Atypical Face Versus Object Processing and Hemispheric Asymmetries in 10-Month-Old Infants at Risk for Autism

Joseph P. McCleery, Natacha Akshoomoff, Karen R. Dobkins, and Leslie J. Carver

Background: Previous studies have documented atypicalities in face/object processing in children and adults with autism spectrum disorders (ASDs). 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 toys. Latencies and amplitudes of four ERP components (P100, N290, P400, and Nc) were compared between 20 high-risk infants and 20 low-risk control subjects (infants with no family history of ASD).

Results: Responses to faces versus 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). Object responses were also faster in high-risk than low-risk infants (both N290 and P400). Left versus 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 versus object processing and an atypical lack of hemispheric asymmetry early in life. These atypicalities might contribute to development of the disorder.

Key Words: Autism spectrum disorders, endophenotype, event-related potentials, face processing, hemispheric asymmetry

Autism spectrum disorders (ASDs) 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., [8–12] 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 nonface 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 versus 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 faces versus 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. Also, direct group comparisons show that N290 responses to faces are slower in ASD than in typical children. In addition to atypicalities in face versus 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 versus object processing and atypical hemispheric processing in ASD, which can be observed by 3 years of age.

Although there is no clear consensus about the origins of face/object atypicalities in ASD (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 individuals with ASD. Recently, the concept of an endophenotype in ASD has emerged to refer to a measurable trait (like atypical face-processing) 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

From the Departments of Psychology (JPM, KRD, LJC) and Psychiatry (NA), University of California, San Diego, La Jolla, California.

Address correspondence to Karen R. Dobkins, Ph.D., University of California, San Diego, Psychology Department, 0109, La Jolla, CA 92093-0109; E-mail: kdobkins@ucsd.edu.

Received Jan 5, 2009; revised Jul 20, 2009; accepted Jul 22, 2009.

0006-3223/09/$36.00
doi:10.1016/j.biopsych.2009.07.031

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 (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 (52–54). Their risk of developing ASD, 5% to 10% (55,56), is roughly tenfold to twentyfold higher than that seen in the general population, .2% to .6% (57,58). And, as explained above, even high-risk infants who never develop ASD are likely to exhibit differences compared with low-risk control subjects, i.e., 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). 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 versus 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 and Materials

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 the University of California, San Diego (UCSD). The older siblings of the high-risk infants were diagnosed with an ASD (Autistic Disorder, Aspergers 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 (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.

Table 1. Older Sibling Information for Each of the 20 High-Risk Infants in Our Study

Subject	Gender	Age at Outside Clinical Diagnosis	Original Outside Clinical Diagnosis	Age at Clinical Best Estimate Diagnosis	Clinical Best Estimate Diagnosis
S1	M	2 years 10 months	AD	4 years 11 months	AD
S2	M	2 years 4 months	PDD	4 years 8 months	PDD
S3	M	2 years 1 month	AD	5 years 3 months	AD
S4	M	2 years 8 months	Autism	5 years 5 months	AD
S5	M	2 years 6 months	AD	7 years 2 months	AD
S6	F	22 months	Provisional PDD	4 years	AD
S7	M	2 years 7 months	PDD	3 years 2 months	PDD
S8	M	16 months	AD	5 years 8 months	AD
S9	M	2 years	Provisional AD	4 years 9 months	AD
S10	M	4 years	PDD	7 years 6 months	AD
S11	M	—	None	5 years 2 months	PDD
S12	M	5 years 6 months	AD	16 years 9 months	AD
S13	M	2 years 11 months	AD	3 years 9 months	AD
S14	M	2 years 5 months	AD	3 years 11 months	PDD
S15	M	3 years 5 months	Mild ASP	4 years 11 months	AD
S16	M	2 years 9 months	AD	5 years	PDD
S17	M	3 years 4 months	AD	7 years 3 months	PDD
S18	F	3 years 9 months	AD	5 years 5 months	AD
S19	M	21 months	AD	6 years 6 months	PDD
S20	M	20 months	AD	2 years 6 months	AD

Outside clinical diagnosis was made by an outside clinical professional in the community, usually when the child was under age 3. A clinical best estimate diagnosis was made by our clinical psychologist (N.A.) 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 2 and 5 (97,98).

AD, autistic disorder; ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; ASP, Aspergers Syndrome; F, female; M, male; PDD, Pervasive Developmental Disorder Not Otherwise Specified.

