

Abnormal Magnocellular Pathway Visual Processing in Infants at Risk for Autism

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Background: A wealth of data has documented impairments in face processing in individuals with autism spectrum disorders (ASD). Recently, the suggestion has been made that these impairments may arise from abnormal development of a subcortical system involved in face processing that originates in the magnocellular pathway of the primate visual system.

Methods: To test this developmental hypothesis, we obtained visual perceptual data from 6-month-old infants who were at risk for ASD because they had an older sibling diagnosed with the disorder ("high-risk infants"). To measure sensitivity of the magnocellular (M) pathway and, for comparison, of the parvocellular (P) visual pathway, we employed visual stimuli designed to selectively stimulate the two. Sensitivity data from high-risk infants ($n = 13$) were compared with data from matched control infants (i.e., "low-risk" infants with no family history of ASD, $n = 26$).

Results: On the P pathway stimulus, high-risk infants exhibited sensitivities that were identical to those of control infants. By contrast, on the M pathway stimulus, high-risk infants exhibited sensitivities nearly twofold greater than those of control infants.

Conclusions: Given that ASD and its symptoms are known to run in families, these preliminary results suggest that ASD may be associated with abnormal M pathway function early in infancy, which may aid in early diagnosis of the disorder.

Key Words: Autism spectrum disorders, face processing, infancy, magnocellular, parvocellular, visual system

Autism spectrum disorders (ASD) are pervasive developmental disorders characterized by deficits in a variety of social, communicative, and emotional behaviors (1–3). In addition to these well-known higher level deficits in ASD, there also exists substantial evidence for atypicalities in lower level visual (4–6) and auditory (7,8) perception. Most notably, in the visual domain, it is well documented that individuals with ASD exhibit impairments in face processing (9,10). Given that face processing is a socially relevant aspect of visual perception and that social deficits are a core component of ASD, several researchers have suggested that face-processing deficits and the neural systems that underlie them may play an important role in the development of ASD (11–14).

There are several models of what leads to the face-processing impairment in ASD (see 12 for review). Most relevant to the current study, it has recently been posited that the impairment may arise from abnormal development of a subcortical face-processing system (11). This subcortical system originates in the magnocellular (M) visual pathway and projects to the amygdala (see Discussion for details). The M pathway is one of the three pathways from the eye to the brain, the other two being the parvocellular (P) and koniocellular (K) pathways.¹ The amygdala is a limbic system structure involved in processing emotion, including facial expressions of emotion (e.g., 15,16). It has been suggested (11) that abnormalities of the amygdala (known to exist in individuals with ASD, 17,18) are likely to be responsible

for developmental abnormalities of the subcortical face-processing system. However, it is also possible that the problem originates in the M pathway, which provides the input to the amygdala. This is especially true given that the M pathway develops very early (19,20), and thus early abnormalities in this pathway hold the potential to create a cascade of abnormalities in later developing brain regions downstream, including (but perhaps not limited to) those involved in face processing. In the current study, we tested this "abnormal M pathway" developmental hypothesis by studying M pathway functioning in 6-month-old infants at risk for ASD. The logic behind this approach is described below.

Because ASD cannot currently be diagnosed reliably before 24 months of age (21), a recent way investigators have been studying early stages of development of the disorder has been to track the development of infant siblings of children diagnosed with ASD (22,23). These infants are referred to as "high-risk infants" because their likelihood of developing ASD, ~9% (24), is roughly tenfold to twentyfold higher than that seen in the general population, .2% to .6% (25,26), suggesting a strong genetic component in ASD (27,28). (Note that there are also retrospective approaches to studying early development of ASD [e.g., 29–34]; however, they are potentially limited by parental bias and/or lack of experimental control). One type of analysis performed in these prospective infant studies involves measuring a given behavior in high-risk infants early in development (typically within the first 18 months), waiting until each infant is old enough to be tested reliably for ASD (between 24 and 36 months), and then comparing the early data between infants who did versus who did not develop the disorder. To date, initial results from these analyses suggest that there are social, communicative, and language deficits in high-risk infants who go on to develop ASD, starting as early as 4 months of age (e.g., 35–38).

Another type of analysis from these prospective studies focuses on differences between high-risk infants and low-risk control infants (e.g., 37,39), the latter defined as infants without a family history of ASD. This approach capitalizes on what is referred to as the broader autism phenotype (BAP), i.e., behavioral markers of ASD, such as impairments on social, communi-

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Received September 29, 2006; revised January 9, 2007; accepted February 9, 2007.

¹Because relatively little is known about the K pathway (53,91), we restrict our discussion to that of the M and P pathways.

cative, and cognitive measures (40–43), as well as abnormalities in face processing (13), that are often seen in unaffected relatives of probands with ASD. Like the relatively high recurrence rates in families with an affected child (see above), the BAP phenomenon also suggests a strong genetic component in ASD. With the ultimate goal of revealing the particular genes involved, the concept of an endophenotype has emerged to refer to these measurable traits (physiological, cognitive, or behavioral) that occur more commonly in both affected and unaffected family members than in the general population (44,45, and see 46 for a more comprehensive description of the term and its application to other disorders like schizophrenia). The advantage of exploring an endophenotype of a disorder is that it is thought to be a simpler marker than the full diagnosis (and presumably lies closer to the basic mechanisms underlying the diagnosis), as well as the fact that the inclusion of both unaffected and affected family members increases the subject sample size and thus potentially the sensitivity of the measure.

In the current study, we investigated visual sensory processing in young infants at familial risk for developing ASD in an effort to uncover an endophenotypic marker for ASD. Specifically, we tested the hypothesis that high-risk infants might show abnormal sensitivity for visual stimuli that are detected by the M visual pathway, since this pathway feeds the subcortical face-processing system conjectured to develop abnormally in ASD. To this end, we measured sensitivity to an M pathway stimulus in both high-risk infants and low-risk control infants, and for comparison, sensitivity to a P pathway stimulus was also measured.

Methods and Materials

Subjects

The data from 13 6-month-old high-risk infants contributed to this study (5 female infants, 8 male infants). These infants were recruited through advertisements in the San Diego area, as well as referrals from other laboratories studying autism at the University of California, San Diego (UCSD). The older siblings of the high-risk infants were diagnosed with ASD (autistic disorder; Asperger syndrome; or pervasive developmental disorder-not otherwise specified [PDD-NOS]) by a licensed clinical psychologist or medical doctor not associated with this research, based on DSM-IV criteria (47). They had no known specific neurological or genetic conditions (e.g., fragile X) that could account for their diagnosis of ASD. We also verified the ASD diagnosis of most of the older siblings using research-based methods, specifically, the Autism Diagnostic Observation Schedule (ADOS) (48) and the Autism Diagnostic Interview-Revised (ADI-R) (49), as described further below. Detailed information for each older sibling is presented in Table 1. Each high-risk infant was matched to two low-risk control infants, defined as infants from families with no history of ASD. The match was based on gender, age on the first day of testing, number of days that birth date was pre/post due date, and having an older sibling. Infants in the low-risk control group were recruited from the San Diego area via letters sent to parents, and they were screened through parent report questionnaires for any abnormal medical conditions. We required that biological siblings, parents, aunts, uncles, and cousins of these infants to have never been diagnosed with ASD.

The mean age on the first day of testing was 182.2 days (SD = 4.3 days) for the high-risk infants and 182.1 days (SD = 3.6 days) for the low-risk infants. All infants were screened through parent report questionnaires for family history of color blindness

Table 1. Older Sibling Information for Each High-Risk Infant in Our Study

Subject	Age at Clinical Diagnosis	Clinical Diagnosis	Age at Research Diagnosis	Research Diagnosis
S1	1.6	AD	4.6	AD
S2	4.5	ASP	6.8	PDD-NOS
S3	1.7	PDD-NOS	5.4	PDD-NOS
S4	2.9	AD	5.1	PDD-NOS
S5	2.7	PDD-NOS	4.7	PDD-NOS
S6	2.5	ASP	4.9	AD
S7	2.6	AD	4.4	PDD-NOS
S8	1.5	PDD-NOS	4.8	AD
S9	2.0	AD	3.5	AD
S10	1.3	AD	3.8	AD
S11	~2.0	AD	N/A	N/A
S12	3.2/2.9	AD/AD	N/A	N/A
S13	2.0	AD	TY	TY
S14	4.0	PDD-NOS	7.8	AD
S15	2.3	AD	5.3	PDD-NOS
S16	~2.0	AD	6.5	PDD-NOS
S17	2.8	AD	4.6	PDD-NOS
S18	1.7	AD	4.0	PDD-NOS

