Atypical neural specialization for social percepts in autism spectrum disorder

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Abstract

The social motivation hypothesis posits that aberrant neural response to human faces in autism is attributable to atypical social development and consequently reduced exposure to faces. The specificity of deficits in neural specialization remains unclear, and alternative theories suggest generalized processing difficulties. The current study contrasted neural specialization for social information versus non-social information in 36 individuals with autism and 18 typically developing individuals matched for age, race, sex, handedness, and cognitive ability. Event-related potentials elicited by faces, inverted faces, houses, letters, and pseudoletters were recorded. Groups were compared on an electrophysiological marker of neural specialization (N170), as well as behavioral performance on standardized measures of face recognition and word reading/decoding. Consistent with prior results, individuals with autism displayed slowed face processing and decreased sensitivity to face inversion; however, they showed comparable brain responses to letters, which were associated with behavioral performance in both groups. Results suggest that individuals with autism display atypical neural specialization for social information but intact specialization for non-social information. They concord with the notion of specific dysfunction in social brain systems rather than non-specific information processing difficulties in autism.

Preserved neural specialization for non-social information in autism

The ability to efficiently perceive the human face is a crucial and early-emerging social ability. Specialized processing for faces emerges in the first days of life (Bushnell, Sai & Mullin, 1989; Goren, Sarty & Wu, 1975; Johnson, Dziurawiec, Ellis & Morton, 1991; Meltzoff & Moore, 1977) and is honed by developmental experience (Nelson, 2001). Faces come to be encoded using configural processing mechanisms (Farah, Tanaka & Drain, 1995), reflected in disproportionate impairments in recognizing both upside down faces (the inversion effect (Yin, 1970) and facial features out of context (Tanaka & Farah, 1993). Functional neuroimaging studies show that faces elicit selective, right-lateralized hemodynamic activity in a portion of occipitotemporal cortex, the fusiform gyrus (Haxby et al., 1994; Kanwisher, McDermott & Chun, 1997; Puce, Allison, Gore & McCarthy, 1995), and intra-cranial electrophysiological recordings reveal face-related negative electrical activity originating from this portion of cortex (Allison, McCarthy, Novbre, Puce & Belger, 1994). Likewise, event-related potentials (ERPs) recorded from corresponding scalp regions show a negative-going electrical deflection approximately 170 milliseconds after viewing a face (N170; Bentin, Allison, Puce, Perez & McCarthy, 1996). The N170 putatively reflects structural encoding, an early stage of face processing preceding higher-order processes like recognition (Bentin, Deouell & Soroker, 1999), and is sensitive to perturbations in face configuration, including inversion (Rossion et al., 2000). Neural generators of the N170 have been localized to occipitotemporal sites including the fusiform gyrus (Itier & Taylor, 2002; Rossion, Joyce, Cottrell & Tarr, 2003; Shibata et al., 2002), as well as the superior temporal sulcus (Itier

& Taylor, 2004), lingual gyrus (Shibata et al., 2002), and posterior inferotemporal gyrus (Schweinberger, Pickering, Jentzsch, Burton & Kaufmann, 2002; Shibata et al., 2002).

These processing strategies and brain regions are also observed in the perception of visual stimuli with which viewers have extensive experience (Diamond & Carey, 1986; Gauthier, 2000). Experts at perceiving and discriminating among exemplars within a visually homogenous class (e.g., Greebles, birds, or cars (Gauthier, Skudkarski, Gore & Anderson, 2000; Gauthier, Williams, Tarr & Tanaka, 1998) develop face-like patterns of brain activity, in terms of both hemodynamic (Tarr & Gauthier, 2000) and electrophysiological response, as indexed by the N170 (Rossion, Gauthier, Goffaux, Tarr & Crommelinck, 2002). According to this model, these brain regions subserve a processing style rather than specific content, and face-related brain activity reflects, in large part, human beings' extensive experience processing human faces during development (Gauthier & Nelson, 2001).

Analogous specialization through developmental experience occurs in brain mechanisms subserving letter and word processing. Perception of printed letters (James, James, Jobard, Wong & Gauthier, 2005) and words (McCandliss, Cohen & Dehaene, 2003) selectively activates left fusiform gyrus and elicits a left-lateralized N170 in literate children as young as eight years of age (Bentin, Mouchetant-Rostaing, Giard, Echallier & Pernier, 1999; Maurer et al., 2006). A maturational course independent of higher-order phonological or semantic processes (Grossi, Coch, Coffey-Corina, Holcomb & Neville, 2001; Holcomb, Coffey & Neville, 1992) and an early time course suggest that this "letter N170" marks pre-linguistic processes related to visual perception of form (Bentin, Mouchetant-Rostaing et al., 1999) and, like the N170 elicited by faces, automatic

perceptual categorization within a domain of expertise (Maurer, Brem, Bucher &

Brandeis, 2005). Neural specialization for letters is revealed by enhanced N170

amplitude to familiar alphabets but not foreign alphabets or nonsensical letter

approximations (pseudoletters; Wong, Gauthier, Woroch, DeBuse & Curran, 2005).

Converging evidence from neuroimaging studies and ERP source localization suggest

left-lateralized sources in the fusiform gyrus and the inferior occipitotemporal cortex

(Cohen et al., 2000; Maurer et al., 2005; Rossion et al., 2003). Though letter-related brain

activity is typically contralateral to face processing areas (Rossion et al., 2003), there is

some degree of functional overlap; under special circumstances, such as precocious

reading ability, right fusiform gyrus is recruited for letter and word recognition

(Turkeltaub et al., 2004).

