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Spatial Working Memory Deficits in Autism

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Abstract Previous studies have reported working memory deficits in autism, but this finding has been inconsistent. One possibility is that deficits in this domain may be present only when working memory load exceeds some limited capacity. High-functioning individuals with autism performed the CANTAB computerized test of spatial working memory. Individuals with autism made more errors than a matched group of typically developing controls on this task, and were less likely to consistently use a specific organized search strategy to complete the task. Overall, these results demonstrate reduced spatial working memory abilities in autism, and extend previous findings by demonstrating that these deficits are significant when tasks impose heavier demands on working memory.

Keywords High functioning autism · CANTAB · Executive function · Frontal lobes · Cognition · Neuropsychology

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Introduction

Many studies have examined higher-order executive functions in individuals with autism (Bennetto, Pennington, & Rogers, 1996; Hughes, Russell, & Robbins, 1994; Minshew & Goldstein, 1998; Ozonoff & Jensen, 1999; Ozonoff, Pennington, & Rogers, 1991). Individuals with this disorder perform less well than matched comparison groups on tasks of set shifting (Hughes et al., 1994; Ozonoff et al., 1991), tasks requiring inhibition of prepotent responses (Hughes & Russell, 1993; Minshew, Luna, & Sweeney, 1999), and tasks requiring planning abilities such as the Towers of London and Hanoi (Bennetto et al., 1996; Ozonoff et al., 1991; Ozonoff & Jensen, 1999).

Another important executive function that has been investigated in autism is working memory. Working memory involves both the ability to maintain information ''on-line'' over brief periods of time to support a temporal continuity of behavior, and to manipulate ideas internally to plan complex responses (Baddeley, 1986). Deficits in spatial working memory abilities have been reported in individuals with autism (Minshew et al., 1999), in their unaffected family members (Hughes, Leboyer, & Bouvard, 1997; Koczat, Rogers, Pennington, & Ross, 2002), and in individuals with Asperger's syndrome (Morris et al., 1999).

We previously reported spatial working memory deficits in a sample of 26 high-functioning individuals with autism using an oculomotor delayed response task (Minshew et al., 1999). In this simple task, a single target is presented very briefly in the visual periphery while participants maintain central fixation, and after a few seconds they are cued to look to the location where the peripheral target was presented. In a follow-up

study with an independent sample, we linked this abnormality to reduced task-related activation in dorsolateral prefrontal cortex using fMRI (Luna et al., 2002).

Not all studies of autism, though, have found deficits in spatial working memory. One approach used in previous studies required participants to remember spatial location information over trials, such as when searching under a group of boxes for hidden targets. In tasks of this nature, participants need to remember where targets have been found previously to avoid searching for targets under boxes that have already been inspected. Griffith, Pennington, Wehner and Rogers (1999) reported that very young children with autism (mean age = 51 months) performed as well as matched developmentally delayed individuals on a task of this type. However, the performance of typically developing individuals was not evaluated to determine whether both of these clinical groups might perform more poorly than would be expected of individuals of that age. Also, because boxes in the study were distinguishable by features such as color and design, as well as by location, the task could be performed using figural episodic memory which further complicates interpretation of findings from that study with regard to spatial working memory abilities.

Ozonoff and Strayer (2001) used a computerized spatial memory-span task with a progressively increasing memory load that required participants to remember the location of (1, 3, or 5) colored geometric shapes over varying delay periods (1 or 5 seconds). They reported no significant difference in the performance of 25 high-functioning individuals with autism (ages 7–18), 15 individuals with Tourette syndrome (ages 8–17), and 15 healthy children (ages 8–19). Although this task systematically increased memory load, the total amount of information to be held in memory even in the most difficult task condition was limited, and maintenance of information across trials was not required.