Older sibling information is presented for the 13 high-risk subjects in the matched analysis (S1–S13), as well as the additional 5 high-risk infants (S14–S18) included in the nonmatched analysis. Original clinical diagnoses were made when the children were typically under age 3 by a variety of clinical professionals in the community. The research diagnoses were based on the algorithms of the Autism Diagnostic Observation Schedule and Autism Diagnostic Interview-Revised and clinical judgment. For some subjects, there was a difference between the original clinical diagnosis and later research diagnosis, which is consistent with previous studies demonstrating that change in diagnosis is most likely to occur between the ages of 2 and 5 (92,93). Subject S12 had two older siblings with ASD and thus information is provided for both. AD, autistic disorder; ASP, Aspergers syndrome; N/A, not available for research diagnosis; PDD-NOS, pervasive developmental disorder not otherwise specified; TY, too young for research diagnosis.

(since this study used chromatic stimuli, see below). All infants met a minimum number of trials criterion (200), and the mean number of trials obtained for high-risk infants (267, SD = 27.8) and low-risk infants (263, SD = 31.6) was not different ($p = .76$). Testing was typically completed in 2 to 3 days (each day's session lasting 20 to 40 minutes). In accordance with guidelines at UCSD, each parent in our study signed a consent form to have their infant participate.

These subject data were drawn from a larger sample (18 high-risk infants and 132 low-risk control infants), where number of days that birth date was pre/post due date and having an older sibling were not matched between groups.² The data from this larger nonmatched sample were nearly identical to those from the smaller, matched sample. Detailed information for each older sibling in this nonmatched sample is presented in Table 1.

Stimuli

Because neurons of the primate M and P pathways have distinct visual response properties, there are several different visual stimuli that, in theory, could be used to separately assess

²Note that the low-risk infants chosen for our matched analysis (consisting of 13 high-risk and 26 low-risk infants) were selected by a naïve laboratory assistant who did not have access to the performance data. This assured that there was no bias in the selection. Also note that we were only able to find matched control subjects for 13 of the 18 high-risk infants (for example, because some of the high-risk infants were quite premature), which is why the number of high-risk infants is lower in our matched, as compared with our nonmatched, analysis.

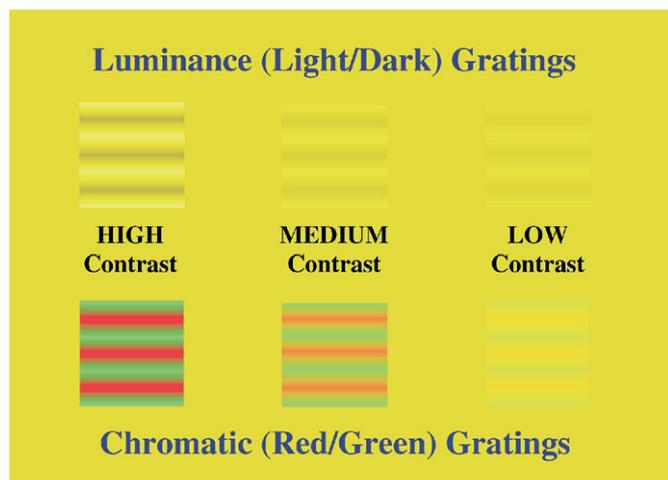


Figure 1. Stimuli. Luminance (light/dark) and chromatic (red/green) gratings. These stimuli were presented at different contrasts (three shown here) to obtain contrast sensitivities.

the two (see 50 for review). Relevant to the current study, neurons of the M pathway exhibit high luminance contrast (light/dark) sensitivity, yet low chromatic contrast (red/green) sensitivity, while neurons of the P pathway exhibit the converse, i.e., high chromatic, low luminance sensitivity (51–53). Thus, like our previous studies of typically developing infants (19,54), we obtained chromatic and luminance contrast sensitivities as a way of measuring the integrity of M and P pathway functioning, respectively.