Because face perception is a well-studied social behavior, it has been employed as

an avenue to understand social development in autism spectrum disorder (ASD). In ASD,

decreased attention to human faces is evident by 6 to 12 months (Maestro et al., 2002;

Osterling & Dawson, 1994), and abnormalities in face perception and recognition have

been observed throughout the lifespan (Hobson, 1986; Hobson, Ouston & Lee, 1988;

Klin et al., 1999; Langdell, 1978; Schultz, 2005; Wolf et al., 2008). Individuals with ASD

often exhibit abnormal viewing patterns to faces (Jones, Carr & Klin, 2008; Klin, Jones,

Schultz, Volkmar & Cohen, 2002) and hypoactivation in face-related brain areas

(Schultz, 2005; Schultz et al., 2000). Studies of electrophysiological markers of face

perception suggest delayed N170 to human faces and decreased sensitivity to face

inversion in individuals with ASD, as well as first degree relatives (Dawson et al., 2002;

Dawson, Webb, Wijsman et al., 2005; McCleery, Akshoomoff, Dobkins & Carver, 2009;

McPartland, Dawson, Webb, Panagiotides & Carver, 2004; O'Connor, Hamm & Kirk, 2005, 2007; Webb, Dawson, Bernier & Panagiotides, 2006) though some studies suggest at least partially preserved face perception in some subgroups of individuals with ASD (Webb et al., 2010; Webb et al., 2009).

One theoretical explanation for these observed differences in face perception in ASD focuses on the role of developmental exposure to faces. The social motivation hypothesis (Dawson, Webb & McPartland, 2005; Schultz, 2005) posits that, due to abnormalities in social drive very early in childhood, children with ASD do not attend to faces during sensitive developmental periods. Consequently, people with ASD fail to develop typical proficiency in face processing and associated patterns of behavioral and brain specialization (Behrmann, Thomas & Humphreys, 2006). Because the social motivation hypothesis implicates social drive as the dysfunction from which face perception difficulties originate (rather than specific dysfunction of brain regions subserving face perception), it presumes that individuals with ASD, given appropriate exposure to and interest in a stimulus class, should develop both behavioral and brain specialization (Sasson, 2006). This notion is supported by a single-case study revealing behavioral and neural indices of specialization in a child with ASD during perception of cartoon characters associated with a circumscribed interest (Grelotti et al., 2005). Though others have attempted to investigate brain response associated with experience in this population (Boeschoten, Kenemans, van Engeland & Kemner, 2007), research has been stymied by difficulty finding shared areas of expertise in ASD; whereas groups of study participants experienced in perceiving faces are common, groups of individuals with ASD who share a common non-face area of expertise are rare.

The current work circumvented this difficulty by examining brain activity reflecting neural specialization for letters of the alphabet. As described above, development of specialization for letters and words is well studied and elicits brain activity similar to faces in terms of temporal characteristics and scalp topography (despite lateralization differences). This is a novel and uniquely appropriate comparison because, despite developmental disinterest towards faces and characteristic weakness in language, facility with reading has been a noted strength in ASD since Kanner's original account (Kanner, 1943). High-functioning individuals on the autism spectrum display age-appropriate skills in single word-reading and word-decoding ability (Huemer & Mann, 2009; Nation, Clarke, Wright & Williams, 2006; Newman et al., 2006), and a subgroup possesses precocious interest and proficiency in reading, or *hyperlexia* (Burd, Kerbeshian & Fisher, 1985; Grigorenko et al., 2002; Klin, 2004). In this study, electrophysiological and behavioral methods were applied to compare neural specialization for faces and letters in individuals with ASD. Experiments contrasted neural response to faces versus houses, faces versus inverted faces, and letters versus pseudoletters and compared these parameters to behavioral measures assessing proficiency in face recognition and letter and word perception. Consistent with previous work, it was hypothesized that individuals with ASD would exhibit impaired face recognition and delayed brain response to faces in the right hemisphere, as well as decreased sensitivity to face inversion. In keeping with the notion that these atypicalities reflect developmental sequelae of social deficits, it was predicted that similar anomalies would not be observed for non-social stimuli; individuals with ASD would show typical skills in terms of letter and word perception and comparably enhanced response to letter stimuli with respect to unfamiliar pseudoletters.

As prior work has revealed relationships among neural correlates of face perception and behavioral measures of face recognition (McPartland et al., 2004), exploratory analyses examined relationships among neural and behavioral measures of face and letter perception.

Methods

Participants

  Two groups participated in the study: individuals with ASD and medically and

neuropsychiatrically healthy individuals with typical development. Exclusionary criteria

for participants with ASD included seizures, neurological disease, history of serious head

injury, sensory or motor impairment that would impede completion of the study protocol,

active psychiatric disorder (other than ASD; screened with the Child Symptom Inventory:

Fourth Edition (Gadow & Sprafkin, 1994), or medication known to affect brain

electrophysiology. Additional exclusionary criteria for typical participants included the

above plus learning/language disability or family history of ASD. From an existing pool

of subjects involved in ongoing research at the Yale Child Study Center, participants

were selected based on having a Full Scale IQ in the average range or higher (Standard

Score of 80 or above; Differential Ability Scales: Second Edition (Elliott, 2007);

Wechsler Intelligence Scale for Children – Fourth Edition (Wechsler, 2003); Wechsler

Adult Intelligence Scale: Third Edition (Wechsler, 1997)). All individuals with ASD had

a pre-existing diagnosis that was confirmed with gold standard diagnostic assessments for

research: combination of parent interview (Autism Diagnostic Interview-Revised (Lord,

Rutter & Le Couteur, 1994; ADI-R), semi-structured social behavior and communication

assessment (Autism Diagnostic Observation Schedule; Lord et al., 2000), and clinical

diagnosis based on DSM-IV-TR (American Psychiatric Association, 2000) criteria by an

expert clinician. The ADI was not administered to one subject because a parent was

unavailable for interviewing, and two individuals were included in the sample who failed

to meet ADI-R onset criteria; for both of these high-functioning, verbal individuals,

problems were not detected until enrolled in school with peers. In addition to the

aforementioned exclusionary criteria, typical participants were recruited to match the

ASD sample in terms of sex ethnicity, handedness (Edinburgh Handedness Inventory

(Oldfield, 1971), chronological age, and Full Scale IQ (Wechsler Abbreviated Scale of

Intelligence; Psychological Corporation, 1999). Groups did not significantly differ on any

of these variables. Behavioral assessments could not be administered to one typical

participant due to time limitations. All procedures were approved by the Human

Investigation Committee at Yale School of Medicine and were carried out in accordance

with the Declaration of Helsinki (1975/1983). Of an initial sample of 57 individuals with

ASD and 25 typically developing participants, adequate artifact-free data was obtained

from 36 and 18 participants, respectively, in the letter/pseudoletter experiment, and 32

and 17, respectively, in the face/house experiment. Table 1 displays demographic data for

the complete sample; variation in sample between experiments did not introduce

differences on demographic characteristics.

