# Functional Disconnection of Frontal Cortex and Visual Cortex in Attention-Deficit/Hyperactivity Disorder

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**Background:** Current pathophysiologic models of attention-deficit/hyperactivity disorder (ADHD) suggest that impaired functional connectivity within brain attention networks may contribute to the disorder. In this electroencephalographic (EEG) study, we analyzed cross-frequency amplitude correlations to investigate differences in cue-induced functional connectivity in typically developing children and children with ADHD.

**Methods:** Electroencephalographic activity was recorded in 25 children aged 8 to 12 years (14 with ADHD) while they performed a cross-modal attention task in which cues signaled the most likely (.75 probability) modality of an upcoming target. The power spectra of the EEG in the theta (3–5 Hz) and alpha (8–12 Hz) bands were calculated for the 1-sec interval after the cue and before the target while subjects prepared to discriminate the expected target.

**Results:** Both groups showed behavioral benefits of the predictive attentional cues, being faster and more accurate for validly cued targets (e.g., visual target preceded by a cue predicting a visual target) than to invalidly cued targets (e.g., visual target preceded by a cue predicting an auditory target); in addition, independent of cue-target validity, typical children were faster to respond overall. In the typically developing children, the alpha activity was differentially modulated by the two cues and anticorrelated with midfrontal theta activity; these EEG correlates of attentional control were not observed in the children with ADHD.

**Conclusions:** Our findings provide neurophysiological evidence for a specific deficit in top-down attentional control in children with ADHD that is manifested as a functional disconnection between frontal and occipital cortex.

**Key Words:** ADHD, alpha, attentional control, children, disconnection, EEG, theta

Attention-deficit/hyperactivity disorder (ADHD) is characterized by symptoms of inattention, impulsivity, and hyperactivity. Some of the current pathophysiological models of ADHD suggest that the symptoms of ADHD may be related to impaired interactions (i.e., functional connectivity) within brain networks, rather than impaired function of specialized cortical regions (1).

Electroencephalography (EEG) is a noninvasive method of recording human brain activity that provides a real-time measure of neuronal activity. The oscillatory activity in the EEG is believed to index the neurobiological organization of frequency-specific networks in the brain, with event-related changes in the EEG reflecting the reorganization of these networks in relation to event-specific computational demands (2,3).

In the present study, we investigated possible differences in cue-related changes in oscillatory EEG activity between typically developing children and those diagnosed with ADHD. We employed a cross-modal attentional cuing paradigm where the cues signaled the modality of upcoming stimuli (Figure 1). The focus of our analysis was on the oscillatory activity in theta and alpha frequency ranges or bands, because prior studies have implicated the involvement of these bands in various aspects of visual processing, attentional orienting, and cognitive control (4–7) in typically developing children and adults and in children with ADHD (8).

First, we examined the differences in the cue-induced posterior alpha modulation between typical and ADHD children. Then, we examined the trial-by-trial correlations in power between the alpha activity and theta activity across the scalp. Such an approach, although relatively new, provides a powerful method for investigating functional connectivity in human electrophysiological data (6,9). We found clear evidence for a functional disconnection of frontal cortex and occipital cortex in children with ADHD. It should be noted that most prior studies in this field have examined either relationships between the neural responses to different experimental conditions averaged across a group of subjects or the relationship between neural responses and behavior on a subject-by-subject basis. However, the strongest evidence that baseline activity modulates sensory processing comes from showing a trial-by-trial relationship between the two (10–12).

## Methods and Materials

### Subjects and Inclusion Criteria

Children aged 8 to 12 years with typical development or ADHD-combined type were enrolled following informed written parental consent. The inclusion criteria for typically developing children was that, based on parent interview, they be free from neurodevelopmental disorders, including autism spectrum disorder and ADHD, using the Diagnostic Interview Schedule for Children, and that they be unrelated to the ADHD children. The inclusion criteria for the ADHD-combined type were as follows. The diagnosis of ADHD was based on DSM-IV criteria established by 1) a previous diagnosis of ADHD by either a psychologist, psychiatrist, or behavioral paediatrician; 2) clinical judgment by a licensed clinical psychologist (B.A.C.); and 3) a semistructured parent interview extracted from the Diagnostic

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Received Aug 21, 2009; revised Oct 7, 2009; accepted Nov 11, 2009.