Our stimuli consisted of chromatic (red/green) and luminance (light/dark) horizontally oriented sinusoidal gratings, as shown in Figure 1. They were presented on a Nanao F2-21 video monitor (1152 × 870 pixels, 75 Hz) (Eizo Nanao Technologies Inc., Cypress, California) driven by a PowerMac 7100 computer (Apple Computer, Inc., Cupertino, California) and viewed from a distance of 38 cm. Chromatic gratings varied only in chromaticity, i.e., the red and green stripes of the grating were equiluminant.³ Luminance gratings varied only in luminance, i.e., the light and dark stripes of the grating were of the same chromaticity (see 19 for further details). Chromatic and luminance gratings subtended 11.1° by 11.1° (a total of three cycles), were presented at a spatial frequency of .27 cycles per degree, and moved (upward or downward) at a temporal frequency of 4.2 Hz with direction counterbalanced across trials. These specific spatial and temporal frequencies were chosen because they are near optimal for young infants (e.g., 19,55–57), and our choice of moving, rather than counterphase, gratings was based on the finding that infants are more sensitive to the former (57).

Forced-Choice Preferential Looking Paradigm

Infants' contrast sensitivity to the chromatic and luminance gratings was assessed using the forced-choice preferential looking (FPL) technique (58), as described in detail previously (59). The FPL technique relies on the fact that infants prefer to look at a patterned stimulus on one side of a display rather than a uniform field on the other side. In our study, each trial began with a small orienting stimulus (consisting of a rotating figure) presented in the center of the uniform background display to get the infant centrally focused. At that point, either a chromatic or

luminance grating appeared on the video monitor, centered 15° to the left or right of monitor center, with contrast ramped on in the first 240 msec (to avoid an abrupt stimulus onset). Chromatic or luminance gratings were presented randomly across trials. Stimulus contrast was also randomized across trials (luminance = 1.25% to 80% contrast; chromatic = .30% to 24.7% contrast), with contrast defined in terms of cone contrast, i.e., the amount of response modulation produced in the long-wavelength-selective and medium-wavelength-selective cones in the eye (see 19 for methodological details).

On each trial, an adult experimenter (highly trained in the FPL method), who held the infant up 38 cm from the monitor, used the infant's head turning and eye gaze behavior (viewed with a video camera aimed at the infant's face) to judge the (left vs. right) stimulus location. This judgment was made after each trial (i.e., in real time) and computer beeps provided feedback as to whether the judgment was correct/incorrect. The rationale behind this paradigm is as follows: because the background luminance (12.6 candela [cd]/m²) and chromaticity ($x = .478, y = .425$ in International Commission on Illumination [CIE] color space) of the monitor is the same as the mean luminance and chromaticity of both the chromatic and luminance gratings, if the gratings are below contrast threshold, they simply blend into the background and the entire video monitor appears uniform. At that point, FPL performance should fall to chance (i.e., 50% correct). Conversely, for contrasts the infant can detect, FPL performance should yield performance >50% correct. A picture of the FPL setup is presented in Figure 2.

Visual Data Analyses

These FPL studies yielded performance data that went from 50% to 100% correct as a function of increasing contrast. To obtain luminance and chromatic contrast thresholds, for each infant, psychometric curves were fit to the data points (separately for chromatic and luminance data) using Weibull functions and maximum likelihood analysis (60,61), and contrast threshold was



Figure 2. Forced-choice preferential looking (FPL) technique used in the current study. On each trial, the grating stimulus appears on the left or right side of the display and an adult experimenter uses the infant's head-turning and eye gaze behavior (viewed with a video camera aimed at the infant's face, projected onto the camera monitor above) to judge the stimulus location. Note that the adult experimenter is blind to the stimulus location, because a piece of cardboard blocks her view of the video monitor. Above chance (i.e., >50% correct) performance indicates an ability of the infant to detect the stimulus.

