
Clinical Investigative Study

Event-Related fMRI of Inhibitory Control in the Predominantly Inattentive and Combined Subtypes of ADHD

Mary V. Solanto, PhD, Kurt P. Schulz, PhD, Jin Fan, PhD, Cheuk Y. Tang, PhD, Jeffrey H. Newcorn, MD

From the Department of Psychiatry, Mount Sinai School of Medicine, New York, New York (MVS, KPS, JF, JHN); and Departments of Radiology and Psychiatry, Mount Sinai School of Medicine, New York, New York (CYT).

[Correction added after online publication 10-June-2009: Received and revised dates have been corrected.]

ABSTRACT

BACKGROUND AND PURPOSE

To examine the neurophysiological basis for the pronounced differences in hyperactivity and impulsiveness that distinguish the predominantly inattentive type of attention-deficit/hyperactivity disorder (ADHD-PI) from the combined type of the disorder (ADHD-C).

METHODS

Event-related brain responses to a go/no-go test of inhibitory control were measured with functional magnetic resonance imaging (fMRI) in 11 children with ADHD-C and 9 children with ADHD-PI, aged 7 to 13 years, who were matched for age, sex, and intelligence.

RESULTS

There were no significant group differences in task performance. Children with ADHD-C and ADHD-PI activated overlapping regions of right inferior frontal gyrus, right superior temporal lobe, and left inferior parietal lobe during inhibitory control. However, the magnitude of the activation in the temporal and parietal regions, as well as in the bilateral middle frontal gyrus, was greater in children with ADHD-PI than those with ADHD-C. Conversely, children with ADHD-C activated bilateral medial occipital lobe to a greater extent than children with ADHD-PI.

CONCLUSIONS

The results provide preliminary evidence that phenotypic differences between the ADHD-C and ADHD-PI subtypes are associated with differential activation of regions that have previously been implicated in the pathophysiology of ADHD and are thought to mediate executive and attentional processes.

Keywords: Attention-deficit/hyperactivity disorder, AD/HD, subtypes, inhibitory control, go/no-go, fMRI.

Acceptance: Received July 19, 2007, and revised form February 26, 2008, July 10, 2008. Accepted for publication July 22, 2008.

Correspondence: Address correspondence to Dr. Mary V. Solanto, Department of Psychiatry, Box 1230, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029. E-mail: mary.solanto@mssm.edu.

J Neuroimaging 2009;19:205-212.
DOI: 10.1111/j.1552-6569.2008.00289.x

Introduction

The predominantly inattentive type of attention-deficit/hyperactivity disorder (ADHD-PI) is characterized by difficulties with attention without the pronounced hyperactivity-impulsivity that is diagnostic for the more widely recognized combined type of ADHD (ADHD-C).¹ Attention problems also differ qualitatively between the subtypes, with more sluggish cognitive tempo in the ADHD-PI type.^{2,3} However, linking these differences in behavioral phenotype with neuropsychological mechanisms has presented a challenge. Some studies have shown slower processing speed in the ADHD-PI subtype,⁴⁻⁶ consistent with reports of sluggish cognitive tempo. The literature is inconsistent with respect to differences in inhibitory control,⁶ with some showing longer stop signal reaction time (SSRT)^{5,7} or increased continuous performance test (CPT) commission errors⁸ in children with ADHD-C, and others failing to find subtype differences on one or more of these measures.^{4,9} Given the inconsistencies in results of neurocognitive studies of the ADHD-PI and ADHD-C subtypes, the use

of functional magnetic resonance imaging (fMRI) may help to resolve continuing controversy concerning whether these subtypes are variants of the same condition or completely different disorders.^{10,11} Beyond the heuristic value of this research, these results have implications for the selection of subjects for functional neuroimaging studies that seek to isolate specific cognitive processes involved in the etiology of ADHD.