All subjects were screened through parent report questionnaires for any abnormal medical conditions. In accordance with UCSD guidelines, the parent of each subject in our study signed a consent form to participate. Parents were asked to bring their infant in 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 1) age on first day of testing (high-risk = 306.5 days ± 14.5, low-risk = 302.9 days ± 14), 2) 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), 3) proportion of female subjects (high-risk = 40%, low-risk = 45%), and 4) total number of retainable trials (high-risk = 47.5 trials ± 20.1, low-risk = 44.1 trials ± 14.5). Detailed information about the low-risk 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 9 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 samples 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 >3 SD 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 objects 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 (Canon, Lake Success, New York) against a gray 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 candela/meter^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 (Supplement 1).

ERP Recordings and Analyses

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

Electroencephalogram recordings were processed offline using Netstation 3.0 software (Electrical Geodesics Inc., Eugene, Oregon) (low-pass filter = 40 Hz, data rereferenced to an average reference). Each segment consisted of 1300 msec: 100 msec of baseline recording, 500 msec of stimulus presentation, and 700 msec of poststimulus 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 versus objects in infants/children (see above). We also examined the Nc component, which in typical infants/children (32,84,85) but not children with ASD (81), differentiates familiar versus 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 versus 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 eight amplitude/latency values: two stimulus types (faces vs. objects), two familiarity levels (familiar vs. unfamiliar), and two 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 occipitotemporal montage. The P100, N290, and P400 components can be seen in each subject's waveform.

Data Analyses

Four-factor analyses of variance (ANOVAs) (subject group [high-risk vs. low-risk] × stimulus type [faces vs. objects] × familiarity level [familiar vs. unfamiliar] × 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.

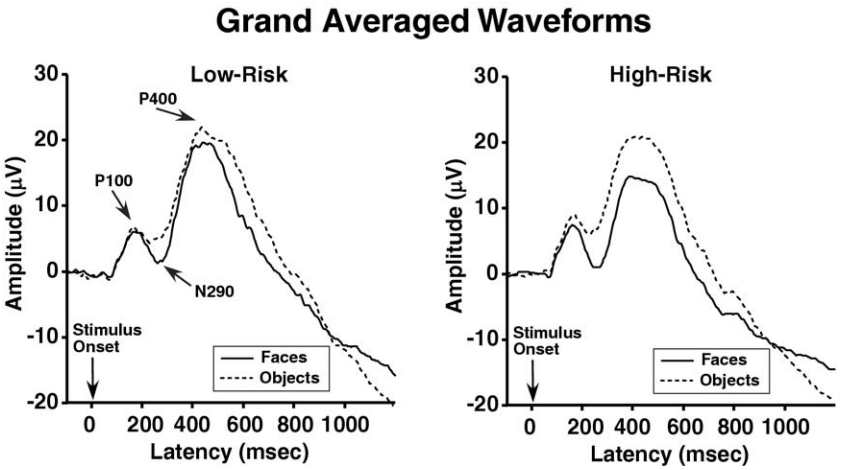

Figure 1. Grand averaged waveforms showing the P100, N290, and P400 occipital-temporal components for low-risk (left panel) and high-risk (right panel) infants. Amplitude (μV) versus latency (msec) is plotted for faces (solid lines) and objects (dashed lines). Waveforms reflect data collapsed across familiar/unfamiliar stimuli and left/right hemispheres. For clarity, P100, N290, and P400 components are labeled for the low-risk infants. See text and Figure 2 legend for full description of statistical analyses based on individual subject values.

Results

Group Differences in Face versus 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 [$F(1,38) = 4.87$, $p = .033$] and P400 latency [$F(1,38) = 7.08$, $p = .011$], indicating differential face versus object processing between groups. These group differences are shown in Figure 1, which plots grand averaged waveforms for faces versus 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 versus 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. Post hoc 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, $p = .004$, two-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 (Table 2). In addition, direct comparisons between groups showed that the N290 response to objects was significantly faster in high-risk, compared with low-risk, infants (by 24.4 msec, $p = .009$, two-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, $p = .0035$, two-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, compared with low-risk, infants (by 36.7 msec, $p = .004$, two-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 [$F(1,38) = 8.60$, $p = .006$], the N290 [$F(1,38) = 16.88$, $p < .0001$], and the P400 [$F(1,49) = 9.90$, $p = .003$]. 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