³The chromatic grating was set to the mean equiluminance point determined for 24 adult subjects tested with motion photometry (19).

calculated as the contrast yielding 75% correct performance (i.e., halfway between 50% and 100%). Contrast sensitivity was then determined from the inverse of threshold (i.e., sensitivity = 1/threshold) and then logged, because log, but not linear, sensitivity values conform to a normal distribution (19). In addition to determining absolute sensitivity, we also computed a chromatic versus luminance difference score for each infant: log luminance sensitivity – log chromatic sensitivity. The advantage of this difference score is that it factors out effects of attention/alertness (which could differ from infant to infant and/or between subject groups), providing a metric of the relative sensitivity to the two stimulus types.

Cognitive and Motor Development/Autism Assessments

To assess cognitive and motor development, infants were tested using the Mullen Scales of Early Learning (62), which is administered by a trained experimenter and evaluates cognitive/motor development. Note that we do not have Mullen Scales of Early Learning data from all subjects (matched analysis: 8 high-risk and 10 low-risk control infants, nonmatched analysis: 11 high-risk and 46 low-risk control infants). This is because at the beginning of our project, we obtained parent report data on their infant's development via the Ages and Stages Questionnaire (ASQ) (63). However, we have since switched to the Mullen Scales of Early Learning because they are a more objective measure of cognitive/motor performance. The results of the Mullen Scales of Early Learning data revealed a small and nonsignificant performance difference between high-risk and low-risk infants (matched analysis: high-risk infants performed 4.4% lower, $p = .10$, one-tailed t test; nonmatched analysis: high-risk infants performed 3.1% lower, $p = .13$, one-tailed t test). These Mullen Scales of Early Learning data, which suggest no cognitive/motor delay in the high-risk group, are in line with negative findings comparing 6-month Mullen Scales of Early Learning data between infants who do versus who do not develop ASD (38), as well as from studies reporting no global cognitive delays in siblings of children diagnosed with ASD (64,65).

At both 24 and 36 months, all children are assessed for ASD with the Autism Diagnostic Observation Schedule (ADOS), which is a play-based assessment designed to elicit behaviors (or lack of behaviors) associated with a diagnosis of ASD. If the child's ADOS score falls above the cutoff for ASD, the Autism Diagnostic Interview-Revised (ADI-R), which is a parent interview, is administered. Also, at 24 and 36 months, all children are assessed using the Preschool Language Scales (PLS-IV) (66), which measures expressive and receptive language skills, as well as the Mullen Scales of Early Learning. The final ASD diagnosis is dependent on the results from all of these assessments (ADOS, ADI-R, PLS-IV, Mullen Scales of Early Learning).

Of the 18 high-risk infants in our study (13 in the matched analysis, 5 additional infants in the nonmatched analysis), 12 have been tested for ASD at 24 months or at both 24 and 36 months (5 are not old enough to be tested and 1 has moved away). None has received a positive ASD diagnosis. Based on statistics of recurrence (9%), of the remaining seven untested infants, none or one is expected to develop ASD. For this reason, we believe that any observed abnormalities in our high-risk group reflect the broader phenotype of autism rather than being driven by infants who will later be diagnosed with autism. (Note that of the 26 low-risk infants in the matched analysis, 6 have been tested and are negative for ASD. The chance for ASD in the other 20 infants, who were not tested either because they

were not old enough or could not be brought back in, is extremely low). However, two other infants in our study (one low-risk infant and one high-risk infant) were diagnosed with autistic disorder at both 24 and 36 months of age in our laboratory and by a licensed clinical psychologist not associated with our research. Note that the data from these two infants were not included in the group analyses but, rather, were analyzed separately (see Results).

Results

Shown in Figure 3A are group mean log luminance and chromatic contrast sensitivities for 13 high-risk infants (white bars) and 26 low-risk matched control infants (grey bars). The results of a two-factor analysis of variance (ANOVA) (1 = subject group, 2 = stimulus type [luminance vs. chromatic]) yielded no significant main effects. However, the interaction between subject group and stimulus type was significant [$F(1,37) = 10.45$, $p = .0026$]. As can be seen in Figure 3A, this interaction was driven by the fact that chromatic contrast sensitivity was statistically indistinguishable between groups ($p = .45$), while luminance contrast sensitivity was significantly greater in the high-risk group by 1.82-fold (i.e., .260 log units, $p = .0313$, two-tailed t test). Note that the enhanced luminance sensitivity strongly suggests that the observed group differences were not driven by some sort of general delayed development in the high-risk group (because a delay would predict the opposite result, i.e., relatively poor luminance contrast sensitivity). Along a similar line, group differences cannot be due to differences in attention or alertness between groups, because any attention effects would be expected to alter both luminance and chromatic sensitivity, which was not the case.