Studies using fMRI to date have depicted a complicated picture of functional brain anomalies related to executive and inhibitory processes in ADHD. For example, of 5 studies that have used go/no-go paradigms to test inhibitory control, 3 reported increased activation of ventral prefrontal brain regions in children with ADHD^{12,13} and adolescents diagnosed with ADHD during childhood,¹⁴ a fourth study found decreased activation of ventral prefrontal cortex in children with ADHD,¹⁵ and the fifth reported no prefrontal cortical abnormalities in adolescents with ADHD-C.¹⁶ Similarly, divergent results were reported regarding activation of the striatum and anterior cingulate gyrus during the go/no-go task.¹²⁻¹⁶ These

inconsistencies have frustrated efforts to pinpoint the precise frontostriatal impairments in the pathophysiology of ADHD. Several factors are likely to contribute to these inconsistencies, including the heterogeneous nature of the ADHD samples that have been studied. The samples in most fMRI studies have combined individuals with ADHD-C and ADHD-PI^{12-15,17-19} despite evidence that the subtypes may imperfectly represent independent forms of ADHD with genetic influences specific to each.²⁰ Recent studies have attempted to address this heterogeneity by restricting the sample to youth with ADHD-C only.^{16,21,22} However, no studies have directly compared the ADHD-C and ADHD-PI subtypes to disentangle subtype differences in the neural mechanisms of inhibitory control.

The present study used fMRI with a go/no-go task to examine event-related brain activation during inhibitory control in children with ADHD-C and ADHD-PI. The go/no-go task used in this study has been previously characterized in healthy children and adults^{23,24} and has been used to test children with ADHD.¹³ Based on the phenotypic differences between groups in impulsivity/hyperactivity, as well as the fMRI findings available at the time,^{12,18} we predicted that children with ADHD-C would have worse inhibitory control and activate ventral prefrontal cortex and striatum less than children with ADHD-PI. In addition, given hypothesized deficits in alerting and orienting functions mediated by posterior parietal cortex in the ADHD-PI group,⁶ we were particularly interested in comparisons between subtypes in activation of this region. Further analyses examined subtype similarities in activation.

Method

Participants

Twenty children (14 boys, 6 girls) were recruited from a larger pool of 7 to 13 year-old participants in a study of the neurocognitive functioning of ADHD. All the children met DSM-IV diagnostic criteria for either the ADHD-C or ADHD-PI subtype as assessed by clinical interview and confirmed by parental responses to the NIMH diagnostic interview schedule for children version IV (NIMH-DISC).²⁵ In addition, all children met symptom severity thresholds of at least 1.5 standard deviations (SD) \geq age and gender means on both Conners' parent rating scale-Revised (CPRS-R)²⁶ and Conners' teachers rating scale-revised (CTRS-R)²⁷ according to diagnostic subtype: (1) DSM-IV inattentive symptoms scale score ≥ 65 for both subtypes; and (2) DSM-IV hyperactive-impulsive symptoms scale score ≥ 65 for the ADHD-C subtype or < 65 for the ADHD-PI subtype. Finally, general cognitive ability was assessed with the Wechsler Intelligence Scale for Children-Third Edition (WISC-III). Children with a chronic medical or neurological condition, diagnosis of pervasive developmental disorder, psychosis, or Tourette's syndrome, WISC-III Full Scale Intelligence Quotient (FSIQ) < 80 , or who were currently receiving psychotropic medication (other than stimulants) were excluded from participation in the parent study. The final sample consisted of 11 children with ADHD-C and 9 children with ADHD-PI.

Participants were scanned on average 2.1 ± 1.3 years following their initial evaluation for the neurocognitive study. The children remained symptomatic as demonstrated by mean \pm SD scores on the DSM-IV inattentive and hyperactive-impulsive symptoms scales of the CPRS-R of 75.4 ± 11.0 and 77.9 ± 9.5 for children with ADHD-C and 70.0 ± 13.2 and 58.5 ± 11.7 for children with ADHD-PI. The ADHD-C and ADHD-PI groups did not differ in mean \pm SD elapsed time since evaluation (2.4 ± 1.5 years vs. 1.6 ± 1.0 years), age (11.2 ± 1.9 years vs. 10.7 ± 1.3 years), FSIQ (108.0 ± 13.8 vs. 107.9 ± 10.0), gender (64% male vs. 78% male), or handedness (64% right-handed vs. 78% right-handed) (all $p > .10$). One child with ADHD-C and 2 children with ADHD-PI had specific learning disabilities. SES, as indexed by mother's education, was equivalent between groups in that 57% of the ADHD-C and 50% of the ADHD-PI had completed a 4-year college degree. None of the families in either group were receiving public assistance.

ADHD-CB and ADHD-PI groups were nearly equal with respect to the percentages who were stimulant-naïve (18% vs. 22%, respectively) or who had been treated with stimulants for more than 1 month (73% vs. 67%, respectively). At the time of the study, 5 (44%) children with ADHD-C and 6 (67%) children with ADHD-PI were receiving stimulant treatment and all were withdrawn from medication for at least 24 hours prior to the scan. The study was approved by the Institutional Review Board committee of the Mount Sinai School of Medicine. Written informed consent was obtained from the parents of participants and signed assent from the children. Participants and parents were compensated for their participation.

Go/No-Go Paradigm

Durston et al.^{13,23,24} designed the go/no-go task used in this study to measure the ability to inhibit responses to rare nontargets (no-go trials) in the context of frequent targets (go trials). The task consisted of 5 238-second blocks that began with a 10-second period of fixation. Each block contained 57 trials, with 43 (75%) go trials and 14 (25%) no-go trials, yielding a total of 70 no-go trials across the task. The Lilo and Stitch characters from the "Lilo and Stitch" movie (© Disney Enterprises, Inc.) served as the stimuli for go trials, the stimulus for no-go trials was the Cobra Bubble character from the same movie, and fixation was depicted by a small image of Earth. Stimuli were presented for 500 msec with an interstimulus interval of 3,500 msec. Trial order was pseudorandomized so that the occurrence of no-go trials was jittered from 4 to 20 seconds (ie, preceded by 1 to 5 go trials). Participants were reminded at the beginning of each block to respond as quickly as possible while trying not to make mistakes.

The go/no-go task was compiled and run using E-PrimeTM software (Psychology Software Tools, Inc., Pittsburgh, PA;²⁸). Stimuli were projected via an SVGA projector system onto a rear-projection screen mounted at the head of the magnet bore. Participants viewed the stimuli through a mirror on the head coil positioned above their eyes and responded with the right hand using the BrainLogics fiber optic button system (Psychology Software Tools, Inc., Pittsburgh, PA). Responses were recorded on a personal computer and provided measures of reaction time and accuracy.

MRI Image Acquisition

All structural and functional scans were acquired on the same 3.0 Tesla Siemens Allegra (Siemens Medical Systems, Erlangen, Germany) head-dedicated MRI scanner equipped with a high-performance head gradient system that was designed especially for functional brain imaging. Firm foam padding was used to restrict head motion. Following sagittal localization and shimming, a high-resolution T2-weighted anatomical volume of the whole brain was acquired with a turbo spin-echo (TSE) pulse sequence (28 axial slices, repetition time [TR] = 5,380 msec, echo time [TE] = 99 msec, flip angle = 170°, field of view [FOV] = 210 mm, matrix = 512 × 336, voxel size = 0.41 × 0.41 × 4 mm). Functional T2*-weighted images depicting the blood oxygenation level-dependent (BOLD) signal were acquired at the same 28 slice locations using gradient-echo echo-planar images (EPI) with a TR of 2,000 msec, TE of 40 msec, flip angle of 90°, FOV of 210 mm, and a matrix of 64 × 64. Each functional image comprised a full brain volume of 28 axial slices (thickness = 3 mm, skip = 1 mm, in-plane resolution = 3.28 × 3.28 mm). All images were acquired with slices positioned parallel to the anterior commissure-posterior commissure line. The participants each completed 5 runs of 238 seconds, resulting in 120 time points per participant.

Statistical Analyses

Group differences in the percentage of commission errors on no-go trials of the go/no-go task, as well as the percentage of omission errors and mean reaction time on go trials, were analyzed with Student's *t*-tests. Pearson's product-moment correlations between percent change in MRI signal intensity and behavioral measures were calculated for regions that demonstrated significant activation. The 2-tailed probability level was set at $p < .05$ for statistical significance.

Image preprocessing and analyses were conducted using statistical parametric mapping (SPM2).²⁹ The first 5 volumes of each functional time series were discarded and the functional scans were then realigned to the remaining first volume, coregistered with the high-resolution TSE image, spatially normalized to a Montreal Neurological Institute (MNI) T2-weighted template image, and spatially smoothed. General linear modeling (GLM) was then conducted for the functional scans from each participant by modeling the observed event-related BOLD signals and regressors to identify the relationship between the experimental parameters and the hemodynamic response. Event-related analyses were performed by convolving the default SPM basis function with a train of delta functions that represent the individual trial events to create regressors, the linear combination of which was used to model the hemodynamic response to 4 conditions: correct and incorrect no-go and go trials. The 6 parameters generated during motion correction were entered as covariates in the GLM. The 4 conditions were then estimated for each participant and the effects of inhibitory control were tested by applying appropriate linear contrasts to the parameter estimates for the correct no-go minus correct go contrast, resulting in a contrast image for each participant.

The contrast images of all participants were entered into second-level group analyses conducted with random effects sta-

tistical models that accounted for intrasubject variability. The first analysis examined regions in which there was evidence of a conjunction between inhibitory control-related activations in the ADHD-C and ADHD-PI groups. We employed here the method described by Friston et al.³⁰⁻³² that tests the minimum *t* statistic against the global null hypothesis with a global false-positive rate of .01 for the height threshold. This is one of the 2 accepted methods for conducting conjunction analyses, yielding a more inclusive interpretation of common activations. The a priori hypothesis that children with ADHD-CB would activate ventral prefrontal cortex and striatum less than children with ADHD-PI was then tested with direct between-group contrasts. The resultant voxel-wise statistical maps were then thresholded for significance using a cluster size algorithm that protects against an inflation of the false-positive rate. Results are reported at an uncorrected height (intensity) threshold of $p < .05$ and an extent threshold of $k = 100$ voxels, corresponding to a whole brain false-positive rate of approximately .05, according to a Monte Carlo simulation of the current brain volume.³³ This more liberal alpha level was selected in order to minimize Type II error, given that this first fMRI comparison of subtypes was intended to be exploratory and hypothesis-generating rather than definitive. Simultaneously, however, we employed a relatively conservative extent threshold of 100 voxels, rather than 50, in order to provide additional protection against findings of spurious activations. Coordinates of activation were converted to the Talarach and Tournoux³⁴ coordinate system using a nonlinear transformation (<http://www.mrc-cbu.cam.ac.uk/Imaging/mnispac.html>).

Results

Behavioral Data

There were no significant differences between children with ADHD-C and those with ADHD-PI in percent commission errors on no-go trials [$t_{18} = .48, p = .64$] or mean reaction time [$t_{18} = .90, p = .38$] and percentage of omission errors on go trials [$t_{18} = .21, p = .84$]. Both groups of children made a large number of commission errors; percent commission errors on no-go trials were $41.2 \pm 16.6\%$ for children with ADHD-C and $37.9 \pm 13.1\%$ for children with ADHD-PI. Mean reaction time and percent omission errors on go trials were 460 ± 55 msec and $6.4\% \pm 7.4\%$ for the ADHD-C group and 488 ± 84 msec and $5.7\% \pm 5.7\%$ for the ADHD-PI group. Mean translational movement during the echoplanar time series was $1.74 \pm .119$ mm for children with ADHD-C and $1.71 \pm .85$ mm for children with ADHD-PI [$t_{18} = .06, p = .95$]. Mean rotational displacement was less than .10 for both groups [$t_{18} = .95, p = .36$].

fMRI Data

Conjunction Analysis

Brain regions that were conjointly activated during inhibitory control (ie, correct no-go event minus correct go event) by children with ADHD-C and ADHD-PI are shown in Figure 1 and listed in Table 1. Regions with overlapping activation included:

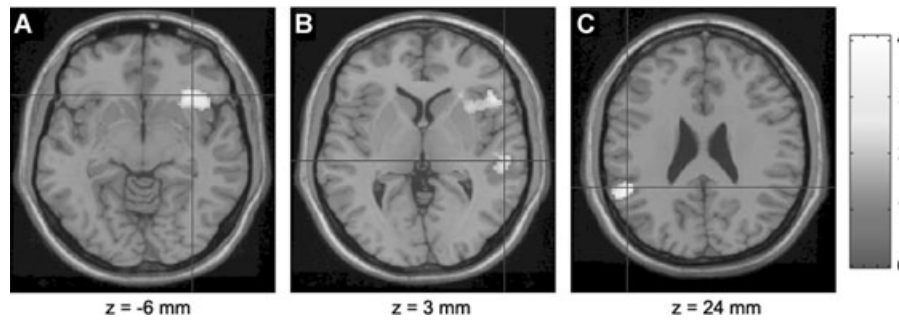


Fig 1. Children with the combined and predominantly inattentive types of attention-deficit/hyperactivity disorder conjointly activated the right inferior frontal gyrus (A), right superior temporal gyrus (B), and left inferior parietal lobule (C) during inhibitory control ($t > 1.96$, $p < .05$). Crosshairs indicate cluster maxima. Values below the images refer to the Talarach and Tournoux (1988) coordinates for the sections.

Brodmann's Area (BA 47) in the ventrolateral convexity of the right inferior frontal gyrus; the right superior temporal gyrus (BA 22); and the left inferior parietal lobule (BA 40). There were no significant correlations between the magnitude of these activations and the percentage of commission errors on no-go trials (all $p > .10$).

Between-Group Analyses

Significant differences in activation between children with ADHD-C and those with ADHD-PI revealed by direct voxel-by-voxel between-group comparisons are depicted in Figure 2 and detailed in Table 2. Children with ADHD-PI had markedly greater activation of bilateral middle frontal gyrus (BA 9/10) and inferior parietal lobule (BA 40) during the inhibition of prepotent responses than children with ADHD-C. In addition, the magnitude of activation of the right superior temporal gyrus (BA 22) region identified in the conjunction analysis was greater in the ADHD-PI than the ADHD-C group. Conversely, children with ADHD-C had greater activation of a large bilateral region of the cuneus (BA 19) during inhibitory control than children with ADHD-PI. There were no significant correlations

between activation and the percentage of commission errors on no-go trials (all $p > .10$).

Exploratory Analyses

Exploratory analyses capitalized on the large number of commission errors on no-go trials in the present study to test the neural consequences of error trials. Error trials were modeled individually in 18 of the 19 children with the incorrect no-go events minus correct go events contrast using the methods described above; one child with PI did not make enough commission errors to model incorrect no-go events. Conjunction analysis of the error trials contrasts revealed several regions that were activated following commission errors by both the CB and PI groups (Table 3). Both groups of children produced robust activation of bilateral inferior frontal gyrus (BA 45/47) that extended into the insula, as well as of regions in the left anterior (BA 24/32) and middle cingulate gyrus (BA 24). Direct between-group comparisons revealed no clusters of significant differences in activation between the CB and PI groups.

Discussion

The present results provide the first evidence of both of common and distinct neural mechanisms during the successful inhibition of prepotent responses in school-aged children with ADHD-C and ADHD-PI. Specifically, both groups of children activated the right ventrolateral prefrontal cortex, right superior temporal lobe, and left inferior parietal lobe during successful inhibition, but the magnitude of the activation in the latter 2 regions, as well as bilaterally in ventral-most prefrontal cortex, was greater in children with ADHD-PI than those with ADHD-C. In contrast, children with ADHD-C activated a bilateral region of superior occipital lobe to a greater extent during inhibitory control than children with ADHD-PI. The equally poor performances on the go/no-go task by the 2 groups of children suggest that these differences in brain activation reflect differences in the magnitude to which these regions were engaged under conditions that elicited comparable performance³⁵ and are not simply artifacts of impaired performance.³⁶ Under these circumstances, greater activation by one group suggests less efficient processing by the brain regions in question.

Similar activation of ventrolateral prefrontal, dorsal superior temporal, and inferior parietal regions during inhibitory

Table 1. Regions Conjointly Activated During Inhibitory Control by Children with the Combined and Predominantly Inattentive Types of Attention-Deficit/Hyperactivity Disorder

Brain Region	BA	Side	Coordinates			<i>t</i>	Cluster Size
			x	y	z		
Inferior frontal gyrus	47	R	34	23	-6	3.34	938
Superior temporal gyrus	22	R	55	-25	3	2.33	143
Inferior parietal lobule	40	L	-51	-43	24	4.07	281

Note: BA refers to Brodmann's area; L and R refer to the left and right cerebral hemispheres; x, y, and z refer to the Talarach and Tournoux³⁴ coordinates of the maximally activated voxel; *t* refers to the *t* score of the of maximally activated voxel ($p < .05$).

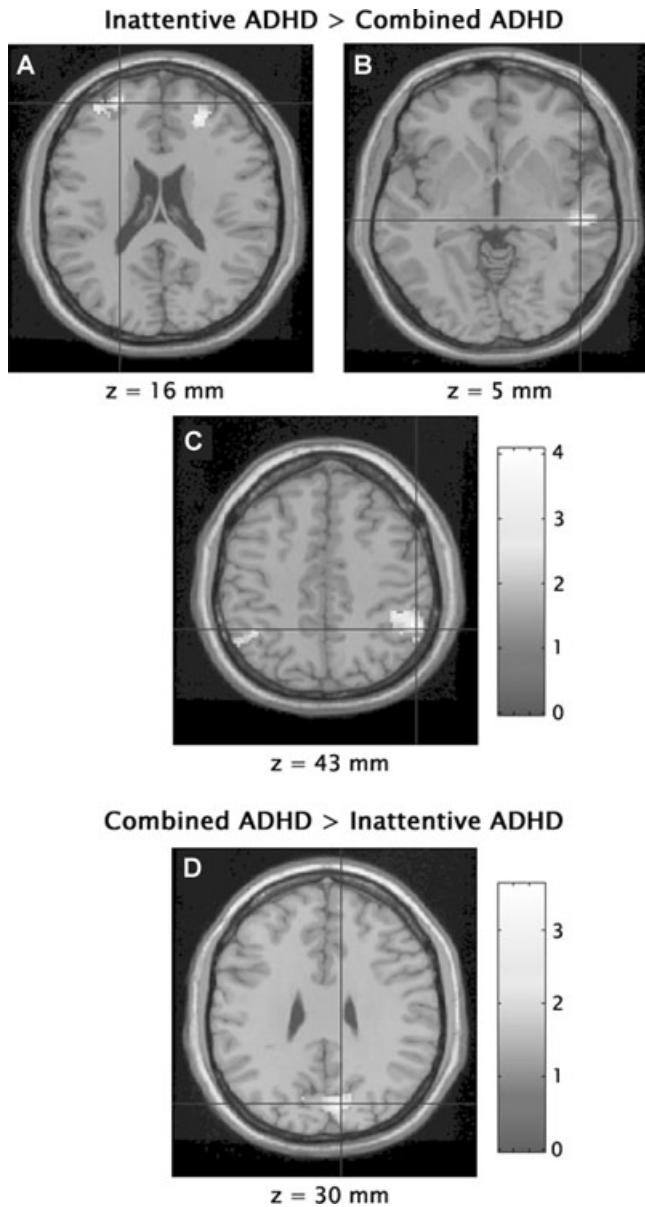


Fig 2. Children with the combined and predominantly inattentive types of attention-deficit/hyperactivity disorder had significant differences in activation during inhibitory control in bilateral middle frontal gyrus (A), right superior temporal gyrus (B), bilateral inferior parietal lobule (C), and bilateral cuneus (D) ($t > 1.96$, $p < .05$). Crosshairs indicate cluster maxima. Values below the images refer to the Talarach and Tournoux (1988) coordinates for the sections.

