

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research report

Atypical category processing and hemispheric asymmetries in high-functioning children with autism: Revealed through high-density EEG mapping

Ian C. Fiebelkorn^{a,b}, John J. Foxe^a, Mark E. McCourt^b, Kristina N. Dumas^a and Sophie Molholm^{a,*}

^aThe Sheryl and Daniel R. Tishman Cognitive Neurophysiology Laboratory, Children's Evaluation and Rehabilitation Center (CERC), Departments of Pediatrics and Neuroscience, Albert Einstein College of Medicine, Van Etten Building, 1C, Bronx, NY, USA

^bCenter for Visual and Cognitive Neuroscience, Department of Psychology, North Dakota State University, Fargo, ND, USA

ARTICLE INFO

Article history:

Received 27 October 2011

Reviewed 20 March 2012

Revised 1 April 2012

Accepted 17 April 2012

Action editor Mike Anderson

Published online xxx

Keywords:

Autism spectrum disorders

Category processing

Hemispheric asymmetries

Attention

Electroencephalography

ABSTRACT

Behavioral evidence for an impaired ability to group objects based on similar physical or semantic properties in autism spectrum disorders (ASD) has been mixed. Here, we recorded brain activity from high-functioning children with ASD as they completed a visual-target detection task. We then assessed the extent to which object-based selective attention automatically generalized from targets to non-target exemplars from the same well-known object class (e.g., dogs). Our results provide clear electrophysiological evidence that children with ASD ($N = 17$, aged 8–13 years) process the similarity between targets (e.g., a specific dog) and same-category non-targets (SCNT) (e.g., another dog) to a lesser extent than do their typically developing (TD) peers ($N = 21$). A closer examination of the data revealed striking hemispheric asymmetries that were specific to the ASD group. These findings align with mounting evidence in the autism literature of anatomic underconnectivity between the cerebral hemispheres. Years of research in individuals with TD have demonstrated that the left hemisphere (LH) is specialized toward processing local (or featural) stimulus properties and the right hemisphere (RH) toward processing global (or configural) stimulus properties. We therefore propose a model where a lack of communication between the hemispheres in ASD, combined with typical hemispheric specialization, is a root cause for impaired categorization and the oft-observed bias to process local over global stimulus properties.

© 2012 Elsevier Srl. All rights reserved.

1. Introduction

The current diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) diagnostic criteria for autism spectrum disorders (ASD) describe a “persistent preoccupation with parts of objects” as a core component of the

phenotype. In the words of a familiar proverb, individuals with typical development (TD) first see the forest (Navon, 1977), while individuals with ASD first see the trees (Plaisted et al., 1999). The weak central coherence theory of autism emphasizes that this well-established tendency to focus on details at the expense of configural information is a cognitive style rather than a deficit

* Corresponding author.

E-mail address: sophie.molholm@einstein.yu.edu (S. Molholm).

0010-9452/\$ – see front matter © 2012 Elsevier Srl. All rights reserved.

doi:10.1016/j.cortex.2012.04.007

(Frith, 1989; Happé and Frith, 2006), and experimental evidence supports this characterization. Individuals with ASD are able to use global stimulus properties when cued to do so, but otherwise have an inherent bias to process local stimulus properties (Plaisted et al., 1999). Under normal circumstances, when there are no explicit instructions to use global stimulus properties, this bias toward local processing has been shown to lead to atypical performance in various cognitive tasks (Bölte et al., 2007; see Dakin and Frith, 2005 for a review; O’Riordan et al., 2001; Plaisted et al., 1999; Scherf et al., 2008). Such a bias might have implications for categorization (i.e., the grouping objects based on similar physical or semantic properties), particularly when the to-be-categorized objects differ in their specific features but are similar in their global stimulus properties. A chair, for example, is not a chair because of any single feature, but rather because of its configuration of features; likewise, a face is a face because it has two symmetrically placed eyes, a nose below, and so on. We would thus predict that a local processing bias interferes with the activation of broader category representations, leading to impaired categorization in ASD.

Despite the strong theoretical basis for hypothesizing atypical categorization among individuals with ASD, existing evidence is mixed, with some studies reporting impaired categorization (e.g., Gastgeb et al., 2006; Klinger and Dawson, 2001; Vladusich et al., 2010) and others not (e.g., Bott et al., 2006; Molesworth et al., 2005; Soulières et al., 2007, 2011; Tager-Flusberg, 1985). A closer examination of these disparate findings suggests that impaired categorization in ASD indeed depends on the extent to which category membership is based on global rather than local stimulus properties (Gastgeb et al., 2006; Klinger and Dawson, 2001; Vladusich et al., 2010). This hypothesis was explicitly tested in Vladusich et al. (2010), where participants classified novel dot patterns into two categories. In one experiment, category designations had to be made based on the configuration of all the constituent dots within a stimulus. In a separate experiment, category designations could instead be made at the featural level, based on a subset of dots that remained stationary across stimuli. Supporting the notion that impaired categorization in ASD arises from a bias toward local over global processing, performance in the ASD group was impaired during the first experiment, which favored global processing, and fully intact during the second experiment, which favored local processing.

Although impaired categorization might only be observed when membership is based on global stimulus properties, presumably atypical neural processes are operating even when behavioral differences in categorization are not observed (i.e., when category designations can be made based on local

stimulus properties alone). A direct examination of these atypical neural processes would therefore provide important clues regarding the etiology of impaired categorization, and possibly the autism phenotype more generally. To this end, we recorded event-related potentials (ERPs) to determine the extent to which children with ASD automatically process the similarities between exemplars of the same well-known object class (dogs, cars, or guitars). That is, we measured whether electrophysiological markers for object-based selective attention (Molholm et al., 2004, 2007) occur in response to same-category non-targets (SCNT) in children with ASD (Fig. 1). The well-established bias among individuals with ASD to process local over global stimulus properties led us to predict reduced generalization (or a reduced spread of attention) from targets to SCNT as compared to children with TD.