[PLEASE INSERT TABLE 1 ABOUT HERE]

EEG procedures

    Stimuli. Stimuli were administered in pseudorandom sequence in two

counterbalanced blocks. The first block consisted of gray-scale digitized images of

neutral faces, houses, inverted faces, and inverted houses (not included in current

analyses), all displayed from a direct frontal perspective. The second block included

letters and a confabulated alphabet of pseudoletters (Wong et al., 2005). Example stimuli

are displayed in the legends of Figures 1 and 2. Subjects were presented with 23 stimuli

from each category four times, for a total of 92 stimuli per category. Stimuli were

standardized in terms of size (approximately five degrees of visual angle), background

color (gray), and average luminance. To maximally engage attention to individual

stimuli, participants were asked to press a button whenever a stimulus repeated (9 times

for each stimulus category). Because this behavioral task was confounded with face

recognition, attention to task was monitored in real time through closed-circuit video,

enabling pausing of data collection and redirection of attention to stimulus presentation if

needed.

   Data collection. Stimuli were presented on a Pentium-IV computer controlling a

51 cm color monitor (75-Hz, 1024x768 resolution) running E-Prime 2.0 software

(Schneider, Eschman & Zuccolotto, 2002). Displays were viewed at a distance of 90 cm

in a sound attenuated room with low ambient illumination. EEG was recorded using

NetStation 4.3. A 256 lead Geodesic sensor net (Electrical Geodesics Incorporated;

(Tucker, 1993) was dampened with potassium-chloride electrolyte solution, placed on the

participant's head, and fitted according to the manufacturer's specifications. Impedances

were kept below 40 kilo-ohms. ERP was recorded continuously throughout each stimulus

presentation trial, consisting of a fixation cross (randomly varying from 250-750 ms),

stimulus (500 ms), and blank screen (500 ms). The EEG signal was amplified (x1000)

and filtered (0.1 Hz high-pass filter and 100 Hz elliptical low-pass filter) via a

preamplifier system (Electrical Geodesics Incorporated). The conditioned signal was

multiplexed and digitized at 250 Hz using an analog-to-digital converter (National

Instruments PCI-1200) and a dedicated Macintosh computer. The vertex electrode was

used as a reference, and data were re-referenced to an average reference after data collection.

Data editing and reduction. Data were averaged for each subject by stimulus type across trials. Averaged data were digitally filtered with a 30 Hz low-pass filter and transformed to correct for baseline shifts. The window for segmentation of the ERP was set from 100 ms before and 500 ms after stimulus onset. NetStation artifact detection settings were set to 200 μv for bad channels, 150 μv for eye blinks, and 150 μv for eye movements. Channels with artifacts on more than 50 percent of trials were marked as bad channels and replaced through spline interpolation. Segments that contained eye blinks, eye movement, and those with more than 20 bad channels were also excluded. Participants with less than 46 good trials for any stimulus category were excluded from analysis. Electrodes of interest were selected based on maximal observed amplitude of the N170 to faces and letters in grand averaged data and to conform to those used in previous research. Data were averaged across eight electrodes over the left (95, 96, 97, 106, 107, 108, 116, 117) and right lateral posterior scalp (151, 152, 153, 160, 161, 162, 170, 171). The time windows for P1 and N170 analysis, extending from 108 ms to 327 ms and 56 ms to 206 ms post-stimulus onset, respectively, were chosen by visual inspection of grand averaged data and then customized for each subject to confirm that the component of interest was captured at each electrode. Peak amplitude and latency to peak were averaged across each electrode group within the specified time window and were extracted for each participant for each stimulus category.

Data analysis. P1 and N170 amplitudes and latencies to peak were separately analyzed using univariate repeated measures analyses of variance (ANOVA) with two

within-subject factors, condition (face/house; face/inverted face, letter/pseudoletter) and

hemisphere (left/right). The between subjects factor was Group (ASD/Typical). A

planned comparison using one-way ANOVA was employed to test the specific

hypothesis that N170 to faces would be delayed in the right hemisphere in the ASD group

relative to the typical group.

Behavioral procedures

Face perception. Face recognition was measured with the Benton Facial

Recognition Test (Benton, Sivan, Hamsher, Varney & Spreen, 1994). Participants viewed

a grayscale image of a face and specified one or three matches from an array of six faces,

varying in shadowing and orientation.

Letter perception. The Letter-Word Identification and Word Attack subtests of the

Woodcock-Johnson Tests of Achievement – Third Edition (Woodcock, McGrew &

Mather, 2001) required the participant to read words aloud, with the former using

genuine English words and the latter using novel words. Both subtests yielded a standard

score (Mean = 100, SD = 15) derived from an age-based standardization sample.

Data analysis. Between-group differences in behavioral measures were analyzed

with independent samples t-tests. Interrelationships among behavioral measures and ERP

parameters (N170 latency, amplitude) were computed using Pearson Product-Moment

Correlations.

Results

<u>Electrophysiological measures</u>

Faces versus houses: P1 Amplitude. Figure 1 displays waveforms depicting ERPs to faces and houses, and Table 2 displays mean amplitudes and standard deviations for both groups across both hemispheres and all conditions. Faces elicited smaller P1 amplitudes across hemisphere and group (main effect of Condition; $F(1,47) = 18.01$, $p \leq .01$). No other significant effects were observed (all Fs < 2.44; all ps > .05).

Faces versus houses: P1 Latency. Table 3 displays mean latencies and standard deviations for both groups across both hemispheres and all conditions. Faces elicited shorter P1 latencies across hemisphere and group (main effect of Condition; $F(1,47) = 63.92$, $p \leq .01$). No other significant effects were observed (all Fs < 3.10; all ps > .05).

