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Variability in Post-Error Behavioral Adjustment Is Associated with Functional Abnormalities in the Temporal Cortex in Children with ADHD

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Abstract

Background—Error processing is reflected, behaviorally, by slower reaction times (RT) on trials immediately following an error (post-error). Children with Attention-Deficit Hyperactivity Disorder (ADHD) fail to show RT slowing and demonstrate increased intra-subject variability (ISV) on post-error trials. The neural correlates of these behavioral deficits remain unclear. The dorsal anterior cingulate cortex (ACC) and lateral prefrontal cortex (PFC) are key regions implicated in error processing and subsequent behavioral adjustment. We hypothesized that children with ADHD, compared to typically developing (TD) controls, would exhibit reduced PFC activation during post-error (versus post-correct inhibition) trials and reduced dACC activation during error (versus correct inhibition) trials.

Methods—Using fMRI and a Go/No-Go task, we analyzed the neural correlates of error processing in 13 children with ADHD and 17 TD children.

Results—Behaviorally, children with ADHD showed similar RT slowing but increased ISV compared to controls. The post-error contrast revealed a relative increase in BOLD signal in the middle/inferior temporal cortex (TempC), the ACC/supplementary motor area (SMA) and the somatosensory/auditory cortex (AudC) in children with ADHD compared to controls. Importantly, in the ADHD group, increased post-error temporal cortex activity was associated with lower ISV. During error (versus correct inhibition) trials, no between group differences were detected. However, in children with ADHD lower ISV was associated with decreased insula and increased precentral gyrus activity.

Conclusions—In children with ADHD, post-error neural activity suggests first, a shift of attention towards task-irrelevant stimuli (AudC) and second, a recruitment of compensatory regions that resolve stimulus conflict (TempC) and improve response selection/execution (ACC/SMA). ADHD children with higher temporal cortex activation showed lower ISV, suggesting that functional abnormalities in the compensatory temporal regions contribute to increased variability. Moreover, increased ISV may be related to an over-sensitivity to negative outcomes during error trials in ADHD (insula correlation).

Keywords

error processing; variability; temporal cortex; medial frontal cortex; ADHD; children; fMRI

Error processing is an executive control process that refers to the detection of an error and the subsequent behavioral adjustment (Gehring & Fencsik, 2001; Taylor, Stern & Gehring, 2007). When healthy adults and children are engaged in a fast reaction time tasks, error processing is reflected by longer reaction times (RT) on trials immediately following the error (post-error trials) (Rabbitt, 1966; Sergeant & van der Meere, 1988). This post-error slowing is interpreted as a sign of ongoing cognitive control processes, allowing subsequent improvement in task performance.

Functional magnetic resonance imaging (fMRI) and electrophysiological findings have identified the posterior part of the medial frontal cortex (pmFC), which comprises the dorsal anterior cingulate cortex (dACC), and the lateral prefrontal cortex (PFC), as key regions involved in error processing and subsequent behavioral adjustment. Although the specific role of these regions is unclear, it has been suggested that the pmFC may be important during error monitoring while the lateral PFC may be recruited to regulate subsequent task performance (Ridderinkhof et al., 2004; Taylor et al., 2007). In healthy adults, fMRI studies using fast response inhibition tasks, including the Go/No-Go and the Stop-Signal tasks, have consistently reported activation of the dACC when comparing error versus correct inhibition trials (Hester, Fassbender & Garavan, 2004; Menon et al., 2001), and increased ventrolateral PFC when comparing post-error versus post-correct inhibition trials (Li et al., 2008).

Error processing abnormalities in children with Attention-Deficit Hyperactivity Disorder (ADHD) have been previously reported in electrophysiological and behavioral studies. Specifically, children with ADHD fail to exhibit the post-error slowing that is seen in typically developing (TD) children and show high intra-subject variability (ISV) in their post-error RT (Epstein et al., 2009; Schachar et al., 2004; Sergeant & van der Meere, 1988; Wiersma, van der Meere & Roeyers, 2005). Moreover, a decrease in electrophysiological components associated with error processing, the error-related negativity (ERN) and error positivity (Pe), has been reported in children with ADHD using a variety of paradigms (Liotti et al., 2005; Overtom et al., 2002; Wiersma et al., 2005, see also review by Shiels & Hawk 2010). Moreover, recent electrophysiological data in adolescents with ADHD using the Go/No-go task show a significant reductions in late evoked theta power and early and late theta inter-trial phase coherence, suggesting suggest that a weaker error-related signal from the ACC to the PFC, important for guiding future behavior, may underline poor performance in ADHD (Groom et al. 2010).

