Functional Evaluation of Object Analysis in Children with Autistic Disorder

K. Malisza[1,2], D. Shiloff[3], C. Jones[3], D. Foreman[3], K. Paulson[4], C. Yu[5], S. Longstaffe[6], and A. Chudley[7,8]

[1]MR R&D, Institute for Biodiagnostics-NRC, Winnipeg, MB, Canada, [2]Physiology, University of Manitoba, Winnipeg, MB, Canada, [3]Institute for Biodiagnostics, [4]Medicine, University of Manitoba, [5]St. Amant Centre, Winnipeg, MB, Canada, [6]Pediatrics & Child Health, Health Sciences Centre, Winnipeg, MB, Canada, [7]Pediatrics & Child Health, Children's Hospital, Health Sciences Centre, [8]Biochemistry & Medical Genetics, University of Manitoba, Winnipeg, MB, Canada

Introduction

Autism spectrum disorders (ASDs) are complex genetic disorders characterized by a triad of social relating and communication impairments, with restricted, repetitive or stereotyped behaviours (1). Autistic disorder (AD) is a subtype. Previous studies involving functional magnetic resonance imaging (fMRI) of ASD have shown conflicting results, which may be attributed, in part, to imaging ASD subjects as one group instead of focusing on different subtypes of the disorder. There are clear developmental areas where autistic children differ from typically developing children. One area in which autistic subjects were shown to perform well is object analysis, in terms of embedded figures (2). In this task, subjects must decide if a simple figure shown to them is also present in a complex illustration. To date, all fMRI studies involving embedded figures were performed on only adult ASD volunteers. This is the first study involving functional imaging of children with autism and looking specifically at high-functioning Autistic Disorder.

Methods

Embedded figures FMRI experiments were completed with 7 children with AD, 7 healthy controls (age-, sex-matched) and 7 control subjects with attention deficit hyperactivity disorder (ADHD) (age-, sex- and IQ-matched) all of whom were able to perform the task with >50 % accuracy. Images were shown in which target shapes were presented along with a complex figure that may or may not contain it. The subject determined if the simple object was part of the complex one and responded accordingly. During the control or rest period, only the simple figure was shown. Reaction times were recorded for all of the tasks. Standard gradient-echo EPI with 128 x 128 matrix and 20 cm field of view (echo time (TE) = 40 ms, repetition time (TR) = 3.25 s) was used for functional MRI acquisition. A block design with a total of 80 volumes of 23 contiguous, 5 mm thick slices acquired parallel to the anterior-posterior commissure line were acquired. FMRI data were analyzed using FSL (3) and corrected for multiple comparisons by False Discovery Rate statistics.

T1-weighted anatomical images (TE/TR = 20 ms/500 ms) were acquired (20 cm field of view and 256 x 256 matrix) for reference. Additionally, 3-D SPGR (rf-spoiled gradient echo) images were acquired (5 ms TE, 24 ms TR, 256 x 192 x 124 matrix in a 26 x 24 x 18.8 cm field of view) to overlay fMRI activity.

Results

No significant differences were observed in number of incorrect responses, number of no responses or response latency between healthy controls and children with AD. Significant difference was observed in the number of correct responses, with significantly fewer correct responses in the AD group compared to the healthy control group ($p=0.0178$). No significant differences were observed between the AD group response accuracy or rate, compared to ADHD controls. No significant group differences to any of the measures above were observed between the two control groups. Functional images showed significant activity in the cerebellum in all subjects. Activity in the occipital lobe was observed in all healthy controls, in all but one AD subject, but in only four of seven ADHD subjects. Similarly, the fusiform gyrus showed mainly bilateral activity in all subjects with the exception of one ADHD control. All subjects showed substantial activity in inferior frontal and middle frontal brain regions (except one ADHD individual), particularly in more superior slices. Overall, greater activity was observed in the healthy controls compared to AD and ADHD. While significant activity was typically observed in the occipital-temporal region in children with AD, greater activity was observed in age and sex matched healthy controls. Activity in AD subject was comparable to ADHD controls (figure).

