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CONDITIONAL ASSOCIATIVE LEARNING OF SPATIAL AND OBJECT INFORMATION IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER

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The present study assessed frontostriatal mediated memory functions in children with ADHD (N = 12) and healthy control participants (N = 12) using two tests of conditional associative learning (i.e., object and spatial) that shared similar stimulus-response association structures but that differed in terms of the demands placed upon strategic processes. Children with ADHD displayed normal performance on the object learning task but were impaired on the spatial learning task that placed greater demands on internally derived strategic processes. Secondary analyses further indicated that this strategic processing impairment cannot be attributed specifically to perseverative or working memory errors but rather appears to be related to a more general inability to maintain a high degree of consistency in responding across trials. Although the results of this study must be interpreted in light of the small sample sizes, they suggest that ADHD does not produce a basic deficit in acquiring stimulus-response associations previously shown to be associated with basal ganglia dysfunction. Rather, these findings suggest that the impaired conditional associative learning performance of children with ADHD is attributable to deficits in strategic processes previously been found to be dependent upon the integrity of the prefrontal cortex.

Attention deficit/hyperactivity disorder (ADHD), one of the most prevalent psychological disorders of childhood (Barbaresi et al., 2004) is characterized behaviorally by the presence of age-inappropriate inattention, hyperactivity, and impulsivity. Studies investigating the neuropathological correlates of ADHD have most consistently implicated frontostriatal circuitry components such as the prefrontal cortex, caudate nucleus, and globus pallidus (for a review, see Giedd, Blumenthal, Molloy, & Castellanos, 2001). Morphometric studies using Magnetic Resonance Imaging (MRI), for example, have revealed volumetric reductions in the prefrontal cortex, globus pallidus, and caudate nucleus, as well as right greater than left caudate asymmetry (Aylward et al., 1996; Castellanos et al., 2001; Castellanos et al., 1996; Filipek et al., 1997; Hynd et al., 1993; Schrimsher, Billingsley, Jackson, & Moore, 2001). Functional studies using either functional Magnetic Resonance

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Imaging (fMRI) or Position Emission Tomography (PET) have also demonstrated hypoperfusion in prefrontal cortical regions and the striatum (Vaidya et al., 1998; Zametkin et al., 1990).

Consistent with the presence of frontostriatal neuropathology, participants with ADHD have frequently been found to display deficits in cognitive functions that have previously been shown to be dependent upon the integrity of these brain regions. Several reviews, for example, have highlighted the similarities of ADHD symptomatology to the executive function deficits displayed by patients with damage to the prefrontal cortex (Barkley, 1997a; Sergeant, Geurts, & Oosterlaan, 2002; Voeller, 2001). In particular, children with ADHD have been found to be impaired on tests of working memory, interference control, response inhibition, and strategic planning (Barkley, 1997b; Kerns, McInerney, & Wilde, 2001; Pliszka, Liotti, & Woldorff, 2000; Scheres et al., 2003; Slaats-Willemse, Swaab-Barneveld, de Sonneville, van der Meulen, & Buitelaar, 2003; Sonuga, Edmund, Dalen, Daley, & Remington, 2002). Previous studies have also been able to demonstrate direct associations between executive or cognitive control deficits and frontostriatal structural or functional brain abnormalities in children with ADHD. For example, Casey and colleagues (1997) found that the impaired performance of children with ADHD on computerized measures of response inhibition correlated with anatomical measures of the prefrontal cortex, caudate nucleus, and globus pallidus, while Semrud-Clikeman, Steingard, Filipek, Bekken, and Renshaw (2000) found an association between inhibition as measured by the Stroop Interference Test and reversed caudate asymmetry.

Frontostriatal dysfunction may also be contributing to the memory deficits displayed by children with ADHD. However, the majority of studies that have examined memory functioning in children with ADHD have utilized tasks previously found to be dependent primarily on medial temporal lobe rather than frontostriatal structures (Berlin, Bohlin, Nyberg, & Janols, 2004; Klingberg, Forssberg, & Westerberg, 2002; Muir-Broaddus, Rosenstein, Medina, & Soderberg, 2002; Sergeant et al., 2002). In the frequently used Paired-Associate Learning Task, for example, children first study a set of word pairs (e.g., “apple-house”) and are then tested by being presented with the first word of each pair and asked to recall the second word of that pair. Previous studies in both humans and animals have found that paired-associate learning is particularly sensitive to damage to medial temporal lobe structures with several investigators suggesting that the medial temporal system is particularly crucial for binding the associations between unrelated stimuli in these tasks (Eichenbaum, Otto, & Cohen, 1994; Squire, 1992). Although children with ADHD have been found to be impaired relative to age-matched controls on Paired-Associate Learning Tasks (Chang et al., 1999; Douglas & Benezra, 1990; Kinsbourne, 1977), this impairment does not appear to reflect a primary memory deficit similar to that seen in patients with medial temporal lobe damage. Rather, this impairment appears to be secondary to deficits in those executive processes that impact memory performance, such as rehearsal, conceptual organization, and elaboration (Berlin, Bohlin, Nyberg, & Janols, 2004; Klingberg, Forssberg, & Westerberg, 2002; Muir-Broaddus, Rosenstein, Medina, & Soderberg, 2002; Sergeant et al., 2002).