Data on the neural correlates of error processing in children with ADHD are limited and findings from existing studies are inconsistent. Pliszka et al. (2006) contrasted unsuccessful and successful Stop-Signal trials, and found that children with ADHD fail to show patterns of dACC and ventrolateral PFC activation observed in TD children (Pliszka et al., 2006). These findings align with previous studies reporting decreased ERN in ADHD, the electrophysiological component considered to be localized in the dACC (Liotti et al., 2005), and suggest that reduced dACC activity in ADHD may compromise recruitment of ventrolateral PFC regions involved in post-error behavioral adjustment. In contrast, Rubia et al. (2005) found that adolescents with ADHD exhibited reduced activation in the precuneus and posterior cingulate cortex (PCC), relative to controls, when unsuccessful inhibition trials were compared to go trials (Rubia et al., 2005). The PCC is important for the allocation of visuospatial attention (Mohanty et al., 2008). Attentional fluctuations are hypothesized to compete with goal-directed activity and affect task performance by increasing intra-subject variability (ISV) in responding (Sonuga-Barke & Castellanos, 2007). Increased ISV in response RT is a consistent finding in ADHD (Castellanos & Tannock, 2002; Vaurio, Simmonds & Mostofsky, 2009). Therefore it is possible that error processing deficits in ADHD are related to attentional impairments and abnormal precuneus/PCC neural activity. While these studies have provided some initial insight into the neural correlates of error

processing in children with ADHD, no studies have examined whether the behavioral findings of decreased RT slowing and increased ISV for post-error trials are related to functional abnormalities of the dACC, the precuneus/PCC, or both.

The present study examines the neural correlates of error processing in children with ADHD using fMRI and the Go/No-Go task by comparing neural activity during two contrasts, errors versus correct inhibition trials and post-error versus post-correct inhibition trials. Based on previous data, we hypothesized that children with ADHD would show less RT slowing and higher ISV on post-error trials compared to TD children. We further predicted that, compared to TD children, children with ADHD would show decreased activation in both the dACC and the precuneus/PCC in during error trials, and would show reduced ventrolateral PFC activation during post-error trials.

Methods

Subjects

Thirteen children with ADHD [9 males; mean age=10.6 years, SD=1.4 (range: 8–13 years); mean IQ=109.2, SD= 5.2 (range: 88–137); Conner's parent rating scale-revised (CPRS-R) mean=74.3, SD= 10.9 (range: 54–90)] and seventeen TD children [8 males; mean age=10.5 years, SD 1.2 (range: 8–13 years); mean IQ=108.8, SD= 15.4 (range: 81–135); CPRS-R mean=45.1, SD=4.3 (range: 40–55)] were matched in terms of age, gender, IQ and commission error rate in the go/no-go task. Only children with a commission error rate of 25 percent or greater were included in the analysis. Three children with ADHD had comorbid oppositional-defiant disorder and one of these children also met criteria for simple phobia. Two children with ADHD were being treated with stimulant medication and their parents were asked to withhold the medication on the day prior and day of testing (see Supplemental Information).

The study was conducted at the Kennedy Krieger Institute in Baltimore, MD. Written consent was provided by a parent or guardian for all subjects, and assent was obtained from the participating child. All study procedures were approved by the Johns Hopkins Medicine Institutional Review Board.

