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Attentional Control Activation Relates to Working Memory in Attention-Deficit/Hyperactivity Disorder

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Abstract

Background—Attentional control difficulties in individuals with attention-deficit/ hyperactivity disorder (ADHD) might reflect poor working memory (WM) ability, especially as WM ability and attentional control rely on similar brain regions. The current study examined whether WM ability might explain group differences in brain activation between adults with ADHD and normal controls during attentional demand.

Methods—Participants were 20 adults with ADHD combined subtype with no comorbid psychiatric or learning disorders, and 23 controls similar in age, IQ, and gender. WM measures were obtained from the WAIS-III and WMS-R. Brain activation was assessed with functional magnetic resonance imaging (fMRI) while performing a Color-Word Stroop task.

Results—Group differences in WM ability explained a portion of the activation in left dorsolateral prefrontal cortex (DLPFC), which has been related to the creation and maintenance of an attentional set for task-relevant information. In addition, greater WM ability predicted increased activation of brain regions related to stimulus-driven attention and response selection processes in the ADHD group, but not in the control group.

Conclusions—The inability to maintain an appropriate task set in young adults with combined type ADHD, associated with decreased activity in left DLPFC, may in part be due to poor WM ability. Furthermore, in individuals with ADHD, higher WM ability may relate to increased recruitment of stimulus-driven attention and response selection processes, perhaps as a compensatory strategy.

Keywords

attention-deficit/hyperactivity disorder; ADHD; working memory; attentional control; Stroop task; functional magnetic resonance imaging; fMRI; adults

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Introduction

A defining characteristic of attention-deficit/hyperactivity disorder (ADHD) is a difficulty in controlling, maintaining, and directing attention (1). However, ADHD affects executive function more widely, compromising processes such as response inhibition and planning (2). Such deficits may account for the negative outcomes of individuals with ADHD in academic, social, and workplace settings (3).

Some theories suggest that reduced WM ability in individuals with ADHD contributes to their deficits in attentional control and executive function (5,6). Indeed, lower WM ability in non-ADHD individuals is associated with poorer cognitive ability (7) and increased mind-wandering away from challenging activities in real-life settings (8). Furthermore, poorer WM ability has been correlated with poorer performance on the Stroop color-word task (9,10), a classic measure of attentional control (11). Computational models of the Stroop task have suggested that maintenance of a task set provides support for top-down bias toward task-relevant processing (12), and other studies suggest that better WM ability improves the active maintenance of task-relevant information (13).

Attentional control and WM rely on a common set of neural structures, many of which have been implicated as dysfunctional in ADHD. Meta-analyses of both the Stroop task (14,15) and WM tasks (16,17) have implicated bilateral dorsolateral prefrontal cortex (DLPFC), bilateral inferior frontal gyrus (IFG), dorsal anterior cingulate cortex (dACC), inferior parietal lobule, and precuneus. These same regions show atypical functioning in individuals with ADHD (18). Despite these similarities, no studies have investigated directly how the neural substrates that support both WM ability and attentional control, namely DLPFC, might be altered in young adults with ADHD.

The current study investigated whether WM ability in adults with ADHD and controls could explain differences in performance and attentional-control activity during the Stroop color-word task. We used a data set from our laboratory (see reference 19 for details) that demonstrated significant effects of ADHD on activation of attentional-control regions. Of note, relative to controls, the ADHD group showed significant yet reduced DLPFC activation during three Stroop conditions (incongruent, congruent, neutral), suggesting that individuals with ADHD have reduced maintenance of the attentional set to the task-relevant ink color. Furthermore, the ADHD group showed increased activation in linguistic regions such as the left temporal gyrus relative to controls, which suggests increased processing of the task-irrelevant word dimension.

We expected WM differences between ADHD and control groups to relate to attentional control in two different ways. First, WM ability may capture group differences in performance and brain activation associated with attentional control, suggesting that attentional control deficits in ADHD arise, in part, from WM deficits. Second, the relationship between WM ability and brain activation related to attentional control might differ between the groups, suggesting that WM ability affects different pathways and/or processes in the ADHD group compared to controls. For example, in individuals with ADHD, high WM ability might promote activation of brain regions associated with compensatory attentional processes, while in controls, recruitment of those same neural processes may be unnecessary due to effective task-set maintenance. Importantly, the two groups can show different associations between WM ability and activity in some brain region whether or not differ in average activation. Consequently, we may observe relationships with WM ability in brain regions that show group differences in average activity, as well as those that do not.

The relationship of WM ability with performance and brain activation associated with attentional control may depend on the type of attentional demand. The Stroop task contains at

least three levels of attentional demand: selection and maintenance of a task set for task-relevant information (i.e., attend to chromatic color), selection of the task-relevant stimulus dimension (i.e. the chromatic color blue, not the semantic meaning "RED"), and response selection (the response associated with blue versus with red). We propose that WM networks may maintain representations of task sets, resulting in a relationship between WM ability and task-set maintenance.

