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# Atypical Faces vs. Object Processing and Hemispheric Asymmetries in 10-Month-Old Infants at Risk for Autism

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## Abstract

**Background—**Previous studies have documented atypicalities in face/object processing in children and adults with autism spectrum disorders (ASD). To investigate whether such atypicalities may reflect a genetically-mediated risk factor present early in development, we measured face/object processing in 10-month-old "High-Risk" infants, who carry some of the genes associated with ASD because they have an older sibling diagnosed with the disorder.

**Methods—**We employed event related potentials (ERPs) to measure cortical responses to pictures of faces and objects, the objects being pictures of toys. Latencies and amplitudes of four ERP components (P100, N290, P400 and Nc) were compared between 20 High-Risk infants and 20 Low-Risk controls (infants with no family history of ASD).

**Results—**Responses to faces vs. objects differed between High- and Low-Risk infants, for the latencies of the N290 and P400. Differences were driven by faster responses to faces than objects in Low-Risk, but not High-Risk, infants (P400), and conversely, faster responses to objects than faces in High-Risk, but not Low-Risk, infants (N290). And, *object* responses were faster in High-Risk than Low-Risk infants (both N290 and P400). Left vs. right hemisphere responses also differed between High- and Low-Risk infants, for the amplitudes of the P100, N290 and P400; collapsed across faces/objects, Low-Risk, but not High-Risk, infants exhibited hemisphere asymmetries.

**Conclusions—**Genetic risk for ASD is associated with atypical face vs. object processing, and an atypical lack of hemispheric asymmetry, early in life. These atypicalities might contribute to development of the disorder.

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Note that differences between means observed in the grand averaged waveforms (Figure 1) vs. subject group means (Figure 2) result from the fact that grand averages get compressed due to variation in amplitude and latencies across subjects. Because the statistics are conducted on values that make up the subject group means, the group means are a more accurate representation of the results than the grand averages.

Akin to the N290 latency result of the current study, Webb et al. reported that the N290 *amplitude* response to objects was larger in ASD, than in typical, children. Note, however, they were referring to the absolute (positive) value of the N290 being larger in ASD children. Because the N290 is a *negative*-going component, it is probably more proper to describe their result as showing that the N290 response to objects is larger (i.e., more negative) in typical, than in ASD, children. In any event, their results show that the N290 amplitude in ASD children differs from that of typical children for objects, but not faces.

**Keywords**

autism spectrum disorders; face processing; hemispheric asymmetry; event-related potentials; endophenotype

Autism spectrum disorders (ASD) are pervasive developmental disorders characterized by impairments in social interaction and communication and the presence of repetitive behaviors and restricted interests (1,2). In addition to these well-described hallmarks of ASD, there also exists substantial evidence for atypicalities in visual perception (e.g., 3–5) and auditory perception (e.g., 6,7). Most notably, in the visual domain, it is well known that individuals with ASD often exhibit impairments in tests of face perception (e.g., 8–10, see 11,12 for reviews), and abnormal cortical responses to pictures of faces (e.g., 13–18 but cf. 19). In contrast to these reported impairments in face processing, there are several reports that young children with ASD show normal or even enhanced processing of non-face objects (e.g., 20–25).

Most relevant to the current study, a number of event-related potential (ERP) studies have documented atypical cortical responses to faces vs. objects in individuals with ASD. In typical adults, there is a face sensitive ERP component, the N170, recorded over occipital and temporal scalp locations, which is consistently larger and faster in response to face vs. objects (e.g., 26–28). By contrast, in adults with ASD, the N170 has been shown to exhibit the reverse pattern, i.e., faster responses to objects than faces, and direct group comparisons show that N170 responses to faces are slower in ASD, than in typical, adults (29). Atypicalities have also been reported in children with ASD. In typical infants/children, there are two components that have each shown some degree of face sensitivity: the N290 and the P400 (30–32), which are thought to merge together during development to produce the adult N170 (31,33). Like the results from adults with ASD, the N290 face/object responses of 3- to 4-year old children with ASD have been shown to differ from those of typically developing children (34). While the N290 of typical children shows faster responses to faces than objects, the N290 of children with ASD shows faster responses to objects than faces. And, direct group comparisons show that N290 responses to faces are slower in ASD, than in typical, children. In addition to atypicalities in face vs. object processing, the results of the above-described adult/children studies show less hemispheric asymmetry of the N170/N290 amplitude (data collapsed across faces and objects) in ASD, than in typical, individuals. In sum, these ERP studies reveal atypical face vs. object processing, and atypical hemispheric processing, in ASD, which can be observed by three years of age.