Faces versus houses: N170 Amplitude. Faces elicited N170s with larger amplitudes (main effect of Condition; $F(1,47) = 49.77$, $p \leq .01$) across hemispheres for both groups. N170 amplitude to houses was reduced in the left hemisphere across groups (Hemisphere by Condition interaction; $F(1,47) = 6.80$, $p \leq .01$), and, relative to typical individuals, bilaterally in the ASD group (Condition by Group interaction; $F(1,47) = 5.17$, $p \leq .05$). Right-lateralization was evident only in typically developing individuals (Hemisphere by Group interaction; $F(1,47) = 7.22$, $p \leq .01$). No other significant effects were observed (all Fs < 0.90; all ps > .05).

Faces versus houses: N170 Latency. Faces elicited N170s with shorter latencies (main effect of Condition; $F(1,47) = 30.10$, $p \leq .01$) across hemispheres for both groups. A planned comparison confirmed the predicted differences in latency between groups in the right hemisphere, N170 latency to faces was significantly faster (a difference of

approximately 20.4 milliseconds) in typically developing individuals than those with ASD ($F(1, 47) = 5.57; p \leq .05$). Figure 2 displays N170 amplitudes for faces and houses, highlighting this difference. No other significant effects were observed (all Fs < 3.09; all ps > .05).

[PLEASE INSERT FIGURE 1 ABOUT HERE]

[PLEASE INSERT FIGURE 2 ABOUT HERE]

Face versus inverted faces: P1 Amplitude. Waveforms depicting ERPs to faces and inverted faces are displayed in Figure 1. Inverted faces elicited larger P1 amplitudes across hemisphere and group (main effect of Condition; $F(1,47) = 12.41, p \leq .01$). P1 amplitude to inverted faces was larger relative to upright faces in the right hemisphere across groups (Hemisphere by Condition interaction; $F(1,47) = 5.88, p \leq .05$). No other significant effects were observed (all Fs < 3.25; all ps > .05).

Face versus inverted faces: P1 Latency. Faces elicited shorter P1 latencies across hemisphere and group (main effect of Condition; $F(1,47) = 19.80, p \leq .01$). No other significant effects were observed (all Fs < 3.31; all ps > .05).

Face versus inverted faces: N170 Amplitude. Across faces and inverted faces, typically developing individuals displayed enhanced amplitude in the right hemisphere, while those with ASD exhibited equivalent amplitude in both hemispheres (Hemisphere by Group interaction; $F(1,47) = 7.70, p \leq .01$). Across hemisphere, typically developing individuals displayed an inversion effect in the expected direction, with larger amplitude to inverted relative to upright faces, whereas individuals with ASD displayed attenuated

N170 amplitudes to inverted faces relative to upright faces (Condition by Group

interaction; $F(1,47) = 5.84$, $p \le .05$). No other significant effects were observed (all Fs <

1.40; all ps > .05).

Face versus inverted faces: N170 Latency. Inverted faces elicited N170s with

longer latencies than upright faces (main effect of Condition; $F(1,47) = 4.66$, $p \le .05$)

across hemispheres for both groups. No other significant effects were observed (all Fs <

2.69; all ps > .05).

Letters versus pseudoletters: P1 Amplitude. Figure 3 displays waveforms

depicting ERPs to letters and pseudoletters. No significant effects were observed (all Fs <

3.08; all ps > .05).

Letters versus pseudoletters: P1 Latency. Across hemisphere and group, letters

elicited shorter P1 latency than pseudoletters (main effect of Condition; $F(1, 52) = 16.28$,

$p \le .01$). Across group and condition, P1 latency was shorter in the right hemisphere

(main effect of Hemisphere; $F(1, 52) = 4.15$, $p \le .05$). No other significant effects were

observed (all Fs < 1.07; all ps > .05).

Letters versus pseudoletters: N170 Amplitude. For both groups, letters elicited

N170s with larger amplitudes than pseudoletters across hemispheres (main effect of

Condition; $F(1, 52) = 14.67$, $p \le .01$). As displayed in Figure 4, paired samples t-tests

revealed that this effect was carried by significantly enhanced amplitude to letters versus

pseudoletters in the typical group in the left hemisphere ($t(1,17) = 2.12$, $p \le .05$) and in

the ASD group in both left ($t(1,35) = 2.90$, $p \le .01$) and right hemispheres ($t(1,35) = 3.34$,

$p \le .01$). No other significant effects were observed (all Fs < 2.68; all ps > .05).

Letters versus pseudoletters: N170 Latency. No significant effects were observed (all *F*s < 3.58; all *p*s > .05).

[PLEASE INSERT FIGURE 3 ABOUT HERE]

[PLEASE INSERT FIGURE 4 ABOUT HERE]

Behavioral measures

Face perception. Table 2 displays mean score and standard deviation on behavioral measures for both groups. Individuals with ASD obtained significantly lower face recognition scores than typically developing individuals (*t*(1,51)=3.29, *p* ≤ .01). For both groups, N170 latency to faces in the right hemisphere was correlated with face recognition skill; individuals with faster N170s displayed better face recognition performance (ASD: *r* = -.39, *p* ≤ .05; Typical: *r* = -.53, *p* ≤ .05). Among individuals with ASD, N170 amplitude to inverted faces was correlated with face recognition performance; those with better face recognition abilities were more likely to display an enhanced N170 associated with inversion (*r* = -.47, *p* ≤ .01).

Letter perception. Groups performed comparably and in the average range on word reading and decoding tasks. Among typically developing individuals, longer N170 latency to letters in the right hemisphere was correlated with word reading score; those with longer latencies tended to perform better on the measure of single word reading (*r* = .64, *p* ≤ .01).