Others have argued that the demands of task set maintenance vary across different Stroop task conditions (9). On incongruent trials, the inherent conflict between the ink color and the word provides a subtle reminder that only one of those task sets is correct (i.e., ink color identification). Hence, the conflict present during incongruent trials may serve as a reminder to reactivate the correct task set of identifying the ink color (20-23). In contrast, on congruent and neutral trials, the word name does not conflict with the ink color, resulting in no reminder of the need to identify the ink color (i.e., "goal neglect"; 9). Consequently, task set maintenance may be more contingent upon intrinsic WM ability during the congruent and neutral conditions compared to the incongruent condition. Consistent with such an idea, Kane & Engle (2003) demonstrated that low WM ability results in greater interference on Stroop accuracy when blocks are mostly congruent compared to when blocks are mostly incongruent. Hence, we expect the effects of WM ability on group differences in DLPFC activation to be stronger during congruent and neutral blocks and weaker during incongruent blocks.

According to our Cascade-of-Control model (20), posterior regions of DLPFC implement a task set to exert top-down attentional control (24,25). When top-down control from posterior DLPFC is inadequate, other brain regions must resolve difficulties at later stages of processing (26,27). In particular, we have posited that anterior regions of DLPFC are involved in selecting the task-relevant dimension of the stimulus, and that dACC is involved in selecting the response (23,28). For selecting the task-relevant stimulus dimension, attentional demands will be less for neutral trials than for incongruent and congruent trials, when two sources of color information must be disambiguated (i.e., the ink color and the word identity; 23,29). For response selection, attentional demands will be greater for incongruent than congruent and neutral trials, because the two sources of color information in incongruent trials relate to potential responses that conflict. We hypothesize that individuals with ADHD may compensate for poorer task-set maintenance using these later-stage attentional processes.

Of note, we examined these issues in high-functioning (i.e. college-enrolled) young adults with ADHD combined type versus a control group consistent in age, IQ, and gender. The ADHD group was not comorbid for other psychiatric disorders or learning disabilities. This means that between-group differences likely result from ADHD rather than other conditions that might influence WM and attentional control.

Methods and Materials

Participants

Twenty-seven adults with DSM-IV ADHD combined subtype and 24 normal controls participated in this study. Participants were screened for comorbid psychiatric, psychological, and learning disorders, a history of head injury, and conditions contraindicated for MRI before participating in the fMRI session. Section 1 in Supplement 1 contains more details regarding subject selection.

Data from 5 individuals (4 ADHD, 1 control) were unusable due to excessive movement (i.e., greater than 2mm) during scanning. Furthermore, three individuals with ADHD were identified as outliers on WM measures. These individuals were excluded prior to subsequent analyses,

to avoid spurious correlations between WM ability and brain activity. Section 2 in Supplement 1 contains more information about outlier identification.

Hence, the final sample consisted of 20 individuals with ADHD (12 male) and 23 control individuals (13 male). Groups did not differ in IQ, reading and spelling performance, or math performance, and were consistent in overall age. As expected, however, the ADHD and control groups differed in the number of ADHD symptoms and impairment in real-world functioning (Table 1).

Individuals provided informed consent before participating. All procedures were approved by the Colorado Multiple Institutional Review Board. Participants were asked to refrain from stimulant medications for 24 hours prior to the fMRI session. Section 3 in Supplement 1 contains additional information regarding medication history.

WM Ability Scores

The measure of WM ability was the average of two WM measures from the WAIS-III (30) – forward digit span and backward digit span – and two WM measures from the WMS-R (31) – forward spatial span and backward spatial span. Performance on each measure was z-scored across all participants, and the average of the four z-scores for each participant was used as an estimate of overall WM ability.

fMRI Paradigm

Participants performed a Color-Word Stroop task (11) in the scanner. A series of words were printed in one of four ink colors (red, blue, green, or yellow). Participants indicated the ink color of the item with a manual keypress. The word named either a color word or a non-color word, resulting in three trial types: congruent trials, in which the word name matched the ink color (e.g., “red” in red ink), incongruent trials, in which the word name did not match the ink color (e.g. “red” in green ink), and neutral trials, in which the word did not name a color (e.g. “bond” in blue ink).

Three types of task blocks were used – congruent, incongruent, and neutral – in addition to resting fixation blocks. Within each task block, half of the trials were block-specific (congruent, incongruent, or neutral) and half were neutral trials that were identical across all three blocks (referred to as N_C, N_I, and N_N trials, depending on the block in which they were presented). This design allowed the estimation of both blocked and event-related effects.

There were three scan runs, each comprising 163 volumes. Seven null trials were dropped from the beginning of each run to ensure steady-state magnetization, leaving 156 volumes in each run. Each run was composed of 13 blocks of 12 volumes: four blocks of resting fixation and nine task blocks. Each task block consisted of 12 trials – one for each volume acquired. Fixation blocks (F) alternated with triads of task blocks. Each triad consisted of one incongruent block (I), one neutral block (N), and one congruent block (C). For example, the block order for one run could be F-INC-F-NCI-F-CIN-F. The order of blocks was counterbalanced across triads, and the triad order was counterbalanced across participants. In total, there were 324 task trials, with 54 trials in each of the six trial conditions.

fMRI Data Acquisition

Functional images were acquired with a GE Signa (3T) MRI scanner using a T2*-weighted gradient-echo, echo-planar imaging (repetition time [TR] = 2000 ms, echo time [TE] = 40 ms, flip angle = 90°, 29 slices parallel to the AC-PC line, thickness = 4 mm, gap = 0 mm, 64 × 64 in-plane resolution, in-plane FOV = 22cm). A high-resolution T1-weighted anatomical scan was collected for each participant to localize functional activity.