FMRI paradigm

The Go/No-Go paradigm is a response inhibition task in which, either a green or a red spaceship is presented on the screen; subjects are asked to push a button as quickly as possible each time a green spaceship appeared (go trials), and to refrain from pushing the button when a red spaceship appeared (no-go trials). Stimuli were presented for 300ms, followed by a fixation cross that was displayed for 1500ms. Subjects had time to respond until the next stimulus appeared (see Supplemental Information). There were four trials of interest: successful withholding of a no-go trial (correct inhibition), failure to inhibit responding to a no-go stimulus (commission error), go trials after correct inhibition (post-correct), go trials after a commission error (post-error). As a behavioral measure of post-error behavioral adjustment, we calculated the percent difference in mean RT and ISV for three types of go trials: post-error, post-correct inhibition, and go trials after correct go. The ISV was calculated as the standard deviation of the RT divided by the mean RT (Stuss et al., 2003).

Scanning procedures

Images were acquired on a 1.5 Tesla ACS-NT Powertrack 6000 MRI scanner (Philips Medical Systems) using a body coil transmission and quadrature end-capped head-coil

reception, and image processing was carried out using SPM2 (Wellcome Department of Imaging Neuroscience) [see Supplemental Information].

Data analysis

Behavioral data were examined using repeated measures analysis of variance (RM-ANOVA) with diagnostic status (ADHD, TD) as between subject variable and trial category (post-error, post-correct inhibition and go trials after correct go) as within subject factor. Analyses were conducted using StatView 5.0.1 (SAS Institute, Inc., Cary, NC). All data were reported as mean $\pm$ standard error of the mean (SEM), and significance was set at $p < 0.05$ two-tailed alternatives.

Functional data were analyzed using SPM5 to construct and examine the fit of the voxelwise time course data to a general linear model (GLM). Event-related response amplitudes were estimated using the GLM. Nine regressors were modeled: correct inhibition, commission error, post-correct inhibition, post-error, correct go trials after correct go response, omissions (failure to respond to go stimuli), correct go trials after omissions, anticipatory responses (defined as go responses occurring less than 200ms after stimulus presentation), and correct go trial after anticipatory responses [see Supplemental Information].

Whole-brain random effects analyses was performed using a spatial extent cluster size threshold to achieve a corrected statistical threshold of $p = 0.05$, based on the number of voxels included in the ROI and the spatial smoothness of the data.

Percent signal change in each functional ROI was calculated using Marsbar from the SPM toolbox (<http://marsbar.sourceforge.net/>) by comparing mean voxel values within the specified ROI for the ADHD and TD groups. A linear regression model in SPM5 was used to assess brain-behavior correlations.

Results

Behavioral data

Table 1 presents the mean RT and ISV for the ADHD and TD groups as well as the mean % difference in for each of these behavioral measures. The 2 (diagnostic group) $\times$ 3 (trial category) RM-ANOVA of the mean RT for each go trial category showed a significant main effect of category ($F(2,56) = 13.12$, $p < 0.001$), but no effect of diagnosis ($F(1,28) = 1.38$, $p > 0.24$) or category $\times$ diagnosis interaction ($F(2,56) = 1.87$, $p > 0.16$). Fisher's post hoc analysis indicated that the RT of post-error trials and RT of post-correct inhibition trials were significantly slower than the RT of go trials after correct go ($p < 0.05$, Table 1).

The 2 (diagnostic group) $\times$ 3 (trial category) RM-ANOVA of the mean ISV values for each go trial category showed no effect of category ($F(2,56) = .97$, $p > 0.38$), but a significant main effect of diagnosis ($F(1,28) = 11.90$, $p < 0.002$) and a category $\times$ diagnosis interaction ($F(2,56) = 3.97$, $p < 0.03$). Unpaired t-test for each ISV category indicated that compared to the TD group, ISV was higher in the ADHD group for go trials after correct go ($t(28) = 2.82$, $p < 0.01$) and for post-error trials ($t(28) = 3.75$, $p < 0.001$). However, there was no group difference in ISV for post-correct inhibition trials ($t(28) = 1.19$, $p < 0.24$).

fMRI Data

BOLD signal during post-error versus post-correct inhibition trials—Results of the two-sample t-tests examining group differences in the neural correlates of post-error versus post-correct inhibition trials are presented in Table 2 and Figure 1A. These data showed higher activation in the ADHD group compared to the TD group in three

suprathreshold clusters (corrected $p=0.05$) that correspond to the bilateral superior/medial frontal and cingulate gyri (BA6/32/24; pMFC), the right postcentral/transverse gyri (BA43/41; secondary somatosensory and auditory cortex), and the right middle/inferior temporal gyri (BA21/20) [results for post-error trials versus go trials after correct go and post-correct inhibition versus go trials after correct go are reported in Supplemental Information].

