the development of autism symptoms. The findings are relevant to studies of interactions between early experience, brain plasticity, and the ultimate shaping of developmental trajectories. They also inform potential sources of variability and threats to replicability in experimental studies where sex effects go unexamined. Finally, these findings, which highlight specific traits associated with genetic autism risk rather than traits specifically associated with an outcome of autism, may also prove to be of interest to evolutionary biologists who consider trait benefits in special populations. Replication of this work in larger and more diverse samples and extension to other social and nonsocial contexts would contribute to elucidating the attentional mechanisms that influence outcomes in high-risk sibling populations and may suggest potential targets for early intervention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The study was supported by the National Institute of Child Health and Development, P01 HD003008, Project 1 (K.C.), National Institutes of Mental Health R01 MH087554 (K.C.), and the Simons Foundation (187398, Ami Klin).

The authors thank Gabriella Greco, BA, Lilli Flink, BA, Sharlene Lansiquot, BA, Carla Wall, BA, Elizabeth Kim, PhD, and Quan Wang, PhD, of Yale University School of Medicine, for assistance in data collection and manuscript preparation. The authors wish to express their appreciation to the families and their children for their participation.

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A

B

Figure 1.

(A) Frame from video stimulus with (B) regions of interest (ROIs) used in analysis. Note: The ROIs are scene (face + body + toys + background), face, and toys.

Figure 2.

Marginal means ($\pm$ 1 standard error) in proportion of looking at the scene, face, and toys in high- (HR) and low-risk (LR) males and females at 6, 9, and 12 months.

Table 1

Sample Characteristics at 6, 12, and 24 Months

	High Risk		Low Risk	
	Males	Females	Males	Females
N (%)	71 (70)	30 (30)	32 (52)	29 (49)
	6 months			
Age (mo)	6.5 (0.7)	6.4 (0.3)	6.1 (0.4)	6.2 (0.5)
Verbal DQ	76 (14)	76 (14)	83 (8)	77 (17)
Nonverbal DQ	89 (16)	97 (18)	97 (11)	96 (11)
	12 months			
Age (mo)	12.4 (0.6)	12.2 (0.4)	12.2 (0.3)	12.5 (0.8)
ADOS-T Total	10.77 (5.5)	7.95 (5.9)	9.27 (4.2)	7.15 (3.7)
Verbal DQ	82 (17)	90 (18)	87 (18)	96.74 (18)
Nonverbal DQ	109 (12)	116 (10)	114 (13)	117.51 (11)
	24 months			
Age (mo)	24.9 (1.9)	24.4 (1.1)	24.3 (1.1)	24.4 (.6)
ADOS-T Total	7.91 (5.4)	6.84 (5.8)	4.29 (3.1)	4.04 (4.3)
Verbal DQ	105 (24)	113 (20)	113 (17)	123 (20)
Nonverbal DQ	101 (12)	111 (16)	108 (13)	114 (11)

Note: ADOS-T = Autism Diagnostic Observation Schedule – Toddler Module; DQ = Developmental Quotient.

Table 2

Means (SD) for %Scene, %Face, and %Toy in High- and Low-Risk Males and Females Averaged Across 6, 9, and 12 Months

	High Risk		Low Risk	
	Males	Females	Males	Females
%Scene	66 (26)	80 (20)	71 (26)	71 (26)
%Face	65 (20)	73 (16)	67 (18)	65 (17)
%Toy	17 (13)	13 (09)	17 (11)	16 (09)