To presage our results, the data reveal (1) atypical category processing and (2) marked hemispheric asymmetries in children with ASD. Years of research have demonstrated hemispheric specialization in the processing of local and global stimulus properties, with the left hemisphere (LH) specialized toward scrutinizing constituent features and the right hemisphere (RH) toward grouping features into whole objects (e.g., Atchley and Atchley, 1998; Flevaris et al., 2010; Robertson et al., 1988, 1993; Volberg et al., 2009; Weissman and Woldorff, 2005; but see Kéita and Bedoin, 2011). What’s more, a separate line of research has revealed consistent neuroanatomic and functional evidence for reduced inter-hemispheric connectivity in autism (Alexander et al., 2007; Barnea-Goraly et al., 2004; Chung et al., 2004; Just et al., 2007; Piven et al., 1997). Here, we combine these previous observations with our own data to introduce a model where isolation of the cerebral hemispheres in ASD leads to functional separation of local (LH) and global (RH) processing. We argue that impairments in categorization thus stem from diminished global–local integration, which is expressed behaviorally as a bias to process local over global stimulus properties.

2. Methods

2.1. Participants

Seventeen high-functioning children with ASD (two left-handed, three females) and 21 TD children (one left-handed, 10 females) between the ages of eight and 13 years participated in this study. The two groups were statistically equivalent (i.e., $p > .05$) in terms of mean age and performance intelligence quotient (IQ) (Table 1). In accordance with the

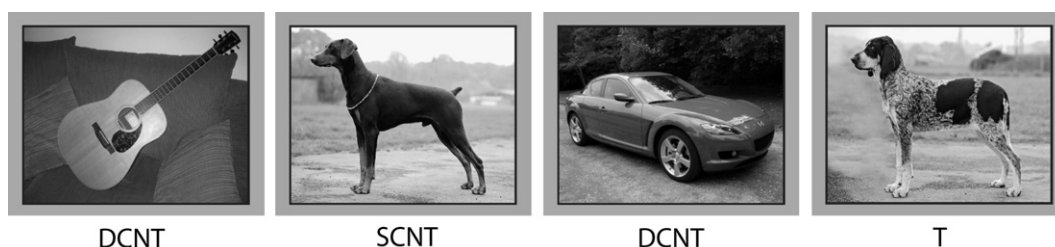


Fig. 1 – Examples of the stimuli presented during a target-dog block. There were three stimulus types: targets (T), SCNT, and DCNT.

Declaration of Helsinki, the parents of all the participants provided written informed consent, and when appropriate, children provided written assent. All the procedures and consent forms were approved by the Institutional Review Boards of the City College of New York and the Albert Einstein College of Medicine. Participants, who were recruited through referrals, as well as advertising and health fairs, were paid \$12.00 an hour. Exclusionary criteria for both groups included uncorrected vision problems or a history of seizures. Parents were asked to refrain from giving their children stimulant medication in the 24-h period before the testing session. TD children were excluded if they had a history of educational, attentional, psychiatric, or developmental difficulties as assessed by a history questionnaire, and were also excluded if their parents endorsed six items of inattention or hyperactivity on a DSM-IV behavioral checklist of attention deficit disorder (with and without hyperactivity). For the ASD group, diagnoses were made based on an assessment that included both the Autism Diagnostic Observation Schedule (Lord et al., 1999) and the Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994), and were confirmed by clinical judgment for 16 of the 17 children. For one of the children, the ADI-R was not performed. Of the 17 children in the ASD group, seven had a diagnosis of Autistic Disorder, eight had a diagnosis of Asperger's Disorder, and two had a diagnosis of Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS). An additional 11 participants (six ASD and five TD) were excluded based on unusually poor task performance or an overabundance of electroencephalography (EEG) artifacts.

2.2. Stimuli and task

Two black and white photographs were used to represent three well-known objects: dogs, cars, and guitars (Fig. 1). The centrally presented images, which appeared on a gray background, subtended 4.4° of the visual angle in the vertical plane and 5.8° of the visual angle in the horizontal plane. The images were presented for 300 msec, and the interstimulus interval was 300–600 msec. Within a given block, participants were asked to maintain central fixation and to press the left mouse button whenever a target photograph (shown to them at the onset of the block) appeared within a stimulus stream that included photographs of all three well-known objects. There were target-dog, target-car, and target-guitar blocks, where a single photograph was designated as the target. A second exemplar of the target object was also included in the stimulus stream, but was treated as a non-target (i.e., within a given block, participants only responded to one of the two photographs of the target object). Each block therefore included one exemplar of each of the non-target objects and

two exemplars of the target object (the target itself and the SCNT), with each exemplar being presented 18 times within a block. Across a total of 15 blocks, each of the six photographs (two for each object) was used as the target at least twice, with one of the two exemplars of each object being used as the target three times. Blocks were further broken into mini-blocks (of 20 stimuli), which allowed for short breaks in the stimulus stream where participants would get feedback on their performance, and could rest their eyes and refocus on the task at hand. Recording sessions typically lasted for approximately 1 h. The experimental paradigm also included task-irrelevant auditory representations of dogs, cars, and guitars, but here analyses and results are focused strictly on the visual-alone stimuli.

2.3. Data acquisition and processing

Continuous EEG recordings were acquired through the ActiveTwo BioSemi (Amsterdam) electrode system from 72 scalp electrodes, digitized at 512 Hz. These recordings were initially referenced online relative to a common mode active electrode. One electrode placed 1 cm posterior to each orbital canthus and one electrode placed on the nasion were used to monitor eye movements.

EEG data were processed using the FieldTrip toolbox (Donders Institute for Brain, Cognition and Behavior, Radboud University Nijmegen, the Netherlands) for MATLAB (The MathWorks Inc., Natick, Massachusetts). The continuous EEG was first low-pass filtered below 45 Hz, then divided into epochs (–100 msec pre-stimulus to 500 msec poststimulus onset) and baseline corrected from –100 msec to stimulus onset. An artifact rejection criterion of $\pm 80 \mu\text{V}$ was used at an electrode placed on the supranasion to reject trials with blinks, and an artifact rejection criterion of $\pm 100 \mu\text{V}$ was used at all other scalp sites to reject trials with eye movements, excessive EMG, or other noise transients. EEG epochs were averaged for each participant to compute ERPs. To ensure that we only considered data where participants were actively engaged in the experimental task, we eliminated data from mini-blocks where target detection fell below 75 percent. The averaged waveforms were algebraically re-referenced to an average reference (i.e., an average of the activity at all electrodes). Separate group-averaged ERPs for each stimulus type were generated for display purposes. Because the time between stimuli was rather short, 300–600 msec, we used the Adjacent Response (Adjar) algorithm on our subject-level data to model and remove any response overlap (Woldorff, 1993).

2.4. Statistical analysis

For all of our analyses we collapsed across the object categories (dogs, cars, and guitars). To test whether behavioral performance differed across the two groups, we conducted independent samples t-tests with hit rates and then reaction times as the dependent measure. For our initial statistical analysis of the ERPs, we conducted repeated measures analysis of variance (ANOVAs) with a between-subjects factor of group (two levels: ASD and TD) and a within-subjects factor of stimulus type (three levels: target, SCNT, and DCNT). The dependent measure for this analysis was the response to each of the

Table 1 – Age and IQ.

Group	Age	Performance intelligence quotient (PIQ)	Verbal intelligence quotient (VIQ)
ASD (N = 17)	11.2 (1.8)	104.5 (17.8)	97.3 (19.2)
TD (N = 21)	10.5 (1.5)	109.0 (11.9)	116.8 (14.0)
Standard deviation in parentheses.			

stimulus types during five different 20-msec windows from 200 msec to 300 msec (i.e., we conducted five ANOVAs, one for each temporal window). This sliding window approach is a common way to capture the relative evolution of overlapping effects, which might be expected, for example, to have different onsets (Fiebelkorn et al., 2010; Talsma et al., 2007). We chose the starting point (200 msec poststimulus) based on previous studies that have demonstrated object-based selective attention effects (e.g., Molholm et al., 2004, 2007). Based on those same studies, we averaged across four electrodes of interest: two each over the left and right lateral occipital regions.

In response to unpredicted processing asymmetries in the ASD group, which were readily apparent in our scalp topographies, we undertook a second, pointed statistical analysis. Here, we conducted repeated measures ANOVAs with a between-subjects factor of group and a within-subjects factor of hemisphere (two levels: left and right). The dependent measure for this analysis was category-specific effects (i.e., the difference between the responses to SCNT and DCNT). The time windows of interest were limited to those where significant category-specific and target-specific effects had been observed for the ASD group in the initial analysis (240–280 msec). We conducted the same analysis on target-specific effects (the difference between the responses to targets and DCNT) to confirm that no such hemispheric asymmetries were observed in response to targets. The alpha level for all statistical analyses was set at .05.

3. Results

For each block, participants were asked to respond to a specific exemplar (black and white photographs) of one of three well-known objects: dogs, cars, and guitars. In addition to the target (e.g., a specific dog) and exemplars of two non-target objects (e.g., cars and guitars), the stimulus stream included a second exemplar from the same category as the target (e.g., another dog). This second exemplar was included to test for electrophysiological evidence of differences in categorization across the two groups of participants (Fig. 1).

Independent samples *t*-tests on the behavioral data revealed nearly identical performance across the ASD and TD groups. The average hit rates for the two groups were both 95 percent ($t_{1,36} = -.1, p = .92$), and the average reaction times for the two groups were 525 msec and 529 msec, respectively ($t_{1,36} = -.2, p = .82$). False alarm rates in response to SCNT were below 1 percent for all participants.

Because equivalent behavioral performance might emerge from non-equivalent underlying neural processes, we also examined ERPs. Previous studies in normative adults have demonstrated object-based selection negativities [i.e., ERP components that track visual selective attention (Hansen and Hillyard, 1980)] that begin at approximately 200 msec post-stimulus (e.g., Molholm et al., 2004, 2007). These ERP effects, which occur in response to visual targets presented in a stimulus stream that also includes visual non-targets, are most evident at electrode sites positioned over the lateral occipital complex—a cluster of brain regions known to contribute to object processing (e.g., Doniger et al., 2000; Lucan et al., 2010;

Sehatpour et al., 2006, 2008). Based on these earlier findings, we began our statistical analyses of ERPs at 200 msec poststimulus and focused on similar lateral occipital electrode sites. To track the evolution of responses both within and between our groups, we used five consecutive 20-msec windows up to 300 msec poststimulus (Fiebelkorn et al., 2010; Talsma et al., 2007).

Our initial goal was to establish whether there were significant category-specific and target-specific responses, and whether those responses differed between the ASD and TD groups. To this end, we conducted repeated measures ANOVAs with a between-subjects factor of group (two levels: ASD and TD) and a within-subjects factor of stimulus type (three levels: target stimulus, SCNT, and DCNT). Important to our central hypotheses, there was a significant interaction between group and stimulus type from 200 to 280 msec ($F_{2,72} = 3.7\text{--}4.4, p's < .05$), but the pattern of results underlying this significant interaction changed depending on the time window. Prior to 240 msec, pairwise comparisons revealed enhanced processing of targets ($p's < .05$) and SCNT ($p's < .05$) relative to DCNT within the TD group, and insignificant results within the ASD group. From 240 to 280 msec, significant differences persisted in the TD group ($p's < .001$), but a different pattern of results emerged in the ASD group. Here, pairwise comparisons revealed enhanced processing of targets relative not only to DCNT ($p's < .01$), but also relative to SCNT ($p's < .03$). The results of the stimulus type by group analysis thus demonstrated (1) that object-based selective attention effects were delayed in children with ASD, and (2) that children with ASD processed the similarity between targets and SCNT to a lesser extent than did TD children (Figs. 2 and 3).