In contrast to paired-associate learning, conditional associative learning (which has not been previously examined in children with ADHD) appears to be more directly dependent upon the integrity of the corticostriatal circuitry implicated in ADHD (Postle, Locascio, Corkin, & Growdon, 1997). In conditional associative learning tasks, fixed arbitrary mappings of stimulus-response pairs are learned incrementally through a process of trial and error with repeated exposure to correct and incorrect pairs. For example, participants

attempting to learn arbitrary associations between six colors and six abstract designs would begin by guessing which of the six designs was paired with a particular color. If the participant made a correct response (indicated by positive feedback), then the participant would move on to guess which of the remaining five designs was associated with a different color. If, however, the participant made an incorrect response (indicated by negative feedback), then the participant would continue making response selections until the correct design was chosen. While some aspects of the basic conditional associative learning task are similar procedurally to implicit learning tasks in which explicit learning and memory skills are minimized (Sprengelmeyer, Canavan, Lange, & Homberg, 1995), successful task completion also appears to require controlled processes such as inhibition of interference in order to select correct rather than incorrect responses (Levine, Stuss, & Milberg, 1997; Pillon et al., 1998). These strategic processes are thought to be particularly critical for facilitating the formation of robust associations in situations in which there is minimal external cuing available to support learning.

A number of studies have demonstrated the critical dependence of conditional associative learning on frontostriatal rather than medial temporal lobe structures in both human and infrahuman species (Levine et al., 1997; Petrides, 1982, 1985; Petrides, Alivisatos, Evans, & Meyer, 1993; Winocur, 1991). While most of these studies have emphasized the role of the frontal lobes in conditional associative learning, several studies have also found that damage to basal ganglia structures can produce impaired conditional associative learning as well (Jahanshahi et al., 2002; Postle, Locascio, Corkin, & Growdon, 1997). Recent studies have also demonstrated the occurrence of simultaneous electrophysiological changes in basal ganglia regions and frontal cortex during conditional associative learning performance (Brasted & Wise, 2004; Schultz, Tremblay, & Hollerman, 2003). Moreover, there is some evidence to suggest that damage to basal ganglia structures (particularly the caudate nucleus) results in a primary impairment in forming the stimulus-response associations necessary for adequate performance on all conditional associative learning tasks (Winocur & Eskes, 1998), whereas the effect of damage to the frontal lobes may disrupt those strategic control processes necessary to facilitate the efficient organization of complex information during conditional associative learning (Pillon et al., 1998).

Given that conditional associative learning appears to be mediated by the same frontostriatal structures consistently implicated in ADHD, children with ADHD should display impairments on conditional associative learning tasks. Moreover, these impairments could be attributable either to a primary deficit in the ability to acquire the conditional associations regardless of task demands or complexity, or to a deficit in those strategic control processes that facilitate conditional associative learning. In the latter case, children with ADHD should still be able to perform adequately on simple conditional associative learning tasks, but they should demonstrate impaired performance under conditions of minimal external cuing that require internally derived strategic processing for successful task completion.

To our knowledge, the status of conditional associative learning in children with ADHD has not been addressed in previous studies. The present study was designed to directly address this issue by comparing the performance of children with ADHD on two conditional associative learning tasks (i.e., spatial and object) that shared similar stimulus-response association structures but that differed in terms of the demands placed on strategic processes. The spatial task required associations to be made between two sets of stimuli based solely on their spatial locations, minimizing any additional potential external cues. Because successful completion of the spatial task required the simultaneous mapping of all

stimuli pairings where individual items had to be considered in relation to each other, this task also placed maximal demands on strategic control processing. The nonspatial object task, in contrast, incorporated stimuli with distinctive features that served to reduce the demands placed on strategic processes, while at the same time maintaining the same basic conditional associative learning requirements as found in the spatial task. If children with ADHD have a primary deficit in conditional associative learning, then these children should display deficits on both the object and spatial versions of the task. If, on the other hand, ADHD is associated more with a deficit in strategic processing rather than with a fundamental deficit in conditional associative learning per se, then children with ADHD should display impairments on the spatial but not the object version of the task.

In addition to manipulating the demands on strategic processing through the use of both spatial and object versions of the conditional associative learning, several other manipulations were included to better characterize the nature of any learning deficit observed in children with ADHD. First, a performance criterion was developed that required a high degree of consistency in responding in order to assess the ability to effectively sustain the established learning set over time. Second, children were administered each task a second time after achieving criterion using a novel set of stimulus-response pairings in order to assess their ability to inhibit previously learned associations. Finally, operationally defined measures of working memory errors and perseverative responses were developed in order to more fully assess the degree to which any impairment is associated with deficient working memory capacity or inhibitory control.

METHOD

Participants

Twelve children (5 female) diagnosed with Attention Deficit/Hyperactivity Disorder (ADHD) and 12 healthy control participants (8 female) completed this study. The children with ADHD were recruited through a preexisting database of children with "pure" ADHD (i.e., no comorbid externalizing behavior disorders, learning disorders, or mood disorders) established at the neurodevelopmental evaluation center at a local hospital (Gitten, Marcotte, Stern, Lockwood, & Heindel 2002). All children in the ADHD group currently met DSM-IV diagnostic criteria for ADHD according to a structured parent interview and were previously diagnosed with ADHD by a clinical neuropsychologist. Nine of the children with ADHD met criteria for ADHD, Combined Type, and three (all females) met criteria for ADHD, primarily Inattentive Type. The healthy control participants were recruited from local schools. None of the children in the control group met DSM-IV diagnostic criteria for ADHD according to a structured parent interview.

Children were included in the study if they met the following criteria: (1) possessed at least average intelligence as estimated using the Block Design and Vocabulary subtests of the Wechsler Intelligence Scale for Children-Third Edition (WISC-III; (Sattler, 1992), (2) did not exhibit a significant discrepancy (i.e., ≥2 SD) between IQ and achievement based upon screening using the Wide Range Assessment Test—3rd Edition (WRAT-3), and (3) did not have neurological or sensory problems based upon parental report. Two potential participants with ADHD were excluded due to a history of migraines and chronic fatigue syndrome. Ten potential participants were excluded from the study due to a history of learning difficulties or evidence of learning difficulties on the screening measures. Participants were compensated for their time with gift certificates of a five-dollar value.