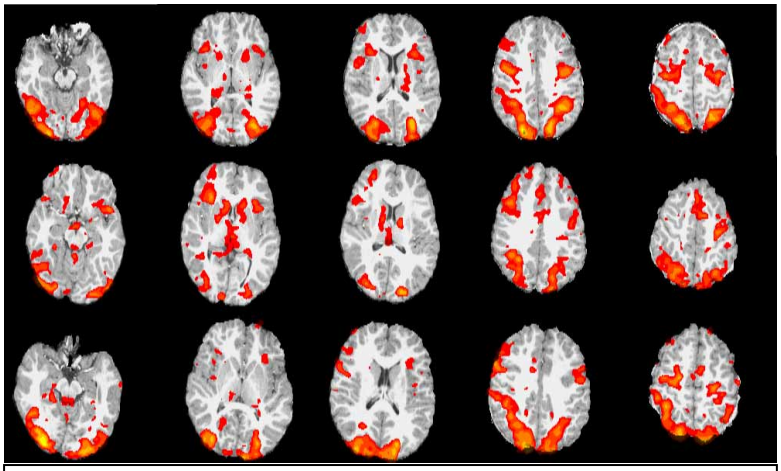

Figure: Example depicting occipitotemporal fMRI activity in a 10 year old male with AD (top), ADHD control (middle) and a healthy control (bottom).

Discussion and Conclusions

In general, individuals with autism perform well on tests that require local processing and visual search. Our study, however, shows the AD group did not perform the embedded figures task more accuracately nor more quickly than healthy individuals. This is contrary to results found in adult ASD populations (2). In the current study, comparison of individual task performance accuracy was not correlated with degree of occipitotemporal fMRI activity. In the example presented in the figure, the subject with high-functioning AD was the worst performer in task accuracy, compared to the age- and sex-matched healthy control, who was among the best in task performance. Yet, fMRI activity in the occipitotemporal region was very similar in the two subjects.

FMRI was recently used to examine the neural correlates of this cognitive skill in autistic adults (2). Normal controls showed more extensive task-related activations generally, but also activated prefrontal cortical areas that were not activated in the autism group (2). Adults with autism showed greater activation in ventral occipitotemporal regions during performance on the embedded figures task, suggesting that their superior performance on the task may reflect greater involvement of cortical regions dedicated to object feature analysis. Again, however, the subjects were from different populations (Asperger and autism), which may potentially prove to be a confounding effect.

This study focused only on high-functioning children with AD. Studies to date have not delineated different subgroups of this disorder in order to understand autism, but tend to view much of the spectrum of disorders together. Previous studies therefore, frequently include a broad range of affected individuals (i.e. Asperger, Pervasive Developmental Disorders-non-specific (PDD-NOS), etc.). The present study provides important information for imaging children with AD only (excluding Asperger syndrome and PDD-NOS). Since the disorders are on a continuous spectrum, it is important to determine if differences are observable between the subgroups, or if consistent patterns of fMRI activity are characteristic of particular subgroups. This can lead to increasing diagnostic specificity and tailored treatment decisions of the individuals.

Acknowledgements: Funding was received from The Canadian National Autism Foundation, The Health Sciences Centre Foundation and Winnipeg Foundation and ASD-CARC (CIHR-IHRT).

References:

1. APA. Diagnostic and statistical manual of mental disorders. DSM-IV. Washington: APA; 1994.
2. Ring, H. A., et al. Cerebral correlates of preserved cognitive skills in autism: a functional MRI study of embedded figures task performance. Brain 1999; 122 (Pt 7): 1305-1315.
3. Smith, S. M., et al. Advances in functional and structural MR image analysis and implementation as FSL. Neuroimage 2004; 23 Suppl 1: S208-S219.