A closer look at the scalp topographies associated with the category-specific effects (i.e., the difference between ERPs in response to SCNT and DCNT) suggested a more complex pattern of results, with striking hemispheric asymmetries in the ASD group that were not present in the TD group (Figs. 2 and 3). To further investigate these findings, we tested whether the category-specific effects differed significantly across hemisphere. We conducted repeated measures ANOVAs with a between-subjects factor of group (two levels: ASD and TD) and a within-subjects factor of hemisphere (two levels: left and right). The dependent measure for this statistical analysis was the difference between the response to SCNT and DCNT (i.e., enhanced processing associated with a non-target being from the same category as the target). To be conservative, we further limited our analysis to time windows of interest (240–260 msec and 260–280 msec) from the previous ANOVAs (i.e., time windows where pairwise comparisons revealed significant differences among the stimulus types within the ASD group). The results of this second statistical analysis demonstrated a significant interaction between group and hemisphere from 240 to 280 msec ($F_{1,36} = 4.9\text{--}6.3, p's < .03$). Pairwise comparisons further revealed that this interaction was attributable to a significant difference in category-specific effects between hemispheres within the ASD group ($p's < .01$), and no such significant difference between hemispheres within the TD group. More specifically, category-specific effects were significantly greater over the right than the LH of the ASD group (Fig. 4), and category-specific effects over the LH of the ASD group were significantly smaller than those over the LH of the TD group

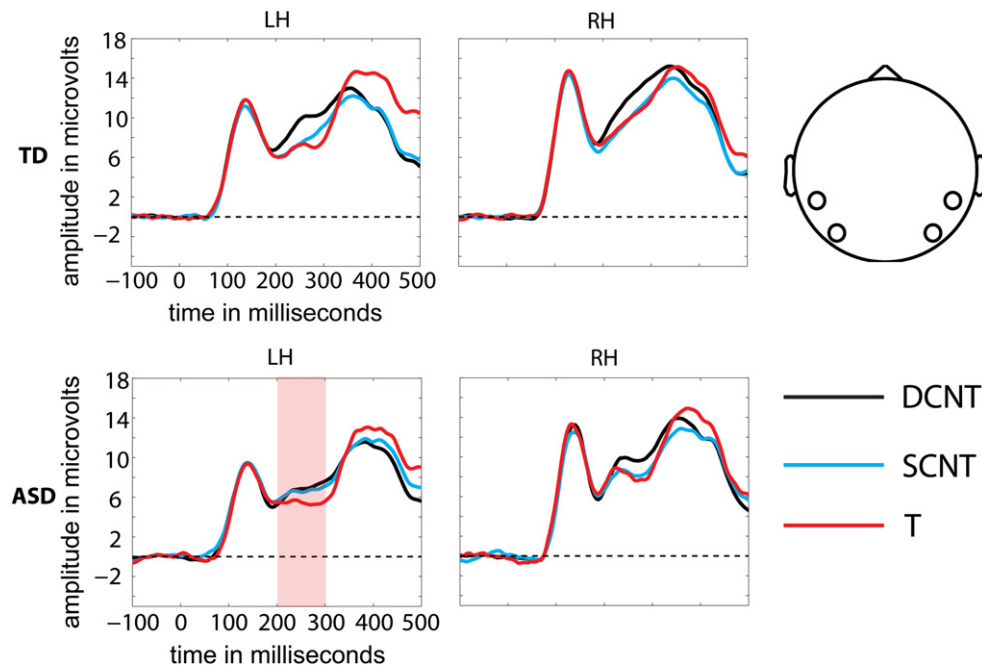


Fig. 2 – Electrophysiological evidence for differential category processing and hemispheric asymmetry in children with ASD. A between groups comparison of the ERPs in response to targets (T), SCNT, and DCNT from electrodes positioned over lateral occipital regions in the LH and RH. The pink rectangle denotes the time period during which we conducted our statistical analyses.

(p 's < .005). An identical analysis of target-specific effects (i.e., the difference between targets and DCNT) revealed no significant hemispheric differences in either the ASD or TD group, confirming that the occurrence of targets led to enhanced processing in both hemispheres.

Given the different ratios of males to females in the ASD and TD groups, as well as some evidence that there are hemispheric differences between the sexes (see Garn et al., 2009), we re-analyzed the data after females were removed from both groups. In other words, we investigated whether the hemispheric asymmetries observed within the ASD group would also be apparent in the TD group when both were limited to males. This yielded the same pattern of results as did the full sample, indicating that gender did not account for the observed differences. Specifically, there was a significant interaction between group and hemisphere from 240 to 280 msec ($F_{1,36} = 4.3–5.4$, p 's < .05), and pairwise comparisons demonstrated a significant difference in category-specific effects between hemispheres within the ASD group (p 's < .04), with no such significant difference between hemispheres within the TD group.

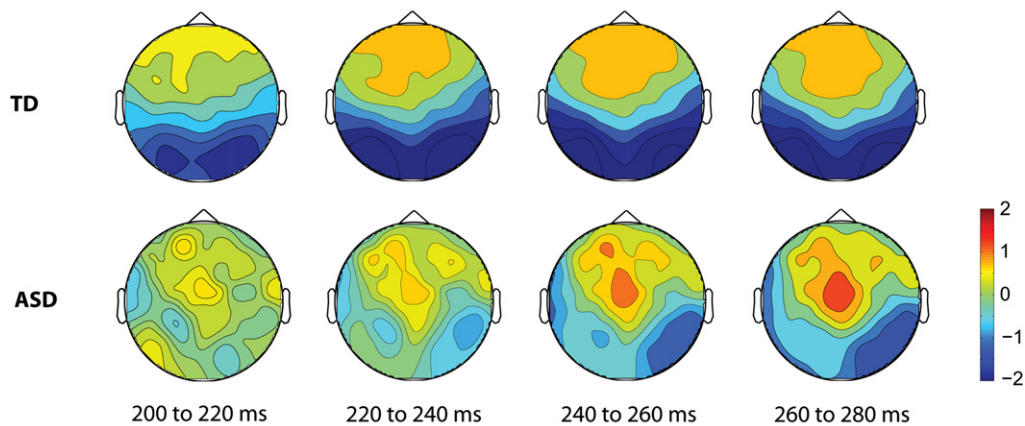
4. Discussion

The current data—presented in the context of a visual-target detection task where behavioral performance across the two groups was equivalent—provide electrophysiological evidence that children with ASD process the relationship among stimuli that are similar in both form and semantic identity to a lesser extent than do TD children (Figs. 2 and 3).