Image preprocessing

Image preprocessing was conducted using the FMRIB Software Library (FSL; http://www.fmrib.ox.ac.uk/fsl/index.html). Images were motion corrected using MCFLIRT, and brain extracted using BET to remove all non-brain tissue from the images. Before statistical analysis, each participant's images were spatially smoothed using a Gaussian kernel (FWHM = 8mm); mean-based intensity normalized; high-pass temporal filtered with a cut-off period of 100s to remove low-frequency noise; and intensity-normalized to allow valid analyses across participants.

Statistical Analyses

Statistical analyses were conducted using FILM. Analyses on the BOLD timecourses were run separately for each participant and for blocked versus event-related analyses. Blocked and event-related regressors were convolved with a double-gamma hemodynamic response function. Event-related regressors included correct trials only.

Our analyses focused on processes that promote attention toward color naming and away from word reading. As laid out in the introduction, those processes will likely be both sustained (e.g., active maintenance of task set) and transient (e.g., stimulus-driven and response-related attention) in nature. Sustained control processes should be active across task blocks, and should be present in contrasts of I, C, and N (versus baseline). Furthermore, the recruitment of sustained processes was expected to be greatest during C blocks, intermediate for N blocks, and least for I blocks. Hence, we examined contrasts of C-N, N-I, and C-I. In terms of transient processes, significant activity was expected for incongruent - N_I and congruent - N_C, because incongruent and congruent trials require greater control than neutral trials due to the presence of two sources of color-related information.

For comparisons across individuals and groups, parameter and variance estimates from each participant were registered to Montreal Neurological Institute standard stereotaxic space (MNI152) using the two-stage registration procedure implemented in FLIRT. FLAME was used to model the mixed-effects variance for each contrast of interest, taking into account both fixed effects (within-participants variability) and random effects (between-participants variability).

Separate general linear models (GLM) were run to test three potential relationships of brain activity with ADHD and WM ability. The first GLM contained separate predictors for each group, in order to test for differences in average activation between the two groups. The second GLM contained an additional predictor for WM ability as a covariate. This model tested group differences in the average activation after controlling for WM ability. The third GLM contained separate WM variables for each group. This model tested whether the relationship of brain activity with WM ability differed significantly between groups after controlling for group differences in average activation.

To simultaneously increase our sensitivity and avoid spurious results, we constrained our search space to regions that have shown Stroop effects in previous studies conducted in our lab (23-25,32,33). Section 4 in Supplement 1 contains a description of brain regions included in this mask. We used the AlphaSim algorithm within AFNI (34) to conduct Monte Carlo simulations to estimate cluster-wise false positive rates of alpha=.05 within this a priori search space. Regions were considered statistically significant, correcting for multiple comparisons, if they surpassed a voxelwise threshold of z=2.58 (one-tailed p = .005) and a cluster size of 69 voxels.

Results

Behavioral results

In a set of unpaired samples t-tests (Table 2), the ADHD group performed significantly worse than controls on the forward digit span, t(41) = -3.260, p = .002, backward digit span, t(41) = -2.131, p = .039, and forward spatial span, t(41) = -3.313, p = .002, and marginally worse than controls on the backward spatial span, t(41) = -1.922, p = .062. The composite WM ability score from these four measures was significantly lower for ADHD individuals than controls, t(41) = -3.804, p=.0005. These results suggest that reduced WM associated with ADHD could give rise to group differences in attentional control during the Stroop color-word task.

For Stroop performance (Table 2), an unpaired samples t-test conducted on proportion RT facilitation scores [(mean RT for N_C trials - mean RT for congruent trials) / mean RT for N_C trials] revealed significantly greater facilitation for the ADHD than control group, t(41)=2.385, p = .022. This group difference remained significant after controlling for WM ability, t(40) =2.510, p = .016, using hierarchical regression with WM ability entered before the group factor. These results suggest increased task-irrelevant processing (i.e., word reading) for congruent items in individuals with ADHD compared to controls. Increased WM ability was related to increased RT facilitation in the ADHD group, r(20)=.468, p = .038, but not for the control group, r(23)=.111, p > .60, suggesting that WM ability increased task-irrelevant processing in the ADHD group, but not in the control group. Accuracy facilitation scores did not differ, before or after controlling for WM ability, p's > .20. Task-set maintenance does not explain the correlation of WM performance with facilitation in the ADHD group. Because the opposite relationship has been reported previously in controls (9), these results suggest that WM performance in the ADHD group relates to attentional processes other than task-set maintenance.

In contrast, an unpaired samples t-test revealed that proportion RT interference scores [(mean RT for incongruent trials - mean RT for N_I trials) / mean RT for N_I trials] were reduced for the ADHD group relative to controls, t(41)=-2.329, p = .025. This group difference was still significant after controlling for WM ability in a hierarchical regression, t(40)=-2.356, p = .023. The groups did not differ on accuracy interference scores, or on the correlation between WM ability and behavioral interference scores.