It is possible that failures to demonstrate spatial working memory deficits in some prior studies of individuals with autism result from an insufficient level of task difficulty relative to the ability level of participants. For example, individuals with autism might show working memory deficits only when memory load exceeds a threshold beyond which working memory capacity is sufficiently taxed to reveal deficits. Morris et al. (1999) used a spatial working memory task with high memory load, similar to the task used in the present study, that required maintenance of information across trials and reported deficits in individuals with Asperger's syndrome. Whether the spatial working memory abilities of high-functioning individuals with autism are intact on tasks with a high memory load is not known. However, literature documenting abnormal prefrontal cortical function in autism (Horwitz, Rumsey, Grady, & Rapoport, 1988; Luna et al., 2002; Ohnishi et al., 2000; Zilbovicius et al., 1995) suggests that working memory systems might be compromised. Therefore, we conducted the present study using the Spatial Working Memory task from the Cambridge Neuropsychological Test Automated Battery (CANTAB). This task examines spatial working memory ability by systematically varying the working memory load which increases the amount of information that needs to be remembered and the number of trials over which it needs to be maintained.

Method

Participants

Participants in this study included 29 high-functioning individuals with autism and 29 typically developing individuals group matched in Verbal IQ (VIQ), Performance IQ (PIQ), age and the socioeconomic status (Hollingshead & Redlich, 1958) of their parents (see Table 1 for descriptive characteristics of the participant groups).

IQ was assessed with the age appropriate Wechsler Intelligence Scale and all participants were required to have a Full Scale score (FSIQ) greater than 80. Additional exclusionary criteria for all participants included a history of traumatic brain injury, birth related injury, poor physical health, or a seizure disorder. Demographic, medical, and personal history information was collected from each participant (and/or their parents) through the completion of a questionnaire and through direct interview.

Diagnostic confirmation of autism was provided by the results from the Autism Diagnostic Interview (ADI and ADI-Revised; Le Couteur et al., 1989; Lord, Rutter, & Couteur, 1994), the Autism Diagnostic Observation Schedule (Lord et al., 1989, 2000) and expert clinical opinion. All participants met ADI and ADOS cut-off criteria for autism, in addition to DSM-IV criteria for Autistic Disorder, confirmed by expert clinical opinion. Individuals were excluded if found to have a history of any medical disorder associated with features of autism such as tuberous sclerosis, fragile-X syndrome, or fetal cytomegalovirus infection.

The comparison group of typically developing individuals was comprised of community volunteers recruited from neighborhoods with similar socioeconomic status (SES) as the participants with autism.

Table 1 Demographic characteristics of participants with autism and typically developing individuals

Variables	Participants with autism (n = 29)			Typically developing individuals (n = 29)			p value
	Mean	SD	Range	Mean	SD	Range	
Age (years)	14.83	5.47	8–29	16.93	5.40	8–29	0.15
Verbal IQ	107.52	13.02	88–135	110.14	9.49	88–129	0.39
Performance IQ	106.21	11.82	77–137	110.07	9.93	86–126	0.18
Full scale IQ	107.76	10.99	93–135	110.79	9.91	90–129	0.27
ADOS social + communication	14.86	2.85	10–20	–	–	–	–
ADOS play	1.20	0.58	0–2	–	–	–	–
ADOS stereotyped behavior	1.50	1.45	0–5	–	–	–	–
ADI-R social	25.00	7.76	10–44	–	–	–	–
ADI-R communication	18.22	5.83	9–30	–	–	–	–
ADI-R stereotyped behavior	7.74	4.11	3–19	–	–	–	–
SES (parents)	2.77	1.03	1–4	3.25	1.17	1–5	0.30
Gender (M:F)	29:0			27:2			

ADOS = Autism Diagnostic Observation Schedule; ADI-R = Autism Diagnostic Interview-Revised; SES = socioeconomic status, using the Hollingshead-Redlich Scale

Specific exclusionary criteria for this group included a history of developmental abnormalities, a current or past history of psychiatric or neurological disorder, or a family history of either autism, a developmental cognitive disorder, or a neuropsychiatric disorder thought to have a genetic component. All participants and their guardians (if they were minors) provided informed consent prior to participating in the study.