0006-3223/10/$36.00
doi:10.1016/j.biopsych.2009.11.022

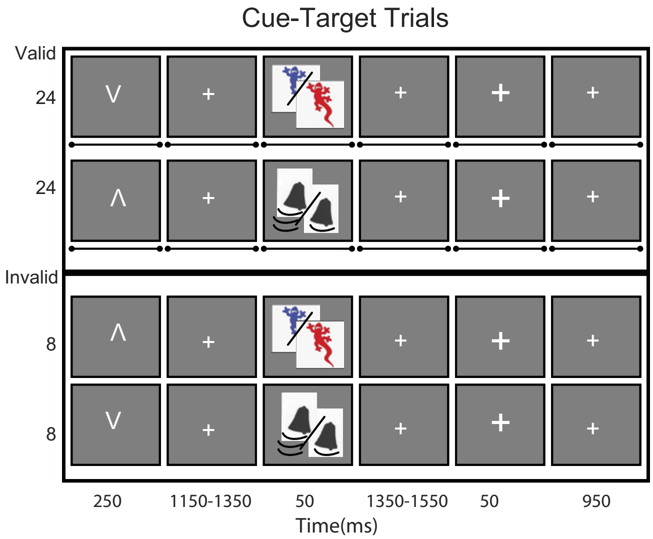


**Figure 1.** The paradigm consisted of a cross-modal attention task, where symbolic cues, presented visually (V for visual or inverted V, represented by the letter A, for auditory) either validly (probability = .75) or invalidly (probability = .25) predicted the modality of an upcoming target stimulus. Subjects pressed a button with the index or middle finger of the right hand upon presentation of a red versus blue picture, respectively, or for a tone of high versus low frequency, respectively. Valid trials are shown in the top two rows, while invalid trials are shown in the bottom two rows of the figure. The numbers at left indicate the numbers of trials of the valid cues (24 each of visual and auditory cues) and of invalid cues (8 each of visual and auditory cues) in each block; 8 blocks were presented.

Interview Schedule for Children (13). Through a basic prescreening interview, the subjects were determined to be free from autism spectrum disorder, neurological disorders, psychiatric illness, mood disorders, and learning disabilities. Stimulant medication was withheld 24 hours before testing. The groups were roughly matched on socioeconomic-status, being recruited from the same school districts, recreational facilities, and physician offices.

Electroencephalography and behavioral measures of performance were recorded in 30 children (16 with ADHD); all 30 children were included in the behavioral analyses. However, for some of these subjects, the EEG data were unusable (i.e., due to electrophysiological artifacts); therefore, the EEG analyses were conducted with 25 children (14 with ADHD). For demographic and diagnostic information please refer to Supplement 1.

### Cross-Modal Attentional Switching Task

In our cross-modal attention task, symbolic visual cues validly or invalidly signaled the modality of an upcoming target (valid probability = .75). As shown in Figure 1, all cues were themselves presented visually and consisted of either the letter "V" to indicate the most likely target was visual or an inverted "V" (described as the letter "A" without the horizontal line to equate the cues for overall luminance) to indicate the most likely target was auditory. On a random 25% of the trials, the cues incorrectly (invalidly) predicted the target modality. Whether a validly cued or invalidly cued target, the subjects were required to discriminate and respond to its features as follows. The subject's task was to maintain fixation on a central fixation point, use the cue information to prepare for the upcoming target of the cued modality, and then press a button with the index or middle finger of the right hand upon discrimination of a red versus blue picture (visual target), respectively, or for a tone of high versus low frequency (auditory target), respectively. Subjects completed eight runs of the paradigm.

### EEG Recording

Electroencephalography was recorded from 20 scalp electrodes located at the sites of the International 10–20 System of Electrode Placement. The signals were acquired using a bandpass of DC-100 Hz and an analog-to-digital sampling rate of 1000 samples per second. The left mastoid served as the reference electrode site.