Imaging results

Group differences in blocked activity—We propose that posterior DLPFC is involved in activating a top-down attentional set towards task-relevant information (20,35), and that WM ability may aid in maintaining that activation. Although each group activated posterior DLPFC during all blocked conditions (19), activity was significantly greater for the control group than the ADHD group in the C and N blocks only (Table 3). When WM ability was added as a covariate, the posterior DLPFC region that showed a group difference was no longer statistically significant after controlling for multiple comparisons (Figure 1). The two groups also differed in precuneus activation for the blocked contrast of C-N. This region did not show a group difference after WM ability was added as a covariate. Overall, this pattern suggests that WM ability may mediate some of the group differences in brain activity related to the maintenance of a top-down attentional set in the Stroop task.

Group differences in event-related contrasts—Transient aspects of attentional control may differ between trial types within the same task block. The congruent-N_C contrast yielded significantly greater activation for controls relative to the ADHD group in left angular gyrus and right DLPFC. The control group activated these regions, but the ADHD group did not. After adding WM ability as a covariate, these effects remained significant (Table 3). In

combination with the blocked analyses, this pattern is consistent with our hypothesis that group differences in WM ability are more related to sustained maintenance of the task set than to transient fluctuations in attentional control.

The event-related contrast of incongruent-N_I yielded significantly greater activation for controls versus ADHD in right dACC. However, after controlling for WM ability, activation in right dACC no longer differed between the two groups. The exact basis of the relationship of dACC with WM ability is unclear. Unlike other regions discussed above (e.g., DLPFC), dACC has not been not strongly implicated in WM function (17). However, activation of dACC during response conflict is typically reduced in individuals with ADHD (19,36). Therefore, the reduction of the group difference in dACC may have arisen because individuals with ADHD independently show both dACC dysfunction and reduced WM ability.

Group differences in the correlation of WM ability with activity—In several brain regions, the correlation of WM ability with blocked activity related to attentional control differed significantly between the two groups (Table 4). These differences in correlations, which were more evident during I and C blocks than N blocks, were observed in bilateral temporal lobe (BA22), bilateral precentral gyrus / premotor cortex (BA6), and right medial frontal gyrus / pre-SMA (BA6). In each case, greater WM ability was associated with greater activation in the ADHD group, whereas in the control group, the relationship between WM ability and blocked activity was either negative (i.e. greater WM, less activity) or non-significant (cf. Figure 2).

For between-block contrasts, the correlation with WM ability demonstrated group differences in right inferior parietal lobule (BA40). Here, the correlation of WM ability with the C-N blocked contrast was significantly greater for the ADHD group than controls. Again, this difference arose from a positive correlation in the ADHD group and a non-significant correlation in the control group. Altogether, these results suggest that, when there are two sources of color-related information, individuals in the ADHD group with high WM ability recruit additional attentional control processes. However, this relationship of WM ability with additional recruitment does not exist in the control group.

The correlations between WM ability and event-related activity also suggest that higher WM ability resulted in greater transient activation of left PFC regions within the ADHD group only. Namely, the correlation of WM ability with the incongruent-N_I contrast was significantly more positive in the ADHD group than the control group in three prefrontal regions involved in top-down control (Table 4). Thus, higher WM ability in individuals with ADHD may relate to increased transient recruitment of left PFC regions related to attentional control.

In contrast, the group difference in the WM correlation was in the opposite direction within three other regions. These regions included ventromedial PFC (BA10), which has been implicated in “default mode” processing (38). The control group deactivated this region during task relative to rest (i.e., I, C, and N blocked contrasts), but the ADHD group did not show this sustained deactivation. Instead, high WM individuals with ADHD deactivated this region in a transient manner for more-difficult incongruent trials relative to neutral trials (i.e., inc-N_I contrast). Controls did not show transient deactivation of this region, either related to WM ability or for the group on average. This suggests that sustained deactivation of default mode is dysfunctional in individuals with ADHD (39), but high WM individuals with ADHD attempt to overcome this dysfunction by deactivating this region transiently.

Discussion

These results suggest that WM ability can account for a portion of the effects of ADHD on attentional control. Reduced WM ability in individuals with ADHD relates to compromised performance and reduced activity in posterior DLPFC regions, which have been implicated in task-set maintenance. It is unclear whether reduced WM ability causes reduced task-set maintenance and increased task-irrelevant processing, or whether interference from task-irrelevant processing reduces task-set maintenance and WM ability. We suggest the former explanation for two reasons. First, reduced active maintenance sometimes precedes increased activation of inhibitory mechanisms (13,40), suggesting that inadequate task-set maintenance may increase subsequent interference. Second, in the current study, performance was affected in individuals with ADHD by task-irrelevant information during the congruent condition only. This pattern was unexpected if interference (which is present in both incongruent and congruent conditions) reduces task-set maintenance.

These results suggest that intrinsic WM ability affects attentional control less when task stimuli support task-set activation (20-23). Consistent with this, left DLPFC activity was reduced for the ADHD group versus controls during C and N blocks, but not during I blocks. These group differences were no longer significant after controlling for WM ability. This pattern suggests that attentional control depended upon task-set maintenance during the C and N blocks, but not during the I blocks.