Procedure

The Spatial Working Memory task from the CANTAB battery was presented on a high-resolution touch-screen computer monitor (Robbins et al., 1994). In this self-ordered serial search task, participants were shown a group of boxes on the computer screen. They were told that a token was hidden beneath one of the boxes on the screen and that they were to search through the boxes to find it. Participants did this by touching a box to discover whether or not a token was hidden beneath it. After participants found the token, they were shown the same set of boxes and instructed to find the next token. Participants were told that once a token had been found under a particular box, the box would never again hide a token. In a set of trials, each box eventually had a hidden token beneath it. Thus, to perform this task with the fewest number of errors, participants needed to remember which of the boxes had previously hidden a token within a set of trials.

The number of boxes on the screen under which participants needed to find tokens determined the level of working memory load. Either four, six, or eight boxes were presented on the screen at one time. As the memory load increased from four to six to eight boxes, participants needed to remember whether or not a token had been previously located under a larger number of boxes and over a larger number of trials.

After a participant had found every token in a set of boxes, both the color and position of the boxes changed to begin the next set of trials; the dimensions of the boxes did not change throughout the task. Each memory load condition (i.e., number of boxes on the screen) was presented four times, with the four 4-box sets followed by the four 6-box sets and then the four 8-box sets. Thus, a total of 72 tokens needed to be located in 12 search sets. To insure that participants understood the task, testing began with a practice set in which targets were hidden sequentially beneath three search boxes.

Performance on the test was evaluated by quantifying (1) between-trial search errors (i.e., searching a box in which a token had been found on a previous trial in a set) and (2) within-trial search errors (i.e., searching the same box twice during a single trial). To facilitate comparison of between-trial search errors across memory load conditions, the percentage of possible errors was calculated (i.e., the number of between-trial search errors divided by the number of potential errors at each memory load condition). This was done to compensate for the fact that it was possible to make many more errors on the higher memory load conditions due to a greater number of trials. The ability of participants to adopt a sequential search pattern, or ''strategy'', to facilitate task performance was also evaluated. Previous studies have shown that repeatedly applying the same search sequence when completing this task can facilitate performance (i.e., beginning each search sequence with a specific box and then, once a token has been found, to begin the next trial by returning to that same starting point and following the

same search sequence again, excluding locations from the search sequence where tokens were previously found; Owen, Downes, Sahakian, Polkey, & Robbins, 1990). Use of this specific search strategy is computed for the CANTAB test by tallying the number of different search sequences participants made within each set (at the levels of six and eight boxes). A low strategy score represents a more consistent use of the effective search strategy. The minimum strategy score possible was 8 (1 for each of the 4 sets at the level of 6 and 8 boxes) and the maximum score possible over the six and eight box conditions is 56 (1 for each trial within the 8 sets).

Data were checked for outliers and the most conservative score-changing option (Tabachnik and Fidell, 1989) was applied for those individuals who deviated from the group mean by greater than 2 SD. Five outliers were identified in distributions of between search error scores, three from the comparison group and two from the autism group. These scores were replaced with the next highest score in the distribution, plus one unit. This score-changing correction decreased the skewness of the distribution, and allowed the outliers to remain at the extreme of the distribution. Outliers were not detected with strategy scores or within search errors. Group by Memory Load (number of search boxes) mixed ANOVAs were performed on the two types of search errors separately (the number of within and the proportion of between search trial errors). The Greenhouse-Geisser correction was used to control familywise error. This procedure lowered degrees of freedom when utilized.

