



Neural processing of intentional biological motion in unaffected siblings of children with autism spectrum disorder: An fMRI study



Alex A. Ahmed, Brent C. Vander Wyk*

Child Study Center, Yale University School of Medicine, 230 South Frontage Road, New Haven, CT 06519, United States

ARTICLE INFO

Article history:

Accepted 22 September 2013

Available online 12 October 2013

Keywords:

Action perception

Autism

Endophenotype

Superior temporal sulcus

fMRI

ABSTRACT

Despite often showing behaviorally typical levels of social cognitive ability, unaffected siblings of children with autism spectrum disorder have been found to show similar functional and morphological deficits within brain regions associated with social processing. They have also been reported to show increased activation to biological motion in these same regions, such as the posterior superior temporal sulcus (pSTS), relative to both children with autism and control children. It has been suggested that this increased activation may represent a compensatory reorganization of these regions as a result of the highly heritable genetic influence of autism. However, the response patterns of unaffected siblings in the domain of action perception are unstudied, and the phenomenon of compensatory activation has not yet been replicated. The present study used functional magnetic resonance imaging to determine the neural responses to intentional biological actions in 22 siblings of children with autism and 22 matched controls. The presented actions were either congruent or incongruent with the actor's emotional cue. Prior studies reported that typically developing children and adults, but not children with autism, show increased activation to incongruent actions (relative to congruent), within the pSTS and dorsolateral prefrontal cortex. We report that unaffected siblings did not show a compensatory response, or a preference for incongruent over congruent trials, in any brain region. Moreover, interaction analyses revealed a sub-region of the pSTS in which control children showed an incongruency preference to a significantly greater degree than siblings, which suggests a localized deficit in siblings. A sample of children with autism also did not show differential activation in the pSTS, providing further evidence that it is an area of selective disruption in children with autism and siblings. While reduced activation to both conditions was unique to the autism sample, lack of differentiation to incongruent and congruent intentional actions was common to both children with ASD and unaffected siblings.

© 2013 Elsevier Inc. All rights reserved.

1. Introduction

Research focusing on unaffected siblings of individuals with autism spectrum disorder (ASD) is critical to understanding how the disorder impacts both individuals and families. Recently published studies have examined not only quantitative measures of mental health in siblings, but also their subjective experiences and perceptions (Angell, Meadan, & Stoner, 2012; Petalas, Hastings, Nash, Reilly, & Dowey, 2012; Shivers, Deisenroth, & Taylor, 2012). Furthermore, study of the “broader phenotype” of autism traits has consistently shown that siblings of children with autism exhibit behavioral deficits in social, communication, and learning do-

mains (see Dawson et al., 2002, for a review). Moreover, Kates et al. (2004) reported shared structural deficits in frontal, temporal, and occipital lobes between discordant twin pairs (one child diagnosed with autism and one unaffected). In this study, all but one of the nine twin pairs contained a unaffected sibling who exhibited the broad autism phenotype, which was defined as showing a language or social delay that was either subclinical (undiagnosed but indicating mild impairment), or clinical (diagnosed as developmental delay or pervasive developmental disorder, but not as autism).

Neuroimaging data from unaffected siblings have also been presented in terms of their similarities to and differences from control children, as well as children with ASD. Dalton, Naciewicz, Alexander, and Davidson (2007) found that unaffected siblings showed decreased fixations onto faces, decreased fusiform gyrus activation, and decreased amygdala volume compared with controls; all of these deficits were also present in the autism group. Belmonte, Gomot, and Baron-Cohen (2010) showed that both unaffected

Abbreviations: ASD, autism spectrum disorder; US, unaffected siblings; CC, control children; pSTS, posterior superior temporal sulcus; dlPFC, dorsolateral prefrontal cortex; BOLD, blood oxygen level-dependent; ROI, region-of-interest.

* Corresponding author.

E-mail address: brent.vanderwyk@yale.edu (B.C. Vander Wyk).

siblings and children with ASD were behaviorally impaired in a non-social visual attention task and also showed atypical brain activations in frontal and cerebellar regions. However, they also noted that a measure of overall functional correlation was decreased in autism but not in siblings. Barnea-Goraly, Lotspeich, and Reiss (2010) reported that deficits shared between children with ASD and siblings extend to the structural modality (measured by significantly reduced white matter fractional-anisotropy values compared to controls) in regions of the brain associated with social cognition. Baron-Cohen's group reported that neural activations in unaffected siblings are similar to individuals with autism in a face processing task (Spencer et al., 2011). In a visual search task, Spencer et al. (2012) showed not only that unaffected siblings and children with autism show similar reductions in activation, but also that these reductions were correlated with behavioral measures of social interaction. These studies demonstrate that unaffected siblings expressing the broader autism phenotype also have structural and functional neurological deficits, some of which they share with children with ASD.

Taking a different approach, Kaiser et al. (2010) used a social task (point-light displays of biological motion). Crucially, the unaffected siblings were matched with controls on measures of social responsiveness and lacked characteristics of the broader autism phenotype. Thus, any shared neural response patterns could be classified as an endophenotype reflecting ASD vulnerability rather than an epiphenomenon resulting from subclinical behavioral features of the disorder. In that study, children with ASD and unaffected siblings both showed hypoactivations in cortical regions, consistent with prior work. However, they also reported atypical hyperactivations, relative to controls, that were unique to the unaffected siblings. Kaiser et al. hypothesized that these hyperactivations may be neural "compensatory" mechanisms.