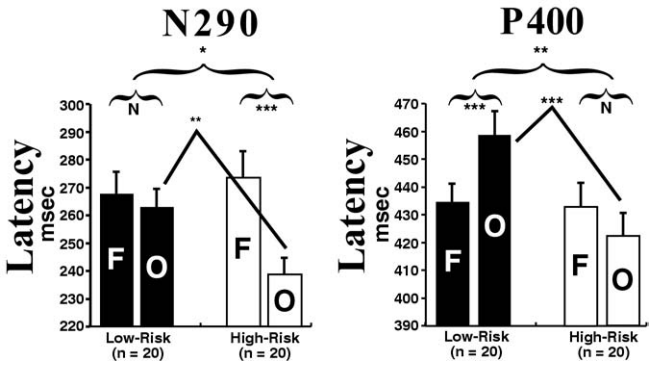

Figure 2. Group mean face (F) and object (O) data for low-risk (black bars) and high-risk (white bars) infants: N290 and P400 latency. Each subject's data were collapsed across left/right hemispheres and familiar/unfamiliar stimuli, separately for face and object responses. Group means were then obtained by averaging individual subject data, with error bars denoting standard errors of the means. Large brackets denote the interaction between subject group × stimulus type. Smaller brackets denote comparisons between face versus object responses, separately within each group. Bent lines denote comparisons between groups, separately for faces and objects. ***$p < .005$, **$p < .01$, *$p < .05$. N, nonsignificant.

[1]Note that differences between means observed in the grand averaged waveforms (Figure 1) versus 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.

Table 2. Main Effects of Subject Group, Stimulus Type, and Hemisphere

Component	*F*(1,38)	*p* Value	Driven by
Main Effects of Subject Group			
P400 Latency	4.16	.048	Faster responses in high-risk than low-risk infants[a]
Nc Amplitude	4.69	.037	Larger negative responses in low-risk than high-risk infants[b]
Main Effects of Stimulus Type			
N290 Latency	8.63	.006	Faster responses to objects than faces[a]
N290 Amplitude	5.12	.030	Larger negative responses to faces than objects[c]
P400 Amplitude	6.69	.014	Larger positive responses to objects than faces[d]
Nc Amplitude	8.69	.005	Larger negative responses to objects than faces[e]
Main Effects of Hemisphere			
P100 Amplitude	5.27	.027	Larger positive responses in left than right hemisphere[f]
N290 Amplitude	8.32	.006	Larger negative responses in right than left hemisphere[f]
P400 Amplitude	7.57	.009	Larger positive responses in left than right hemisphere[f]

ASD, autism spectrum disorder; ERP, event-related potential; fMRI, functional magnetic resonance imaging.

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

[b]This effect, which does not interact with stimulus type, indicates that low-risk infants may have allocated more overall attention than high-risk infants.

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

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

[e]The Nc is generally believed to be tied to salience/attention (which is thought to differ between familiar and unfamiliar stimuli) not face versus object processing per se (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 versus 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 versus unfamiliar faces between individuals with ASD and typical control subjects (ERPs [81], fMRI [99]). Again, the null finding of the current study could result if our familiar versus 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.

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

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, $p = .0014$, two-tailed *t* test), right greater than left hemisphere responses for the N290 (by 5.14 μV, $p < .0001$, two-tailed *t* test), and left greater than right hemisphere responses for the P400 (by 6.41 μV, $p = .0005$, two-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, compared with high-risk, infants (by 5.69 μV, $p = .005$, two-tailed *t* test). In sum, these analyses reveal significantly less hemispheric asymmetry in high-risk than in low-risk infants.

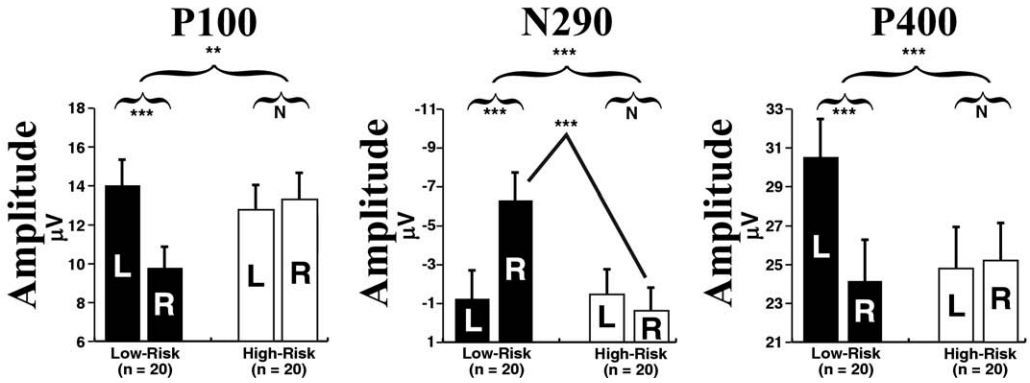

Figure 3. Group mean left hemisphere (L) and right hemisphere (R) data for low-risk (black bars) and high-risk (white bars) infants: P100, N290, and P400 amplitude. Each subject's data were collapsed across faces/objects and familiar/unfamiliar stimuli, separately for left and right hemisphere responses. Group means were then obtained by averaging individual subject data, with error bars denoting standard errors of the means. Large brackets denote the interaction between subject group × hemisphere. Smaller brackets denote comparisons between left versus 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. ***$p < .005$, **$p < .01$. N, nonsignificant.