Although there is no clear consensus about the origins of face/object atypicalities in ASD (see 35,36), there is speculation that they are *genetically*-mediated. In support of this possibility are studies showing atypical face processing in first-degree family members of individuals with ASD, specifically, parents of children with ASD (37,38, and see 39 for commentary), and siblings of children with ASD (mean age ~12 years, 40,41, but see 42). Because of the strong (but complex) genetic contribution in ASD, these family members are likely to carry some of the genes associated with ASD, and thus their face processing atypicality is believed to reflect a genetic predisposition that runs in families of ASD. Recently, the concept of an "endophenotype" in ASD has emerged to refer to a measurable trait (like face processing atypicality) that occurs more commonly in both individuals with ASD and their family members (i.e., without ASD) than in the general population (e.g., 43,44 and see 45 for a more comprehensive description of the term and its relevance in other disorders). Note that while an endophenotype is considered a genetically-mediated risk factor for a disorder, by definition, its presence alone is not thought to correlate with the presence of the disorder. With this in mind, there are several ways that an endophenotype could be associated with development of ASD. First, it may be that an endophenotype is more severe in individuals with ASD than in

family members without ASD. This notion is consistent with the report of milder versions of the hallmarks of ASD in family members, referred to as the "broader autism phenotype" (see 46–49). Second, the severity of an endophenotype may be similar between individuals with ASD and their family members without ASD, but what leads to the development of ASD is an inability to compensate for the endophenotype (often referred to as "lack of resilience" in the developmental disorder literature, see 50,51 for reviews). This lack of compensation could be in the form of being deficient in some critical biological protection factor (e.g., hormones or a particular gene) or an inability to compensate at the behavioral level (e.g., because of a personality trait or temperament). Third, developing ASD may result from possessing a critical number of different endophenotypes, even if each on its own is mild.

Given that atypical face/object processing is an endophenotype in ASD, it is of interest to determine when in development it emerges. To this end, we tested face/object processing in 10-month-old "High-Risk" infants, i.e., infant siblings of children diagnosed with ASD (see 52–54). Their risk of developing ASD, 5 – 10% (55,56), is roughly 10- to 20-fold higher than that seen in the general population, 0.2 – 0.6% (57,58). And, as explained above, even High-Risk infants who never develop ASD are likely to exhibit differences compared to controls, i.e., "Low-Risk" infants from families without history of ASD. Indeed, several studies of High-Risk infants (who were known to not have developed ASD or were too young to be tested for ASD) have shown that they differ from Low-Risk infants in visual responses (23,59–61), motor activity (62,63), social interactions (64–70), and language skills (62,68,69,71–73). And, High-Risk infants who do go on to develop ASD often exhibit more severe atypicalities on these same measures (visual responses: 23, 53, motor activity: 53, 74, social interactions: 53, 75 and language skills: 53, 72–74, 76, 77).

In the current study, we used the same ERP paradigm employed in previous studies of adults and children with ASD (29,34) and parents of children with ASD (37). Like these previous studies, our results reveal atypical face vs. object processing, and atypical hemispheric processing, in 10-month-old infants at genetic risk for developing ASD, revealing potential endophenotypes for ASD early in development.

## Methods

### Subjects

High-Risk infants (defined as infants with an older sibling diagnosed with ASD) were recruited through advertisements in the San Diego area as well as referrals from other laboratories studying ASD at UCSD. The older siblings of the High-Risk infants were diagnosed with ASD (Autistic Disorder, Asperger's 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-TR criteria (1). They had no known specific neurological or genetic conditions (e.g., Fragile X, Rett Syndrome) that could account for their diagnosis of ASD. For each case, we verified the ASD diagnosis of the older sibling using 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 (78), and the *Autism Diagnostic Interview-Revised (ADI-R)* (79), which is a parent interview. Detailed information for the older sibling of each High-Risk infant whose data contributed to the results is presented in Table 1. Low-Risk infants (defined as infants from families with no history of ASD, i.e., no biological siblings, parents, aunts/uncles, or cousins diagnosed with ASD) were recruited from the San Diego area via letters sent to parents. All subjects were screened through parent report questionnaires for any abnormal medical conditions. In accordance with UC San Diego guidelines, the parent of each subject in our study signed a consent form to participate. Parents were asked to bring in their infant for the current study at 10 months of age.

Data from a total of 20 Low-Risk and 20 High-Risk 10-month-old infants contributed to the results in this study. The two subject groups, which were drawn from a larger sample of infants, did not differ on: (A) age on first day of testing (High-Risk = 306.5 days ± 14.5, Low-Risk = 302.9 days ± 14), (B) gestational period, based on number of days that birth date was pre/post due date (High-Risk = 5.6 days early ± 8.6, Low-Risk = 2.5 days early ± 8.1, see 80 for discussion of why this factor might affect visual measures), (C) proportion of females (High-Risk = 40%, Low-Risk = 45%) and (D) total number of retainable trials (High-Risk = 47.5 trials ± 20.1, Low-Risk = 44.1 trials ± 14.5). Detailed information about the Low- and High-Risk groups, including retention rates, sample selection and outcome assessments conducted at 24 and 36 months, is presented in Supplement 1. Note that because the outcome of nine of our 20 High-Risk infants is currently unknown, we cannot rule out the possibility that differences observed between our High-Risk and Low-Risk sample of infants may be driven by High-Risk infants who are destined to develop ASD. We think this unlikely, however, because our statistical tests indicate normality in the ERP data and no outliers (defined as subjects whose data fall > 3SD outside the mean). Still, it will be important to determine whether infants who go on to develop ASD differ on our ERP measure from those who do not. Note that we have had three infants develop ASD, which is currently not enough to investigate this question. Data from these three ASD infants are *not* included in the current analyses, and instead will be presented in a future report when we have more data from infants in this category. Thus, at the current time, differences observed between our High-Risk and Low-Risk sample of infants should be viewed as reflecting the endophenotype of ASD (i.e., traits that run in individuals with ASD and their family members) rather than reflecting predictors of developing ASD *per se*.

## Stimuli

Stimuli consisted of four pictures, a familiar and unfamiliar face and a familiar and unfamiliar object (the object being toys), which was motivated by the design of a previous ERP study in children with ASD (81). The “familiar” face was the mother’s face (neutral expression, earrings and other jewelry removed) and the “unfamiliar” face was another mother’s face. The “familiar” object was the infant’s favorite toy and the “unfamiliar” object was another infant’s favorite toy (verified by the mother to be unfamiliar). (Only toys without faces were employed). The pictures were taken with a Canon 5.0 megapixel digital color camera against a grey background. They were scaled in size so that when presented on the video monitor positioned 65 cm away from the subject, the faces/toys subtended approximately 13.8 × 13.8 degrees of visual space, and were positioned in the center of a background subtending 24.6 × 18.3 degrees. The mean luminance of all stimuli was approximately 24.9 $cd/m^2$. Results from fast fourier transform (FFT) analyses (e.g., 82, 83) showed that faces and objects were equated in terms of spatial frequency makeup, although objects had more contrast than faces (see Supplement 1).

## ERP Recordings and Analyses

Event-related potentials (ERPs) were recorded from 124 electrodes using a 128-channel Geodesic Sensor Net (Electrical Geodesics, Inc). EEG was recorded continuously and referenced to a single vertex electrode, Cz (sample rate = 250 Hz; gain = 10,000x; online bandpass filter = 0.1–100 Hz). Infants passively viewed the stimuli while seated on their parent’s lap, 65 cm from the video monitor (Dell Dimension, 8300) in a dimly lit electromagnetically and acoustically shielded chamber. Stimuli were presented for 500 msec using E-Prime software, and EEG recording continued for an additional 700 msec. Each trial was followed by an inter-trial interval that varied randomly between 500 and 1200 msec. The different stimulus types were presented with equal probabilities in pseudo-random order. More detail about EEG recording, including trial/artifact rejection, is presented in Supplement 1.

EEG recordings were processed off-line using Netstation 3.0 software (low-pass filter = 40 Hz, data re-referenced to an average reference). Each segment consisted of 1300 msec: 100 ms of baseline recording, 500 ms of stimulus presentation, and 700 ms of post-stimulus recording). All infants produced at least 20 artifact-free trials, which was sufficient to provide reliable data, i.e., ERP components with electrode distribution and timing consistent with previous studies of face and object processing in infancy (e.g., 30). Specifically, we examined four ERP components. The N290 and P400 were examined because they have been shown to differentiate faces vs. objects in infants/children (see *Introduction*). We also examined the Nc component, which in typical infants/children (32,84,85), but not children with ASD (81), differentiates familiar vs. unfamiliar faces. Because the Nc is thought to index attention (86, 87), in the current study we examined the Nc as a way of assessing potential group differences in attention allocated to faces vs. objects. Finally, we examined the P100 to determine whether group differences observed in the N290 were driven by earlier differences in the P100.

For each infant, EEG data were averaged across trials and the relevant electrode montage (see Supplement 1 for details). For each component and electrode montage, the *peak amplitude* and *latency to peak amplitude* were derived using individualized time windows to capture each subject's components (referred to as "peak-picking", see 88), which is particularly important if the High-Risk group were to exhibit atypical latencies (mean window durations: P100 = 101.6 ± 29.6 msec, N290 = 143.9 ± 34.7 msec, P400 = 242.6 ± 49.6 msec, Nc = 357.0 ± 65.8 msec). In total, for each subject, we obtained 8 amplitude/latency values: 2 stimulus types (faces vs. objects), 2 familiarity levels (familiar vs. unfamiliar) and 2 electrode montages (left vs. right hemisphere). This was performed for each of the four components (P100, N290, P400 and Nc). In Supplement 1, we present mean waveforms for each infant (20 High-Risk, 20 Low-Risk) obtained over the occipito-temporal montage. The P100, N290 and P400 components can be seen in each subject's waveform.

### Data Analyses

Four-factor ANOVAs: *subject group (High-Risk vs. Low-Risk) × stimulus type (faces vs. objects) × familiarity level (familiar vs. unfamiliar) and hemisphere (left vs. right))* were conducted on amplitude and latency data for the four different ERP components: P100, N290, P400, and Nc. For each condition and each ERP component, the data satisfied Kolmogorov-Smirnov tests for normality and Levene's tests of homogeneity of variances between Low-Risk and High-Risk data.

## Results

### Group Differences in Face vs. Object Processing

The results of our ANOVAs revealed two-way interactions between *subject group (High-Risk vs. Low-Risk) × stimulus type (faces vs. objects)* for N290 Latency ($F(1,38) = 4.87$, $p = 0.033$) and P400 Latency ($F(1,38) = 7.08$, $p = 0.011$), indicating differential face vs. object processing between groups. These group differences are shown in Figure 1, which plots grand averaged waveforms for faces vs. objects, and in Figure 2, which plots subject group means and standard errors for faces and objects for N290 and P400 Latency[1]. There were no three-way interactions between these factors and familiarity or between these factors and hemisphere, indicating that the *subject group × stimulus type* interactions did not differ between familiar and unfamiliar stimuli or between left and right hemispheres. (We did, however, find two-way interactions between *subject group × hemisphere*, which are presented below). For the Nc component, which is thought to index attention (86,87), we did not find a *subject group × stimulus type* interaction. This may indicate that the High- and Low-Risk infants did not differ in the amount of attention allocated to faces vs. objects, which, if true, suggests that the group differences seen for the earlier N290 and P400 components reflect group differences in processing at a

more *sensory-perceptual* level. Main effects of the ANOVAs, which are unrelated to our main hypothesis, are presented in Table 2.

The data presented in Figure 2 also depict what drives the *subject group* × *stimulus type* interactions for N290 and P400 Latency. Posthoc analyses showed that for *N290 Latency*, High-Risk, but not Low-Risk, infants exhibited an "object advantage", i.e., significantly faster responses to objects than faces (by 35.1 msec, p = 0.004, 2-tailed t-test). [Note, however, that for N290 *Amplitude*, we did find faces-larger-than-objects in both subject groups, in line with previous ERP studies of typical infants (30), which is revealed as a main effect of stimulus type for N290 Amplitude, see Table 2]. In addition, direct comparisons between groups showed that the N290 response to objects was significantly faster in High-Risk, as compared to Low-Risk, infants (by 24.4 msec, p = 0.009, 2-tailed t-test). For *P400 Latency*, Low-Risk, but not High-Risk, infants exhibited a "face advantage", i.e., significantly faster responses to faces than objects (by 24.1 msec, p = 0.0035, 2-tailed t-test), which is in line with results from previous ERP studies of typical infants (32). In addition, as was seen for N290 Latency, direct comparisons between groups showed that the P400 response to objects was significantly faster in High-Risk, as compared to Low-Risk, infants (by 36.7 msec, p = 0.004, 2-tailed t-test). In sum, these analyses reveal a greater face advantage in Low-Risk than High-Risk infants (P400), a greater object advantage in High-Risk than Low-Risk infants (N290), and faster *object* responses in High-Risk than Low-Risk infants (N290 and P400).

### Group Differences in Hemisphere Asymmetries

The results of our ANOVAs revealed *subject group* × *hemisphere* interactions for the amplitudes of the P100 ($F(1,38) = 8.60$, $p = 0.006$), the N290 ($F(1, 38) = 16.88$, $p < 0.0001$), and the P400 ($F(1, 49) = 9.90$, $p = 0.003$). These effects are shown in Figure 3, which plots group means and standard errors for left and right hemisphere responses. (See Table 2 for main effects). As noted above, there were no three-way interactions between these factors and *stimulus type* (or *familiarity*), indicating that the *subject group* × *hemisphere* interactions did not differ between faces and objects (or between familiar and unfamiliar stimuli). For all three ERP components, the *subject group* × *hemisphere* interaction was driven by a significant hemisphere asymmetry in *Low-Risk*, but not High-Risk, infants. Collapsed across stimulus type (faces and objects), Low-Risk infants showed *left* greater than right hemisphere responses for the P100 (by 4.27 μV, p = 0.0014, 2-tailed t-test), *right* greater than left hemisphere responses for the N290 (by 5.14 μV, $p < 0.0001$, 2-tailed t-test), and *left* greater than right hemisphere responses for the P400 (by 6.41 μV, p = 0.0005, 2-tailed t-test). We return to a possible explanation for this reversal in hemisphere advantage over time (from left, to right, to left, for the P100, N290 and P400, respectively) in the *Discussion.* In addition, direct comparisons between groups showed that the N290 right hemisphere response was significantly larger in Low-Risk, as compared to High-Risk, infants (by 5.69 μV, p = 0.005, 2-tailed t-test). In sum, these analyses reveal significantly less hemispheric asymmetry in High-Risk, than in Low-Risk, infants.

## Discussion

The results of the current study demonstrate that cortical processing of faces vs. objects, as well as hemispheric asymmetries, are atypical in 10-month-old infants at genetic risk for ASD. Our findings are remarkably similar to those observed in previous studies that used the same or similar ERP paradigm to compare typical individuals vs. those with ASD (adults: 29, 3- to 4-year-old children: 34), as well as typical parents vs. parents of children with ASD (37). The unique contribution of the current results is revealing the existence of these atypicalities in the first year of life, well before ASD is reliably diagnosed.

With regard to *hemispheric asymmetries*, the current and previous three ERP studies all found significant *subject group* × *hemisphere* interactions, driven by greater hemispheric asymmetry in the typical than the ASD group. For N290 amplitude (data combined across faces and objects), the direction of the current results was similar to that of the previous studies, i.e., a right hemisphere advantage in the typical, but not the ASD, group (for 37, this effect was only seen for face responses). However, in the current study, we believe the N290 right hemisphere advantage in Low-Risk infants may have been driven by a "carry-over" from the significant left hemisphere advantage for the (positive-going) P100, which could also carry-over to produce the apparent left hemisphere advantage in the (positive-going) P400 waveform. This possibility is supported by a peak-to-peak (PTP) analysis on the data from Low-Risk infants, which showed no hemispheric asymmetry for the P100-N290 PTP ($p = 0.31$, 2-tailed t-test) or the N290-P400 PTP ($p = 0.38$, 2-tailed t-test), thus suggesting that the N290 and P400 effects are likely accounted for by the P100 left hemisphere advantage. The previous ERP studies did not report results for the P100 amplitude, but it would be interesting to see if their N290 hemispheric asymmetry is likewise driven by an earlier P100 asymmetry. Nonetheless, it is very interesting that, like previous ERP studies of individuals with ASD and their parents, the current study revealed a lack of hemispheric asymmetry in High-Risk infants (and see 89–93 for similar differences between typical and ASD individuals in hemispheric asymmetries, revealed with other paradigms). Because infants are thought to start out with roughly symmetrical hemispheric processing, becoming more asymmetrical over the course of development (see 31,33,94 for discussion), the lack of hemispheric asymmetry in our High-Risk infants, in conjunction with that seen in adults/children with ASD and their parents, suggests that hemispheric asymmetry may fail to develop in these individuals.

With regard to *face vs. object processing*, the current and previous three ERP studies all found significant *subject group* × *stimulus type* interactions. And, interestingly, a very recent ERP study complements the results of the current study by showing atypical responses to pictures of faces with eyes "directed" vs. "averted" in High-Risk infants, as compared to Low-Risk infants, at 10 months of age (60). Together, these findings may help to inform the origins of face processing atypicalities known to exist in individuals with ASD, which have been conjectured to originate from: (A) impaired social motivation to attend to faces, which results in failure to develop expertise in processing faces (e.g., 35,81,95), (B) fundamental impairments in brain areas involved in face processing (17,36,40,59) and (C) general deficits in visual processing (e.g., 59,96). The face/object ERP results of the current study, which revealed faster-than-normal *object* responses in High-Risk infants (and see $34^2$), suggest a new hypothesis; perhaps face processing atypicalities in ASD originate from atypical processing of *objects* instead of, or in addition to, atypical face processing, early in development. For example, it may be that the early endophenotype in ASD results in fundamental enhancements in brain areas involved in object processing or enhanced motivation to attend to objects (although this latter possibility is inconsistent with our finding of a lack of *subject group* × *stimulus type* interaction for the Nc, see *Results*), or both. In line with the possibility of enhanced responses to objects, there are several reports that young children with ASD exhibit *increased* looking times to, and exploration of, objects (e.g., 21–23, but see 20,24). Thus, we speculate that the face/object endophenotype observed in the current study might lead to a propensity for processing objects at the expense of processing faces properly.

In sum, the results of the current study suggest that two endophenotypes in ASD – atypical face vs. object processing and atypical hemispheric asymmetries, are present in the first year of life. Note that we cannot yet determine whether the observed endophenotypes (atypical face vs. object processing and atypical hemispheric asymmetries) are associated with development of ASD, *per se*, because we do not know the diagnostic outcome of all of our subjects. In the future when we have enough data from infants who go on to develop ASD, it could turn out that these infants: 1) exhibit a more severe version of the observed endophenotype(s), 2) show

signs of being unable to compensate for carrying the endophenotype(s), or 3) possess some critical combination of endophenotypes (i.e., the ones observed in the current study, as well as others). For this reason, we are hopeful that the endophenotypic markers revealed in the current study may ultimately aid in the early diagnosis of ASD.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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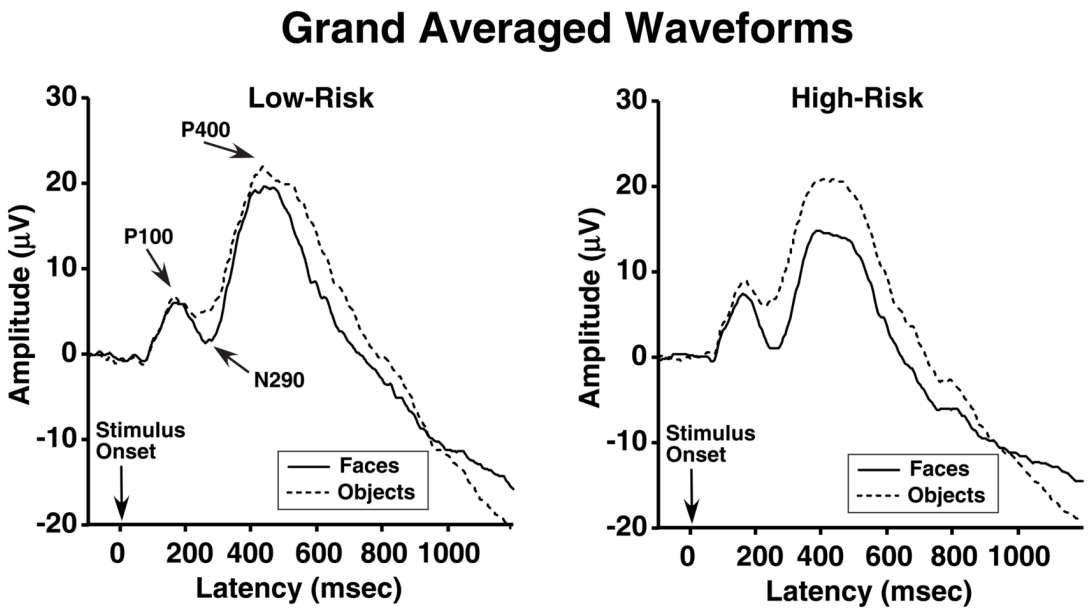


**Figure 1. Grand Averaged Waveforms Showing the P100, N290 and P400 Occipital-Temporal Components for Low-Risk (*Left Panel*) and High-Risk (*Right Panel*) Infants**

Amplitude (mv) vs. Latency (msec) is plotted for Faces (*solid red lines*) and Objects (*dashed blue lines*). Waveforms reflect data collapsed across familiar/unfamiliar stimuli and left/right hemispheres. For clarity, P100, P290 and P400 components are labeled for the Low-Risk infants. See text and Figure Legend 2 for full description of statistical analyses based on individual subject values.

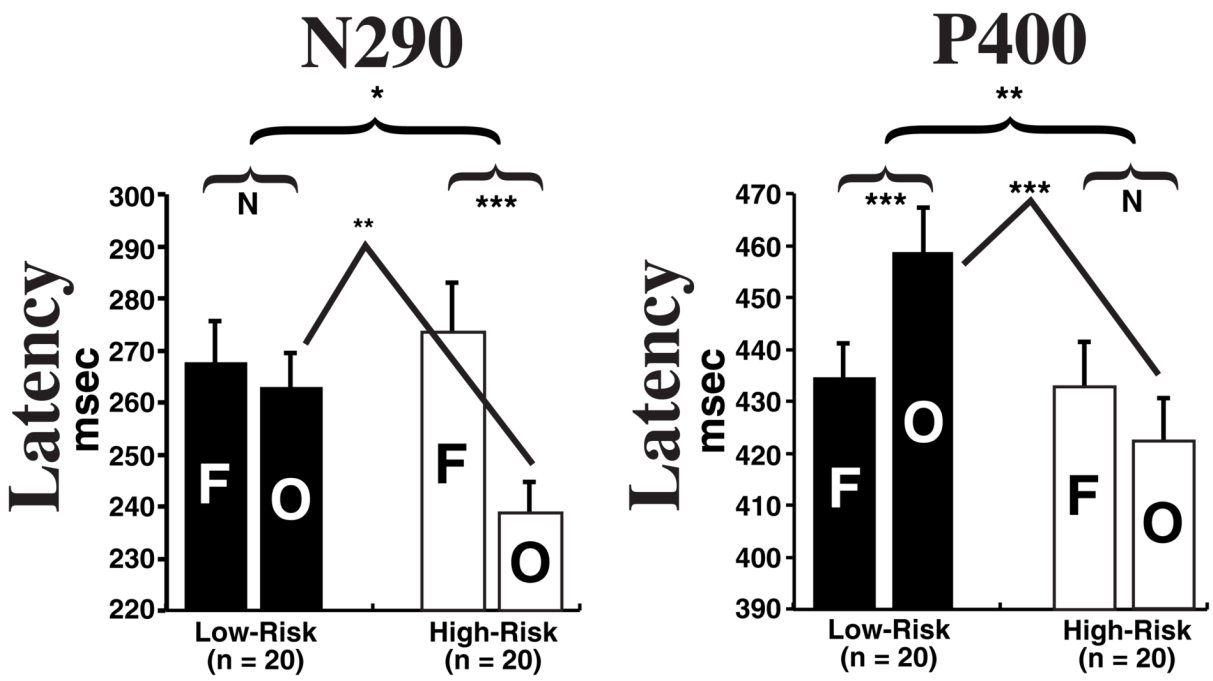


**Figure 2. Group Mean Face (F) and Object (O) Data for Low-Risk (*black bars*) and High-Risk (*white bars*) Infants: N290 and P400 Latency**

Each subject's data were collapsed across left/right hemispheres and familiar/unfamiliar stimuli, separately for face and object responses. Group means were then obtained by averaging individual subject data, with error bars denoting standard errors of the means. Large red brackets denote the interaction between *subject group* × *stimulus type.* Smaller black brackets denote comparisons between face vs. object responses, separately within each group. Bent lines denote comparisons between groups, separately for faces and objects. *** = $p < 0.005$, ** = $p < 0.01$, * = $p < 0.05$, N = Non-Significant.

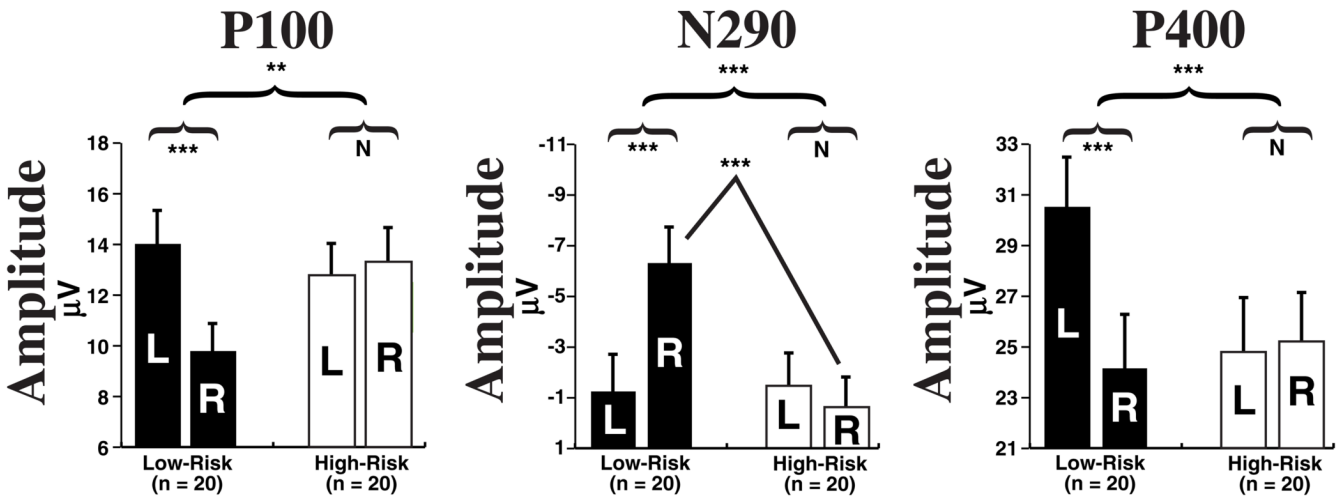


**Figure 3. Group Mean Left Hemisphere (L) and Right Hemisphere (R) Data for Low-Risk (*black bars*) and High-Risk (*white bars*) Infants: P100, N290 and P400 Amplitude**

Each subject's data were collapsed across faces/objects and familiar/unfamiliar stimuli, separately for left and right hemisphere responses. Group means were then obtained by averaging individual subject data, with error bars denoting standard errors of the means. Large red brackets denote the interaction between *subject group* × *hemisphere*. Smaller black brackets denote comparisons between left vs. right hemisphere responses, separately within each group. Bent lines denote comparisons between groups, separately for left and right hemispheres. Note that for the N290 data, the Y axis increases in negativity so that larger bars reflect a larger (negative) response. *** = $p < 0.005$, ** = $p < 0.01$, N = Non-Significant.

**Table 1**

**Older Sibling Information for Each of the 20 High-Risk Infants in Our Study**

"Outside Clinical Diagnosis" was made by an outside clinical professional in the community, usually when the child was under age three. A "Clinical Best Estimate Diagnosis" was made by our clinical psychologist (N. Akshoomoff) based on information from research diagnoses (ADOS and ADI-R) and clinical judgment using DSM-IV-TR criteria. There was sometimes a difference between the original outside clinical diagnosis and our Clinical Best Estimate Diagnosis, which is consistent with previous studies demonstrating that change in diagnosis is most likely to occur between the ages of two and five (97, 98).

| Subject | Gender | Age at Outside Clinical Diagnosis | Original Outside Clinical Diagnosis | Age at Clinical Best Estimate Diagnosis | Clinical Best Estimate Diagnosis |
|---|---|---|---|---|---|
| S1 | M | 2 yr, 10 mo | AD | 4 yr, 11 mo | AD |
| S2 | M | 2 yr, 4 mo | PDD | 4 yr, 8 mo | PDD |
| S3 | M | 2 yr, 1 mo | AD/DD | 5 yr. 3 mo | AD |
| S4 | M | 2 yr, 8 mo | Autism | 5 yr, 5 mo | AD |
| S5 | M | 2 yr, 6 mo | AD/Mild MR | 7 yr, 2 mo | AD |
| S6 | F | 22 mo | Provisional PDD | 4 yr | AD |
| S7 | M | 2 yr, 7 mo | PDD (HF) | 3 yr, 2 mo | PDD |
| S8 | M | 16 mo | AD | 5 yr, 8 mo | AD |
| S9 | M | 2 yr | Provisional AD | 4 yr, 9 mo | AD |
| S10 | M | 4 yr | PDD | 7 yr, 6 mo | AD |
| S11 | M | -- | None | 5 yr, 2 mo | PDD |
| S12 | M | 5 yr, 6 mo | AD/MR | 16 yr, 9 mo | AD |
| S13 | M | 2 yr, 11 mo | AD | 3 yr, 9 mo | AD |
| S14 | M | 2 yr, 5 mo | AD | 3 yr, 11 mo | PDD |
| S15 | M | 3 yr, 5 mo | Mild ASP | 4 yr, 11 mo | AD |
| S16 | M | 2 yr, 9 mo | AD | 5 yr | PDD |
| S17 | M | 3 yr, 4 mo | AD | 7 yr, 3 mo | PDD |
| S18 | F | 3 yr, 9 mo | AD | 5 yr, 5 mo | AD |
| S19 | M | 21 mo | AD | 6 yr, 6 mo | PDD |
| S20 | M | 20 mo | AD | 2 yr, 6 mo | AD |

AD = Autistic Disorder, ASP = Asperger's Disorder, PDD = Pervasive Developmental Disorder Not Otherwise Specified. N/A = Not available for research diagnosis, and thus no clinical best estimate could be made.

## Table 2

Main Effects of Subject Group, Stimulus Type and Hemisphere.

| **Main Effects of Subject Group:** | | | |
|---|---|---|---|
| **Component** | **F(1,38)** | **p value** | **Driven By** |
| P400 Latency | 4.16 | 0.048 | Faster responses in High-Risk than Low-Risk infants[1] |
| Nc Amplitude | 4.69 | 0.037 | Larger negative responses in Low-Risk than High-Risk infants[2] |
| **Main Effects of Stimulus Type:** | | | |
| **Component** | **F(1,38)** | **p value** | **Driven By** |
| N290 Latency | 8.63 | 0.006 | Faster responses to Objects than Faces[1] |
| N290 Amplitude | 5.12 | 0.030 | Larger negative responses to Faces than Objects[3] |
| P400 Amplitude | 6.69 | 0.014 | Larger positive responses to Objects than Faces[4] |
| Nc Amplitude | 8.69 | 0.005 | Larger negative responses to Objects than Faces[5] |
| **Main Effects of Hemisphere:** | | | |
| **Component** | **F(1,38)** | **p value** | **Driven By** |
| P100 Amplitude | 5.27 | 0.027 | Larger positive responses in Left than Right hemisphere[6] |
| N290 Amplitude | 8.32 | 0.006 | Larger negative responses in Right than Left hemisphere[6] |
| P400 Amplitude | 7.57 | 0.009 | Larger positive responses in Left than Right hemisphere[6] |

[1] The interpretation of this main effect is modified by the *subject group* × *stimulus type* interaction, see *Results*.

[2] This effect, which does not interact with *stimulus type*, indicates that Low-Risk infants may have allocated more overall attention than High-Risk infants.

[3] This result mirrors that seen in previous ERP studies of typical infants (30).

[4] This result, although somewhat surprising, is similar to the non-face advantage for the P400 previously reported in ERP studies of typical infants (30).

[5] The Nc is generally believed to be tied to salience/attention (which is thought to differ between familiar and unfamiliar stimuli), not face vs. object processing *per se* (see 33). However, note that the current study did not find familiarity effects for the Nc (in either Low- or High-Risk infants), which could be because our familiar vs. unfamiliar stimuli did not differ sufficiently in salience (see 33 for discussion). Also, note that the current study found no interactions between familiarity and subject group, which is not consistent with results from previous neural imaging studies that reported differences in the response to familiar vs. unfamiliar faces between individuals with ASD and typical controls (ERPs: 81, fMRI: 99). Again, the null finding of the current study could result if our familiar vs. unfamiliar stimuli did not differ sufficiently in salience. Other reasons for a discrepancy between the current and previous studies include different ages (infants vs. children) and different diagnostic categories (High-Risk infants vs. individuals diagnosed with ASD) across studies.

[6] The interpretation of this main effect is modified by the *subject group* × *hemisphere* interaction, see *Results*.