As described previously, the Stroop task involves multiple stages of attentional demand, each of which recruits different brain regions and responds differently to various conditions. The Cascade-of-Control model (20) suggests that, when earlier-stage attentional control processes are ineffective, individuals direct performance using later-stage attentional control processes. The brain regions differentially related to WM ability in the ADHD group have been implicated in later-stage processes, such as stimulus-driven attention (41), and response selection (23). These relationships were especially evident during incongruent and congruent conditions, when task stimuli contain multiple stimulus dimensions and/or potential responses. Altogether, the relationships of WM ability with behavioral facilitation and with activity in brain regions previously implicated in later-stage attentional processes suggest that better performance on WM tasks in individuals with ADHD may be less related to sustained activation of the task set and more related to compensatory attentional processes such as stimulus-driven attention and response selection. However, we believe that these findings need to be replicated and further investigated in future studies.

Altogether, these results suggest that the relationships observed among attentional control, WM ability, and ADHD may depend upon factors that vary across situations. WM deficits might not affect attentional control adversely in individuals with ADHD when the task design or stimuli provide extrinsic reinforcement of the task set. Such situations might elicit fewer deficits, or even improved performance, in individuals with ADHD. Furthermore, WM ability in individuals with ADHD might relate to attentional control processes other than task-set maintenance, such as stimulus-driven attention and response selection. If these processes can augment performance, the relationship between ADHD, task-set maintenance, and attentional control may be obscured. Further consideration of these factors may explain some of the inconsistencies in the literature regarding effects of WM ability on attentional control in individuals with ADHD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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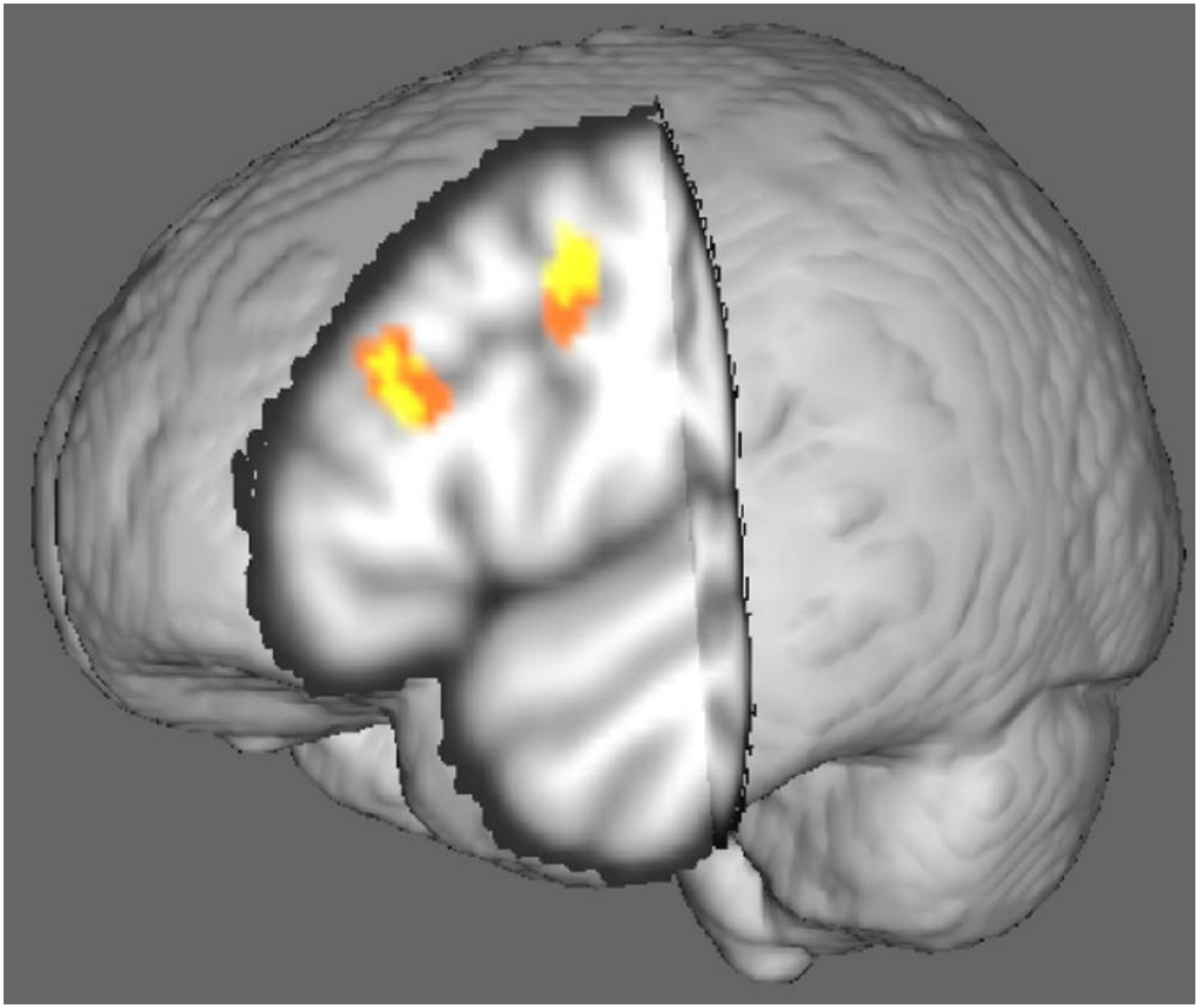

Figure 1.
Brain regions that showed greater activation for Controls than ADHD during congruent block. The yellow subregions show the group difference in activation, after partialling the influence of WM ability. These subregions were not significant after correcting for multiple comparisons.