control by children with ADHD-C and ADHD-PI is both consistent with findings of largely similar executive function deficits in the subtypes^{6,37} and noteworthy, given previous findings of abnormal activation of these regions during go/no-go tasks in youth with ADHD.¹³⁻¹⁵ The dorsal superior temporal and inferior parietal regions together form the temporo-parietal junction (TPJ), a cortical association area specialized for the detection of behaviorally relevant signals.³⁸ The TPJ provides afferent input to the ventrolateral prefrontal cortex,^{39,40} which in turn, is unique among frontal regions in that it contains populations of neurons that code for sensory cues that signal the suppression

Table 2. Regions of Significant Differences in Activation During Inhibitory Control in Children with the Combined Type versus the Predominantly Inattentive Type of Attention-Deficit/Hyperactivity Disorder

Brain Region	BA	Side	Coordinates			t	Cluster Size
			x	y	z		
Combined ADHD > Inattentive ADHD							
Cuneus	19	R	10	-74	30	3.63	563
	19	L	-10	-71	24	2.82	
Inattentive ADHD > Combined ADHD							
Middle frontal gyrus	9	R	22	44	16	3.50	287
	10	L	-24	51	16	4.46	
Superior temporal gyrus	22	R	50	-25	5	2.95	111
Inferior parietal lobule	40	R	53	-46	43	4.21	695
	40	L	-40	-48	41	2.83	

Note: BA refers to Brodmann's area; L and R refer to the left and right cerebral hemispheres; x, y, and z refer to the Talarach and Tournoux³⁴ coordinates of the maximally activated voxel; t refers to the t score of the of maximally activated voxel ($p < .05$).

rather than execution of behavior.⁴¹ The data suggest that children with both subtypes recruited a similar neural network, and presumably cognitive processes, to successfully inhibit responses.

The finding of significantly greater activation of the parietal and temporal regions by children with ADHD-PI than those with ADHD-C, in the context of equivalent task performance, suggests that the ADHD-PI group recruits alerting and/or orienting processes less efficiently than does the ADHD-C group. The use of a control group as well as a task such as the attentional network task,^{38,42} which more specifically assesses orienting and alerting functions than does the go/no-go task used in this

Table 3. Regions of Significant Activation During Error Trials (Incorrect NOGO Trials Minus Correct GO Trials) in Children with Both the Combined and Predominantly Inattentive Types of ADHD

Brain Region	BA	Side	Coordinates			t	Cluster Size
			x	y	z		
Inferior frontal gyrus/insula	45/47	R	55	16	1	3.54	1,884
		L	-38	20	3	3.99	628
Anterior cingulate gyrus	24/32	L	-4	24	23	3.01	947
Middle cingulate gyrus	24	L	-6	-16	36	2.93	293

Note: x, y, z refer to Talarach and Tournoux³⁴ of maximally activated voxel ($p < .01$ uncorrected). Cluster size refers to the number of voxels in region of activation.

study, will be necessary to definitively determine whether the ADHD-PI group is more or less effective in the recruitment of these processes than children without ADHD and children with ADHD-C. In this context, it must be noted, however, that performance differences in spatial orienting have not been found thus far in several studies that have compared the subtypes, with numbered citations as indicated.^{6,43-45} Differences in the activation of bilateral cuneus between children with ADHD-C and ADHD-PI point to other potential differences in attentional processes between children with ADHD-C and those with ADHD-PI. The cuneus is also a part of the dorsal visual system⁴⁶ and has afferent connections with the inferior parietal cortex among other regions.⁴⁷ In addition to its role in visual processing, this medial parietal region has been implicated in uncued spatial and nonspatial shifts in attention.^{48,49} The divergent recruitment of inferior and medial parietal regions by children with ADHD-PI and ADHD-C during inhibitory control suggests subtle subtype differences in attentional and/or sensory processing that may relate to phenotypic differences between the ADHD-C and ADHD-PI subtypes. This result is intriguing given that most investigations have focused on the motor output stage of information processing in ADHD, for example.^{50,51}