Participants were asked to respond to a specific exemplar of a well-known object (e.g., a dog) embedded in a stimulus stream that included a second exemplar of the same object (e.g., another dog), as well as exemplars of other well-known objects (e.g., cars and guitars). Unlike TD children, for whom electrophysiological markers of selective attention appeared to be identical in response to targets and SCNT, selective attention effects in children with ASD were greatly diminished in response to SCNT. These results reveal that selective attention was more specifically oriented in children with ASD (i.e., selective attention effects were stronger in response to targets than in response to SCNT). The combined behavioral and electrophysiological data thus indicate that children with ASD followed a different, though equally effective path to visual-target detection.

The data further reveal hemispheric asymmetries in children with ASD that were not apparent in their TD counterparts (Figs. 3 and 4), with category-specific selective attention effects that were strongly weighted toward the RH. The absence of selective attention effects in response to SCNT over the LH in ASD aligns well with one of the more consistent findings in autism: underconnectivity among anatomically separate brain regions (Anderson et al., 2011; Casanova et al., 2002, 2011; Castelli et al., 2002; Darmala et al., 2010; Just et al., 2004, 2007; Kumar et al., 2010; Luna et al., 2002). In particular, several studies have reported that the corpus callosum, the primary white matter tract connecting the hemispheres, is reduced in size among individuals with ASD (Alexander et al., 2007; Barnea-Goraly et al., 2004; Casanova et al., 2011; Chung et al., 2004; Just et al., 2007; Piven et al., 1997). What's more, David et al. (2010) recently provided behavioral evidence that

a Category-specific effects



b Target-specific effects

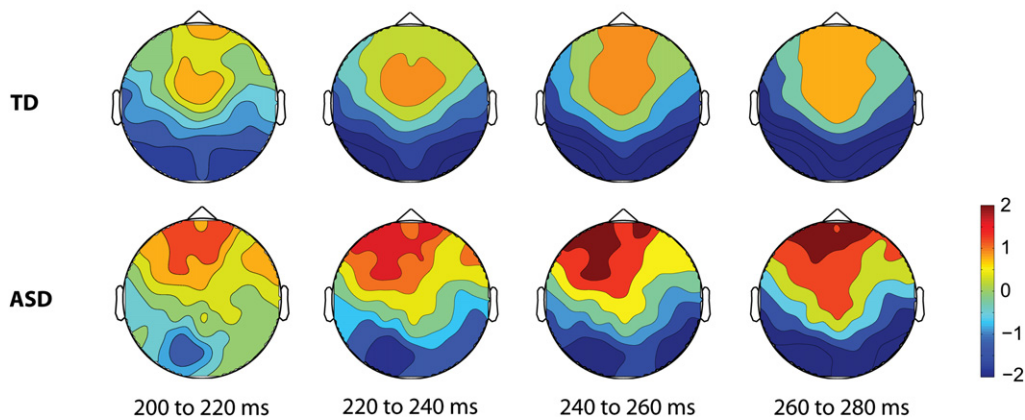


Fig. 3 – Scalp topographies of the (a) category-specific and (b) target-specific effects for both groups. Category-specific effects were bilateral in the TD group and weighted toward the RH in the ASD group.

this hemispheric isolation has functional consequences. Individuals with ASD were shown to perceive coherent motion when dots were sequentially presented at locations within a single hemisphere (i.e., vertical motion), but not when the dots were sequentially presented at locations that

crossed the hemispheres (i.e., horizontal motion), thus demonstrating atypical perception when there was a need for interhemispheric integration.

In the current experiment, the absence of selective attention effects in the LH in response to SCNT suggests a greater degree of independence between the hemispheres in children with ASD as compared to children with TD (Figs. 2 and 3). An abundance of data from the normative population have shown that the LH is specialized toward scrutinizing constituent features and the RH toward grouping features into whole objects (e.g., Flevaris et al., 2010; Robertson et al., 1988, 1993; Volberg et al., 2009; Weissman and Woldorff, 2005; but see Kéita and Bedoin, 2011). Although selective attention can accentuate this hemispheric specialization (Flevaris et al., 2010; Volberg et al., 2009), typical object processing engages both hemispheres. Expert discrimination, such as that required for facial recognition, is based not only on the parsing of separate features but also on determining the unique quantitative or configural relationship among those features (i.e., expert discrimination requires an integration of local and global stimulus properties). In individuals with ASD, on the other hand, there is a well-documented overreliance on local

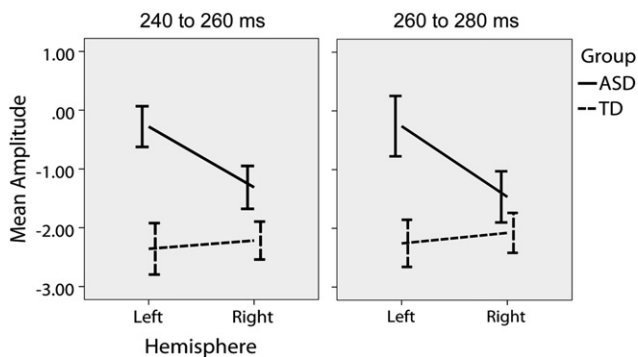


Fig. 4 – A representation of the significant interaction between group and hemisphere for the category-specific effects (i.e., the response to SCNT minus the response to DCNT). The error bars denote one standard error of the mean.