To more directly examine group differences in relative sensitivity to luminance versus chromatic contrast, a difference score (log luminance sensitivity – log chromatic sensitivity) was obtained for each infant and then averaged across infants. Difference scores are plotted in Figure 3B. As would be expected from the data presented in Figure 3A, the mean difference score for the high-risk group (.149) was markedly and significantly higher than that of the control group (–.192). Frequency histograms for difference scores plotted separately for low-risk infants (Figure 3C) and high-risk infants (Figure 3D) indicate that group differences were not driven by outliers in the high-risk group but, rather, are best represented by a shift in the overall distributions. (See Supplement 1 for nearly identical results obtained from the larger, nonmatched subject sample).

To date, two infants in our study have been diagnosed with autistic disorder (see Methods and Materials). Their data were therefore not included in the group means but, rather, were analyzed separately. One of these infants (Figure 3, grey circle), who was a low-risk infant, exhibited high luminance contrast sensitivity, 1.9-fold (i.e., .270 log units) greater than the mean for control infants, yet his chromatic contrast sensitivity was close to the mean for control infants. Accordingly, his difference score (.147) was higher than the mean for control infants. (Note that his data were close to the mean of the high-risk group). The other infant, who was a high-risk infant (Figure 3, white triangle), exhibited luminance sensitivity near the mean for control infants and chromatic sensitivity lower than the mean for control infants. However, like the other infant diagnosed with autistic disorder, his difference score (–.077) was substantially higher than the mean for control infants. The differences we observed between the two infants who went on to develop autistic disorder are