Table 1 Participants' Mean Age, Years of Education, and Intelligence/Achievement Screening Standard Scores.

	Group			
	ADHD		Control	
	M	*(SD)*	*M*	*(SD)*
n [m,f]	12 [7,5]		12 [4,8]	
Age	10.65	(2.26)	11.59	(2.75)
Education	4.83	(2.13)	5.58	(2.97)
IQ	105.3	(12.7)	113.8	(14.3)
Reading	102.3	(8.1)	115.3	(8.0)
Spelling	102.0	(12.7)	116.1	(10.2)
Mathematics	106.4	(13.3)	103.7	(8.0)

The demographic characteristics of the ADHD and control groups are shown in Table 1. The two groups did not differ significantly in age [$t(22) = .91$, $p = .37$] or years of education [$t(22) = 0.71$, $p = .48$]. The intelligence and achievement scores for the ADHD and control groups are also shown in Table 1. The estimated IQ scores for both the ADHD and the control participants ranged from Average to Superior, and both groups scored at or above the Average range on measures of mathematics achievement. The two groups did not differ significantly in estimated IQ [$t(22) = 1.53$, $p = .14$] or math achievement [$t(22) = .61$, $p = .55$]. Although both groups also performed at or above the Average range on screening measures of reading and spelling achievement, the control group performed significantly better than the ADHD group on both measures [reading: $t(22) = 3.98$, $p < .01$; spelling: $t(22) = 3.0$, $p < .01$].

Nine of the 12 children with ADHD were prescribed medication for management of ADHD symptomatology. Seven children with ADHD were prescribed stimulant medication (e.g., methylphenidate): Five of these seven children were prescribed a long-acting form of stimulant medication and had taken it on the morning of the evaluation; the other two children were prescribed a short-acting form of stimulant medication and had not taken their medication on the day of testing. Two children with ADHD were prescribed non-stimulant medication (e.g., guanfacine).

Procedure

Testing occurred in a 60–90 minute session interspersed with short breaks between tasks. During the first half of the session, participants were administered the intelligence and achievement screening measures. During the second half of the session, each participant was administered the computerized spatial and object conditional associative learning tasks. Each task is described in detail below. The order of administration of the spatial and object tasks was counterbalanced across participants.

The tasks were programmed using E-Prime software, V1.1 (Psychology Software Tools, 2002). The tasks were run on a Pentium II 450 MHz computer, and the stimuli were viewed on a 19 inch, ViewSonic PS 790 monitor.

Spatial Learning Task. In the Spatial Task, participants viewed a screen consisting of five identical pictures of a caterpillar evenly spaced in a semicircle in the top half of the screen and five identical pictures of a butterfly evenly spaced in a horizontal ellipse in the bottom half of the screen (see Figure 1A). The specific caterpillar-butterfly pairs were

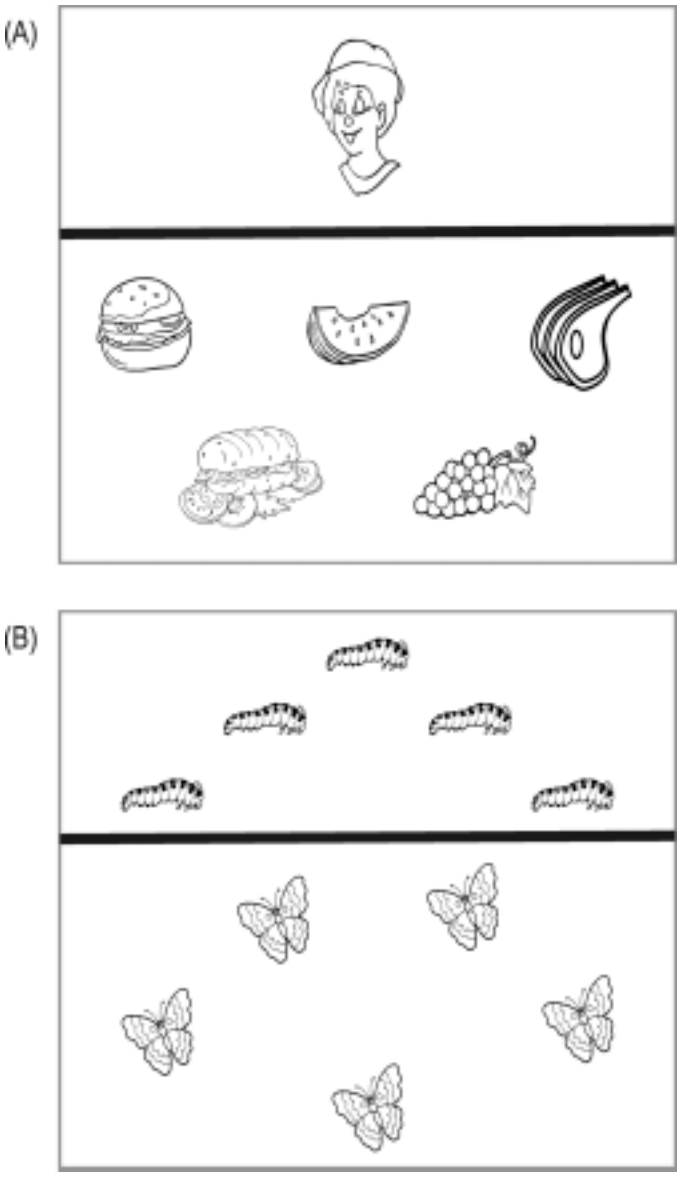

Figure 1 Schematic of stimuli used in the (A) Spatial Task and (B) Object Task. Actual stimuli used in the experiment were made from color photos or images of children, food items, caterpillars, and butterflies.

randomly defined by the computer program at the start of each participant's testing session. Participants were instructed to choose the correct caterpillar-butterfly pairs (i.e., "the butterfly that each caterpillar will grow up to be"). Because all of the caterpillar (and butterfly) stimuli were identical in appearance, correct pairs were based only on the spatial location of the stimuli. Pairs were chosen at random.

At the start of each trial, one caterpillar was framed with a red box, and the participant then had to choose the matching butterfly. Using a mouse, the participant indicated a

response by clicking on a butterfly, guessing if necessary. Positive or negative feedback followed correct or incorrect responses, respectively. The positive feedback included the correct caterpillar-butterfly pair. Following an incorrect response, the same caterpillar was framed and the participant was provided another attempt. There was no limit on the number of responses that could be made for each caterpillar. After a correct response, a new caterpillar was framed, signaling the start of a new trial. Thus, a trial was defined as one successfully completed stimulus-response pairing, and a participant could make multiple responses before achieving a correct trial. Perfect performance would therefore be reflected in a single correct response for each caterpillar-butterfly pairing. Total trials and number of correct and incorrect responses were recorded.

Object Learning Task. In the object task, the participant viewed a screen consisting of a picture of a child centered in the top half of the screen and five pictures of different food items evenly spaced in two rows across the bottom half of the screen (see Figure 1B). Participants were instructed to choose the correct child-food pair (i.e., "the picture of the child's favorite food item"). In order to control for any positional effects in learning, the positions of the five food pictures were randomly changed when a new child was presented. Therefore, correct pairs were based only on the features of the stimuli.

At the start of each object trial, one child appeared in the top half of the screen and the five food items were displayed in the bottom half of the screen. Using a mouse, the participant indicated a response by clicking on a food picture, guessing if necessary. Positive or negative feedback followed correct or incorrect responses, respectively. The positive feedback included the correct child-food pairing. Following an incorrect response, the participant was presented with the original screen and was provided another attempt. As with the spatial task, there was no limit on the number of responses that could be made for each child. After a correct response, a new child appeared at the top of the screen, signaling the start of a new trial. As with the Spatial Task, a trial was defined as one successfully completed stimulus-response pairing, and a participant could make multiple responses before achieving a correct trial. Perfect performance would therefore be reflected in a single correct response for each child-food pairing. Again, total trials and number of correct and incorrect responses were recorded.

Initial Learning. For both the Spatial and Object Tasks, the Initial Learning trials continued until the participant either reached criterion or made a maximum number of 500 responses. In order to reach criterion, participants needed to: (1) achieve greater than 70% accuracy within a complete response set; and (2) consistently maintain that level of accuracy for five consecutive complete response sets. A complete response set was defined as a sequence of at least 10 consecutive responses comprising a series of successfully completed trials. Since a set was only considered complete if the final response was correct (i.e., a set could not terminate in the middle of a trial), a complete response set could contain greater than ten responses. For example, if the participant's 10^{th} response was not correct, the set would continue until the participant provided a correct response to the final trial (see Figure 2 for a sample of a complete response set with more than 10 responses. When the participant achieved greater than 70% accuracy in five consecutive complete response sets, criterion was achieved and the computer program ended. Our strict criterion was specifically designed to ensure that participants not only mastered the correct stimulus-response pairs, but they also maintained consistent responding over time. All control participants and 11 of the 12 participants with ADHD were able to reach criterion during the Initial Learning trials of the Spatial Task, and all participants reached criterion during the Initial Learning trials of the Object Task.

(A)

TRIAL	RESPONSE	CORRECT
1	1	no
	2	no
	3	YES
2	4	no
	5	YES
3	6	no
	7	no
	8	YES
4	9	no
	10	YES

(B)

TRIAL	RESPONSE	CORRECT
1	1	no
	2	no
	3	YES
2	4	no
	5	YES
3	6	no
	7	no
	8	YES
4	9	no
	10	no
	11	YES

Figure 2 Examples of completed response sets containing four trials. Set A contains exactly 10 responses whereas Set B contains 11 responses. The accuracy is 40% and 36% in Sets A and B, respectively. Learning criterion is reached when participants achieve greater than 70% accuracy in five consecutive response sets.

Negative Transfer. Once the Initial Learning mastery criteria were met, the participant was informed that the caterpillar-butterfly or child-food pairs had changed. The participant was then instructed to learn five new pairs using the same stimuli. The Negative Transfer condition of the Spatial and Object Tasks continued until the aforementioned criteria were again met or until 500 responses were made. Similar to the initial training trials, all control participants and 11 of the 12 participants with ADHD were able to reach criterion during the Negative Transfer trials of the Spatial Task, and all participants reached criterion during the Negative Transfer trials of the Object Task.

Performance Measures

Two dependent measures, number of complete trials and number of incorrect responses, were used to assess associative learning. As indicated, a complete trial was defined as a correct stimulus-response pair (i.e., a child or a framed caterpillar paired with the correct food or butterfly, respectively), regardless of the number of responses made to achieve that correct pairing. Because one complete trial could require multiple attempts to achieve that correct answer, the number of incorrect responses to match an individual child or caterpillar with its food or butterfly was also calculated. Although the number of complete trials and the number of incorrect responses will be correlated to some degree, comparison of the two measures allows for a more thorough assessment of participants' consistency in responding. Participants who perform consistently well and make relatively few errors when attempting to achieve the correct stimulus-response pairs will reach criterion quickly and subsequently earn a low number of trials. In contrast, participants who also make relatively few errors but who are inconsistent in their response pattern will have difficulty achieving the criterion of five complete response sets and will subsequently earn a high number of trials.

Two additional dependent measures were computed in order to more closely evaluate the types of errors that participants made: working memory errors and perseverative errors. For the purpose of this experiment, working memory errors were defined as (a)

within trial errors resulting from a participant returning to an incorrect response that had already received negative feedback within that trial and (b) between trial errors resulting from a participant choosing an incorrect response that had been correct on the previous trial. Perseverative errors were defined as incorrect responses in the Negative Transfer trials that would have previously been correct in the Initial Learning trials. By definition, perseverative errors were only calculated for the Negative Transfer trials of the Spatial and Object Tasks.

Data Analyses

Performance on the Spatial and Object Tasks was compared using mixed-model repeated measures analyses of variance (ANOVAs). To correct for sphericity violations, we used the Greenhouse-Geisser epsilon to adjust the degrees of freedom for within-subject factors with more than two levels.

RESULTS

Initial Learning

Table 2 shows the mean number of trials to criterion for both groups on the Initial Learning trials of the Spatial and Object Tasks. The number of trials to criterion was entered into a two-way repeated measures ANOVA with Group (ADHD, Control) as the between subjects factor and Task (Spatial, Object) as the within subjects factor. The analysis revealed significant main effects of Group [$F(1,22) = 4.88$, $p = .04$; $1 - \beta = .56$, $\eta_p^2 = .18$] and Task [$F(1,22) = 27.28$, $p < .01$; $1 - \beta = .99$, $\eta_p^2 = .55$]. These main effects were qualified by a significant Group by Task interaction [$F(1,22) = 4.35$, $p = .05$; $1 - \beta = .51$, $\eta_p^2 = .17$]. Follow-up t-tests indicated that the interaction was due to the children with ADHD performing significantly worse than the Control participants on the Spatial Task [$t(22) = 2.16$, $p = .04$; $1 - \beta = .66$, $d = .92$] but not on the Object Task [$p = .12$].

In order to further compare the learning patterns of the two groups, we also examined the number of errors as a percentage of total number of responses across the first six blocks of 10 trials for the Spatial and Object Tasks. The results for the Spatial and Object Tasks are presented in the left and right panels, respectively, of Figure 3. The cutoff was set at six blocks because none of the participants reached criterion before the sixth block in either task. Percentage of errors per block was entered into a three-way ($2 \times 2 \times 6$) repeated measures ANOVA with Group (ADHD, Control) as the between-subjects factor and Task (Spatial, Object) and Block as the within-subjects factors. Results revealed a significant three-way interaction [$F(5,110) = 2.93$, $p = .03$, $\varepsilon = .71$, $1 - \beta = .73$, $\eta_p^2 = .12$]. In order to evaluate the significant three-way interaction, we computed

Table 2 Participants' Mean Trials to Criterion.

	Initial Leaning Tasks				Negative Transfer Tasks			
	Spatial		Object		Spatial		Object	
Group	*M*	*(SD)*	*M*	*(SD)*	*M*	*(SD)*	*M*	*(SD)*
ADHD	146.33	(83.08)	59.75	(8.69)	118.50	(88.21)	67.75	(26.53)
Control	90.17	(37.55)	55.17	(3.81)	84.08	(22.31)	56.50	(6.90)

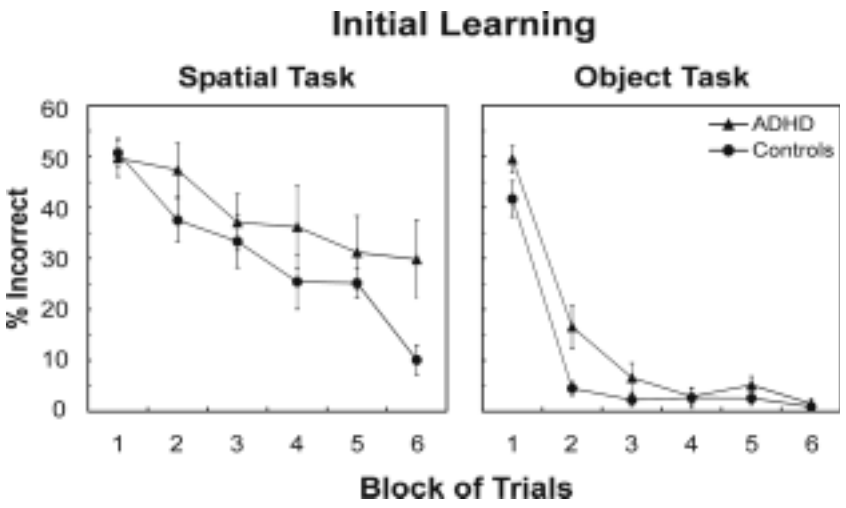

Figure 3 Total number of errors as a percentage of total responses across the first six blocks of 10 Initial Learning trials in the (Left) Spatial Task and (Right) Object Task.

the differences in the percentage of errors between the sixth block and the first block for the Spatial and Object Tasks. Change in percentage of errors was then entered into a two-way (2 × 2) repeated measures ANOVA with Group (ADHD, Control) and Task (spatial, object) as factors. Results again revealed a significant Group by Task interaction [$F(1,22) = 12.98$, $p < .01$, $1 - \beta = .93$, $\eta_p^2 = .37$]. Neither the main effect of Group or Task was significant [*ps* > .08]. Follow-up t-tests revealed a significant difference between the groups on the Spatial Task [$t(22) = 2.565$, $p = .02$; $1 - \beta = .78$, $d = 1.09$], with control participants showing a greater decrease in percentage of errors than the children with ADHD, but no significant difference between the groups on the Object Task [$p > .08$]. Taken together, these results provide additional support that the children with ADHD displayed impaired conditional associative learning performance on the Spatial but not the Object Task.

Secondary analyses were conducted in order to investigate the possibility that the impaired performance displayed by the children with ADHD on the Spatial Conditional Associative Learning Task could be attributed to increased working memory errors. As previously stated, working memory errors are defined within this experimental context as either: (a) within trial errors resulting from a participant returning to an incorrect response that had already received negative feedback within that trial; or (b) between trial errors resulting from a participant choosing an incorrect response that had been correct on the previous trial. Mean working memory error scores through the sixth block for each group are presented in Table 3. Overall, very few working memory errors were committed by either group. When total working memory errors committed during the Initial Learning trials were entered into a two-way repeated measures ANOVA with Group (ADHD, Control) and Task (Spatial, Object) as factors, neither the two main effects nor the interaction effect reached significance [*all ps* > .10]. These results suggest that performance differences between the groups on the Initial Learning trials were not driven by differences in the number of working memory errors.

Table 3 Participants' Mean Working Memory and Perseverative Errors within 1st Six Blocks of Each Task.

		Initial Learning				Negative Transfer			
		Spatial		Object		Spatial		Object	
Error Type	Group	*M*	*(SD)*	*M*	*(SD)*	*M*	*(SD)*	*M*	*(SD)*
Working Memory									
	ADHD	1.92	(1.44)	1.92	(1.38)	2.17	(3.13)	1.83	(1.27)
	Control	1.75	(1.66)	0.75	(0.87)	2.00	(2.76)	0.92	(1.24)
Perseverative									
	ADHD	–	–	–	–	8.50	(6.87)	2.75	(2.70)
	Control	–	–	–	–	8.33	(4.05)	1.75	(1.82)

Negative Transfer Trials

Table 2 also shows the group mean number of trials to criterion for each task during the Negative Transfer trials. As with the analysis conducted on the Initial Learning trials, the number of trials to criterion was entered into a two-way repeated measures ANOVA, with Group (ADHD, Control) as the between subjects factor and Task (Spatial, Object) as the within subjects factor. The analysis revealed a significant main effect of Task [$F(1,22) = 11.21$, $p < .01$, $1 - \beta = .89$, $\eta_p^2 = .34$], with a larger number of trials required to reach criterion on the Negative Transfer trials of the Spatial Task than the Object Task. Neither the main effect of Group nor the Group by Task interaction effect reached significance [*ps* > .08], indicating that the two groups did not differ in the number of trials required to reach criterion on the Negative Transfer trials of the Spatial and Object Tasks.

In order to further compare the learning patterns of each group on the Transfer Trials, we also examined the number of errors as a percentage of total responses across the first six blocks of 10 trials each. The results for the Spatial and Object Tasks are presented in the left and right panels, respectively, of Figure 4. The cutoff was again set at six blocks

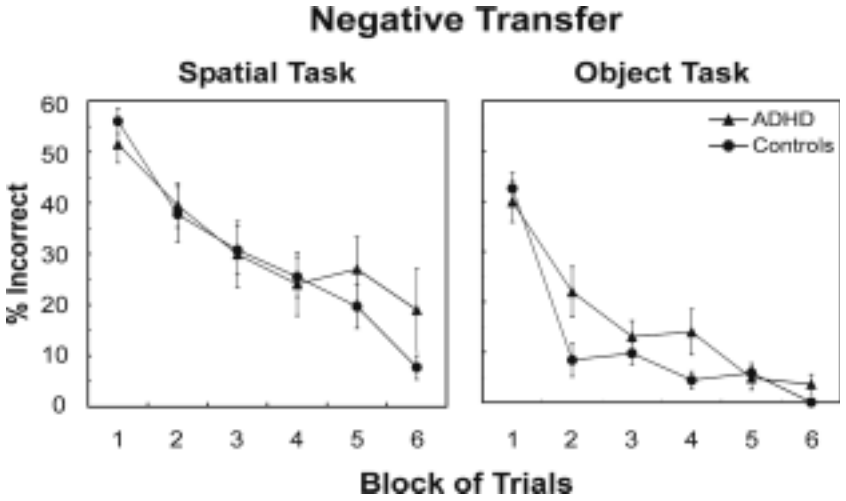

Figure 4 Total number of errors as a percentage of total responses across the first six blocks of 10 Negative Transfer trials in the (Left) Spatial Task and (Right) Object Task.

because none of the participants reached criterion before the sixth block in either Negative Transfer task. Percentage of errors per block was then entered into a three-way ($2 \times 2 \times 6$) repeated measures ANOVA with Group (ADHD, Control) as the between-subjects factor and Task (Spatial, Object) and Block as the within-subjects factors. Results revealed a significant main effect of Task [$F(1,22) = 40.67$, $p < .01$], indicating that more errors overall on the Spatial than the Object Task, as well as a significant main effect of Block [$F(5,110) = 70.34$, $p < .01$, $\varepsilon = .83$], indicating that errors decreased overall across the six blocks. No other main or interaction effects were significant [*ps* > .08].

Finally, secondary analyses were again conducted to evaluate the qualitative nature of the errors committed during Negative Transfer trials. First, the mean number of **working memory errors** committed on the Negative Transfer trials were calculated (Table 3). As with the Initial Learning trials, very few working memory errors were committed by either group. A two-way repeated measures ANOVA confirmed that there was no significant main effect of Group (ADHD vs. Control) or Task (Spatial vs. Object), and no significant interaction effect [*all ps* > .10]. We were also able to evaluate **perseverative errors** committed during the Negative Transfer trials, with perseverative errors defined as incorrect responses during the Negative Transfer trials that would have been correct responses in the Initial Training trials. A two-way ANOVA revealed a significant main effect of Task [$F(1,22) = 33.74$, $p < .01$], with greater preservative errors produced overall on the Spatial than the Object Task. No other effects were significant [all *ps* > .10].

DISCUSSION

Surprisingly few studies have directly assessed learning and memory processes in children with ADHD. While children with ADHD have previously demonstrated impaired performance on tests of paired associative learning, this impairment appears to be due more to executive function deficits rather than to deficits in memory per se. These findings are in fact consistent with previous studies in other patient populations showing that paired associate learning is dependent more on medial temporal lobe structures rather than on the frontostriatal structures implicated in ADHD. The present study was designed to assess the performance of children with ADHD on tests of conditional associative learning that (unlike Paired-Associate Learning Tasks) have previously been shown to be dependent more on frontostriatal structures than on medial temporal lobe structures. In particular, we investigated whether children with ADHD possess a conditional associative learning impairment that can be directly attributable to a basic deficit in acquiring stimulus-response associations or whether a conditional associative learning impairment occurs only under conditions that placed high demands on strategic processes.

In order to address this issue, we compared children's performance on two tests of conditional associate learning (i.e., spatial and object) that shared similar stimulus-response association structures but differed in terms of the demands placed upon strategic processes. On the Spatial Conditional Associative Learning Task, stimulus-response associations were made based solely on their spatial locations, thereby minimizing the potential use of external cues. Because successful completion of the spatial task required the simultaneous mapping of all stimuli pairings (i.e., all individual items had to be considered in relation to each other), this task placed maximal demands on strategic control processing. The Object Conditional Associative Learning Task, in contrast, maintained the same basic conditional associative learning requirements as in the spatial task, but it incorporated stimuli with distinctive features that served to reduce the demands placed on strategic processes.

Children with ADHD were found to display normal performance on the Object Conditional Associative Learning Task but to be significantly impaired relative to control participants on the Spatial Task. The intact performance on the object tasks indicates that ADHD does not produce a general conditional associative learning deficit. The impaired performance on the Spatial Task, however, indicates that deficits in children with ADHD emerge under task conditions in which demands on internally derived strategic processes are maximized. These results are consistent with previous findings indicating that impaired strategic processing underlies conditional associative learning deficits in populations with frontostriatal dysfunction (Levine et al., 1997; Pillon et al., 1998). Results are also consistent with data specifically suggesting that children with ADHD exhibit strategic processing deficits (Douglas & Benezra, 1990; Perchet, Revol, Fourneret, Mauguiere, & Garcia-Larrea, 2001) that may lead to impaired ability to make use of internally derived elaborative or organizational strategies necessary for completion of complex Conditional Associative Learning Tasks.

These results may also help to shed some light on the nature of the frontostriatal pathology contributing to the conditional associative learning impairment in ADHD. Previous studies in other populations have suggested that damage to basal ganglia structures may produce a general impairment in the ability to form critical stimulus-response associations regardless of task demands. Damage to the prefrontal cortex, on the other hand, does not appear to result in complete failure to form stimulus-response associations but rather leads to performance deficits on Conditional Associative Learning Tasks that require a high degree of strategic processing (Levine et al., 1997; Winocur & Eskes, 1998). The demonstration in the present study that children with ADHD can display normal performance on one Conditional Associative Learning Task but display impaired performance on another task that places greater demands on strategic processes suggests that their impaired performance may be associated more with frontal rather than striatal dysfunction. That is, our results indicate that the ADHD group is impaired on a measure of frontal lobe mediated conditional associative learning with high strategic processing demands and is unimpaired on a measure of basic conditional associative learning dependent upon integrity of the basal ganglia.

Several additional analyses were conducted in an attempt to better characterize the nature of the strategic processing impairment displayed by children with ADHD on the Spatial Learning Task. First, perseverative errors (defined as incorrect responses in the Negative Transfer trials that would have previously been correct in the Initial Learning trials) were computed in order to obtain a measure of inefficient response inhibition as reflected in the failure to shift attention away from previously reinforced stimulus-response pairs to new pairings. Both groups produced more perseverative errors on the spatial task than the object task, most likely due to the greater demands the spatial task places on strategic control processes. However, no differences emerged between the two groups, suggesting that the strategic inefficiency that underlies impaired conditional associative learning performance in the ADHD group cannot be attributed to inefficient response inhibition.

Second, working memory errors (defined as the same incorrect pairing made more than once either within a single complete trial or across two adjacent trials) were calculated in order to obtain a measure of the ability to hold online, for short periods of time, useful information regarding incorrect pairings during the completion of an individual trial or adjacent trials. Because working memory errors represent a return to a previously incorrect response despite recent feedback indicating it as such, these types of errors may

also be conceptualized as perseverative errors, with perseveration occurring within a single trial or across two trials. Regardless of the way in which these errors are conceptualized, what is most noteworthy is that very few of these errors were committed by participants in either group in either the Initial Learning or Negative Transfer trials. Moreover, no differences emerged between the two groups, indicating that strategic inefficiency that underlies impaired conditional associative learning performance in the ADHD group also cannot be attributed specifically to working memory deficits.

Rather than being associated with a specific deficit in response inhibition or working memory, the spatial conditional associative learning impairment in children with ADHD appears instead to be related to a more general inability to maintain a high degree of consistency in responding across trials. The performance criteria for the Conditional Associative Learning Tasks used in the present study required a higher degree of consistency in responding across trials than criteria based simply on the total number of correct stimulus-response pairings. Specifically, in order to reach criterion in the current tasks, participants needed to achieve greater than 70% accuracy in a set of responses and to consistently maintain that level of accuracy for five consecutive sets of responses. Because the control participants made relatively few errors and were able to maintain consistently accurate responding across trials they were able to achieve criterion quickly. In contrast, although the participants with ADHD also frequently chose correct stimulus-response pairs and consequently made relatively few errors, they were not able to maintain consistently accurate responding across trials. That is, because the errors generated by the participants with ADHD were interspersed throughout the task, the criteria for achieving criterion were continuously violated and a greater number of correct trials were required before criterion was ultimately achieved. Such impaired consistency is suggestive of deficient attentional resources or higher-order organizational processes.