stimulus properties (or features) in both facial processing (e.g., Boucher and Lewis, 1992; Joseph and Tanaka, 2003; Klin et al., 2002) and visual processing in general (Bölte et al., 2007; see Dakin and Frith, 2005 for a review; O’Riordan et al., 2001; Plaisted et al., 1999; Scherf et al., 2008). Combining our results with those from previous studies, we propose that this oft-observed bias toward local processing in ASD, which leads to impaired categorization, arises from typical hemispheric specialization coupled with atypical hemispheric isolation. In other words, the cerebral hemispheres in ASD differ in their object processing duties (as is the case in TD), but communication between the two hemispheres—and thus global–local integration—is reduced. In TD children, we suspect that bilateral activation in response to both targets and SCNT involves coupling between the hemispheres, with visual-target detection being based on a more holistic (or integrated) representation of local and global stimulus properties. Among children with ASD, visual-target detection might instead be based on a subset of target-specific features, with bilateral activation of the hemispheres in response to targets stemming from independent processing of local and global stimulus properties. As a consequence of this greater functional independence between the hemispheres, children with ASD might need to make a choice between directing processing toward either local or global stimulus properties. Plaisted et al. (1999) indeed demonstrated that individuals with ASD, although having a predisposition toward local stimulus properties, are capable of biasing object processing toward global stimulus properties when cued to do so. The well-established bias toward local stimulus processing in ASD is thus not obligatory, but represents the optimal strategy in the context of reduced global–local integration. That is, if global–local integration is diminished in ASD, focusing on a specific, unique feature (or set of features) will often be a better strategy for visual-target detection, particularly when making within-category discriminations (i.e., when global stimulus properties tend to be similar across objects).

Investigations into neuronal connectivity in individuals with ASD have not only revealed underconnectivity among anatomically separated cortical regions, but also over-connectivity within local cortical regions (Barttfeld et al., 2011; Courchesne and Pierce, 2005; Kéïta et al., 2011). Such excess short-range projections might further contribute to decreased integration by increasing the autonomy of processing within local cortical regions (Liu et al., 2011; Simmons et al., 2009). The enhanced perceptual functioning (EPF) theory of autism posits that overdeveloped low-level sensory processing, which has been hypothesized to arise from over-connectivity, creates a competitive advantage for local features (Motttron et al., 2006; Wang et al., 2007). The bias toward local stimulus properties (or constituent features) in ASD might therefore result from both underconnectivity among anatomically separated cortical regions and over-connectivity within local cortical regions.

In addition to differences in category processing, target-specific ERP effects in our data seemingly began earlier in TD children than children with ASD, but these shorter latency effects were not reflected in reaction times, which were nearly identical across the two groups. Differences in the onset of target-specific ERP effects could simply be attributable to greater variability in the ASD sample, but we offer an

alternative explanation. Based on the scalp topographies, we hypothesize that this apparent electrophysiological difference might result, at least in part, from different generators in the LH. Although speculative at this point, selective attention effects in response to targets appear to be slightly more central in the LH of children with ASD than in the LH of TD children (Fig. 3). Such a shift in the voltage map would be expected if there was a greater reliance on local stimulus properties, leading to greater selective attention effects in earlier regions of the visual processing hierarchy (i.e., regions that would be better represented by electrodes positioned closer to the midline). Future research using a methodology with better spatial resolution, such as functional magnetic resonance imaging (fMRI), will be needed to detect the existence of such subtle differences in the underlying neural generators.

Despite nearly identical behavioral results, we report processing differences between ASD and TD children that demonstrate electrophysiological evidence of a frequently described behavioral effect: impaired categorization. What’s more, apparent hemispheric asymmetries in children with ASD illuminate a possible etiology for a section of the DSM-IV diagnostic criteria: “a persistent preoccupation with parts of objects.” Hemispheric isolation might lead to a reduction in global–local integration and a greater reliance on (or bias toward) local stimulus properties when processing objects and categories. Our data provide electrophysiological evidence in support of the notion that previously described under-connectivity in ASD may be a root cause for some of the characteristic behaviors associated with the autism phenotype.

Acknowledgments

This work was supported by a National Institute of Mental HealthMH-085322 to SM and JFF, and a National Science FoundationBCS0642584 to JFF. ICF and MEM received support from the National Center for Research Resources (NCRR) and the National Institute for General Medicine (NIGMS) of the National Institutes of Health (NIH) through Grants P20 RR020151 and P20 GM103505. The contents of this report are solely the responsibility of the authors and do not necessarily reflect the official views of the NIH, NCRR or NIGMS. We would like to thank Dr. Natalie Russo and Sarah Ruberman for their help at various stages of the project. We would also like to acknowledge the contributions of the staff at the Human Clinical Phenotyping Core (HCP) of the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (IDDRC) during the recruitment and clinical classification of a portion of the participants who served in this study. This core is supported through a P30 center grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (HD071593).

REFERENCES

Alexander AL, Lee JE, Lazar M, Boudos R, DuBray MB, Oakes TR, et al. Diffusion tensor imaging of the corpus callosum in autism. *NeuroImage*, 34(1): 61–73, 2007.