[PLEASE INSERT TABLE 4 ABOUT HERE]

General Discussion

The current study contrasted neural specialization for social and non-social information in individuals with ASD and a cohort of typically developing individuals of comparable age, ethnicity, sex, handedness, and cognitive ability. A critical social stimulus with which most adults possess great experience, the human face, was contrasted with a comparably complex visual stimulus without interpersonal relevance, houses. Consistent with predictions and with prior research (McPartland et al., 2004), individuals with ASD displayed a selective processing delay for human faces in the right hemisphere relative to typical counterparts. Individuals with ASD also showed reduced hemispheric specialization compared to typical counterparts, who showed a marked right lateralization effect for faces. The inversion effect, a marker of neural specialization and processing experience for faces, was evident in typically developing individuals but not those with ASD. On a behavioral measure of face recognition, individuals with ASD, despite comparable intellectual ability, performed significantly worse than typically developing counterparts. Face recognition performance was associated with processing efficiency for faces; in both groups, individuals with better face recognition abilities displayed faster N170 response. Among individuals with ASD, increased inversion effects, as reflected by a stronger response to inverted faces, were associated with better face recognition performance. This pattern of anomalies, i.e., decreased efficiency of processing, insensitivity to inversion, and impaired face recognition, is hypothesized to reflect underdeveloped specialization for faces, a downstream effect of decreased attention to faces during childhood secondary to reduced social drive from infancy (Dawson, Webb & McPartland, 2005). Indeed, the observed correlation between neural

response to face inversion and recognition performance suggests that, in this case,

development of expertise and processing proficiency are related.

Though differences related to condition and lateralization were observed in an

earlier component, the P1, no between-group differences were detected. Given the P1's

role in basic visual attention and low-level sensory perception (Key, Dove, & Maguire,

2005), this pattern of results indicates that children with ASD did not differ from

typically developing peers in terms of fundamental sensory perception. Indeed, despite

observed differences in the basic sensory response to different classes of stimuli, groups

responded similarly. These findings suggest normative sensory perception for visual

information in ASD, with differences emerging at subsequent processing stages related to

social perception.

Current findings concord with prior work describing deviant social development

in ASD. However, scant evidence to-date has informed the specificity of the observed

neural processing anomalies to social information. By measuring responses to non-social

expert stimuli, the current study demonstrated the selectivity of perceptual deficits in

ASD. Following up on work showing N170-related expertise effects for letters, ERP

response to letters of the Roman alphabet were compared to a confabulated alphabet of

pseudoletters (Wong et al., 2005). In contrast to the discrepancies observed during

perception of social stimuli, individuals with ASD displayed neural responses

comparable to typical counterparts; both groups showed enhanced N170 to familiar

letters. Similar results were obtained on behavioral measures, with individuals with ASD

obtaining word reading and decoding scores that were comparable to the typical

participants in this study and within the average range. These results suggest intact

behavioral and brain specialization for non-social information in individuals with ASD.

These results are consistent with prior behavioral work demonstrating preserved word-

reading and word-decoding ability in cognitively able individuals with ASD (Huemer &

Mann, 2009; Nation et al., 2006; Newman et al., 2006) despite complications with

reading comprehension and more sophisticated aspects of language (O'Connor & Klein,

2004). They are consistent with the notion that the social element of communication

rather than language, more generally, may be most directly impacted in ASD (Paul,

2003).

The current findings have significant implications for understanding the

neuropathology of autism spectrum disorders. Two prevailing classes of theories attribute

autistic impairments to dysfunctional brain structures supporting social information

processing (Dawson, Webb & McPartland, 2005) or altered connectivity among

distributed brain regions (Minshew & Williams, 2007). The former emphasizes the

import of the content that is processed, and the latter accentuates the nature of processing

itself. Social brain theories posit that social information is qualitatively unique and that

specific brain systems have evolved to support this type of information processing.

Connectivity theories, in contrast, have traditionally argued that social information is

relevant only insofar as it relies on complex or cortically distributed processing

mechanisms. The current work demonstrates, for the first time in a substantial sample of

children with ASD, preserved specialization for a cognitive process subserved by

distributed cortical regions. Development of specialized letter processing is a process that

develops over time and requires elaborate communication of anterior and posterior

cortical regions (Krigolson, Pierce, Holroyd & Tanaka, 2009). The demonstration of

preserved neural specialization for this type of "expert" processing in ASD is not consistent with models of non-specific, brain-wide dysfunction. Taking into account consideration considerable evidence for atypical patterns of connectivity in ASD (Minshew & Williams, 2007), current findings emphasize the potential value of studying connectivity *within specific brain systems in developmental context*. The observed latency delays may reflect reduced connectivity, and their specificity to social information compared to non-social information may indicate system-specificity in terms of atypical connectivity. By studying connectivity within specific neural circuits, scientists may also extricate atypical connectivity as potential cause or consequence of autistic dysfunction; it is likely that origins of dysfunction in functionally specific brain systems would, through developmental maturation, lead to broader connectivity problems. Such research may also clarify to what degree problems with connectivity uniquely differentiate autism from the diversity of developmental and psychiatric disorders also manifesting atypical connectivity, e.g. obsessive-compulsive disorder, (Garibotto et al., 2010), schizophrenia (Friston, 2002), ADHD (Murias, Swanson & Srinivasan, 2007), and intellectual impairment (Zhou et al., 2008).

This work yields clinically relevant implications for the detection and treatment of ASD. Results are supportive of the broad class of interventions designed to direct the attention of children with ASD to relevant social information. When children are appropriately engaged and attuned to information, in this case, letters, typical patterns of neural specialization develop; given the right input, the brain of a person with autism can function like that a of a typical peer, without ostensible reliance on compensatory mechanisms or alternative processing strategies. Findings add to a body of evidence that

electrophysiological brain activity to faces represents a viable bio-behavioral risk marker

for ASD, as temporal anomalies in neural correlates of face perception have been

observed in children with ASD (Dawson, Webb, Wijsman et al., 2005) and infants at-risk

for ASD (McCleery et al., 2009).

Though the current work replicates initial findings of temporal anomalies to faces

(McPartland et al., 2004), these findings have not fully replicated in all samples (Kemner,

Schuller & van Engeland, 2006; Senju, Tojo, Yaguchi & Hasegawa, 2005; Webb et al.,

2009). Some of this variability may reflect methodological inconsistencies in terms of

electrode selection (e.g., Webb et al., 2009) or employment of gold-standard diagnostic

procedures (e.g., Grice, Halit, Farroni, Baron-Cohen, Bolton & Johnson, 2005); however,

varied results may accurately reflect the phenotypic heterogeneity evident in ASD.