### EEG Preprocessing

Data analysis was completed using the Fieldtrip software package, an open-source toolbox for neurophysiological data analysis, developed at the Donders Institute for Brain, Cognition, and Behaviour (http://fieldtrip.fcdonders.nl). Artifacts (e.g., trials containing eye movements, blinks, muscle potentials, and amplifier or electrode noise) were removed from the EEG using a semiautomatic routine. There was no difference between groups in terms of the number of trials removed.

### Postcue Oscillatory EEG Analyses

The oscillatory EEG activity was characterized by calculating the power spectra for the period 1 second before and 1 second after the cues. A 1 second long Hanning taper was applied to the data before calculating the spectra. The difference between the precue and postcue spectra was calculated for the individual trials and then averaged for each subject.

## Results

### Behavioral Data

Overall, independent of cue validity, the typically developing children had faster reaction times to visual targets than the children with ADHD [$F(1,28) = 4.26$, $p < .048$]; although the effects were in the same direction, for accuracy this main effect did not reach significance for visual discrimination [$F(1,28) = 3.76$, $p > .05$]. The overall group effects were similar for the auditory targets: faster overall reaction times [$F(1,28) = 5.97$, $p < .02$] and higher accuracy [$F(1,28) = 4.88$, $p < .03$] for the typically developing children compared with the children with ADHD. Importantly, in the analysis of variance (ANOVA), there were no significant interactions between validity and group for reaction times or accuracy, in line with the $t$ tests we will report below. Moreover, there were no other significant interactions with the factor group (typical vs. ADHD groups) in the omnibus ANOVAs for reaction times or accuracy.

Both the typically developing children and those with ADHD showed significant benefits of attentional cuing: reaction times were significantly faster for validly cued visual targets (cue correctly predicted the modality of the subsequent target) than for invalidly cued targets (cue incorrectly predicted the modality of the target) for both typically developing children [$t(13) = 3.01$, $p < .010$] and children with ADHD [$t(15) = 2.69$, $p < .017$] (Figure 2). Accuracy was also significantly higher for validly cued visual targets for both typically developing children [$t(13) = 2.705$, $p < .018$] and children with ADHD [$t(15) = 2.382$, $p < .032$]. Similarly, in the auditory modality, there were significant benefits of attentional cuing: reaction times were significantly faster for validly cued auditory targets for the typically developing children [$t(13) = 2.32$, $p < .037$] and children with ADHD [$t(15) = 2.05$, $p = .05$]. Finally, accuracy was significantly higher for validly cued auditory targets for both typically developing