Results

Individuals with autism (M = 0.17, SD = 0.11) made a higher proportion of between trial search errors than the typically developing individuals (M = 0.08, SD = 0.06), F (1, 56) = 20.27, $P < .001$. A significant Group by Memory Load interaction was also observed, F (2, 112) = 7.13, $P < .001$, reflecting a greater impact of increasing memory load on the performance of autistic than typically developing individuals. Follow-up paired samples t-tests (two tailed) indicated that the proportion of between search errors significantly increased from the 4 and 6 box Memory Load levels for participants with autism, t (28) = –6.98, $P < .001$, as well as for the comparison group, t (28) = –4.75, $P < .001$. A significant increase in the proportion of between search errors also occurred between the 6 and 8 box Memory Load levels in typically developing individuals, t (28) = –3.77, $P < .001$, but not in the participants with autism, t (28) = 0.19, $P > .80$. These results indicate that group differences in the proportion of between search errors increased more dramatically for autistic individuals as memory load increased from 4 to 6 boxes, but that beyond this level of memory load further performance impairment was not seen (see Fig. 1).

For analyses of within search errors, the assumption of sphericity was violated and thus all related results are reported using the Greenhouse-Geisser correction. Individuals with autism (M = 2.03, SD = 3.99) did not make more within search errors than typically developing participants (M = 0.69, SD = 1.07), F (1, 56) = 3.08, $P > .08$, and no significant Group by Memory Load interaction, F (1.3, 75) = 2.32, $P > .10$, was observed.

Significant group differences were observed in search strategy scores, F (1, 56) = 8.35, $P < .01$. Participants with autism (M = 34.59, SD = 4.80) used the specific sequential organized search strategy less consistently than typically developing participants (M = 31.34, SD = 3.67). The degree to which participants did not use the sequential search strategy over trials was significantly correlated with increased rates of between search errors in both individuals with autism (r = .84, $P < .001$) and the typically developing comparison group (r = .52, $P < .01$). Using the Fisher z-transform (Papoulis, 1990), the two correlation coefficients were transformed and compared to assess whether there was a significant difference in the degree of correlation between the two participant groups. Results indicated a higher degree of correlation of search strategy scores with the proportion of between search errors in individuals with autism, z = 2.29, $P < .02$. However, the range of search strategy scores was lower in typically developing participants (variance in strategy scores was 71% higher in the autism group) because they utilized the efficient strategy more frequently. This

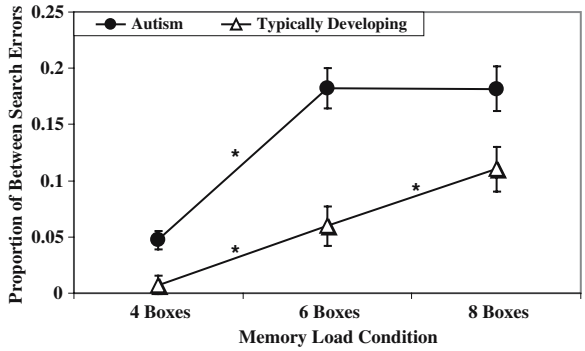

Fig. 1 Between search errors (±SEM) across memory load conditions in individuals with autism and typically developing participants

may have contributed to the ability to detect a more robust relationship with strategy scores in the autism group.

The proportion of between search errors was significantly correlated with Performance IQ ($r = -.47$, $P < .01$), but not Verbal IQ ($r = -.11$, $P > .50$), in participants with autism. Strategy scores were also significantly correlated with Performance IQ ($r = -.45$, $P < .02$), but not Verbal IQ ($r = -.08$, $P > .70$), in the autism group. Correlations between the proportion of between search errors and intelligence test scores, as well as between strategy scores and intelligence, were not significant in the comparison group. Analyses were also conducted to determine whether test performance varied in relation to the severity of autism symptoms, as measured by the algorithm scores from the ADOS-G and ADI-R (Lord et al., 1994, 2000; see Table 2).