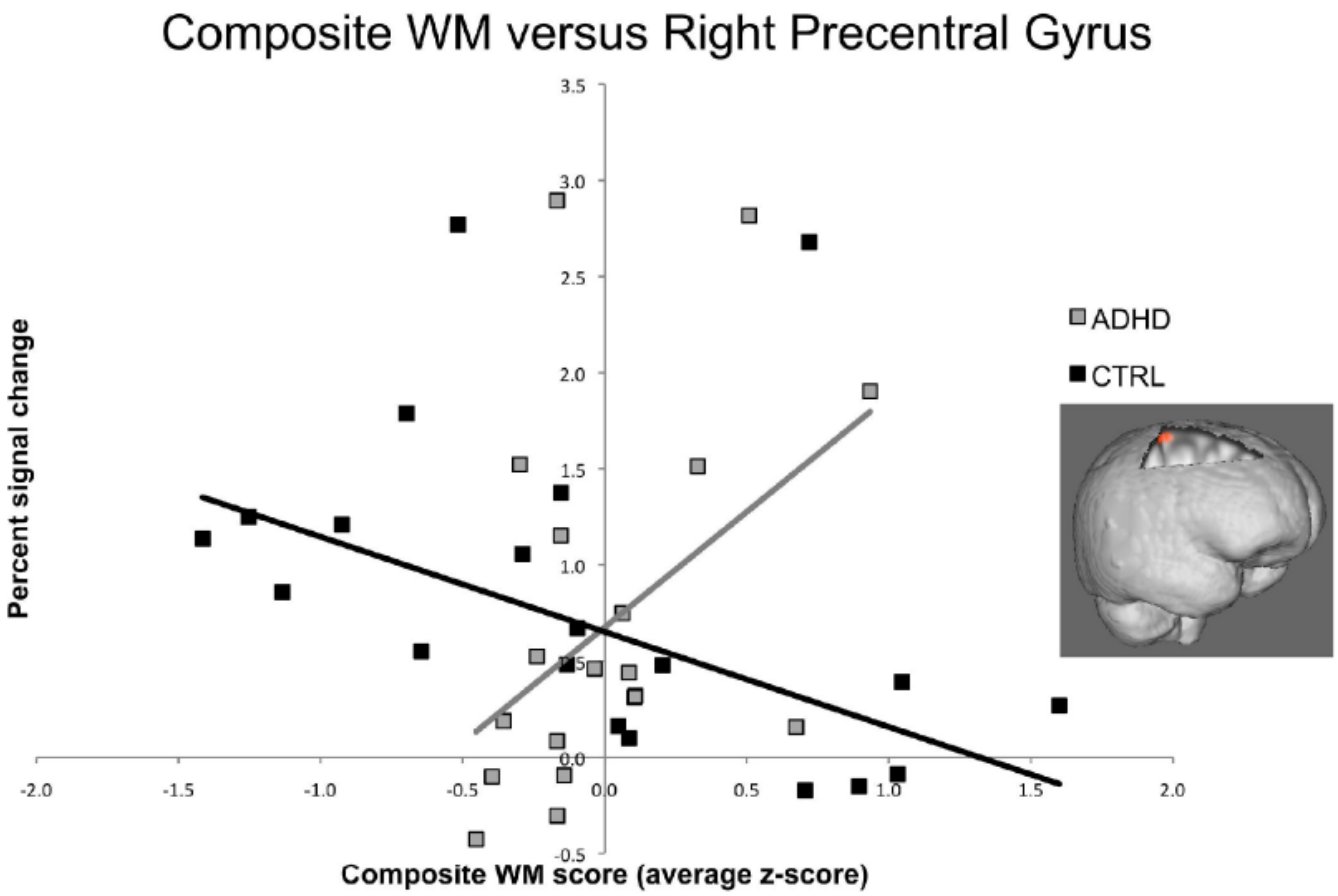

Figure 2.
Scatterplot of the correlations between WM ability and right precentral gyrus activation during the congruent block separately for each group

Table 1

Descriptive characteristics of the Control and ADHD samples

	GROUP		
	Control	**ADHD**	
	M (SD)	**M (SD)**	***t***
Descriptive characteristics			
Age	19.0 (0.9)	20.1 (1.8)	2.48*
DSM-IV ADHD symptoms[a]			
Childhood			
Inattention	0.9 (1.2)	6.3 (2.4)	9.39***
Hyperactivity-impulsivity	0.8 (1.0)	7.3 (2.1)	13.12***
Current			
Inattention	1.3 (1.4)	6.3 (2.4)	7.65***
Hyperactivity-impulsivity	1.5 (1.2)	4.9 (2.3)	6.09***
WAIS-III Estimated IQ scores			
Performance	113.5 (10.5)	114.3 (8.9)	0.26
Verbal	113.3 (10.5)	116.7 (12.0)	1.02
Full Scale	113.3 (8.3)	115.5 (6.6)	0.93
WJ-III			
Reading and Spelling			
Letter Word ID	105.1 (8.9)	99.8 (9.1)	1.95
Word Attack	100.4 (9.7)	99.8 (9.3)	0.23
Spelling	106.9 (7.9)	102.7 (8.5)	1.58
Math			
Calculations	110.7 (13.5)	106.2 (16.0)	0.93
Math Fluency	102.3 (11.2)	96.0 (12.0)	1.68
	Percent Impaired		
	Control	ADHD	
Domain of functioning	N (%)	N (%)	X^2
Global impairment (past 12 months)	5 (22%)	18 (90%)	20.0***
Management of responsibilities	0 (0%)	13 (65%)	21.4***
Academic functioning	1 (4%)	12 (60%)	15.7***
Social relationships	0 (0%)	14 (70%)	23.9***
Driving	2 (9%)	7 (35%)	4.5*
Occupational functioning	2 (9%)	10 (50%)	9.1**
Significant impairment in 1 or more domains	5 (22%)	20 (100.0%)	26.9***
Significant impairment in 2 or more domains	0 (0%)	17 (85%)	32.3***

[a]Parent and self-report ratings were combined to create the total symptom counts by coding each symptom as present if endorsed by either the parent or the participant (see Lahey et al., 1994).

Table 2

Group differences in behavioral performance on Stroop and WM tasks

	GROUP		
	Control	**ADHD**	**T-test**
STROOP	**M (SD)**	**M (SD)**	**T**
Accuracy			
Interference score	0.089 (0.054)	0.086 (0.092)	.165
Facilitation score	-0.010 (0.035)	0.000 (0.040)	-.805
congruent	0.960 (0.034)	0.954 (0.031)	.601
incongruent	0.883 (0.063)	0.877 (0.096)	.243
neutral	0.969 (0.034)	0.956 (0.040)	1.134
N_C	0.969 (0.033)	0.954 (0.038)	1.414
N_I	0.973 (0.036)	0.963 (0.035)	.893
N_N	0.970 (0.028)	0.961 (0.026)	1.106
Reaction Time			
Interference score	0.223 (0.116)	0.146 (0.097)	2.343*
Facilitation score	-0.040 (0.059)	0.015 (0.061)	-2.974*
congruent	711 (76)	697 (90)	.525
incongruent	856 (93)	825 (98)	1.082
neutral	698 (58)	739 (92)	-1.751
N_C	683 (62)	708 (77)	-1.142
N_I	702 (72)	723 (97)	-0.813
N_N	679 (63)	709 (87)	-1.317
WORKING MEMORY			
WAIS			
Forward Digit Span	11.91 (2.29)	10.10 (1.02)	3.260*
Backward Digit Span	8.04 (2.55)	6.65 (1.53)	2.131*
Spatial Span			
Forward Spatial Span	10.48 (1.78)	8.90 (1.64)	3.313*
Backward Spatial Span	8.87 (1.96)	7.80 (1.64)	1.922+

* = p<.05

+ = p < .10

Table 3

Group differences in brain activation before and after partialling out WM ability

Contrast	Region	BA	x	y	z	Original GLM			Partialled GLM
Blocked						**Group Diff. Z**	**ADHD Z**	**CTRL Z**	**Group Diff. Z**
I – Baseline	Middle Frontal Gyrus (L)	45	-44	32	24	5.06	5.02	7.87	4.48
C – Baseline	Middle Frontal Gyrus (L)	45	-44	32	22	5.79	2.55	7.36	4.87
	Precentral Gyrus (L)	6	-48	-2	36	3.73	6.69	8.24	0.88
N - Baseline	Middle Frontal Gyrus (L)	45	-46	30	22	3.60	1.20	5.49	2.39
	Precentral Gyrus (L)	6	-50	4	36	3.55	3.68	7.06	2.82
C - N	Precuneus (L)	31	-6	-60	32	3.15	-1.57	3.05	2.35
I - C	Supramarginal Gyrus (R)	40	66	-38	26	2.86	-.073	3.30	3.38
Event Related									
I - NI	Precentral Gyrus (L)	6	-46	2	44	1.74	1.98	4.30	3.27
	Dorsal ACC (R)	24	6	14	28	3.19	0.99	4.82	2.38
C - NC	Angular Gyrus (L)	40	-38	-58	44	4.03	-1.05	4.57	3.49
	Angular Gyrus (R)	40	46	-54	46	2.24	-0.03	3.12	3.26
	Middle Frontal Gyrus (R)	6	36	12	58	3.36	-2.54	2.39	3.48