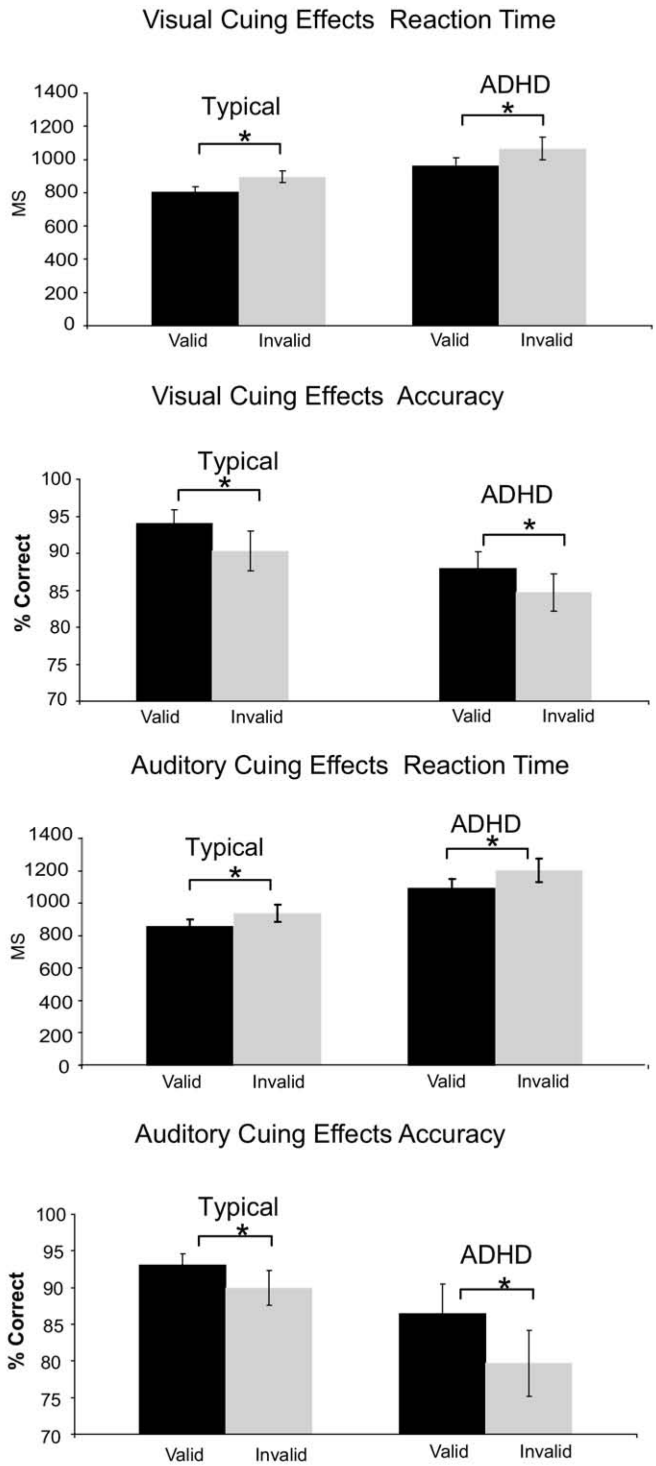


**Figure 2.** The visual cue facilitated performance for both typically developing children and children with ADHD. Reaction times were significantly faster and accuracy was increased for validly cued targets versus invalidly cued targets for both groups. Independent of attentional cuing, the typically developing children had faster reaction times overall than did the children with ADHD. $*p < .05$. ADHD, attention-deficit/hyperactivity disorder.

children [$t(13) = 2.169$, $p < .048$] and children with ADHD [$t(15) = 2.472$, $p < .027$].

In summary, the behavioral results indicate that the attentional cues were used by both groups of children in performing the task because cue-target validity influenced performance. In addition, the children with ADHD were slower, overall, to respond to the targets.

### Cue-Induced Modulation of Alpha Activity

First, we set out to investigate if the presentation of the attentional cues resulted in a difference in the modulation of alpha activity across the scalp as a function of the modality that they signaled. This was done by comparing the postcue relative to precue power spectra for cues signaling visual stimuli with those signaling auditory stimuli. The statistical analyses were conducted separately for each frequency band: theta (3–5 Hz), alpha (8–12 Hz). These frequency bands were selected based on the frequency bands typically used to classify the spontaneous EEG (14) and also based on the literature (4). The difference in EEG power in the different bands between the cue types was quantified by means of *t* values that subsequently were converted to *z* values; this was done for each scalp channel. A similar approach has been used in several previous studies (6,15,16). The scalp topography of these *z* values can be seen in Figure 3 (right column).

We found that in the typically developing children, relative to cues signaling auditory targets, cues signaling visual targets elicited a decrease in alpha activity over posterior scalp [$t(10) = 2.84$, $p < .02$] (Figure 3A). In contrast, in the children with ADHD, the visual compared with auditory cues did not elicit any significant posterior alpha modulations ($p > .5$). Compared with the typical children, the ADHD children showed less alpha modulation overall. We also performed this analysis for theta activity but found no affects of cuing or subject group. There were no significant differences in oscillatory activity in the precue interval between the ADHD and typical children.

### The Relationship Between Alpha Activity and Behavioral Benefit of Cues

To determine if there was a relationship between the cue-related changes in alpha activity (V vs. A cues) and the behavioral benefits imparted by the cues, we correlated (Spearman rank) the power difference of the alpha activity at each electrode for each subject with the corresponding reaction time difference between validly and invalidly cued trials (for visual targets). We found that in the typical children there was a negative correlation between alpha activity and the behavioral benefits of the cue (Figure 4A), which mapped predominantly on to the occipital electrodes ($r = -.61$, $p < .05$). In the ADHD children, however, there was no such relationship between alpha modulation and the behavioral benefits of the cue (Figure 4B).