Despite the unifying characteristic of social impairment, ASD presents in a remarkable

diversity of manifestations, likely representing multiple etiologic pathways and

developmental experiences (Jones & Klin, 2009). Considering the manner in which face

processing (especially in older children and adults) has been actively shaped by

experience, it is intuitive that anomalies might emerge in different ways or might not

emerge universally (Jemel, Mottron & Dawson, 2006). In this regard, like any of the

symptoms characterizing autism, anomalous face perception is neither necessary nor

specific. It is one potential manifestation of atypical social development that, by virtue of

a deep understanding of behavioral and brain bases in typical social development, is a

viable avenue for investigating social disability. Variability in electrophysiological

studies of face perception may also relate to differences in visual attention (Webb et al.,

2009), a trend observed in hemodynamic studies (Dalton, Nacewicz, Alexander &

Davidson, 2007; Dalton et al., 2005). Our employment of a pre-stimulus fixation crosshair reduces the likelihood that between-group differences are attributable to differences in visual attention. Furthermore, given comparable N170 latencies to visual fixations to eyes and mouths in typical development (McPartland, Cheung, Perszyk & Mayes, 2010) and delayed processing in ASD irrespective of point of gaze on the face (McPartland, Perszyk, Crowley, Naples & Mayes, 2011), it is unlikely that variation in visual attention alone could account for observed latency differences; resolution of this matter will ultimately require co-registration of eye-tracking and EEG.

There are several aspects of the current work that are being revisited and improved upon in ongoing research. Limiting the sample to high-functioning individuals was a necessary first step towards addressing the research questions posed in this study, but it limits generalizability to the broader range of individuals with ASD. Given that even many nonverbal children with ASD are capable of reading, these types of experiments offer a window into domains of strength and preserved neural functions of children on the autism spectrum, important goals for tailoring interventions and proscribing specific treatments. The sample in the current study focused on pre-adolescence, a time of rapid maturation of brain systems subserving face perception. Additional research in younger and older children and adults will elucidate the protracted maturational course of specialization for face perception in ASD and of letter expertise in both typical and atypical development. Of note, many participants in the current study displayed the bifid waveform morphology characteristic of pre-adult face responses (Taylor, Batty & Itier, 2004); however, this was not evident for letter N170s. Exploiting the dense spatial sampling afforded by the 256 electrode sensor net, analyses in progress

are using individual-specific three-dimensional head models (computed with sensor registration images acquired with the Geodesic Photogrammetry System) to localize potentially distinct neural sources for these facets of the developing N170 (Perszyk et al., 2010).

Our current results reveal a different relationship between performance on the behavioral face processing task and brain responses in individuals with ASD than observed in a prior study (McPartland et al., 2004). Previously, results indicated slowed processing to be associated with improved face recognition. In the current study, however, the group of people with ASD, like the typically developing counterparts in the current and prior study, displayed an association between faster processing and better face recognition. We hypothesize that this reflects age-related differences in the application of compensatory strategies over time. In this younger sample, more normative brain responses correlated with more normative face recognition ability in ASD. In the older sample studied previously, the opposite trend was observed in the hemisphere contralateral to that typically associated with face perception; we interpret this as reflective of effective compensatory processing strategies. In the approximately 10 years between age 11 (current study) and age 21 (prior study), increased reliance on compensatory strategies may "overtake" weakened default processing mechanisms, ultimately resulting in better performance associated with these compensatory strategies. Though we see the pattern of results as supportive of this interpretation, it is also possible that the differences observed between studies simply reflect task effects, as the prior work relied on a visual recall task and the current study utilized a visual discrimination task

with reduced memory demands. Face recognition performance in ASD is demonstrated to vary with task characteristics (McPartland, Webb, Keehn & Dawson, 2011).

Understanding developmental factors is particularly important in the current context in that neural specialization for letters is clearly a distinct phenomenon from face expertise, occurring over a relatively compressed period of time rather than from birth. Moreover, it is likely that qualitatively different types of experience are associated with the accrual of proficiency in letter versus face processing. It will thus be essential to examine development of specialized processing mechanisms for a greater variety of stimuli. Though it has been proposed that, like faces, letters are encoded using a holistic processing strategy (Martelli, Majaj & Pelli, 2005), unlike faces, letters are processed at a basic rather than subordinate level of identification (James et al., 2005). The N170 has been posited to denote specialization at this basic level of identification, while later components, such as the N250, index expertise at the subordinate level of identification (Scott, Tanaka, Sheinberg & Curran, 2006). Similar mechanisms underlying neural specialization for both faces and letters exist at early processing stages as indexed by the N170, but study of a broader range of electrophysiological components and expert stimuli will paint a clearer picture of the development and potential limitations of neural specialization in ASD.

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Figure Legends

Figure 1. Grand averaged waveforms across entire scalp for faces, houses, and inverted faces for typical participants and those with ASD. Electrodes of interest in right and left hemisphere are highlighted. Subpanels display the averaged waveform across the eight specified electrodes in each hemisphere for both groups.

Figure 2. Mean latency of the N170 component (in milliseconds) elicited by faces and houses for both groups in both hemispheres. Error bars represent +/- 1 S.E. Significance at the $p \leq .05$ level is indicated by *.

Figure 3. Grand averaged waveforms across entire scalp for letters and pseudoletters for typical participants and those with ASD. Electrodes of interest in right and left hemisphere are highlighted. Subpanels display the averaged waveform across the eight specified electrodes in each hemisphere for both groups.

Figure 4. Amplitude of the N170 component (in microVolts) elicited by letters and pseudoletters for both groups in both hemispheres. Error bars represent +/- 1 S.E. Significance at the $p \leq .05$ level is indicated by *, and significance at the $p \leq .01$ level is indicated by **.