Discussion

The results of the current study demonstrate that cortical processing of faces versus 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 versus those with ASD (adults: 29; 3- to 4-year-old children: 34), as well as typical parents versus 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 carryover from the significant left hemisphere advantage for the (positive-going) P100, which could also carryover 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 ($p = .31$, two-tailed t test) or the N290-P400 PTP ($p = .38$, two-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 was 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 the lack of asymmetry seen in adults/children with ASD and their parents, suggests that hemispheric asymmetry may fail to develop typically in these individuals.

With regard to face versus 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" versus "averted" in high-risk infants, compared with 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 1) impaired social motivation to attend to faces, which results in failure to develop expertise in processing faces (e.g., [35,81,95]), 2) fundamental impairments in brain areas involved in face processing (17,36,40,59), and 3) 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 versus 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). Therefore, we are hopeful that the endophenotypic markers revealed in the current study may ultimately aid in the early diagnosis of ASD.

This research was supported by National Institutes of Health (R01 HD052804-01A2), the MIND Institute, and Autism Speaks (KRD and LJC). JPM was supported by a National Science Foundation Integrative Graduate Education and Research Traineeship Program traineeship (DGE-0333451, Principal Investigators: Cottrell, Boynton, Desa, Dobkins, and Kreigman), a MIND Institute Scholars Award, and an American Psychological Association Dissertation Research Award. NA was supported by the National Institute of Mental Health (K23MH071796).

We thank all of the families who generously participated in this study. We also thank Elisa Price, Vanitha Sampath, Karen Burner, Sara Geal-Tougby, Matthew Martin, and Lee Edwards for assistance with data collection and analysis and Elizabeth Dohrmann, Michelle Peltz, and Lisa Tully for assistance with the collection of clinical assessment data.

The authors reported no biomedical financial interests or potential conflicts of interest.

Supplementary material cited in this article is available online.

[2]Akin to the N290 latency result of the current study, Webb *et al.* (34) 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.