### Functional Coupling Between Posterior Alpha and Frontal Theta Activity

A recent study found that in typical adults, posterior alpha activity during directed attention is inversely correlated with frontal theta activity (6). Therefore, we examined the data from the typically developing and ADHD children to determine whether power in posterior alpha activity following the visual cue was correlated with frontal theta power. We chose the posterior scalp site displaying the strongest cue modulation in the alpha band to use as a seed site for the analysis. The trial-by-trial alpha power from this seed electrode was correlated with the theta power across all other sensors to create topographies of the correlation. Correlation coefficients were subsequently converted to *z* values using Fisher's *r*-to-*z* transformation

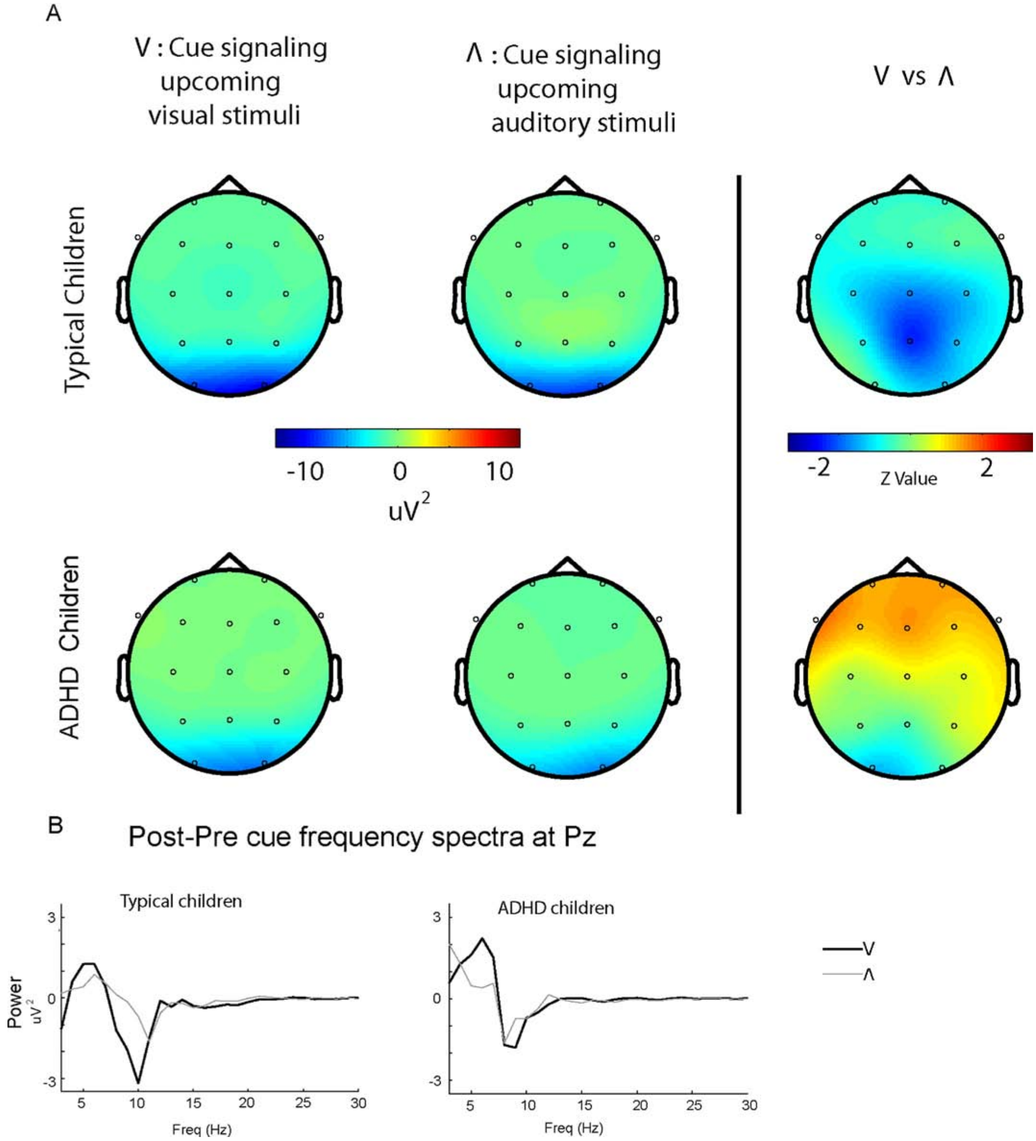


**Figure 3. (A)** The averaged topographies (across each group) of cue-modulated alpha activity characterized in the postcue/pretarget interval. The left column shows the maps in response to a visual cue, and the middle column shows the maps for auditory cues; the right column shows the difference map constructed by subtracting middle from the left maps after *z*-score conversion. In the typically developing children, relative to cues signaling upcoming auditory targets, visual cues signaling upcoming visual targets elicited a decrease in parieto-occipital alpha activity (top row). In the children with ADHD, the cue did not elicit any significant alpha modulation (bottom row). The maps are shown with the nose at the top and left hemisphere is shown on the left of each map. **(B)** The difference frequency spectra (postcue-precue) across the cue and group at the parieto-occipital electrode (Pz). ADHD, attention-deficit/hyperactivity disorder.

to obtain a normally distributed variable (17). Significance of the correlation at each electrode was then assessed at the group level with one-sample $t$ tests.