No index of task performance was significantly correlated with the number of symptoms related to autism. The relationship between chronological age and task performance (strategy score, and proportion of between search) was also examined. The proportion of between search errors was not significantly correlated with age in either autistic ($r = -.04$, $P > .80$) or typically developing participants ($r = -.22$, $P > .20$). Similarly, use of the specific search strategy did not increase with age in either participants with autism or typically developing individuals ($r = -.05$, $P > .80$ and $r = -.24$, $P > .20$, respectively).

Discussion

This study of spatial working memory was undertaken to examine the ability of high-functioning individuals with autism to remember spatial location information under conditions with increasing memory load. Participants with autism demonstrated an impaired capacity to remember the locations of previously searched boxes over trials compared to typically developing individuals, and a reduced ability to consistently utilize a sequential search strategy to facilitate performance. Thus, we extend previous findings with regard to spatial working memory deficits in autism by demonstrating that these deficits are evident when tasks impose heavier demands on working memory capacity. These findings are consistent with other studies of working memory by showing that as task demands increase, performance of individuals with autism becomes impaired relative to that of typically developing individuals (Minshew & Goldstein, 2001). Thus, the failure of some previous studies to detect working memory deficits might be related to their use of tasks with more modest memory loads.

Individuals with autism also failed to effectively use the sequential search strategy when performing this task, and the failure to do so strongly predicted their difficulty remembering where tokens had previously been located. This finding is consistent with several studies of individuals with autism that have shown a reduced utilization of organizational strategies, and in some cases even a failure to use explicitly available structures that typically developing individuals use to enhance memory performance (Ameli, Courchesne, Lincoln, Kaufman, & Grillon, 1988; Bennetto et al., 1996; Joseph, Steele, Meyer, & Tager-Flusberg, 2005; Minshew & Goldstein, 1993, 2001). The results of the present study suggest that a problem using efficient problem solving strategies is related to limitations in working memory capacity. The relationship of spatial

Table 2 Intercorrelations among SWM performance and demographic variables within autism and typically developing participants

	Autism participants ($n = 29$)		Typically developing participants ($n = 29$)	
	Proportion of between search errors	Strategy score	Proportion of between search errors	Strategy score
Age (years)	–0.04	–0.05	–0.22	–0.24
Verbal IQ	–0.11	–0.08	0.16	–0.14
Performance IQ	–0.47**	–0.45*	0.05	–0.18
Full scale IQ	–0.36	–0.30	0.12	–0.17
ADOS social + communication	–0.23	–0.22	–	–
ADOS play	–0.10	0.10	–	–
ADOS stereotyped behavior	–0.21	–0.12	–	–
ADI-R social	–0.14	0.04	–	–
ADI-R communication	0.05	0.04	–	–
ADI-R stereotyped behavior	–0.06	0.03	–	–

*$p < .05$, **$p < .01$

working memory deficits on the CANTAB task to Performance IQ scores in individuals with autism also suggests that deficits in working memory may have a broader significance in relation to general fluid spatial problem solving skills.

Two previous investigations did not report evidence of a spatial working memory deficit in autism. Griffith et al. (1999) found that very young children with autism were able to remember the location of hidden tokens as well as a group of individuals with other developmental delays. However, performance of the children in both groups was well below that of the typically developing individuals on whom the test was developed (Diamond, Prevor, Callender, & Druin, 1997), suggesting that the individuals with autism and the developmentally delayed comparison group both had spatial working memory deficits.

A study by Ozonoff and Strayer (2001), using a spatial memory-span task, found no differences in performance among three groups (individuals with high-functioning autism, individuals with Tourette's Syndrome, and healthy individuals). The present study, using the CANTAB spatial working memory task, required previously searched target locations to be remembered across trials in the presence of increasing memory load. Deficits in individuals with autism were greater when memory load demands were high. Thus, one possible reason why the Ozonoff and Strayer study did not find a similar spatial working memory deficit is that the working memory load requirements of their task may not have been sufficiently taxing to reveal them.