1. American Psychiatric Association (2004): *Diagnostic and Statistical Manual of Mental Disorders, 4th ed*. Washington, DC: American Psychiatric Association.
2. Lord C, Leventhal BL, Cook EH Jr (2001): Quantifying the phenotype in autism spectrum disorders. *Am J Med Genet* 105:36–38.
3. Rivera SM, Koldewyn K (2005): Unraveling the mystery of motion perception impairments in autism: Some further considerations. *Curr Psychol Cogn* 23:189–197.
4. Dakin S, Frith U (2005): Vagaries of visual perception in autism. *Neuron* 48:497–507.
5. Happe F, Frith U (2006): The weak coherence account: Detail-focused cognitive style in autism spectrum disorders. *J Autism Dev Disord* 36:5–25.
6. Kellerman GR, Fan J, Gorman JM (2005): Auditory abnormalities in autism: Toward functional distinctions among findings. *CNS Spectr* 10:748–756.
7. Mottron L, Dawson M, Soulieres I, Hubert B, Burack J (2006): Enhanced perceptual functioning in autism: An update, and eight principles of autistic perception. *J Autism Dev Disord* 36:27–43.
8. Hauck M, Fein D, Maltby N, Waterhouse L, Feinstein C (1998): Memory for faces in children with autism. *Child Neuropsychol* 43:187–198.
9. Klin A, Sparrow SS, de Bildt A, Cicchetti DV, Cohen DJ, Volkmar FR (1999): A normed study of face recognition in autism and related disorders. *J Autism Dev Disord* 29:499–508.
10. Joseph RM, Tanaka J (2003): Holistic and part-based face recognition in children with autism. *J Child Psychol Psychiatry* 44:529–542.
11. Behrmann M, Thomas C, Humphreys K (2006): Seeing it differently: Visual processing in autism. *Trends Cogn Sci* 10:258–264.
12. Jemel B, Mottron L, Dawson M (2006): Impaired face processing in autism: Fact or artifact? *J Autism Dev Disord* 36:91–106.
13. Humphreys K, Hasson U, Avidan G, Minshew N, Behrmann M (2008): Cortical patterns of category-selecive activation for faces, places and objects in adults with autism. *Autism Res* 1:52–63.
14. Pierce K, Muller RA, Ambrose J, Allen G, Courchesne E (2001): Face processing occurs outside the fusiform "face area" in autism: Evidence from functional MRI. *Brain* 124:2059–2073.
15. Schultz RT, Gauthier I, Klin A, Fulbright RK, Anderson AW, Volkmar F, *et al.* (2000): Abnormal ventral temporal cortical activity during face discrimination among individuals with autism and Asperger syndrome. *Arch Gen Psychiatry* 57:331–340.
16. Aylward E, Bernier R, Field K, Grimme A, Dawson G (2004): Normal activation of fusiform gyrus in adolescents and adults with autism during viewing of familiar, but not unfamiliar, faces. Presented at the Collaborative Programs of Excellence in Autism (CPEA)/Studies to Advance Autism Research and Treatment (STAART) Annual Meeting, 17–20 May, Bethesda Maryland.
17. Pierce K, Haist F, Sedaghat F, Courchesne E (2004): The brain response to personally familiar faces in autism: Findings of fusiform activity and beyond. *Brain* 127:2703–2716.
18. Bailey AJ, Braeutigam S, Jousmaki V, Swithenby SJ (2005): Abnormal activation of face processing systems at early and intermediate latency in individuals with autism spectrum disorder: A magnetoencephalographic study. *Eur J Neurosci* 21:2575–2585.
19. Hadjikhani N, Joseph RM, Snyder J, Chabris CF, Clark J, Steele S, *et al.* (2004): Activation of the fusiform gyrus when individuals with autism spectrum disorder view faces. *Neuroimage* 22:1141–1150.
20. Maestro S, Muratori F, Cavallaro MC, Pei F, Stern D, Golse B, *et al.* (2002): Attentional skills during the first 6 months of age in autism spectrum disorder. *J Am Acad Child Adolesc Psychiatry* 41:1239–1245.
21. Swettenham J, Baron-Cohen S, Charman T, Cox A, Baird G, Drew A, *et al.* (1998): The frequency and distribution of spontaneous attention shifts between social and nonsocial stimuli in autistic, typically developing, and nonautistic developmentally delayed infants. *J Child Psychol Psychiatry* 39:747–753.
22. Zwaigenbaum L, Bryson S, Rogers T, Roberts W, Brian J, Szatmari P (2005): Behavioral manifestations of autism in the first year of life. *Int J Dev Neurosci* 23:143–152.
23. Ozonoff S, Macari S, Young GS, Goldring S, Thompson M, Rogers SJ (2008): Atypical object exploration at 12 months of age is associated with autism in a prospective sample. *Autism* 12:457–472.
24. Baranek GT (1999): Autism during infancy: A retrospective video analysis of sensory-motor and social behaviors at 9–12 months of age. *J Autism Dev Disord* 29:213–224.
25. Osterling JA, Dawson G, Munson JA (2002): Early recognition of 1-year-old infants with autism spectrum disorder versus mental retardation. *Dev Psychopathol* 14:239–251.