- Anderson JS, Druzgal TJ, Froehlich A, DuBray MB, Lange N, Alexander AL, et al. Decreased interhemispheric functional connectivity in autism. *Cerebral Cortex*, 21(5): 1134–1146, 2011.
- Atchley RT and Atchley P. Hemispheric specialization in the detection of subjective objects. *Neuropsychologia*, 36(12): 1373–1386, 1998.
- Barnea-Goraly N, Kwon H, Menon V, Eliez S, Lotspeich L, and Reiss AL. White matter structure in autism: Preliminary evidence from diffusion tensor imaging. *Biological Psychiatry*, 55(3): 323–326, 2004.
- Barttfeld P, Wicker B, Cukier S, Navarta S, Lew S, and Sigman M. A big-world network in ASD: Dynamical connectivity analysis reflects a deficit in long-range connections and an excess of short-range connections. *Neuropsychologia*, 49(2): 254–263, 2011.
- Bölte S, Holtmann M, Poustka F, Scheurich A, and Schmidt L. Gestalt perception and local-global processing in high-functioning autism. *Journal of Autism and Developmental Disorders*, 37(8): 1493–1504, 2007.
- Bott L, Brock J, Brockdorff N, Boucher J, and Lamberts K. Perceptual similarity in autism. *Quarterly Journal of Experimental Psychology*, 59(7): 1–18, 2006.
- Boucher J and Lewis V. Unfamiliar face recognition in relatively able autistic children. *Journal of Child Psychology and Psychiatry*, 33(5): 843–859, 1992.
- Casanova MF, Buxhoeveden DP, Switala AE, and Roy E. Minicolumnar pathology in autism. *Neurology*, 58(3): 428–432, 2002.
- Casanova MF, El-Baz A, Elnakib A, Switala AE, Williams EL, Williams DL, et al. Quantitative analysis of the shape of the corpus callosum in patients with autism and comparison individuals. *Autism*, 15(2): 223–238, 2011.
- Castelli F, Frith C, Happé F, and Frith U. Autism, Asperger Syndrome and brain mechanisms for the attribution of mental states to animated shapes. *Brain*, 125(8): 1839–1849, 2002.
- Chung MK, Dalton KM, Alexander AL, and Davidson RJ. Less white matter concentration in autism: 2D voxel-based morphometry. *NeuroImage*, 23(1): 242–251, 2004.
- Courchesne E and Pierce K. Why the frontal cortex in autism might be talking only to itself: Local over-connectivity but long-distance disconnection. *Current Opinion in Neurobiology*, 15(2): 225–230, 2005.
- Dakin S and Frith U. Vagaries of visual perception in autism. *Neuron*, 48(3): 497–507, 2005.
- Darmala SR, Keller TA, Kana RK, Cherkassky VL, Williams DL, Minshew NJ, et al. Cortical underconnectivity coupled with preserved visuospatial cognition in autism: Evidence from an fMRI study of an embedded figures task. *Autism Research*, 3(5): 273–279, 2010.
- David N, Rose M, Schneider TR, Vogeley K, and Engel AK. Brief report: Altered horizontal binding of single dots to coherent motion in autism. *Journal of Autism and Developmental Disorders*, 40(12): 1549–1551, 2010.
- Doniger GM, Foxe JJ, Murray MM, Higgins BA, Snodgrass JG, and Schroeder CE. Activation timecourse of ventral visual stream object-recognition areas: High-density electrical mapping of perceptual closure processes. *Journal of Cognitive Neuroscience*, 12(4): 615–621, 2000.
- Fiebelkorn IC, Foxe JJ, Schwartz TH, and Molholm S. Staying within the lines: The formation of visuospatial boundaries influences multisensory feature integration. *European Journal of Neuroscience*, 31(10): 1737–1743, 2010.
- Flevaris AV, Bentin S, and Robertson LC. Local or global? Attentional selection of spatial frequencies binds shapes to hierarchical levels. *Psychological Science*, 21(3): 424–431, 2010.
- Frith U. *Autism: Explaining the Enigma*. Oxford: Blackwell, 1989.
- Garn CL, Allen MD, and Larsen JD. An fMRI study of sex differences in brain activation during object naming. *Cortex*, 45(5): 610–618, 2009.
- Gastgeb HJ, Strauss MS, and Minshew NJ. Do individuals with autism process categories differently? The effect of typicality and development. *Child Development*, 77(6): 1717–1729, 2006.
- Hansen JC and Hillyard SA. Endogenous brain potentials associated with selective auditory attention. *Electroencephalography and Clinical Neurophysiology*, 49(3–4): 277–290, 1980.
- Happé F and Frith U. The weak coherence account: Detail-focused cognitive style in autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 36(1): 5–25, 2006.
- Joseph RM and Tanaka J. Holistic and part-based face recognition in children with autism. *Journal of Child Psychology and Psychiatry*, 44(4): 529–542, 2003.
- Just MA, Cherkassky VL, Keller TA, Kana RK, and Minshew NJ. Functional and anatomical cortical underconnectivity in autism: Evidence from an fMRI study of an executive function task and corpus callosum morphometry. *Cerebral Cortex*, 17(4): 951–961, 2007.
- Just MA, Cherkassky VL, Keller TA, and Minshew NJ. Cortical activation and synchronization during sentence comprehension in high-functioning autism: Evidence of underconnectivity. *Brain*, 127(8): 1811–1821, 2004.
- Kéita L and Bedoin N. Hemispheric asymmetries in hierarchical stimulus processing are modulated by stimulus categories and their predictability. *Laterality*, 16(3): 333–355, 2011.
- Kéita L, Mottron L, Dawson M, and Bertone A. Atypical lateral connectivity: A neural basis for altered visuospatial processing autism. *Biological Psychiatry*, 70(9): 806–811, 2011.
- Klin A, Jones W, Schultz R, Volkmar F, and Cohen D. Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. *Archives of General Psychiatry*, 59(9): 809–816, 2002.
- Klinger LG and Dawson G. Prototype formation in autism. *Developmental Psychopathology*, 13(1): 111–124, 2001.
- Kumar A, Sundaram SK, Sivaswamy L, Behen ME, Makki MI, Ager J, et al. Alterations in frontal lobe tracts and corpus callosum in young children with autism spectrum disorder. *Cerebral Cortex*, 20(9): 2103–2113, 2010.
- Liu Y, Cherkassky VL, Minshew NJ, and Just MA. Autonomy of lower-level perception from global processing in autism: Evidence from brain activation and functional connectivity. *Neuropsychologia*, 49(7): 2105–2111, 2011.
- Lucan JN, Foxe JJ, Gomez-Ramirez M, Sathian K, and Molholm S. Tactile shape discrimination recruits human lateral occipital complex during early perceptual processing. *Human Brain Mapping*, 31(11): 1813–1821, 2010.
- Luna B, Minshew NJ, Garver KE, Lazar NA, Thulborn KR, Eddy WF, et al. Neocortical system abnormalities in autism: An fMRI study of spatial working memory. *Neurology*, 59(6): 834–840, 2002.
- Lord C, Rutter M, DiLavore PC, and Risi S. Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*, 24(5): 659–685, 1994.
- Lord C, Rutter M, DiLavore PC, and Risi S. *Autism Diagnostic Observation Schedule*. Los Angeles, CA: Western Psychological Services, 1999.
- Molesworth CJ, Bowler DM, and Hampton JA. The prototype effect in recognition memory: Intact in autism? *Journal of Child Psychology and Psychiatry*, 46(6): 661–672, 2005.
- Molholm S, Martinez A, Shpaner M, and Foxe JJ. Object-based attention is multisensory: Co-activation of an object's representation in ignored sensory modalities. *European Journal of Neuroscience*, 26(2): 499–509, 2007.
- Molholm S, Ritter W, Javitt DC, and Foxe JJ. Multisensory visual-auditory object recognition in humans: A high-density electrical mapping study. *Cerebral Cortex*, 14(4): 452–465, 2004.