To identify if the between group differences in activation reported above were related to increased activation in the ADHD group or decreased neural activity in the TD group, we extracted the mean percent signal change of each cluster for post-error and post-correct inhibition trials separately. For post-error trials, children with ADHD showed a relative increase in percent signal change whereas TD children showed a relative decrease across all three clusters (Figure 1B). In contrast, during post-correct inhibition trials, both groups showed a relative increase in percent signal change. However, the increase was relatively small in the ADHD group, but substantial in the TD children (Figure 1B).

Correlation between percent ISV differences and percent signal change during post-error versus post-correct inhibition trials—As a follow up analysis, Pearson's regression analysis was performed to examine the relationship between percent ISV difference and percent signal change (post-error versus post-correct inhibition) in the three clusters reported above. The rationale for performing this analysis was based on our finding of significantly increased ISV in the ADHD compared to the TD group during post-error trials. In the ADHD group, there was a significant negative correlation between percent signal change in the middle/inferior temporal gyrus and percent ISV differences ($R^2=0.44$, $p<0.02$; Figure 2), indicating that low variability in post-error trials was associated with increase neural activity in the temporal gyrus. This correlation was confirmed when a whole brain linear regression analysis was conducted (see Supplemental Results). No other significant correlations were found in the ADHD or TD groups.

BOLD signal during error versus correct inhibition trials—The two-sample t-tests examining group differences in the neural correlates of error trials versus correct inhibition trials contrast showed no suprathreshold activation at a corrected $p=0.05$.

Whole brain correlations between percent ISV differences and neural activity during error trials versus correct inhibition trials—To assess if neural activity during error versus correct inhibition trials was associated with percent ISV difference, we conducted a whole brain linear regression analysis in each group separately. Table 3 presents the results of these correlations. In the ADHD group, percent ISV difference was significantly positively correlated with differences in this contrast in the precentral gyrus (BA4/6) and negatively correlated in the left and right insula/claustrum (corrected $p=0.05$). These results indicate that in children with ADHD, higher variability in post-error trials was associated with greater activity in the bilateral insula and lower activity in the left precentral gyrus. In TD children, the whole brain linear regression analysis showed no significant correlation at the corrected threshold.

Discussion

The present study investigated the neural correlates of error processing in children with ADHD and TD children using the Go/No-Go task. During post-error (versus post-correct inhibition) trials, children with ADHD demonstrated high RT variability and increased neural activity in the right middle/inferior temporal cortex, the pMFC (dorsal cingulate and SMA), and the right secondary somatosensory and auditory cortex when compared to TD children. Moreover, brain-behavior correlation analysis showed that within the ADHD

group, lower RT variability was associated with increased recruitment of the middle/inferior temporal cortex. During error (versus correct inhibition) trials we found no differences in neural activity between the ADHD and the TD group. However, in the ADHD group increased activity in the insula and decreased activity in the precentral gyrus during error (versus correct inhibition) was associated with increased variability for post-error trials.

Behavioral findings of post-error versus post-correct inhibition

Increased ISV in response time is a consistent finding in ADHD and has been proposed as an endophenotype of the disorder (Castellanos & Tannock, 2002; Vaurio et al., 2009). In line with previous behavioral finding (Schachar et al., 2004), we report that post-error behavioral adjustment occurred in children with ADHD but was less consistent and frequent than in TD children, as indicated by increased ISV for post-error trials. Of interest is the fact that children with ADHD showed low ISV for post-correct inhibition trials. This finding is consistent with those from previous behavioral studies showing a higher effect of positive feedback/reward on task performance in ADHD compared to TD children [reviewed by (Luman, Oosterlaan & Sergeant, 2005)], and indicate that when positive feedback is provided, children with ADHD are more able to stay “on task”, whereas negative feedback may detrimentally affect subsequent performance. We can speculate that correct inhibition trials, by activating on brain networks involved in processing positive emotions, are associated with a small dopamine increase, which may be sufficient to keep ADHD children focused, at least for the following trial.