26. Bentin S, Allison T, Puce A, Perez E, McCarthy G (1996): Electrophysiological studies of face perception in humans. *J Cognit Neurosci* 8:551–565.
27. Rebai M, Poiroux S, Bernard C, Lalonde R (2001): Event-related potentials for category-specific information during passive viewing of faces and objects. *Int J Neurosci* 106:209–226.
28. Heisz JJ, Watter S, Shedden JM (2006): Automatic face identity encoding at the N170. *Vision Res* 46:4604–4614.
29. McPartland J, Dawson G, Webb SJ, Panagiotides H, Carver LJ (2004): Event-related brain potentials reveal anomalies in temporal processing of faces in autism spectrum disorder. *J Child Psychol Psychiatry* 45:1235–1245.
30. Halit H, Csibra G, Volein A, Johnson MH (2004): Face-sensitive cortical processing in early infancy. *J Child Psychol Psychiatry* 45:1228–1234.
31. Halit H, de Haan M, Johnson MH (2003): Cortical specialisation for face processing: Face-sensitive event-related potential components in 3- and 12-month-old infants. *Neuroimage* 19:1180–1193.
32. de Haan M, Nelson CA (1999): Brain activity differentiates face and object processing in 6-month-old infants. *Dev Psychol* 35:1113–1121.
33. de Haan M, Johnson MH, Halit H (2003): Development of face-sensitive event-related potentials during infancy: A review. *Int J Psychophysiol* 51:45–58.
34. Webb SJ, Dawson G, Bernier R, Panagiotides H (2006): ERP evidence of atypical face processing in young children with autism. *J Autism Dev Disord* 36:881–890.
35. Carver LJ, Dawson G (2002): Development and neural bases of face recognition in autism. *Mol Psychiatry* 7(suppl 2):S18–S20.
36. Schultz RT (2005): Developmental deficits in social perception in autism: The role of the amygdala and fusiform face area. *Int J Dev Neurosci* 23:125–141.
37. Dawson G, Webb SJ, Wijsman E, Schellenberg G, Estes A, Munson J, *et al.* (2005): Neurocognitive and electrophysiological evidence of altered face processing in parents of children with autism: Implications for a model of abnormal development of social brain circuitry in autism. *Dev Psychopathol* 17:679–697.
38. Adolphs R, Spezio ML, Parlier M, Piven J (2008): Distinct face-processing strategies in parents of autistic children. *Curr Biol* 18:1090–1093.
39. Pellicano E (2008): Autism: Face-processing clues to inheritance. *Curr Biol* 18:R748–R750.
40. Dalton KM, Nacewicz BM, Alexander AL, Davidson RJ (2007): Gaze-fixation, brain activation, and amygdala volume in unaffected siblings of individuals with autism. *Biol Psychiatry* 61:512–520.
41. Dorris L, Espie CAE, Knott F, Salt J (2004): Mind-reading difficulties in the siblings of people with Asperger's syndrome: Evidence for a genetic influence in the abnormal development of a specific cogniitve domain. *J Child Psychol Psychiatry* 45:412–418.
42. Bolte S, Poustka F (2003): The recognition of facial affect in autistic and schizophrenic subjects and their first-degree relatives. *Psychol Med* 33:907–915.
43. Gottesman I, Gould TD (2003): The endophenotype concept in psychiatry: Etymology and strategic intentions. *Am J Psychiatry* 160:636–645.
44. Gottesman I, Shields T (1972): *Schizophrenia and Genetics: A Twin Study Vantage Point*. New York: Acadmic Publishing.
45. Szatmari P, Maziade M, Zwaigenbaum L, Merette C, Roy MA, Joober R, *et al.* (2007): Informative phenotypes for genetic studies of psychiatric disorders. *Am J Med Genet B Neuropsychiatr Genet* 144:581–588.
46. Bailey A, Palferman S, Heavey L, Le Couteur A (1998): Autism: The phenotype in relatives. *J Autism Dev Disord* 28:369–392.
47. Bailey A, Le Couteur A, Gottesman I, Bolton P, Simonoff E, Yuzda E, *et al.* (1995): Autism as a strongly genetic disorder: Evidence from a British twin study. *Psychol Med* 25:63–77.
48. Pickles A, Starr E, Kazak S, Bolton P, Papanikolaou K, Bailey A, *et al.* (2000): Variable expression of the autism broader phenotype: Findings from extended pedigrees. *J Child Psychol Psychiatry* 41:491–502.
49. Piven J, Palmer P, Landa R, Santangelo S, Jacobi D, Childress D (1997): Personality and language characteristics in parents from multiple-incidence autism families. *Am J Med Genet* 74:398–411.
50. Curtis WJ, Cicchetti D (2003): Moving research on resilience into the 21st century: Theoretical and methodological considerations in examining the biological contributors to resilience. *Dev Psychopathol* 15:773–810.
51. Kim-Cohen J (2007): Resilience and developmental psychopathology. *Child Adolesc Psychiatr Clin N Am* 16:271–283.
52. Volkmar F, Chawarska K, Klin A (2005): Autism in infancy and early childhood. *Annu Rev Psychol* 56:315–336.