Tables

Table 1

Participant Characteristics

	Typical (N=18)	ASD (N=36)
Number male (Percent)	15 (83.3)	32 (88.9)
Number White (Percent)	15 (83.3)	34 (94.4)
Number right handed (Percent)	16 (88.9)	31 (86.1)
Mean age (SD)	12.6 (2.4)	11.2 (3.4)
Mean Full Scale IQ (SD)	112.9 (13.4)	105.2 (17.3)

Table 2

P1 and N170 amplitude

Hemisphere	Condition	P1 M (microVolts)	SD	N170 M (microVolts)	SD
Typical group					
Left	Faces	7.77	4.4	0.39	1.7
	Houses	8.60	5.7	2.49	3.5
	Inverted faces	7.70	4.8	0.24	2.8
	Letters	6.28	3.3	- 2.27	3.0
	Pseudoletters	5.89	3.4	- 1.51	3.1
Right	Faces	6.79	5.0	- 0.16	2.0
	Houses	7.94	5.8	0.89	2.6
	Inverted faces	7.50	5.5	- 0.58	2.8
	Letters	5.03	2.5	- 3.03	4.2
	Pseudoletters	5.10	3.0	- 2.53	3.9
ASD group					
Left	Faces	8.94	5.6	- 0.32	3.4
	Houses	10.49	6.2	3.16	4.0
	Inverted faces	9.64	5.4	0.59	3.6
	Letters	6.26	3.8	- 3.09	3.6
	Pseudoletters	6.31	3.6	- 2.22	3.3
Right	Faces	10.10	6.5	0.76	3.6
	Houses	11.11	6.7	3.44	4.2

Inverted faces	11.17	6.7		1.52	3.5
Letters	6.40	3.3	-	3.57	3.1
Pseudoletters	6.59	3.7	-	2.29	2.9

Table 3

P1 and N170 latency

Hemisphere	Condition	P1		N170	
		M (milliseconds)	*SD*	*M* (milliseconds)	*SD*
Typical group					
Left	Faces	115.27	10.9	193.24	37.3
	Houses	134.71	20.6	215.59	43.4
	Inverted faces	119.44	9.7	194.82	35.3
	Letters	106.67	22.0	177.25	26.9
	Pseudoletters	111.58	25.6	179.56	26.8
Right	Faces	118.44	12.2	181.38	31.6
	Houses	133.97	15.0	217.50	36.4
	Inverted faces	121.12	9.6	188.85	32.7
	Letters	104.72	25.8	181.19	25.9
	Pseudoletters	106.89	24.7	176.03	28.5
ASD group					
Left	Faces	118.73	10.3	200.13	24.3
	Houses	134.05	11.3	221.67	31.2
	Inverted faces	125.97	10.5	205.42	27.7
	Letters	102.68	13.4	189.21	26.7
	Pseudoletters	106.29	15.1	178.83	19.3
Right	Faces	117.59	10.8	201.78	27.2
	Houses	130.25	14.4	219.38	27.8

Inverted faces	122.78	15.4	204.66	31.3
Letters	101.53	14.1	188.42	28.0
Pseudoletters	103.97	14.9	183.51	23.6