For the typically developing children, we found significant cross-frequency coupling expressed as anticorrelations between posterior alpha power and theta power at frontocentral scalp for visual [$t(10) = 3.6$, $p < .004$; Figure 5A] but not auditory cues [$t(10) = .1$ $p < .87$; not shown]. However, this functional coupling between posterior alpha activity and frontocentral theta activity was not observed for visual [$t(13) = .68$, $p < .5$; Figure 5B] or auditory cues [$t(13) = .49$, $p < .63$] in children with ADHD.

## Discussion

In the present EEG study of attentional control, we found that during a cross-modal attention task, a cue to expect a visual target induced a decrease in posterior alpha EEG activity for the typically developing children but not the children with ADHD. The posterior alpha decrease was correlated with the behavioral benefits imparted by the cues in the typical children but not so in the ADHD children. Moreover, posterior alpha activity was anticorrelated with a frontal theta activity on a trial-by-trial basis. This pattern can be interpreted as a form of functional connectivity between frontal brain systems involved in attentional control and perceptual systems in posterior cortical areas, a pattern consistent with many models of voluntary attentional control over sensory processing (18,19). That is, we interpret the anticorrelated theta and alpha activity in the typically developing children as an EEG signature of the top-down influence (reflected in the frontal theta) of attentional control systems onto perceptual structures (reflected in the occipital alpha), which

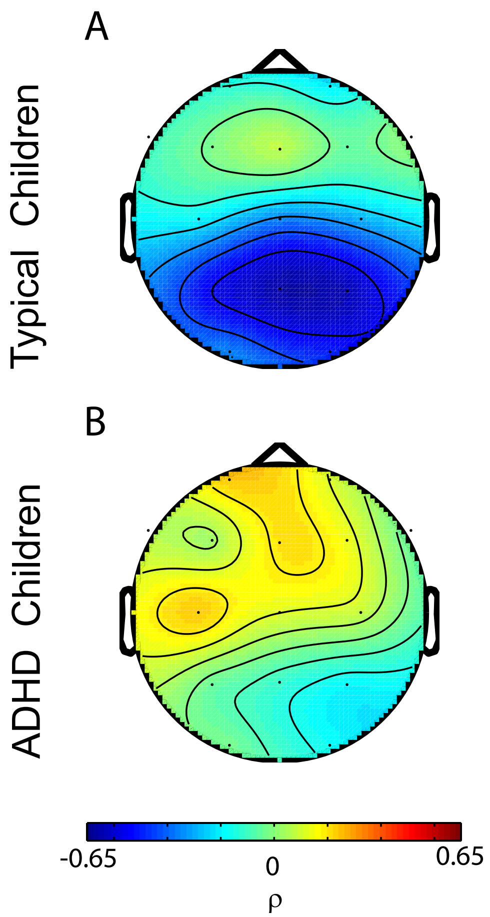


**Figure 4.** The topography of the correlation (Spearman) between cue-related alpha modulation and behavioral benefits across each group. **(A)** Across the typical children, there was significant anticorrelation ($r = -.61$, $p < .05$) between alpha power in the occipital electrodes and the difference in reaction time between validly and invalidly cued trials. This is seen in the map as focus of anticorrelation (deeper blue color) over the posterior scalp (bottom of map). **(B)** No relationship between cue-related alpha modulation and behavioral benefits was observed in the children with attention-deficit/hyperactivity disorder (ADHD).

prepares the brain to selectively process the anticipated upcoming stimulus.