The spatial working memory deficits observed in the present study in individuals with autism are consistent with those observed in our previous studies of spatial working memory using an oculomotor delayed response task (Minshew et al., 1999). The oculomotor working memory task requires participants to merely maintain a single piece of information over time, the location where a dot of light was shown a few seconds previously. It does not require maintenance of information over multiple trials, does not rely on organizational strategies, and thus is much less cognitively demanding than the CANTAB spatial working memory task. Considering the memory load dependency of working memory deficits in autism observed in the present study, it might be surprising that we observed deficits in autism using the very simple oculomotor delayed response task. One explanation for this apparent discrepancy may be related to the fact that the precision with which spatial information needs to be maintained is very different in our oculomotor working memory task in comparison with token-searching paradigms. In tasks hiding targets under boxes, for example, participants merely need to remember which of the boxes they can see on the screen had previously hidden a target. Precise memory of the exact spatial location where a box was presented is not required. In comparison, in oculomotor spatial working memory tasks, participants needed to remember exactly where in space a target was presented without any immediate sensory cues to facilitate their localization. The observations of load-dependent working memory deficits in the present study, together with our previous oculomotor findings, suggest that working memory deficits in autism may exist both in the ability to maintain precise internal representations of spatial location information over time, as well as in the ability to remember even global spatial information when the demands on working memory capacity are high.

There is also an important similarity in the findings of Ozonoff and Strayer (2001) to our previous findings with the oculomotor test of spatial working memory (Minshew et al., 1999). The Ozonoff and Strayer study with their spatial memory-span task increased memory load by varying the delay period over which participants needed to remember spatial information, from one to five seconds. They found that group differences did not increase when delay periods were longer. Similarly, no increased failure to remember spatial location information over longer delay periods was found in our previous work using the oculomotor spatial working memory task (Minshew et al., 1999). This suggests that spatial working memory deficits in autism may not involve an increased rate of forgetting information over time. What seems more important is how much information needs to be kept active in working memory over time, and how precisely that information needs to be encoded.

The prefrontal cortex plays a key role in many executive cognitive processes including spatial working memory and cognitive planning abilities (Fletcher & Henson, 2001; Goldman-Rakic, 1988; Owen, Morris, Sahakian, Polkey, & Robbins, 1996). Studies in non-human primates, as well as lesion and functional neuroimaging studies in humans, have documented that dorsolateral prefrontal cortex (DLPFC) is crucial for maintaining and manipulating information in spatial working memory (Carlson et al., 1998; Fuster, 2000; Goldman-Rakic, 1988; McCarthy et al., 1994; Owen, Evans, & Petrides, 1996; Pierrot-Deseilligny, Rivaud, Gaymard, Muri, & Vermersch, 1995; Sweeney et al., 1996). Functional neuroimaging studies have also reported that the neurophysiology of DLPFC is abnormal in individuals with autism during

performance of spatial working memory tasks (Luna et al., 2002). Reduced metabolism in the prefrontal cortex, delayed maturation of frontal circuitry, and reduced functional connectivity of frontal cortex with other neocortical and subcortical regions have also been reported in individuals with autism (Horwitz et al., 1988; Ohnishi et al., 2000; Zilbovicius et al., 1995). Patients with frontal lobe damage often fail to adopt and effectively utilize organized search strategies on the CANTAB task (Owen et al., 1990), as did our autistic participants. Thus, our results are consistent with a growing body of neuroimaging and neuropsychological evidence indicating that abnormalities in prefrontal systems are a key component of the pathophysiology and cognitive profile of autism.

Further research is needed to address several remaining questions about working memory deficits in autism. Studies are needed to compare verbal and spatial working memory abilities on tasks with varying and matched memory loads to determine whether spatial and verbal working memory are similarly affected in autism. Investigations are also needed to examine working memory deficits across a wider range of autism severity, to better characterize the neural basis of the dysfunction, to examine the developmental profile of cognitive ability in this domain, and to evaluate the implications of deficits in this cognitive domain for day-to-day functioning.

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