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Table 4

Group differences in correlations between brain activation and WM ability

Region	BA	Vox	x	y	z	Correlations with WM: Z values		Main Effect: Z Values	
I - BASELINE									
ADHD>Control									
Precentral gyrus / premotor (R)	6	414	26	0	62	CTRL	-5.30	CTRL	7.03
						ADHD	3.62	ADHD	6.59
						DIFF	-4.90	DIFF	0.42
Precentral gyrus / pre-SMA (R)	6	399	16	4	70	CTRL	0.55	CTRL	3.32
						ADHD	4.79	ADHD	6.91
						DIFF	-4.11	DIFF	-1.50
Precentral gyrus / motor cortex (L)	6/4	238	-52	-12	48	CTRL	0.70	CTRL	3.47
						ADHD	4.26	ADHD	3.72
						DIFF	-3.78	DIFF	0.14
Superior temporal gyrus (L)	22	103	-64	-52	24	CTRL	-1.24	CTRL	1.25
						ADHD	4.09	ADHD	3.46
						DIFF	-4.08	DIFF	-1.78
Superior temporal gyrus (R)	22	98	64	-54	14	CTRL	-0.21	CTRL	-1.41
						ADHD	3.80	ADHD	-0.85
						DIFF	-3.52	DIFF	-0.35
Superior temporal gyrus (R)	22	79	70	-34	6	CTRL	-1.74	CTRL	-0.52
						ADHD	3.59	ADHD	1.00
						DIFF	-3.91	DIFF	-1.09
Superior frontal gyrus (R)	6	73	10	32	56	CTRL	-2.30	CTRL	1.54
						ADHD	2.84	ADHD	4.01
						DIFF	-3.64	DIFF	-0.61
C - BASELINE									
ADHD>Control									
Precentral / superior frontal gyrus (R)	6	831	30	0	66	CTRL	-3.66	CTRL	4.04
						ADHD	4.18	ADHD	4.68
						DIFF	-4.62	DIFF	-2.24

Region	BA	Vox	x	y	z	Correlations with WM: Z values		Main Effect: Z Values	
Angular gyrus/ inferior parietal (R)	40	281	60	-56	28	CTRL	-0.81	CTRL	0.46
						ADHD	3.81	ADHD	0.83
						DIFF	-3.68	DIFF	-0.13
Precentral gyrus (L)	6	221	-52	-4	40	CTRL	0.53	CTRL	5.07
						ADHD	4.43	ADHD	7.11
						DIFF	-5.49	DIFF	2.64
Superior / middle temporal gyrus (R)	22	129	70	-24	8	CTRL	-1.71	CTRL	-0.85
						ADHD	3.34	ADHD	2.07
						DIFF	-3.66	DIFF	-1.75
Superior temporal gyrus (L)	22	123	-64	-22	-4	CTRL	0.48	CTRL	-0.31
						ADHD	4.16	ADHD	0.67
						DIFF	-3.63	DIFF	-0.64
NEUTRAL - BASELINE									
ADHD>Control									
Medial frontal gyrus / pre-SMA (R)	6	262	8	8	54	CTRL	-1.35	CTRL	6.22
						ADHD	4.93	ADHD	6.29
						DIFF	-4.67	DIFF	1.57
Precentral gyrus / premotor (L)	6	144	-54	0	36	CTRL	0.31	CTRL	6.81
						ADHD	7.01	ADHD	6.57
						DIFF	-6.05	DIFF	3.39
Superior parietal lobule (L)	7	135	-30	-54	58	CTRL	-4.10	CTRL	8.27
						ADHD	6.07	ADHD	8.11
						DIFF	-6.30	DIFF	2.66
I – N									
ADHD>Control									
Superior frontal gyrus (R)	6	120	28	10	54	CTRL	-0.60	CTRL	3.57
						ADHD	3.59	ADHD	2.61
						DIFF	-3.57	DIFF	0.38
C – N									
ADHD>Control									

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Region	BA	Vox	x	y	z	Correlations with WM: Z values		Main Effect: Z Values	
Inferior parietal lobule (R)	40	119	56	-44	44	CTRL	-0.69	CTRL	0.96
						ADHD	3.30	ADHD	2.37
						DIFF	-3.26	DIFF	-1.06
INC – Ni									
ADHD>Control									
Precentral gyrus (L)	6	247	-50	-4	36	CTRL	-2.91	CTRL	4.17
						ADHD	2.95	ADHD	2.30
						DIFF	-3.90	DIFF	1.50
Precentral gyrus (L)	6	98	-18	-12	66	CTRL	-1.48	CTRL	2.81
						ADHD	2.94	ADHD	2.49
						DIFF	-3.27	DIFF	0.15
Precentral gyrus (R)	6	86	28	-10	62	CTRL	-0.97	CTRL	2.94
						ADHD	3.24	ADHD	2.12
						DIFF	-3.33	DIFF	0.50
Subgenual ACC (L)	32	429	-6	36	0	CTRL	1.40	CTRL	-0.74
						ADHD	-3.02	ADHD	-0.35
						DIFF	3.28	DIFF	-0.24
Angular gyrus (R)	22	115	56	-50	18	CTRL	1.67	CTRL	1.40
						ADHD	-2.59	ADHD	1.41
						DIFF	3.07	DIFF	0.04
Superior frontal gyrus (R)	6	79	12	20	58	CTRL	-0.40	CTRL	2.87
						ADHD	-4.04	ADHD	2.60
						DIFF	3.50	DIFF	0.02