Study Limitations

The results of this study must be interpreted in light of its methodological limitations. This study compared the performance of relatively small groups of participants, which could result in low power to detect group performance differences. Power analyses suggest we had moderate to good power to detect main and interaction effects for the main analyses. While follow-up studies to replicate our findings with larger sample sizes are clearly warranted, the consistency of our results across the main analyses does suggest that children with ADHD perform more poorly than control participants on measures of conditional associative learning when strategic processing demands are high.

Despite a lack of a significant between-group difference in mean IQ score, the group mean IQs did differ by approximately one-half standard deviation. Because different levels of intelligence could have differentially affected performance on tasks with higher strategic requirements, we investigated the potential impact intelligence may have had on conditional associative learning performance in this study. First, we used a median split to divide the Control and ADHD groups into “lower IQ” (Control Mean: 99; ADHD Mean: 99) and “higher IQ” (Control Mean: 126; ADHD Mean: 116) subgroups, and then we visually inspected the performance of these subgroups on the Initial Learning trials for the Object and Spatial Tasks. The mean numbers of trials required by the “lower IQ” and “higher IQ” Control groups to achieve criterion were similar on both the Object Task (53 and 58, respectively) and the Spatial Task (100 and 90, respectively), suggesting that intelligence level did not substantially impact conditional associative learning in the Control group.

The mean numbers of trials required by the "lower IQ" and "higher IQ" ADHD subgroups on the Object Task were found to be identical (i.e., 60); this observation is consistent with our conclusion that ADHD (regardless of IQ) does not produce a general conditional associative learning deficit. On the Spatial Task, in contrast, the "lower IQ" ADHD group required many more trials to achieve criterion than did the "higher IQ" ADHD group (188 vs. 118, respectively). Moreover, despite nearly equivalent mean IQ performance, the "lower IQ" ADHD group required many more trials to achieve criterion on the Spatial Task than did the "lower IQ" Control group. Although these results need to be verified with larger sample sizes that would allow for direct statistical analyses, they again lend further support to the conclusion that children with ADHD (particularly those for whom IQ performance falls at or below the average range) exhibit impaired performance on measures of spatial conditional associative learning. High intelligence may serve to moderate performance of children with ADHD by allowing them to use compensatory skills to successfully complete spatial conditional associative learning tasks; however, this finding requires further investigation.

An additional methodological limitation of this study is that the groups were not matched for gender, and therefore that performance differences between the groups may be due to differential performance between female and male participants. We investigated the potential impact of gender on conditional associative learning performance by dividing each group into female and male participants and then comparing subgroup means for the number of trials to criterion on the Object and Spatial Initial Learning trials. The mean numbers of trials required to achieve criterion on the Object Task were nearly identical for the female and male participants in both groups (Control Female: 55; Control Male: 56; ADHD Female: 58; ADHD Male: 61). Similarly, the mean numbers of trials required to achieve criterion on the Spatial Task was also similar across female and male participants within each group (Control Female: 93; Control Male: 83 ADHD Female: 142; ADHD Male: 140). Although it will be important to confirm our findings with a follow-up study in which groups are matched for gender, these findings suggest that group differences in performance on the Spatial Conditional Associative Learning Task are not due to performance differences between female and male participants.

The results of this study are also limited by the heterogeneity of the ADHD group with regard to medication status. Although we did not have sufficient power to statistically evaluate performance differences between children with ADHD on and off medication at the time of testing, we investigated the potential impact of medication status by comparing the mean number of trials to criterion for the medicated and nonmedicated ADHD subgroups. The mean number of trials required to achieve criterion for the two subgroups were nearly identical for the Object Task (on medication: 57.2; off medication: 57.6) and were similar for the Spatial Task (on medication: 143; off medication: 127). If anything, medicated children with ADHD had a more difficult time than the nonmedicated children on the Spatial Task. It should be noted in this regard that the one patient with ADHD who was unable to complete the Spatial Task was on medication. Although it will be important to confirm our findings with a follow-up study including large samples of children with ADHD on and off medication at the time of testing, performance on the Conditional Associative Learning Tasks does not appear due to substantially influenced by medication status at the time of testing.

Finally, it is possible that the differential pattern of performance displayed by the children with ADHD on the Object and Spatial Tasks is not due primarily to differences in the demands that the two tasks place on strategic processing, but rather to differences in

the nature of the associative information itself (i.e., object vs. spatial information). While some investigators have suggested that memory for spatial and object memory are mediated by distinct frontostriatal networks, other studies have not supported the segregation of domain-specific modules within frontal cortex (e.g., Postle, Stern, Rosen & Corkin, 2000). Future studies should be conducted to investigate performance differences on tasks with high versus low strategic processing demands within a single domain.

Conclusion

Overall, our results provide evidence of unimpaired conditional associative learning in children with ADHD and evidence of impaired strategic processing in the same sample. Furthermore, results suggest that the primary neuroanatomical locus of the conditional associative learning impairment in children with ADHD lies within frontal regions. Future research should be designed to directly assess participant's mnemonic strategies. This type of assessment will provide direct information about the different strategic processing demands necessary for successful completion of the Spatial and Object Tasks. Additionally, such an investigation will help elucidate the strategic processing failures of children with ADHD. Finally, future work (i.e., functional imaging) needs to be conducted to confirm the suggestion that impaired strategic processing during the completion of a complex Conditional Associative Learning Tasks is directly associated with frontal lobe integrity.

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