Neural correlates of post-error versus post-correct inhibition trials

Compared to the TD group, children with ADHD showed increased activation of the right middle/inferior temporal gyrus. Importantly, increased temporal cortex activation was associated with lower variability in post-error (versus post-correct inhibition) trials, suggesting that the recruitment of the temporal cortex represented a compensatory strategy. Support for this hypothesis comes from a study by Rubia et al. (2007), in which lower variability during the oddball task was associated with increased temporal lobe activation in TD boys (Rubia et al., 2007).

The middle temporal cortex has been implicated in the integration of multisensory information and may be important for resolving ‘stimulus conflict after it has been detected by a cognitive control mechanism’ (Wendelken et al., 2009). In healthy adults, increased middle temporal cortex activity has been reported during tasks of motor inhibition (Go/No-Go) and cognitive inhibition (Stroop) (Bernal & Altman, 2009), as well as during a perceptual decision making task involving stimulus conflict (Wendelken et al., 2009). In the context of post-error behavioral adjustment in children with ADHD, stimulus conflict may be associated with the appearance of a go trial (green spaceship) right after a no-go trial (red spaceship), which immediately requires engaging in a button press; this conflict can be particularly heightened if attention was not allocated to the task when the stimulus was presented. In the ADHD group, this hypothesis is supported by the increased activation in the right secondary somatosensory/auditory cortex during post-error trials in our study, which may reflect an attentional shift towards external stimuli, such as the noise of the scanner.

Despite the increased temporal activation for post-error trials, children with ADHD still showed increased ISV as compared to TD children, suggesting that the recruitment of this compensatory region/network was inconsistent throughout task performance or, that a subgroup of children with ADHD was unable to consistently recruit this temporal region. Overall these data indicate that functional abnormalities in the temporal regions are present in ADHD and need to be further investigated. Previous studies have reported functional

abnormalities in the temporal cortex across different behavioral paradigms in children with ADHD [reviewed by (Cherkasova & Hechtman, 2009)]. For example, Tamm et al. (2004) reported increased neural activity in the middle temporal lobe in boys with ADHD during successful response inhibition in a Go/No-Go task. Importantly, in this study children with ADHD showed more commission and omission error rates than TD children (Tamm et al., 2004). In contrast, decreased activation in the right middle temporal gyrus in boys with ADHD has been associated with successful switching in a task of cognitive flexibility (Smith et al., 2006), and with correct interference inhibition in the Simon task (Rubia et al., 2009). Collectively, these fMRI data suggest that increased temporal lobe activation in ADHD may occur when task conditions are particularly difficult, and thus in association with impairments in behavioral performance, providing further evidence for a compensatory role of the temporal cortex in ADHD [see (Cherkasova & Hechtman, 2009; Fassbender & Schweitzer, 2006)]. However, decreased middle temporal gyrus activation has also been found in association with worse behavioral performance in medication-naïve boys with ADHD performing a visual attention (oddball) task (Rubia et al., 2007), and in adolescent with ADHD during a divided attentional paradigm (Shafritz et al., 2004). It is possible that these attentional tasks rely on temporal networks, which precludes this region from responding in compensatory manner. However, overall these data indicate that functional abnormalities in the temporal regions are present in ADHD and need to be further investigated.

During post-error trials, children with ADHD also showed increased neural activity in the pMFC when compared to TD children. The pMFC, which comprises the SMA and the caudal cingulate zone, is considered to be important for response selection and control, including error monitoring. Functional imaging data in healthy adults have widely implicated the pMFC in monitoring ongoing actions, performance outcome, and subsequent behavioral adjustment [reviewed by (Nachev, Kennard & Husain, 2008; Ridderinkhof et al., 2004; Simmonds et al., 2007)]. Neural activity in this region is increased when subjects are attending to their movement, and it is reduced when motor attention is diverted, for example during a dual task condition (Johansen-Berg & Matthews, 2002).

The relative increase in activation in the pMFC is likely to represent a compensatory process to enhanced cognitive control and adjust motor performance. However, functional abnormalities in the SMA/dACC have also been reported in ADHD during successful response inhibition using the Go/No-Go task (Suskauer et al., 2008a; Tamm et al., 2004). Although ISV was not correlated with pMFC activity, it is possible that the increased ISV in the ADHD group was also related to a limited ability to recruit regions involved in motor control and execution, rather than being uniquely an attentional impairment.

Overall these findings support the hypothesis that children with ADHD had difficulties in reallocating their attention on task-relevant information after an error occurred and thus recruited the temporal cortex to resolve stimulus conflict and the pMFC to adjust their motor response. However, the increased ISV indicates that children with ADHD had a limited ability to recruit compensatory networks to compensate for attentional deficits.

Neural correlates of error versus correct inhibition trials

In contrast to our hypothesis and published data in ADHD, we were unable to report differences in neural activity when comparing error versus correct inhibition trials. However, in the present study the ADHD and TD groups showed no differences in mean RT for post-error trials. It is, therefore, possible that differences in neural activity are found in association with more consistent behavioral impairments, which would also explain the lack of differences in neural activity in the lateral PFC for post-error (versus post-correct inhibition) trials.

Moreover previous fMRI studies of error processing in pediatric ADHD have used the Stop-Signal task. As discussed by Rubia et al. (2005), there are important differences between the Go/No-Go and the Stop-Signal tasks in terms of attentional demand. Lapses of attention are more likely to induce commission errors during the Go/No-Go task, while in the Stop-Signal task commission errors are a more direct measure of the failure to inhibit a motor response that has already been triggered. If, as reported in the present study, error processing impairments in ADHD are related to attentional deficits, it is possible that differences between studies may also be related to differences in attentional processing between the two tasks.

Despite the lack of whole brain findings, when we correlated changes in ISV with BOLD signal for error versus correct inhibition trials, we found that in the ADHD group, high variability was associated with increased activity in the bilateral insula and decreased activity in the left precentral gyrus. The insular cortex is considered to play an important role in decision-making processes that involve integrating information about the internal emotional/arousal states and the risk or uncertainty associated with current decisions (Paulus & Stein, 2006). Increased negative emotionality has been reported in ADHD (Martel, 2009), but the relationship between negative emotions and cognitive performance has been relatively unexplored. The association, between neural activity in the insula during error trials and response variability in the subsequent trial, suggests that in ADHD the internal emotional state associated with making an error may adversely affect the ability to allocate attentional resources in the following trial thereby compromising post-error behavioral adjustment, i.e. the error acted as an emotional distractor.

The correlation of ISV with the left precentral gyrus (BA4/6) is supported by previous data from our lab (Suskauer et al., 2008b) and indicates that deficits in motor preparation and execution contribute to increased variability.

Limitations of the study

Due to the small sample size, the present results should be considered preliminary. The limited sample size prevented us from analyzing age-related changes, as well as the effects of specific ADHD subtypes or psychiatric comorbidities on error processing. Examining these influencing factors will be important in future studies. Moreover, a larger sample size may enable the detection of differences in neural activity during error (versus correct inhibition) trials. The subjects included in the present study were a subset of those used in a previous study and represented a small group of children with a high rate of commission errors. It would be important in future studies to investigate error processing in ADHD using an adapted version of the Go/No-Go task that induces a higher error rate across both groups.

In conclusion, these preliminary findings support previous data demonstrating that post-error behavioral adjustment is not as frequent and consistent in children with ADHD, as in TD controls. Our data revealing high variability for post-error trials and ADHD-associated increases in neural activity in the temporal cortex, the pMFC, and the somatosensory / auditory cortex suggest that error processing deficits are related to difficulties in reallocating attentional resources to task-relevant information after an error has occurred. Moreover, the association between increased temporal cortex activity and lower variability in ADHD indicates that compensatory neural pathways were recruited to compensate for these attentional deficits, albeit with limited efficacy. Our findings showing that high variability in ADHD was associated with increased insula and decreased precentral gyrus activity during error trials further suggest that attentional deficits during post-error behavioral adjustment may be related to an over-sensitivity to negative outcomes and impairments in the motor preparation and execution. Further studies are warranted to confirm these findings.

Key points

- Behavioral and electrophysiological data indicate that post-error behavioral adjustment is impaired in ADHD.
- It is unclear if impairments in attentional allocation, error processing or both are related to deficits in post-error behavioral adjustment in ADHD.
- Previous fMRI studies in ADHD investigated activity during error trails rather than during post-error trials.
- Our preliminary results during post-error trials suggest that post-error behavioral adjustment impairments in children with ADHD are related to attention allocation problems.
- An over-sensitivity to negative outcomes during error trails may underline this attention allocation deficits during post-error trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

A) Glass brain and sectional representation of the regions of increased BOLD fMRI signal in the ADHD group compared to TD group during post-error versus post-correct inhibition trials. Children with ADHD showed higher activation in the posterior medial frontal cortex, the postcentral/transverse gyrus, and the middle/inferior temporal gyrus when compared to TD children. Neurological convention is used (i.e., right = right hemisphere). B) Percent signal change in the posterior medial frontal cortex (pmFC), the postcentral/transverse gyrus, the middle/inferior temporal gyrus for post-error trials and post-correct inhibition trials in the ADHD (gray) and TD (white) groups.

Figure 2. Pearson's correlation between percent ISV difference and percent signal change in the middle/inferior temporal gyrus for post-error versus post-correct inhibition trials in children with ADHD.

Table 1

Behavioral data on go, post-error and post-correct inhibition trials

	GROUP	Go trials after correct go	Post-error trials	Post-correct inhibition trials	% difference
RT (ms)	ADHD	382.7 (9.9)	456.4 (28.7)	419.6 (17.3)	10.4 (7.2)
	TD	359.2 (12.7)	406.1 (18.0)	417.2 (18.5)	-2.0 (3.0)
ISV	ADHD	0.44 (0.04)	0.45 (0.05)	0.37 (0.03)	25.1 (12.9)
	TD	0.32 (0.02)	0.29 (0.02)	0.33 (0.02)	-10.0 (5.9)

Reaction Time (RT) and intra-subject variability (ISV).

Percent difference between post-error and post-correct inhibition trials for RT and ISV was calculated for each subject separately as values for post-error trials minus values for post-correct inhibition trials divided by values for post-correct inhibition trials and multiplied by 100.

Results are reported as mean (SEM).

Between group differences in brain activity associated with post-error versus post-correct inhibition trials.

Table 2

Extent (voxels)	t (Peak voxel)	Region	BA	x	y	z	Hem
530	4.80	Superior Frontal G	6	4	-14	66	R
		Medial Frontal G	32	-6	-6	50	L
		Cingulate G	24	6	-14	46	R
202	4.52	Postcentral G	43	52	-14	22	R
		Postcentral G	43	54	-16	16	R
		Transverse Temporal G	41	58	-20	12	R
213	3.83	Middle Temporal G	21	54	-10	-18	R
		Middle Temporal G	21	56	2	-32	R
		Inferior Temporal G	20	48	0	-44	R

Cluster foci of activation seen in the contrast of post-error versus post-correct inhibition trials using an uncorrected threshold $p=0.005$ and a cluster size threshold equivalent to a corrected threshold $p<0.05$. Coordinates are in MNI space. G=Gyrus; Hem=hemisphere, R=right, L=center.

Regions showing significant correlations between percent ISV difference and neural activity in the contrast of error versus correct inhibition trials in ADHD children.

Table 3

Extent (voxels)	t (Peak voxel)	Region	BA	x	y	z	Hem
Negative correlation							
131	6.32	Precentral G	6	-26	-24	64	L
		Precentral G	4	-34	-	60	L
Positive correlation							
151	7.03	Clausttrum		-38	-8	-4	L
		Insula	13	-44	-4	-10	L
287	5.54	Insula	13	42	-16	12	R
		Clausttrum		40	0	-12	R
		Superior Temporal G	22	54	4	-6	R

Whole-brain analysis with an uncorrected threshold $p=0.005$ and a cluster size threshold equivalent to a corrected threshold $p<0.05$. Coordinates are in MNI space. G=Gyrus; Hem=hemisphere, R=right, L=left.