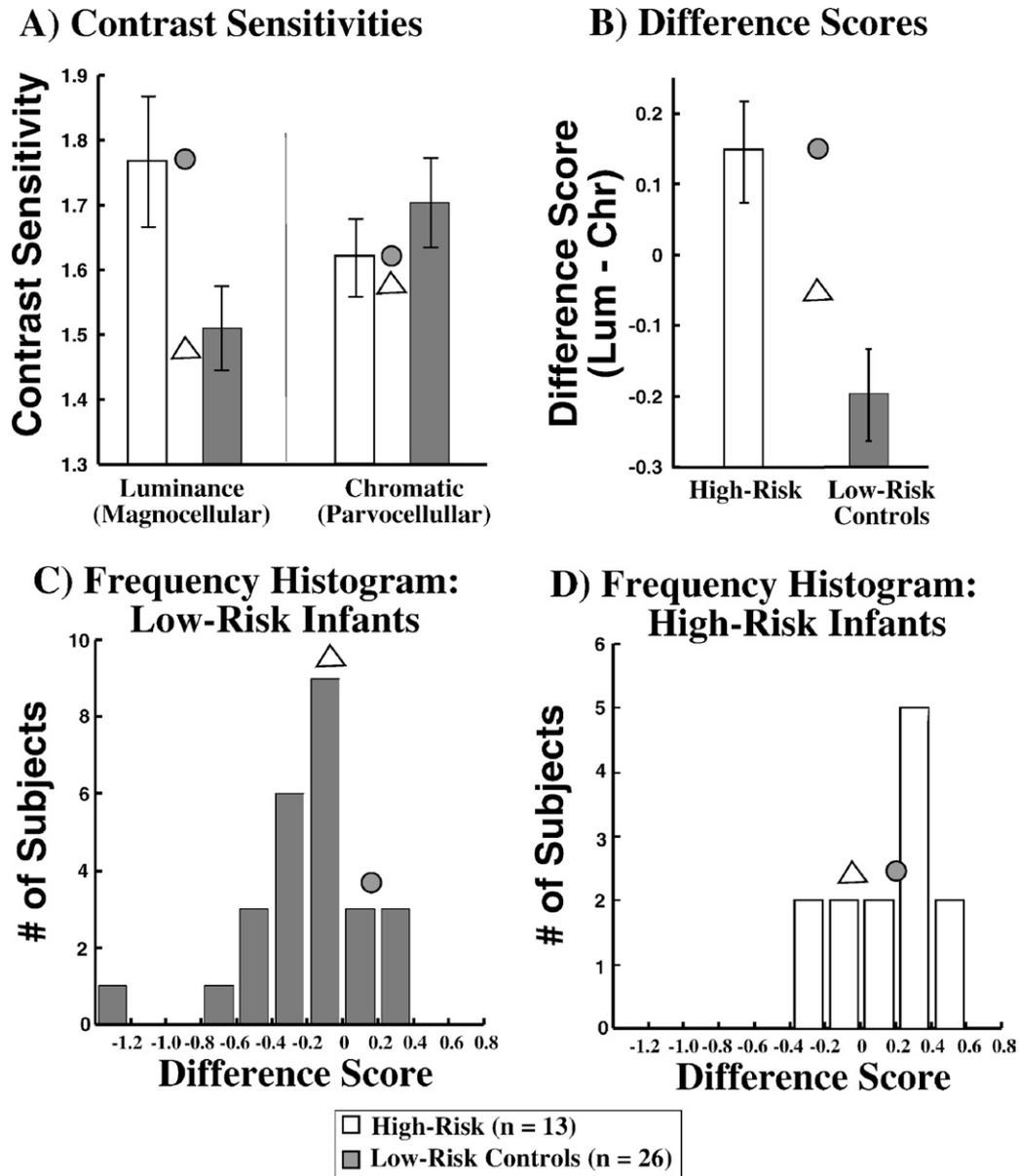


Figure 3. Sensitivity data. **(A)** Log contrast sensitivity for luminance (magnocellular [M] pathway) and chromatic (parvocellular [P] pathway) stimuli for high-risk (white bars) and low-risk control (grey bars) infants. **(B)** Difference scores (log luminance sensitivity – log chromatic sensitivity). Error bars denote standard errors of the means. **(C)** Frequency histograms of low-risk infants for difference scores. With the exception of one low-risk infant (far left in graphs), all low-risk infants fell within 1.7 SD from the mean. We kept the data for this low-risk outlier, whose difference score was 3.3 SD away from the mean, because both his luminance and chromatic contrast sensitivity were within 3 SD of the mean. **(D)** Frequency histograms of high-risk infants for difference scores. All high-risk infants fell within 1.5 SD from the mean for this group. Both groups' data are fairly normal (although the sample size in the high-risk group is too small to ascertain). These frequency histograms suggest that group differences are not driven by outliers in the high-risk group. The grey circle and white triangle represent data from a low-risk control infant and a high-risk infant, respectively, both of whom were later diagnosed with autistic disorder. The data from these infants, which are not included in the group means, are also not outliers.

perhaps not surprising, as we know that there is considerable variability in ASD and even evidence for etiological subtypes (67). More data from infants who go on to develop ASD will be required to determine the significance of intersubject differences.

Discussion

The data from our study of high-risk infants provide preliminary evidence that familial risk for ASD is associated with abnormal processing of luminance contrast in early infancy. Because luminance sensitivity is mediated by the M visual

pathway, these results suggest that abnormal M pathway function may be an endophenotypic marker for ASD. It is important to point out that although the current study observed enhanced luminance sensitivity in high-risk infants, this should still be considered reflective of an abnormality of the M pathway, one that could lead to atypical development of areas that receive input from the M pathway.

Given that our results reflect early developmental abnormalities in M pathway processing associated with ASD, we suggest that such abnormalities might be tied to the face-processing

deficits observed in ASD (10,11) and their family members (13). In line with this notion, Schultz (11) suggested that the face-processing deficit in ASD may arise from abnormal development of a subcortical face-processing system thought to be important for providing an emotional signal to orient to faces. This system projects from the eye to the amygdala, a limbic system structure involved in processing emotion, including facial expressions of emotion (e.g., 15,16). The amygdala, in turn, makes reciprocal connections with the cortical face-processing system in temporal visual cortex (68). In support of the existence of this subcortical face-processing system, it has been shown that the amygdala can be very rapidly activated by faces (69) and that it can be activated in the absence of input from visual cortex (70–72). Because very young infants are believed to rely on the subcortical face-processing system before the more sophisticated cortical face-processing system has fully developed (73), abnormalities in the subcortical system early in development could hinder development of normal face processing.