Table 4

Performance on behavioral measures

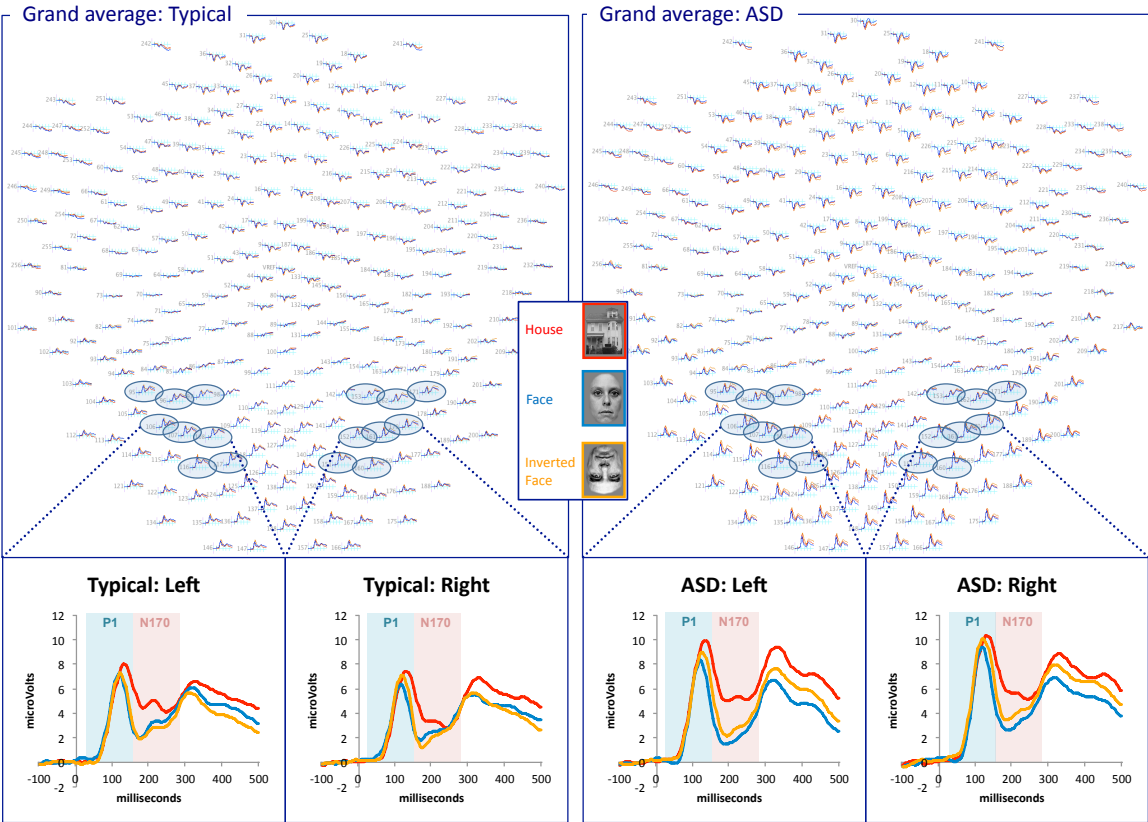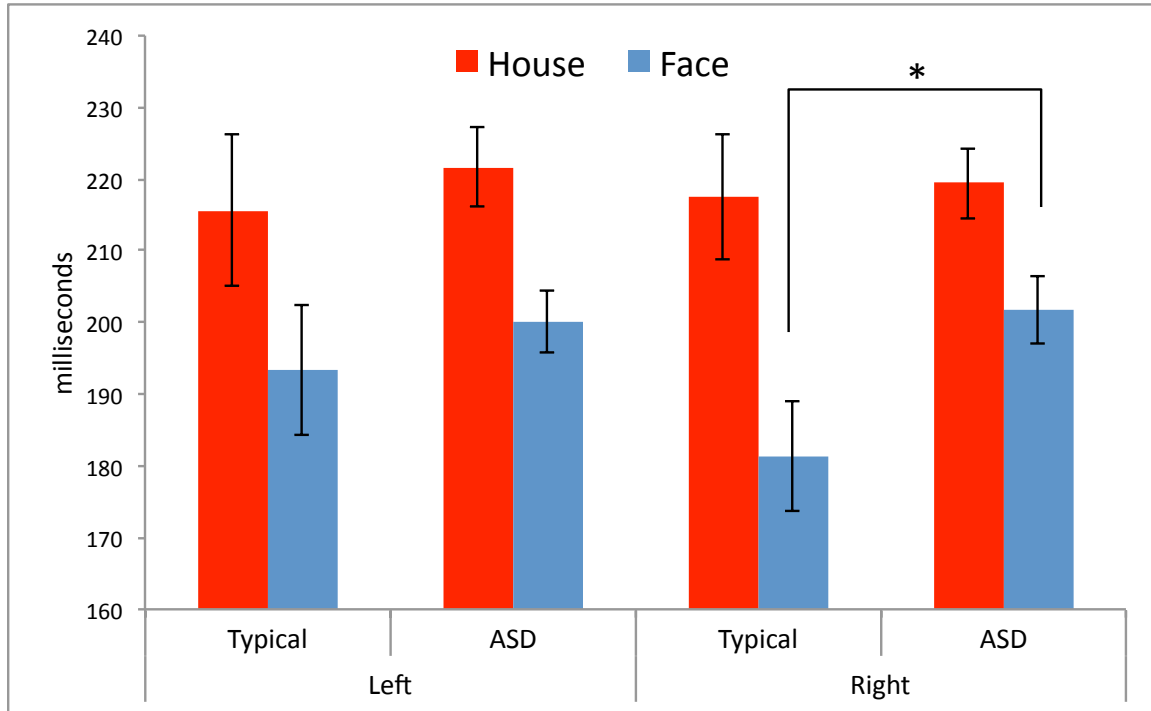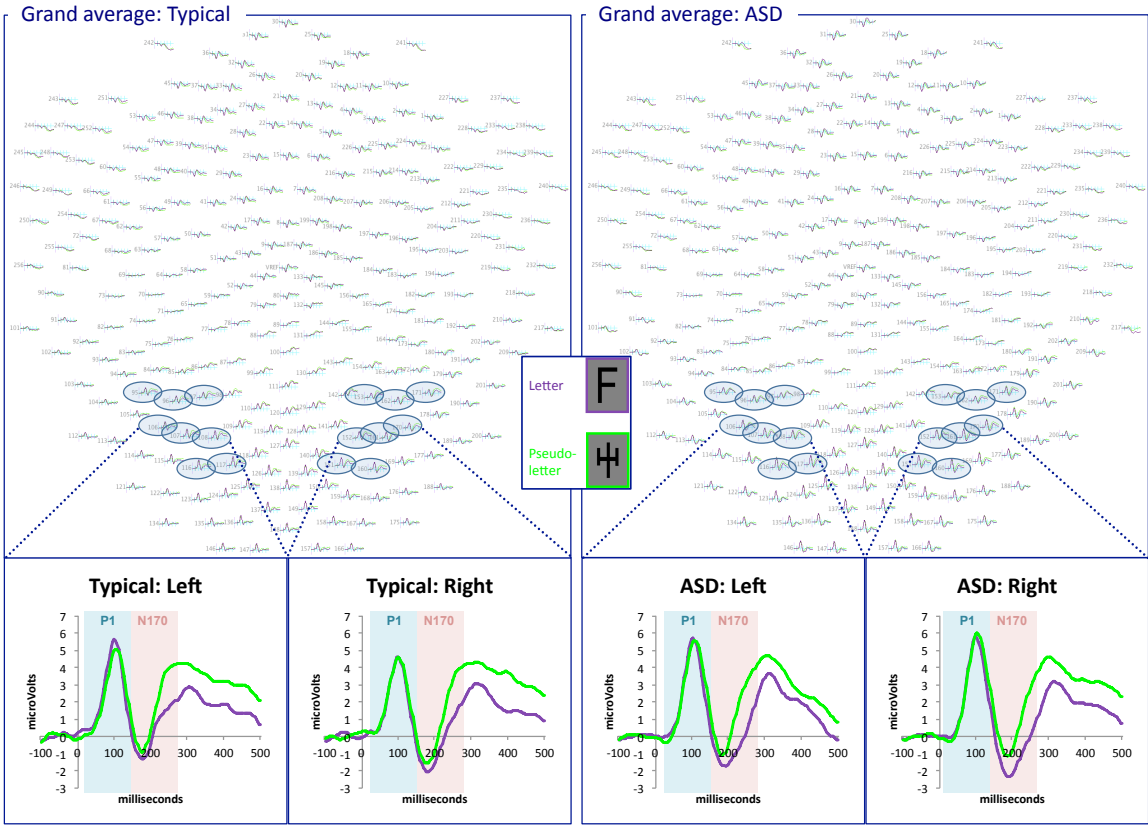|	Typical (N = 17)		ASD (N = 36)	
Measure	*M*	*SD*	*M*	*SD*
Benton Face Recognition Raw Score	41.41	3.6	37.11	4.8
Letter-Word Identification Standard Score	108.41	9.9	105.67	15.0
Word Attack Standard Score	101.41	9.7	103.86	11.6

Figure 1 TOP

Figure 2 TOP

Figure 3 TOP

Figure 4 TOP