- Mottron L, Dawson M, Soulières I, Hubert B, and Burack J. Enhanced perceptual functioning in autism: An update, and eight principles of autistic perception. *Journal of Autism and Developmental Disorders*, 36(1): 27–43, 2006.
- Navon D. Forest before trees: The precedence of global features in visual perception. *Cognitive Psychology*, 9: 353–383, 1977.
- O’Riordan MA, Plaisted KC, Driver J, and Baron-Cohen S. Superior visual search in autism. *Journal of Experimental Psychology Human Perception and Performance*, 27(3): 719–730, 2001.
- Piven J, Bailey J, Ranson BJ, and Arndt S. An MRI study of the corpus callosum in autism. *American Journal of Psychiatry*, 154(8): 1051–1056, 1997.
- Plaisted KC, Swettenham J, and Rees L. Children with autism show local precedence in a divided attention task and global precedence in a selective attention task. *Journal of Child Psychology and Psychiatry*, 40(5): 733–742, 1999.
- Robertson LC, Lamb MR, and Knight RT. Effects of lesions of temporal-parietal junction on perceptual and attentional processing in humans. *Journal of Neuroscience*, 8(10): 3757–3769, 1988.
- Robertson LC, Lamb MR, and Zaidel E. Interhemispheric relations in processing hierarchical patterns: Evidence from normal and commissurotomy subjects. *Neuropsychology*, 7(3): 325–342, 1993.
- Scherf KS, Luna B, Kimchi R, Minschew N, and Behrmann M. Missing the big picture: Impaired development of global shape processing in autism. *Autism Research*, 1(2): 114–129, 2008.
- Sehatpour P, Molholm S, Javitt DC, and Foxe JJ. Spatiotemporal dynamics of human object recognition processing: An integrated high-density electrical mapping and functional imaging study of “closure” processes. *NeuroImage*, 29(2): 605–618, 2006.
- Sehatpour P, Molholm S, Schwartz TH, Mahoney JR, Mehta AD, Javitt DC, et al. A human intracranial study of long-range oscillatory coherence across a frontal-occipital-hippocampal brain network during visual object processing. *Proceedings of the National Academy of Sciences of the United States of America*, 105(11): 4399–4404, 2008.
- Simmons DR, Robertson AE, McKay LS, Toal E, McAleer P, and Pollick FE. Vision in autism spectrum disorders. *Vision Research*, 49(22): 2705–2739, 2009.
- Soulières I, Mottron L, Giguère G, and Larochelle S. Category induction in autism: Slower, perhaps, different, but certainly possible. *Quarterly Journal of Experimental Psychology*, 64(2): 311–327, 2011.
- Soulières I, Mottron L, Saumier D, and Larochelle S. Categorical perception in autism: Autonomy of discrimination? *Journal of Autism and Developmental Disorders*, 37(3): 481–490, 2007.
- Tager-Flusberg H. Basic level and superordinate level categorization by autistic, mentally retarded, and normal children. *Journal of Experimental Child Psychology*, 40(3): 450–469, 1985.
- Talsma D, Doty TJ, and Woldorff MG. Selective attention and audiovisual integration: Is attending to both modalities a prerequisite for early integration? *Cerebral Cortex*, 17(3): 679–690, 2007.
- Vladusich T, Olu-Lafe O, Kim DS, Tager-Flusberg H, and Grossberg S. Prototypical category learning in high-functioning autism. *Autism Research*, 3(5): 226–236, 2010.
- Volberg G, Kliegl K, Hanslmayr S, and Greenlee MW. EEG alpha oscillations in the preparation for global and local processing predict behavioral performance. *Human Brain Mapping*, 30(7): 2173–2183, 2009.
- Wang L, Mottron L, Peng D, Berthiaume C, and Dawson M. Local bias and local-to-global interference without global deficit: A robust finding in autism under various conditions of attention, exposure time, and visual angle. *Cognitive Neuropsychology*, 24(5): 550–574, 2007.
- Weissman DH and Woldorff MG. Hemispheric asymmetries for different components of global/local attention occur in distinct temporo-parietal loci. *Cerebral Cortex*, 15(6): 870–876, 2005.
- Woldorff MG. Distortion of ERP averages due to overlap from temporally adjacent ERPs: Analysis and correction. *Psychophysiology*, 30(1): 98–119, 1993.