Children with ADHD-C and ADHD-PI also differed in bilateral activation of the BA 10 region in the rostral most portion of the prefrontal cortex. This region receives mnemonic input from retrosplenial cortex and polysensory input from superior temporal regions, and is ideally positioned to exert high-order executive control over cognition through reciprocal connections with adjacent prefrontal regions.⁵² However, the exact executive process mediated by this prefrontal region is still debated.^{53,54} The present results suggest that recruitment of higher order executive processes during inhibitory control may account for some of the phenotypic differences between children with ADHD-C and ADHD-PI and could explain the discrepant findings of abnormal BA 10 activation during the go/no-go task that has been found in ADHD samples composed of both the ADHD-C and ADHD-PI subtypes,¹³⁻¹⁵ but not in a sample limited to the ADHD-C subtype.¹⁶

These findings must be considered in the context of several important methodological limitations, including the small sample size, and the lack of a control group against which to compare neural function in children with ADHD-C and ADHD-PI, and the analytic approach. It is certainly possible that greater statistical power in the present study would have revealed significant group similarities and distinctions in activation of other regions in the brain (eg, striatum). For example, the absence of striatal activation during inhibitory control in either group of children with ADHD was unexpected and could reflect the relatively small sample size. However, this finding is not without precedent. Previous studies that used the same go/no-go task have found striatal activation in healthy adults but not healthy children²⁴ and in healthy children but not children with ADHD.¹³ Regrettably, the significance of the lack of striatal activation in this study cannot be determined without a healthy control group against which to compare the children with ADHD. Striatal activation during inhibition may not differ between children with ADHD-C and ADHD-PI (hence the

negative finding here), but may very well differ between the 2 groups of children with ADHD and healthy controls. It is also important that future studies compare groups that are either homogeneous or rigorously matched with respect to such variables as gender, presence of learning disabilities, and history of stimulant treatment, which may affect brain activation.

An additional consideration relates to the approach used in conducting the conjunction analysis. There is currently disagreement in the field regarding which of the 2 approaches is superior, and for which types of analyses. This study followed the method recommended by Friston et al.²⁹⁻³¹ that tests the conjunction effect against the global null hypothesis that none of the comparisons are significant and yields a significant effect for the conjunction if any of the comparisons are significant. An alternative method, advocated by Nichols,⁵⁵ tests the conjunction effect against the conjunction null hypothesis that at least one comparison is nonsignificant, thus yielding a significant result for the conjunction only if all of the comparisons are significant. The Friston et al. method yields a more inclusive interpretation of common activations, while the method of Nichols et al. yields a more restricted view. We acknowledge that using the alternative approach might have yielded a somewhat different pattern of results.

Finally, a methodological limitation of the current study concerns the use of a 40 msec echo time, which is fairly long for the 3T. Current usage is 27 msec. Although some effects in orbital and ventral prefrontal cortex were nonetheless visualized, as reported, it may be that we have underestimated the activation in these regions.

In sum, the present study provides preliminary evidence of both similarities and distinctions in the neural generators of inhibitory control in children with the ADHD-C and ADHD-PI subtypes. The overlapping regions of ventrolateral prefrontal, inferior parietal, and superior temporal activation in children with ADHD-C and ADHD-PI suggests some convergence in the cognitive strategies used to guide the inhibitory control of behavior. In contrast, differential activation of ventral-most prefrontal and medial parietal regions that have previously been implicated in the pathophysiology of ADHD and are thought to mediate executive and attentional processes may account for some of the phenotypic differences between the ADHD-C and ADHD-PI subtypes. The implications of these findings for the classification of the ADHD subtypes and the search for causal factors of the disorder await further investigation with larger samples that include a healthy comparison group.

This work was supported by National Institute of Mental Health grants R03 HD37803 (MVS), K01 MH070892 (KPS) and R21 MH066360 (JHN), and an Elaine Schlosser Lewis Award for Research in ADHD from the American Academy of Child and Adolescent Psychiatry (MVS, JHN). We wish to express our sincere thanks to B.J. Casey for consultation to the study and A.F.T. Arnsten for comments on the manuscript.

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