Further exploration of similarities and differences in neuroimaging measures between individuals with ASD and their siblings seems pertinent. Given the trajectory of research in ASD, it is natural that many of the previous functional neuroimaging experiments have focused on face processing in unaffected siblings. However, no published studies have extended these findings into the domain of intentional action perception. This extension is required if we are to translate current findings from the low-level social cognition to the experience of actively participating in a social world (a much more complex and higher-level activity).

Prior studies of both children and adults show that brain activations in individuals with ASD differ from controls when viewing actions that are congruent with a prior displayed emotion versus those that are incongruent (Pelphrey, Shultz, Hudac, & Vander Wyk, 2011; Vander Wyk, Voos, & Pelphrey, 2012). The pSTS showed differential activations depending on the congruency of the action, suggested that the region is involved in extracting social meaning (intention) from bodily action. We used functional magnetic resonance imaging (fMRI) to investigate brain activations, as measured by the blood oxygen level-dependent (BOLD) response, to congruent and incongruent intentional actions in unaffected siblings of children with ASD, a matched group of control children, and an unmatched, smaller sample of children with ASD.

The primary hypothesis concerns the comparison of differential activation to incongruent actions in unaffected siblings relative to controls. If the hypothesis concerning compensatory activation is correct, unaffected siblings may show overall greater activation to observed actions, regardless of congruency. However, they may also show increased differential activation to incongruent actions relative to congruent actions. The secondary hypothesis concerns the comparison between the control and ASD groups. Based on prior literature, we expect that they ASD sample will show decreased or no differential activation, and lower activation overall, as a function of congruency.

2. Methods

2.1. Subjects

Three groups of participants were recruited. The first group consisted of 22 unaffected siblings (US) of children with ASD with no history of psychiatric disorders (mean age = 12.58, SD = 2.43, range = 9.08–17.25). The second was an age-, gender-, and sample size-matched group of control children (CC) with no presence of ASD in the family and no psychiatric history (mean age = 11.63, SD = 1.85, range = 7.67–15.17). The third group consisted of 14 children diagnosed with ASD (mean age = 10.92, SD = 3.94, range = 5.67–18). Complete sample statistics are presented in Table 1. Between US and CC groups, there were no significant differences in age ($t(39.205) = -1.4703, p = 0.1495$) or IQ as measured by the DAS-II's General Conceptual Ability standard score ($t(41.596) = -0.461, p = 0.6472$). Moreover, they did not differ in gender-normed T-scores on the Social Responsiveness Scale (SRS; $t(36.779) = 1.0717, p = 0.2909$). The SRS is a 65-item parent-report questionnaire that indexes atypical social behavior and responsiveness (Constantino & Todd, 2003). While it is not intended to be diagnostic of ASD, a score of 60 (one standard deviation above the mean) or higher implies risk for the disorder. Because the US and CC groups tested in the typically developing range for social responsiveness, we account for the possibility that neural differences within US are epiphenomenal to subclinical social impairments.

Diagnosis of individuals in the ASD group was determined using the Autism Diagnostic Observation Schedule (Lord et al., 2000) and/or the Autism Diagnostic Interview-Revised (Lord, Rutter, & Le Couteur, 1994) along with the judgment of expert clinicians. A complete list of scores on diagnostic measures for the ASD group is shown in Table 2. The ASD group showed elevated SRS scores, as expected, with an average of 73.21 (SD = 11.0). Analysis of the ASD sample was primarily intended to provide a confirmation of disorder relevance via a qualitative comparison of the brain response of individuals with ASD, within regions identified in direct comparisons between the other two groups. The ASD group was not matched to the other two groups in gender distribution, IQ, or sample size; however, there was no significant difference in age when comparing the ASD group with the CC group ($t(16.698) = -0.6249, p = 0.5405$) and with the US group ($t(19.361) = -1.4146, p = 0.1731$). In one analysis, a smaller subgroup of control subjects was created for direct comparison with the ASD group (see Section 2.8).

The sample sizes and age distributions reported are the final groups after motion correction of the fMRI data was performed. Motion correction led to the removal of some subjects from the analyses (for more details, see Section 2.4). Written informed consent was required from the parents or legal guardians of all child participants, age-appropriate explanations were given to children and their written assent was obtained, and research protocols were approved by the Yale Human Investigation Committee.

2.2. Paradigm

Subjects were first instructed to watch a DVD movie of their choice while anatomical MRI images were acquired (see below for acquisition details). Afterward, they were instructed to passively view a 6 min, 16 s paradigm, during which functional images were acquired. A visual depiction of the paradigm is displayed in Fig. 1. A human actor displayed either positive or negative affect towards a cup, and disregards the other. The actor then reaches for the same cup she regarded or the other. The resulting two-by-two design (positive-same, positive-other, negative-same,

متن کامل مقاله

دریافت فوری ←

ISIArticles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات