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ORIGINAL PAPER

Functional Evaluation of Hidden Figures Object Analysis in Children with Autistic Disorder

Krisztina L. Malisza · Christine Clancy · Deborah Shiloff · Derek Foreman · Jeanette Holden · Cheryl Jones · K. Paulson · Randy Summers · C. T. Yu · Albert E. Chudley

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Abstract Functional magnetic resonance imaging (fMRI) during performance of a hidden figures task (HFT) was used to compare differences in brain function in children diagnosed with autism disorder (AD) compared to children with attention-deficit/hyperactivity disorder (ADHD) and typical controls (TC). Overall greater functional MRI activity was observed in the two control groups compared to children with AD. Laterality differences were also evident, with AD subjects preferentially showing activity in the right medial temporal region while controls tended to activate the left medial temporal cortex. Reduced fMRI activity was observed in the parietal, ventral-temporal and hippocampal regions in the AD group, suggesting differences in the way that children with AD process the HFT.

Keywords Autism Disorder (AD) · Attention Deficit Hyperactivity Disorder (ADHD) · Embedded Figures Task (EFT) · Hidden Figures Task (HFT) · Functional Magnetic Resonance Imaging (fMRI)

Introduction

Autism spectrum disorders (ASDs) are complex genetic disorders characterized by restricted, repetitive, stereotyped patterns of behavior interests and activities, and lack of symbolic/imaginative play that impair social interaction and communication (American Psychiatric Association 1994; Chudley 2004; Rapin and Tuchman 2008). ASDs are a serious and relatively common problem in society; the prevalence of autistic disorder was reported as being between 30 and 60 per 10,000 (Chakrabarti and Fombonne 2005; Chudley et al. 1998; Ouellette-Kuntz et al. 2006; Fombonne 2003). A comprehensive examination of prevalence of ASD across 14 sites in the United States revealed that 0.66% of children at 8 years of age were diagnosed with an ASD, (range = 3.3–10.6 per 1,000 children), with most sites reporting a rate between 5.2 and 7.6 per 1,000 children (Rice 2007).

Autism spectrum disorders are characterized by significant variation in cognitive ability, ranging from profound mental retardation to the superior range of intellectual functioning (American Psychiatric Association 1994). Mental retardation (IQ < 70) occurs in 70–75% of cases with an increased risk of 3–7% for siblings, which is much greater than for the general population (Boddaert and

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Zilbovicius 2002; Rumsey 1996; Chudley et al. 1998). No consistent pattern of cognitive strengths and deficits has been found; however, Asperger Disorder is often associated with better developed verbal than nonverbal skills (VIQ > PIQ), whereas individuals with autism show the opposite pattern (PIQ > VIQ) (Akshoomoff 2005; Klin et al. 1995).

While the etiologies of autism are still unknown, they are thought to be variable and to involve many brain systems (Rumsey 1996). Specifically, temporal lobe dysfunction has been associated with stereotypical autistic-type behaviors (Bolton and Griffiths 1997). The parietal lobe has been implicated in attentional deficits (Belmonte and Carper 1998) and disturbances in cerebellar pathways both have been linked to autism (Courchesne et al. 1988; Chugani et al. 1997; Schmahmann and Sherman 1998).

Children with autism differ from typically developing children across many domains, including local versus global processing style (Crespi and Badcock 2008; Grinter et al. 2009; Russell-Smith et al. 2010). Here, we focus on object analysis in terms of hidden figures. As in the embedded figures task (EFT), in the hidden figures task (HFT) subjects decide if a simple figure shown to them is also present in a complex illustration. This test provides a measure of local versus global processing style. Children with autism differ from typically developing children in how they process complex visual information. It has been well documented that individuals with autism, as a group, perform well on tests that require local processing and visual search. The most robust demonstration of this comes from studies using the embedded figures task in which subjects are required to find a simple shape in a complex design. Children with autism are either more accurate or perform equally well as controls on this test (Jolliffe and Baron-Cohen 1997; Manjaly et al. 2007; Ring et al. 1999; Shah and Frith 1983).

The use of neuroimaging has helped researchers gain a better understanding of autism from a developmental perspective, but only a handful of studies have implemented this approach. Functional magnetic resonance imaging (fMRI) has recently been used to examine the neural correlates of the embedded figures task in autistic adults (Ring et al. 1999) and adolescents (Manjaly et al. 2007). In these studies, normal controls generally showed more extensive task-related activations, but also activated prefrontal cortical areas that were not activated in the autism group. Adults diagnosed with autism also showed greater activation in ventral occipitotemporal regions during performance on the EFT compared to normal controls, suggesting that their superior performance on the task may reflect greater involvement of cortical regions dedicated to object feature analysis (Ring et al. 1999).

Activation of the ventral occipitotemporal regions is consistent with the ventral stream of visual processing, which answers the question “What?” by analyzing form, with specific regions identifying colors, faces, letters and other visual stimuli. Activations in the parietal region suggest involvement of the dorsal stream of visual processing, which answers the question, “Where?” by analyzing motion and spatial relationships between the body and visual stimuli. Activations in the premotor cortex correspond to the frontal eye fields, which are associated with saccadic eye movements towards an object of visual attention (Blumenfeld 2002). In adolescent controls, left lateralization was observed in the parietal and premotor regions, while in subjects with ASD, activations were mainly right lateralized in the primary visual cortex and were found to have bilateral activation in extrastriate regions during the EFT (Manjaly et al. 2007).

A recent study by Lee et al. (2007) showed greater overall fMRI activity in controls than children with ASD during performance on an EFT. In particular, control children demonstrated functional activity in the left dorsolateral frontal and premotor regions, whereas children with ASD activated only the dorsal premotor region. Bilateral activation was observed in controls in the parietal and occipital regions compared to unilateral (left parietal, right occipital) in ASD. In addition, bilateral temporal activation was observed in controls and not in children with ASD (Lee et al. 2007). Studies in adults and adolescents who performed the EFT showed bilateral activation in the occipito-parietal cortex, but only left parietal activity when the local component of the complex form was viewed (Manjaly et al. 2003, 2007; Ring et al. 1999), suggesting that left parietal activity is linked to local object processing in embedded figures.

To date, we are unaware of any fMRI studies to differentiate the subgroups of autism. Instead, many studies have included subjects across the spectrum of the disorder, and in particular Asperger Syndrome. Previous studies involving fMRI of ASD have shown conflicting results (Boddaert and Zilbovicius 2002; Critchley et al. 2000; Ring et al. 1999; Schultz et al. 2000), which we believe may be attributed, in part, to imaging ASD subjects as one group instead of focusing on different subgroups of the disorder (e.g., Autistic Disorder, Asperger Syndrome). Asperger Syndrome is also associated with later diagnosis than autism and near average or higher intelligence. Those diagnosed with Asperger Syndrome do not show developmental language delay and can be differentiated from autistic disorder in this manner (Rumsey and Ernst 2000). In addition, we are unaware of any fMRI study in which either the hidden or embedded figures tasks were used to evaluate brain function in children with ADHD. Children diagnosed with ASD demonstrate significant ADHD-like deficits; comparable deficits have been observed in visual and auditory attention in children with ASD and with ADHD

(Corbett and Constantine 2006). Tamm et al. (2006) used an oddball task that required subjects to press one button when circles appeared on the screen (80% of the time) and another button when triangles were displayed (20% of the time). Significantly less activity was observed in the parietal lobes, which is known to play a role in detection of specific targets in individuals with ADHD (Tamm et al. 2006). We could not find any studies that used an embedded figures or hidden figures task to evaluate children with ADHD.

In the present study, we examined regions of functional brain activity in children diagnosed with Autistic Disorder (AD), excluding Asperger Syndrome (AS) and pervasive developmental disorder—not otherwise specified (PDD-NOS), and compared them to healthy controls and to children with ADHD using a Hidden Figures Task (HFT). As in the embedded figures task, the HFT requires that subjects decide if a simple figure shown to them is also present in a complex illustration. We wished to contrast the fMRI findings on the HFT not only in typically developing healthy control children, but in children with ADHD to determine whether differences existed in the activation patterns within the visual pathway in the parietal lobes (dorsal stream) that process spatial information and the visual pathway in the temporal lobes (ventral stream) that are involved in distinguishing features (Pliszka et al. 2006; Posner and Petersen 1990). We hypothesized that children with AD would show greater fMRI activity in regions of the brain associated with object feature analysis (ventral stream), while controls would show greater overall brain activation, particularly in the frontal cortex.

Methods

Subject Description

Children aged 9–14 years diagnosed with Autistic Disorder (AD), excluding Asperger Syndrome and PDD-NOS, with adequate verbal communication and oral comprehension to understand the requirements of the tasks, were recruited. Eight AD individuals whose diagnoses were confirmed using an objective quantitative and qualitative assessment of their behaviour and communication skills level using the Autism Diagnostic Interview—Revised (Lord et al. 1994) completed the study. Children in the typical healthy control (TC) group were matched to children diagnosed with AD based on age, gender, and handedness. A second group of children diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD) were matched to children diagnosed with AD based on the above criteria as well. A standardized psychological assessment was conducted for the ADHD and AD groups. General cognitive ability was determined using the *Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV*; The Psychological Corporation 2003).

All subjects were either drug naïve or free from medication, such as Ritalin, for 72 h prior to the functional MRI study. Parents of participants were asked to ensure that their children avoided stimulants, such as chocolate and caffeinated beverages on the study day. Children diagnosed with ADHD were recruited at the office of a pediatrician who specializes in diagnosis of ADHD. None of the children recruited in the ADHD group had any comorbid disorders. Typical children were recruited through posters and were screened using a simple parent questionnaire by our collaborating physician, Dr. A. Chudley, who ensured there was no known diagnosis of ADHD, ASD or other physical or behavioral disability or delay.

Of the fifteen AD subjects recruited, four withdrew from the study prior to performing the fMRI. Two did not complete the embedded figures task and one was excluded as ADI-R and ADOS results indicated the subjects' diagnosis as NQA (not quite autism). Of the eight subjects who completed the HFT, responses were not recorded for two subjects due to technical difficulties with the e-prime program. Both of these subjects, however, performed exceptionally well during the training session (100% accuracy) and monitoring of their responses while in the magnet also indicated that they performed the task well (i.e. approximately 100% accuracy). In addition, data was collected for one of these subjects during the mock scanner training period. This data was included in the behavioral data in place of the lost E-prime results from the actual fMRI session. Unfortunately, E-prime data was not collected during the mock scanner session for the second subject for whom there was behavioral data acquisition error in the fMRI experiment. Subject information and group comparisons regarding the matching criteria and across performance measures for the HFT are presented in Table 1.

Table 1 Subject population information and performance measures on the HFT for the AD, ADHD and TC groups

Subject information	AD	ADHD	TC
Sex	6M,2F	7M,2F	7M,2F
Chronological age (years)	11.7 ± 1.4	12.0 ± 1.8	12.1 ± 1.9
fMRI task accuracy			
Correct responses (%)	80.48 ± 13.73 ($n = 7$)	82.59 ± 8.04 ($n = 9$)	92.41* ± 9.21 ($n = 9$)
Response time (ms)	1212 ± 156 ($n = 8$)	1284 ± 131 ($n = 9$)	1250 ± 146 ($n = 9$)

The values represent mean ± SD. No responses were recorded for two children in the AD group during MRI scanning. The data from the practice session inside the mock scanner was substituted for one child. The asterisk represents marginal significant difference at a level of $p < 0.05$ between AD and control subjects

The project was reviewed and approved by the National Research Council's Winnipeg Research Ethics Board and University of Manitoba Biomedical Research Ethics Board.

MRI Procedures

An integral part of this study involved familiarization training of children in a mock MRI scanner prior to performing the actual MRI experiments. Each component of imaging was introduced to allow children to become familiar with all aspects of the study (e.g., preparation, scanner noise) and training to lie still while in the MRI. Subjects were introduced to the paradigm designs for the embedded figures task to ensure satisfactory performance.

All experiments were conducted using a 1.5 T GE Signa MRI system with a standard GE volume coil (General Electric, Healthcare, Waukesha, WI). Pictures presented for the fMRI tasks were viewed through MR compatible goggles (Avotec) while in the magnet. Foam padding was placed under and around the subject's head for comfort and to immobilize the head as much as possible. A child life specialist was present with the child during the scanning procedure. Standard gradient-echo echo-planar imaging was used with a 128 × 128 matrix and a 20 cm field of view to provide a 1.6 × 1.6 mm in-plane resolution for functional MRI acquisition. A repetition time of 3.25 s was used between repeated excitations of each imaging slice. Twenty-three contiguous 5 mm thick slices were positioned parallel to the anterior-posterior commissure (AC-PC) line to cover the entire brain. A 40 ms echo time was used. T1-weighted anatomical images of these same slices, for anatomical reference, were acquired using an RF-spoiled gradient echo (SPGR) sequence (echo time/repetition time = 20/500 ms, 256 × 256 matrix) for each subject. Three dimensional volume images of the whole brain were acquired for each subject onto which individual functional activations were overlaid.

All 3-D SPGR images were combined into a template for each group. Images were then normalized to this template in order to display group activations. SPGR images were acquired with a 5 ms echo time, 24 ms repetition time, 256 × 192 × 124 matrix in a 26 × 24 × 18.8 cm field of view. Two individual scans were acquired, aligned, and added to increase signal-to-noise rather than signal averaging. A movie was projected through the goggles during anatomical image acquisition to capture the subjects' attention and help reduce motion.

FMRI Paradigm

Functional imaging experiments were conducted in which six rest periods, where only the target remained in the centre of the screen, alternated with six stimulation periods

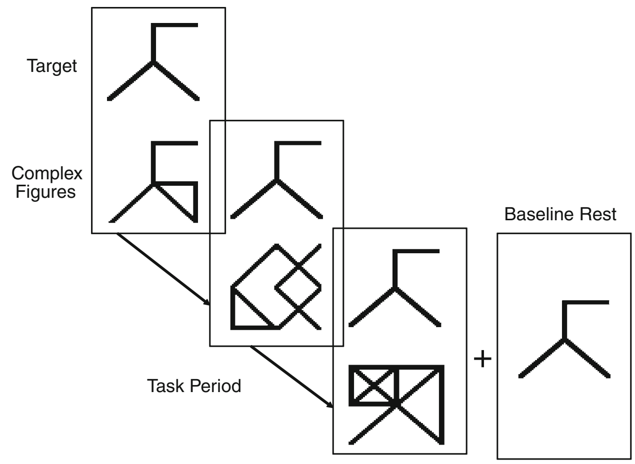

Fig. 1 Example of the hidden figures task (complex figure and target) and baseline rest presented during the fMRI study

where the complex figure appeared directly below the target; ten trials were presented during each stimulation period. Subjects were requested to identify with a button press those stimuli where the target was contained within the complex figure in the exact same orientation for both tasks. Figure 1 depicts the HFT. In all trials, targets appeared in a random order and in approximately 50% of the trials the target was present in the complex figure. Paradigms were constructed using E-Prime (Psychology Software Tools, Inc., PA). The figures used for presentation were a subset of a standardized collection from the Hidden Patterns Test (Ekstrom et al. 1976).

FMRI Data Analysis

Initially, the skull was stripped using the BET tool (Smith 2002). Analysis was carried out using FEAT (FMRI Expert Analysis Tool) Version 5.90 in FSL version 4.0 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl (Jenkinson and Smith 2001; Smith et al. 2004). All data were motion corrected using MCFLIRT and spatially smoothed with a 3 mm full width half maximum Gaussian filter to minimize individual neuroanatomical variation prior to general linear model analysis. FEAT uses univariate general linear modeling (GLM) or multiple regression for fitting the model to the data. Time-series statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) that is incorporated within FEAT. FILM uses nonparametric estimation of time series autocorrelation to prewhiten the time series for each voxel (Woolrich et al. 2001). Z (Gaussianised T/F) statistic images were thresholded using clusters determined by $Z > 2.3$ and 3.0. False Discovery Rate (FDR) corrected ($q \leq 0.05$) statistical maps were generated for individual subjects. Functional activity was overlaid on the individual subjects' high-resolution anatomical images to properly identify regions of the brain showing different activations.

Table 2 Group comparisons on standard IQ measures

WISC IV composite value	AD	ADHD	*p*-Value
VCI*	78.57 ± 21.25	96.89 ± 11.25	0.042
PRI*	84.43 ± 15.00	101.56 ± 11.45	0.021
WMI	75.00 ± 20.36	87.33 ± 11.01	0.142
PSI*	77.71 ± 16.46	93.78 ± 12.66	0.044
FSIQ*	74.71 ± 18.30	94.56 ± 13.17	0.024

The values represent mean ± SD. The asterisk represents significant difference at a level of $p < 0.05$ between AD and ADHD groups

Registration to high resolution images was carried out using FLIRT (Jenkinson and Smith 2001). FDR corrected data was input into the higher level analysis to determine the group mean for all three groups: AD, ADHD and TC. A standard weighted fixed effects modeling was implemented. Fixed effects are known to be more "sensitive" to activation with the error variances consisting of the variances from the previous level. Weighting is introduced by allowing the variances to be unequal and degrees of freedom are calculated by summing the effective degrees of freedom for each input from the previous level and subtracting the number of higher level regressors. Unfortunately, insufficient regions of activity were observed using FLAME (FMRIB's local analysis of mixed effects); however, the fixed effects model analysis was corrected using Bonferroni correction resulting in highly significant activations to the paradigm.

The T_1-weighted (T1W) 3D SPGR whole brain images for all subjects were registered to each other, combined and the skull was stripped, resulting in a combined template used to overlay statistically significant activations. An in-house script was written to perform several operations such as generating individual skull-stripped slices of the T1W images and registration of raw data to the combined template (Smith et al. 2004). After defining the threshold of interest, regions of activity were overlaid onto the combined template to generate functional activity maps.

Group functional activity maps during the HFT at a level of $p < 0.01$ (Bonferroni corrected) are presented in Fig. 1. The corresponding clusters are reported in Table 2. In addition, the level of significance is substantial as only cluster sizes of at least 100 voxels are reported.

Results

Behavioral

Exact 95% confidence intervals and corresponding exact 2-sided *p*-values were calculated for the difference between groups for a difference of two binomial proportions using the software package StatXact, Cytel Corporation. The binomial proportions in our experiment were the proportion of correct answers given for each of the groups AD, TC and ADHD. AD vs. TC: $p = 0.014$ with a 95% confidence interval = (0.007, 0.069), showed a marginally significant difference. AD vs. ADHD: $p = 0.17$ with a 95% confidence interval = (−0.063, 0.012) did not show any significant difference.

Significant differences at $p < 0.05$ were observed for number of correct responses during the HFT in TC children compared to those with AD, however, differences between AD and ADHD subjects were not statistically significant (see Table 1). Groups did not differ significantly in response speed on the task; however, children diagnosed with AD performed these tasks slightly faster on average than the other groups, indicating increased impulsivity in problem solving that may have contributed to their reduced accuracy on the task.

Cognitive

Table 2 displays the means and standard deviations on the WISC-IV by group.

There was a statistically significant difference in overall cognitive ability between the AD and ADHD groups on the *WISC-IV* ($p < 0.05$) favoring the ADHD group. Both the AD and ADHD groups demonstrated PIQ > VIQ; however, the ADHD group performed significantly better on the Perceptual Reasoning Index (PRI), which assesses the interpretation, reasoning and organization of visually presented nonverbal information, than the AD group ($p < 0.05$). More variability across the four composite scores on the *WISC-IV* was evident in the autism group, which is consistent with the heterogeneity in cognitive ability as noted in the literature (Akshoomoff 2005).

fMRI

Overall greater functional activity was observed in typical healthy control children compared to children with AD (Fig. 2; Table 3). Clear occipital activity was present for all subjects. Significant activity was observed in the TC and ADHD controls groups in superior and inferior parietal lobe, in particular at more superior slice levels ($z = 198$–233 mm) and medial frontal gyrus ($z = 213$–228 mm), which was absent in the AD group.

In controls, the activity tended to be either bilateral or mostly in the left hemisphere, while in AD subjects the activity was predominantly in the right hemisphere. Activity in the medial and inferior temporal lobe appears to be significantly greater in controls compared to AD subjects in the left hemisphere, while greater temporal activity was noted in the right hemisphere of subjects with AD

Fig. 2 Functional activity maps showing group analysis during the EFT for **a** AD ($n = 8$), **b** ADHD ($n = 9$), and **c** TC ($n = 9$) at a level of $p < 0.01$ (Bonferroni Corrected). Regions of interest depicted include: inferior temporal gyrus (GTi), occipital gyrus (GO), medial occipital gyrus (GOm), anterior cingulate (AC) and inferior parietal lobe (LPi)

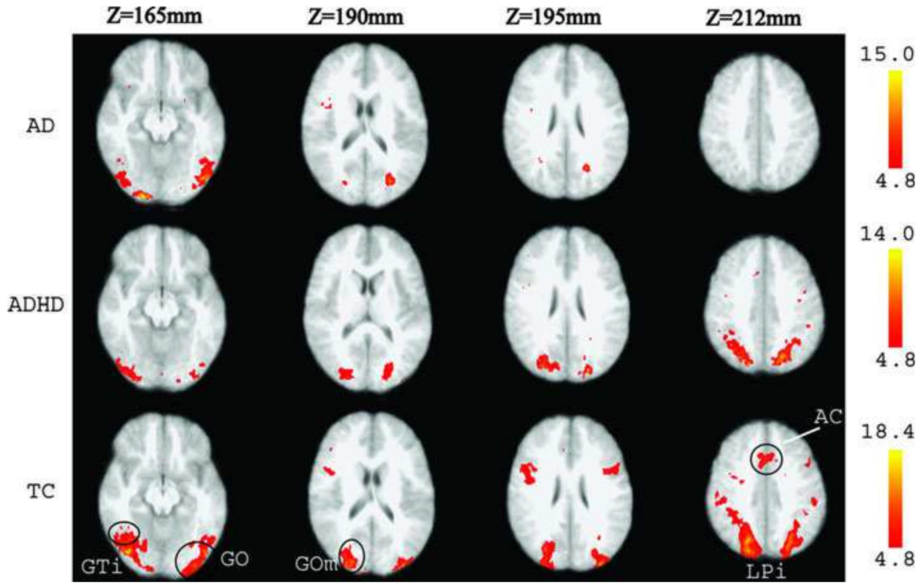

Table 3 Cluster list for individual group activations

Region of interest		CLUSTER size (voxels)	Z-MAX	Z-MAX X (mm)	Z-MAX Y (mm)	Z-MAX Z (mm)
AD ($N = 8$)	Fusiform gyrus, occipital and medial & inferior temporal (R)	7,002	12.5	175	37.5	153
	Fusiform gyrus, occipital and medial & inferior temporal (L)	5,788	15.1	113	19.5	139
	Inferior parietal (L)	381	7.57	95.5	97.5	200
	Inferior frontal (L)	236	6.8	95.5	126	185
ADHD ($N = 9$)	Occipital, superior & medial temporal inferior parietal (L)	11,894	14	108	30	207
	Occipital, superior & medial temporal inferior parietal, cuneus (R)	5,682	11.1	143	31.5	207
	Fusiform (R)	398	7.97	157	42	149
		387	6.65	162	31.5	151
	Medial & inferior frontal (L)	200	6.74	88.4	111	199
	Inferior parietal (L)	120	5.71	83.3	67.5	209
	Medial frontal (L)	119	7.16	109	91.5	220
		107	7.18	95.5	142	199
	Cingulate	104	7.28	137	110	218
TC ($N = 9$)	Fusiform gyrus, occipital and medial & inferior temporal, inferior parietal, cuneus (L)	32,383	18.4	108	21	203
	Fusiform gyrus, occipital and medial & inferior temporal (R)	22,028	15.4	153	13.5	158
	Parietal (L) (precentral gyrus)	4,426	9.66	97.5	91.5	223
	Parietal (R) (precentral gyrus)	4,236	11.8	148	90	226
		1,367	10.7	172	104	208
	Fusiform gyrus (R)	361	7.11	159	43.5	146
	Medial temporal (R)	100	6.48	158	52.5	197

The list shows the main clusters found at a level of $p < 0.01$ (Bonferroni corrected). Only clusters with 100 pixels or more are presented. L and R correspond to left and right sides of brain, respectively

compared to controls (Fig. 3, $Z = 158–161$ mm). While clearly significant activations were observed in the medial temporal region for individual groups (Fig. 2; Table 3), these were greatly reduced in the AD group compared to ADHD and TC groups. However, when comparing the AD to the ADHD and TC groups, this difference did not translate to greater activity in controls (ADHD and TC) in this region of the brain compared to AD subjects (Fig. 3). It is clear that control subjects appeared to activate the left medial temporal cortex to a significantly greater extent,

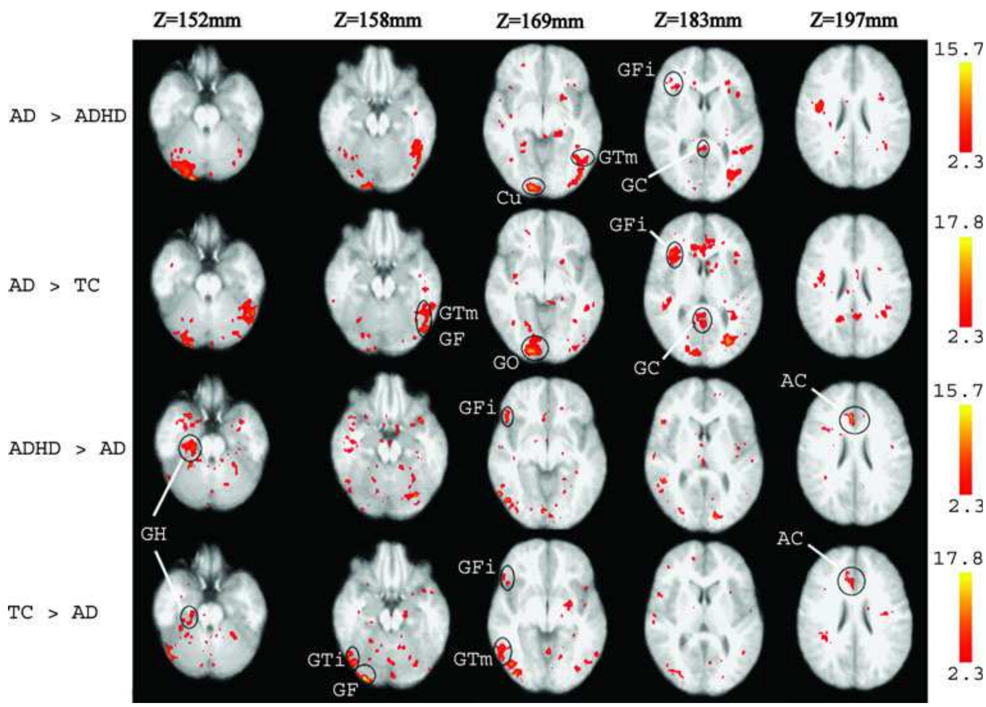

Fig. 3 Group comparisons of functional activity during the EFT where, **a** AD is greater than ADHD, **b** AD is greater than TC, **c** ADHD is greater than AD and **d** TC is greater than AD at $p < 0.01$. Regions of interest depicted include: hippocampal gyrus (GH), inferior temporal gyrus (GTi), medial temporal gyrus (GTm), fusiform gyrus (GF), occipital gyrus (GO), cuneus (Cu), inferior frontal gyrus (GFi), cingulated gyrus (GC) and anterior cingulate (AC)

while AD subjects preferentially showed activity in the right medial temporal region. In addition, AD subjects showed significantly greater activity in the right fusiform gyrus, right inferior temporal gyrus, right parahippocampal gyrus, right caudate nucleus, and left inferior frontal gyrus (Fig. 3).

Greater activity was observed in AD subjects compared to TC in the cingulate gyrus (Fig. 3, $Z = 183$ mm), however, ADHD subjects demonstrated greater cingulate activity compared to subjects with AD (Fig. 3, $Z = 197$ mm). While significant activity was observed in the one sample *t*-tests of the superior and inferior parietal lobe and medial frontal gyrus in the TC and ADHD groups at $z = 198$–233 mm, significant differences were not observed in the group comparisons in these cortical regions.

Discussion

Greater overall brain activation was observed in the TC group compared with AD subjects, which is consistent with previous EFT fMRI studies in adults and children (Ring et al. 1999; Lee et al. 2007; Manjaly et al. 2007). In the present study, similar regions of activity were detected for the autism group and the two control groups (ADHD and TC) but there is reduced cortical activity in the AD group compared to both control groups. This finding is similar to those from Lee et al. (2007) who reported that children with ASD performed the EFT at the same level as controls, but with reduced cortical involvement.

Consistent with the findings of Ring et al. (1999), subjects with autism in the present study demonstrated greater activity in right occipital cortex, which is involved in the visual processing of objects (Kosslyn et al. 1995), extending into the inferior temporal region (Ring et al. 1999). The occipital, inferior temporal, and inferior parietal activity observed is also consistent with the activation patterns in adults with AD (Baron-Cohen et al. 1994) and implicates spatial visual processing pathways (Ungerleider et al. 1998). The parietal and medial temporal regions are involved in complex processing of visual stimuli and visual attention. These regions are associated with working memory for objects and spatial relation (Picchioni et al. 2007; Roth and Courtney 2007). Our study found laterality differences between the AD and control groups, with AD subjects preferentially showing activity in the right medial temporal region, while controls tended to activate the left medial temporal cortex. It is possible that the TC group used internal dialogue to mediate their problem solving approach (Lezak 1995) rather than just a sheer visual matching approach, which may have initiated activation in the left hemisphere. Given the significant differences observed in regions of activity between children with AD and either TC or ADHD and in IQ scores between the TC and AD groups, there appears to be inherent differences in neural recruitment and neuronal connectivity between the groups, with the TC group recruiting more brain regions to solve the task accurately. No activity was observed in the superior parietal region when comparing controls to subjects with autism. This region of interest was also notably absent in the work by Ring et al. (1999), who suggested that these subjects may be sharing these same areas in the processing of the EFT (Ring et al. 1999).

Hemispheric differences are consistent with those noted by Lee et al. (2007), with bilateral ventral temporal and occipital activation (i.e., the "what" visual processing stream) observed in controls and mainly right hemisphere activation in subjects with AD. Ventral temporal and hippocampal activity are typically found during spatial analysis, while the fusiform region is implicated in object analysis (Epstein and Kanwisher 1998; Liu et al. 2008). Both the TC and ADHD groups showed robust activity in the ventral-temporal region and hippocampus (Fig. 3) which is absent in subjects with AD. This may suggest a decreased requirement for visual-spatial attention in children with AD consistent with previous findings (Lee et al. 2007). While the fusiform region showed activity in all subjects, it was mainly right lateralized in subjects with AD and left lateralized in controls. Recent work examining the nature of object processing and particularly structural differentiation by the fusiform region showed greater fusiform activity observed in AD subjects compared to either TC or ADHD groups (Liu et al. 2008). Greater utilization of the fusiform region in distinguishing between simple line shapes in this affected population compared to controls suggests differences in complex visual processing and spatial working memory in children with AD.

Greater inferior frontal, middle temporal and occipital gyri, and parietal lobe activity was observed in the typical healthy control subjects. Activity in these regions is expected based on previous fMRI studies of the EFT in both adults and adolescents (Lee et al. 2007; Manjaly et al. 2007, 2005; Ring et al. 1999). In addition, we found that the activity tended to be left lateralized in control subjects, consistent with left-hemisphere dominance of visual processing in control subjects observed by others (Weissman and Woldorff 2005; Manjaly et al. 2007).

Greater cingulate activity was observed in subjects with AD compared to the TC group; however, subjects with ADHD demonstrated greater cingulate activity than those with AD (Fig. 3, $Z = 183–197$ mm). It is well known that the cingulate plays a role in attention (Posner and Rothbart 2009; Posner et al. 2007). Greater cingulate activity in the AD group suggests that these subjects were required to exert greater effort to sustain their attention during the task than the TC group, while those children with ADHD recruited even more cortical involvement in order to sustain attention and perform the task appropriately. The greater middle temporal and fusiform activity, regions that are known to be involved in attention (Bolton and Griffiths 1997), observed in AD subjects relative to the comparison groups supports this assertion (see Fig. 3). Differences in fMRI activity in these regions suggest increased demand on "top–down" attentional processing in AD compared to comparison groups.

Significant differences were observed in number of correct responses by TC children compared to those with AD. No significant differences were recorded between children with ADHD and AD in either accuracy of responses or time to respond. Though not statistically significant, children with AD performed these tasks slightly faster on average than the other groups, indicating increased impulsivity in problem solving that may have contributed to their reduced accuracy on the HFT. Children with ASD have been shown to perform equally well to controls on an EFT during fMRI studies (Lee et al. 2007); however, better performance on the EFT has not been consistently observed in high functioning children with ASD (Brian and Bryson 1996; de Jonge et al. 2006). In addition, there may be some subtle differences in visual information processing between the EFT and the HFT used in this study.

This is the first study that examines fMRI activation patterns during a HFT using separate subgroup of the spectrum of autism disorders; however, there are a number of limitations of the current study. A significant limitation was the lack of psychological assessment data for the typical control subjects. Inclusion of IQ information for typical control children could have been used to further examine performance differences, which in turn would have allowed us to make more definitive conclusions; however, given the significant differences in activation regions between children with AD and either TC or ADHD, there still appears to be an innate difference in neural recruitment and neuronal connectivity between the groups, with the TC group recruiting more brain regions to solve the hidden figures task accurately. It is quite plausible that the lower cognitive functioning typically observed in children with AD is a direct phenotypic representation of reduced recruitment of brain regions. More studies are needed to examine differences in brain activity and overall cognitive function in children across the autism spectrum. The clinical sample sizes are relatively small with only eight children diagnosed with AD and 9 in each of the ADHD and TC groups. Larger sample sizes would have provided better power in analyzes and greater generalizability. Finally, due to problems with data acquisition, the behavioral data during the fMRI was not captured for two of the AD subjects; this may have affected the differences observed in task performance between groups.

The current study, which used a hidden figures test, is congruent with previous studies involving the embedded figures task in subjects with autism spectrum disorders (Manjaly et al. 2007; Ring et al. 1999; Lee et al. 2007). While previous studies focused on the differences in activation patterns between individuals with autism spectrum disorders and healthy controls during an EFT, we were interested in examining whether consistent results could be obtained in a particular subgroup of individuals diagnosed with autistic disorder and whether functional differences could be observed on a HFT compared to healthy controls and those diagnosed with ADHD. In the present study, we focused only on children diagnosed with autism disorder and excluded those diagnosed with Asperger syndrome and non-specified pervasive developmental disorder. While there is general agreement with previous results in subjects with ASD (Manjaly et al. 2007; Ring et al. 1999; Lee et al. 2007), our findings indicate fewer regions of cortical activation with significantly different activation patterns. Importantly, the current findings show that the differences in brain function in tasks of object evaluation between subjects with AD and age-matched controls can be extended to children between the ages of 9 to 14. In addition, the current study reveals clear differences in visual and attentional processing between children with AD and the comparison groups. Some differences may be explained by variation in methodology between the current study, using a HFT, and previous studies that used an EFT. To date, functional imaging studies of individuals with autism have examined too few subjects to be able to discriminate between these subgroups, but the results of the present study appear consistent when examining neuronal function and clearly show differences from control subjects. Studies with larger sample size are needed in order to further differentiate patterns of functional brain activity between subjects diagnosed with AD and controls.

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