53. Zwaigenbaum L, Thurm A, Stone W, Baranek G, Bryson S, Iverson J, *et al.* (2007): Studying the emergence of autism spectrum disorders in high risk infants: Methodological and practical issues. *J Autism Dev Disord* 37:466–480.
54. Elsabbagh M, Johnson MH (2007): Infancy and autism: Progress, prospects, and challenges. *Prog Brain Res* 164:355–383.
55. Ritvo ER, Jorde LB, Mason-Brothers A, Freeman BJ, Pingree C, Jones MB, *et al.* (1989): The UCLA-University of Utah epidemiologic survey of autism: Recurrence risk estimates and genetic counseling. *Am J Psychiatry* 146:1032–1036.
56. Sumi S, Taniai H, Miyachi T, Tanemura M (2006): Sibling risk of pervasive developmental disorder estimated by means of an epidemiologic survey in Nagoya, Japan. *J Hum Genet* 51:518–522.
57. Chakrabarti S, Fombonne E (2001): Pervasive developmental disorders in preschool children. *JAMA* 285:3093–3099.
58. Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C (2003): Prevalence of autism in a US metropolitan area. *JAMA* 289:49–55.
59. McCleery JP, Allman E, Carver LJ, Dobkins KR (2007): Abnormal magnocellular pathway visual processing in infants at risk for autism. *Biol Psychiatry* 62:1007–1014.
60. Elsabbagh M, Volein A, Csibra G, Holmboe K, Garwood H, Tucker L, *et al.* (2009): Neural correlates of eye gaze processing in the infant broader autism phenotype. *Biol Psychiatry* 65:31–38.
61. Elsabbagh M, Volein A, Holmboe K, Tucker L, Csibra G, Baron-Cohen S, *et al.* (2009): Visual orienting in the early broader autism phenotype: Disengagement and facilitation. *J Child Psychol Psychiatry* 50:637–642.
62. Iverson JM, Wozniak RH (2007): Variation in vocal-motor development in infant siblings of children with autism. *J Autism Dev Disord* 37:158–170.
63. Loh A, Soman T, Brian J, Bryson SE, Roberts W, Szatmari P, *et al.* (2007): Stereotyped motor behaviors associated with autism in high-risk infants: A pilot videotape analysis of a sibling sample. *J Autism Dev Disord* 37:25–36.
64. Carver L, Cornew L, Dobkins KR, McCleery JM (2007): Social referencing in children at risk for autism: Behavior and brain activity. Presented at the International Meeting for Autism Research (IMFAR), 3–5 May, Seattle, Washington.
65. Presmanes AG, Walden TA, Stone WL, Yoder PJ (2007): Effects of different attentional cues on responding to joint attention in younger siblings of children with autism spectrum disorders. *J Autism Dev Disord* 37:133–144.
66. Cassel TD, Messinger DS, Ibanez LV, Haltigan JD, Acosta SI, Buchman AC (2007): Early social and emotional communication in the infant siblings of children with autism spectrum disorders: An examination of the broad phenotype. *J Autism Dev Disord* 37:122–132.
67. Goldberg WA, Jarvis KL, Osann K, Laulhere TM, Straub C, Thomas E, *et al.* (2005): Brief report: Early social communication behaviors in the younger siblings of children with autism. *J Autism Dev Disord* 35:657–664.
68. Toth K, Dawson G, Meltzoff AN, Greenson J, Fein D (2007): Early social, imitation, play, and language abilities of young non-autistic siblings of children with autism. *J Autism Dev Disord* 37:145–157.
69. Yirmiya N, Gamliel I, Pilowsky T, Feldman R, Baron-Cohen S, Sigman M (2006): The development of siblings of children with autism at 4 and 14 months: Social engagement, communication, and cognition. *J Child Psychol Psychiatry* 47:511–523.
70. Merin N, Young GS, Ozonoff S, Rogers SJ (2007): Visual fixation patterns during reciprocal social interaction distinguish a subgroup of 6-month-old infants at-risk for autism from comparison infants. *J Autism Dev Disord* 37:108–121.
71. Gamliel I, Yirmiya N, Sigman M (2007): The development of young siblings of children with autism from 4 to 54 months. *J Autism Dev Disord* 37:171–183.
72. Yirmiya N, Gamliel I, Shaked M, Sigman M (2007): Cognitive and verbal abilities of 24- to 36-month-old siblings of children with autism. *J Autism Dev Disord* 37:218–229.
73. Dobkins KR, Akshoomoff N, Carver LJ, Dorhmann E, McCleery JP (2008): Early cognitive, communicative and social development in infant siblings of children with autism spectrum disorders (ASD). Presented at the International Meeting for Autism Research, 15–17 May, London, England.
74. Landa R, Garrett-Mayer E (2006): Development in infants with autism spectrum disorders: A prospective study. *J Child Psychol Psychiatry* 47:629–638.
75. Sullivan M, Finelli J, Marvin A, Garrett-Mayer E, Bauman M, Landa R (2007): Response to joint attention in toddlers at risk for autism spectrum disorder: A prospective study. *J Autism Dev Disord* 37:37–48.
76. Mitchell S, Brian J, Zwaigenbaum L, Roberts W, Szatmari P, Smith I, *et al.* (2006): Early language and communication development of infants later diagnosed with autism spectrum disorder. *J Dev Behav Pediatr* 27:S69–S78.
77. Bryson SE, Zwaigenbaum L, Brian J, Roberts W, Szatmari P, Rombough V, *et al.* (2007): A prospective case series of high-risk infants who developed autism. *J Autism Dev Disord* 37:12–24.
78. Lord C, Risi S, Lambrecht L, Cook EH Jr, Leventhal BL, DiLavore PC, *et al.* (2000): The Autism Diagnostic Observation Schedule-Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *J Autism Dev Disord* 30:205–223.
79. Lord C, Rutter M, Le Couteur A (1994): Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord* 24:659–685.
80. Dobkins KR, Bosworth RG, McCleery JP (in press): Contributions of biological maturation and visual experience to the development of visual contrast sensitivity. *J Vis*.
81. Dawson G, Carver L, Meltzoff AN, Panagiotides H, McPartland J, Webb SJ (2002): Neural correlates of face and object recognition in young children with autism spectrum disorder, developmental delay, and typical development. *Child Dev* 73:700–717.
82. Balboa RM, Grzywacz NM (2003): Power spectra and distribution of contrasts of natural images from different habitats. *Vision Res* 43:2527–2537.
83. Bosworth RG, Bartlett MS, Dobkins KR (2006): Image statistics of American sign language: Comparison with faces and natural scenes. *J Opt Soc Am A Opt Image Sci Vis* 23:2085–2096.
84. Carver LJ, Dawson G, Panagiotides H, Meltzoff AN, McPartland J, Gray J, *et al.* (2003): Age-related differences in neural correlates of face recognition during the toddler and preschool years. *Dev Psychobiol* 42:148–159.
85. de Haan M, Nelson CA (1997): Recognition of the mother's face by six-month-old infants: A neurobehavioral study. *Child Dev* 68:187–210.
86. Courchesne E (1990): Chronology of postnatal human brain development: Event-related potential, positron emission tomography, myelinogenesis, and synaptogenesis studies. In: Rohrbaugh J, Parasuraman R, editors. *Event-Related Brain Potentials: Basic Issues and Applications*. London: Oxford University Press, 210–241.
87. Nelson CA (1994): Neural correlates of recognition memory in the first postnatal year. In: Dawson G, Fisher K, editors. *Human Behavior and the Developing Brain*. New York: Guilford Publications, 269–313.
88. Handy TC (2005): Basic principles of ERP quantification. In: Handy TC, editor. *Event Related Potentials: A Methods Handbook*. Cambridge, MA: MIT Press.
89. Grice SJ, Halit H, Farroni T, Baron-Cohen S, Bolton P, Johnson MH (2005): Neural correlates of eye-gaze detection in young children with autism. *Cortex* 41:342–353.
90. Prior MR, Bradshaw JL (1979): Hemisphere functioning in autistic children. *Cortex* 15:73–81.
91. Gage NM, Juranek J, Filipek PA, Osann K, Isenberg AL, Flodman P, *et al.* (2009): Rightward hemispheric asymmetries in auditory language cortex in children with autistic disorder: An MRI investigation [published online ahead of print April 4]. *J Neurodev Disord*.
92. Chiron C, Leboyer M, Leon F, Jambaque I, Nuttin C, Syrota A (1995): SPECT of the brain in childhood autism: Evidence for a lack of normal hemispheric asymmetry. *Dev Med Child Neurol* 37:849–860.
93. Escalante-Mead PR, Minshew NJ, Sweeney JA (2003): Abnormal brain lateralization in high-functioning autism. *J Autism Dev Disord* 33:539–543.
94. Mills DL, Coffey-Corina SA, Neville HJ (1993): Language acquisition and cerebral specialization in 20-month-old infants. *J Cogn Neurosci* 5:317–334.
95. Dawson G, Webb SJ, McPartland J (2005): Understanding the nature of face processing impairment in autism: Insights from behavioral and electrophysiological studies. *Dev Neuropsychol* 27:403–424.
96. Scherf KS, Behrmann M, Minshew N, Luna B (2008): Atypical development of face and greeble recognition in autism. *J Child Psychol Psychiatry* 49:838–847.
97. Lord C, Risi S, DiLavore PS, Shulman C, Thurm A, Pickles A (2006): Autism from 2 to 9 years of age. *Arch Gen Psychiatry* 63:694–701.
98. Charman T, Taylor E, Drew A, Cockerill H, Brown JA, Baird G (2005): Outcome at 7 years of children diagnosed with autism at age 2: Predictive validity of assessments conducted at 2 and 3 years of age and pattern of symptom change over time. *J Child Psychol Psychiatry* 46:500–513.
99. Pierce K, Redcay E (2008): Fusiform function in children with an autism spectrum disorder is a matter of "who." *Biol Psychiatry* 64:552–560.