Schultz (11) suggested that abnormalities of the amygdala are likely to be responsible for developmental abnormalities of the subcortical face-processing pathway system, since there are known structural abnormalities of the amygdala in ASD (17,18). However, it is also possible that the problem originates in the M pathway, which provides input to the amygdala. Specifically, anatomical studies in primates have shown that the M pathway (far more so than the P pathway) provides input to the superior colliculus (74,75, see 76,77 for similar findings in cats), which, in turn, projects to the amygdala (78–80).⁴ Thus, abnormal M pathway processing early in development could disrupt the normal development of the subcortical face-processing system.

In addition to the hypothesis outlined above, it is possible that abnormalities in M pathway processing in early infancy may affect visual processing of face (and perhaps other social) stimuli in a more stimulus-driven way, for example, by attracting infants to attend to certain types of visual stimuli at the expense of attending to faces or to attend to less socially relevant aspects of the face (like the moving mouth) rather than the eyes (81,82). We should also note that abnormalities in M pathway processing in early infancy could be tied to the known abnormalities in motion processing, and in particular biological motion processing, seen in ASD (e.g., 83–85, see 5 for review), since the M pathway provides the bulk of the input to motion-processing areas within the dorsal visual cortex (86). Whatever the exact mechanism may be, we believe that M pathway abnormalities associated with ASD could alter the visual world of infants from families with ASD, putting them at risk for visuoperceptual abnormalities, which, in turn, could lead to higher level deficits in visual, social, communicative, and emotional behaviors associated with ASD.

In summary, the current study suggests there are abnormalities in the M visual pathway in the first year of life associated with ASD, which may be an endophenotypic marker for the disorder. The M pathway abnormality appears to be one of enhanced sensitivity, which is opposite to the decreased perceptual sensitivity associated with M pathway function reported for dyslexia and Williams syndrome (e.g., 87,88), suggesting that our results are unlikely to be related to a general dysfunction shared by several developmental disorders. Interestingly, recent psycho-

physical studies in children (youngest age tested = 9 years) and adults with ASD have reported normal M pathway functioning (89,90). Together with the current findings, we suggest that abnormalities in the early-developing M pathway could have negative consequences for neural areas that receive input and rely on the M pathway during a critical period of development, even if the M pathway attains normal functioning later in life. We should note, however, that the relevant factor might not be abnormal M pathway processing *per se* but, rather, an abnormal balance between development of the M and P pathways.

We are currently tracking the development of the infants in our study to see whether M versus P pathway function correlates with assessments of face processing, as well as other assessments of cognitive, social, communicative, and emotional behaviors later in life. From a clinical standpoint, we hope that the visual sensitivity measure of the current study, used in combination with other measures, could aid in early diagnosis of ASD.

This research was supported by grants from the M.I.N.D. Institute and the National Alliance for Autism Research (KRD, IJC) and a M.I.N.D. Institute Scholars Award (JPM). JPM was supported, in part, by a National Science Foundation (NSF) traineeship (DGE-0333451, Principal Investigator G. W. Cottrell).

There are no conflicts of interest, financial or otherwise, related directly or indirectly to the submitted work.

We thank all of the families for their participation in the study, Karen Burner and Lisa Tully for assistance with the data collection, and Dr. Rain Bosworth for statistical assistance. We are especially grateful to clinical psychologist Dr. Natacha Akshoomoff for providing training for, and assistance with, the collection of clinical assessment data and for many helpful discussions.

Supplementary material cited in this article is available online.

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⁴Note that P pathway information can, in theory, reach the amygdala via input from face-processing networks in visual cortex (that receive ample P pathway input). However, given the proposed immaturity of the cortical face-processing system early in development (73), cortical connections to the amygdala carrying P pathway signals would be expected to be relatively limited.

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