Given that the ADHD children performed the task well, exhibiting significant cross-modal attentional cuing effects in reaction times and accuracy measures, our results cannot be attributed to a failure of task performance in the ADHD group. There were, however, significant differences in behavior between the two groups: the children with ADHD were slower overall in performing the task. Therefore, we conclude that although both groups utilized the cue to prepare for the upcoming target stimulus of the expected modality, the children with ADHD could not fully utilize top-down attentional control to bias sensory processing. This deficit is reflected in the slower overall reactions times in the children with ADHD and the absence of both the cue-induced posterior EEG alpha reductions and the typical pattern of anticorrelation between posterior alpha and frontal theta. An alternate, although not mutually exclusive, interpretation could be that the slower reaction times and lower accuracy reflect a basic difference in stimulus processing/discrimination in the ADHD children. Our results are promising for helping to understand the pathophysiology of ADHD. A study with a larger sample size that permits investigation of these effects in different subtypes of ADHD could serve to further broaden the implications of our findings.

Our findings and interpretation are supported by both attention and working memory tasks demonstrating a stimulus-specific alpha decrease in preparation to perform visual tasks (5,20). Additionally, it has been shown that visual discrimination abilities are reduced with an increase in posterior alpha activity (4,21). Previous studies have found an increase in theta activity in relation to tasks requiring executive function (22–25). Since there were no attentional cue-related differences in theta activity alone between the children with ADHD and the typically developing children, it is unlikely that ADHD is associated with a general deficit in executive functioning but rather reflects a more fundamental deficit in attentional control mechanisms.

One influential theory of attention proposes that discrete cognitive processes are supported by independent attentional networks: alerting, orienting, and conflict (26). The alerting network is believed to be involved in acquiring and maintaining an alert state. The orienting network involves the selection of information from sensory input for selective processing, while the conflict network entails the resolution of the conflict that arises between competing stimuli. The Attention Network Test was designed to evaluate alerting, orienting, and executive attention (27). When this paradigm was applied in evaluating attention in ADHD patients, it was found that the children with ADHD demonstrated deficits in the alerting and conflict attention networks but had normal functioning of the orienting network (28). Such differences in the alerting network could be linked to the failure to show alpha reductions after a cue in paradigms similar to ours. However, in the present experiment, the alpha reductions observed are revealed in the contrast of the visual cue (visually presented letter V) and the auditory cue (visually presented inverted V), which would both be expected to elicit alerting. Therefore, the reduction in posterior alpha in the present study is not related merely to generalized alerting to the cues but is specific for the preparation to process a visual event.

Although in the present study the reductions in posterior alpha were observed only for cues predicting an upcoming visual target, we note that these findings do not rule out that the control of auditory attention is similarly affected in ADHD. There is evidence that different processing systems have distinct alpha-like activity, such as the tau rhythm in the auditory cortex (29). However, the tau rhythm has been shown to be greatly attenuated and difficult to record in the EEG due to the anatomical organization of the auditory cortex, which results in reduced volume conduction of this activity to surface electrodes (30). Therefore, based on the results of the present study, we remain agnostic as to whether deficits in attentional control for auditory selective attention are also disordered in ADHD.

Prior studies of EEG changes in ADHD have described various alterations in the ongoing EEG (e.g., [8,31]). The majority of these studies have examined absolute EEG frequency power or the ratio between power in different frequency bands (32). Although useful in understanding neural correlates of ADHD, examining frequency power or power ratios alone does not address functional interactions between distant brain regions. Nor can simple EEG analyses be related to specific cognitive neural processes when the EEG measures are not related to specific task performance. In contrast, the approach used here was designed to examine cross-frequency interactions between distant brain regions and how these interactions were related to attentional control within a well-defined attention task. As a result, the

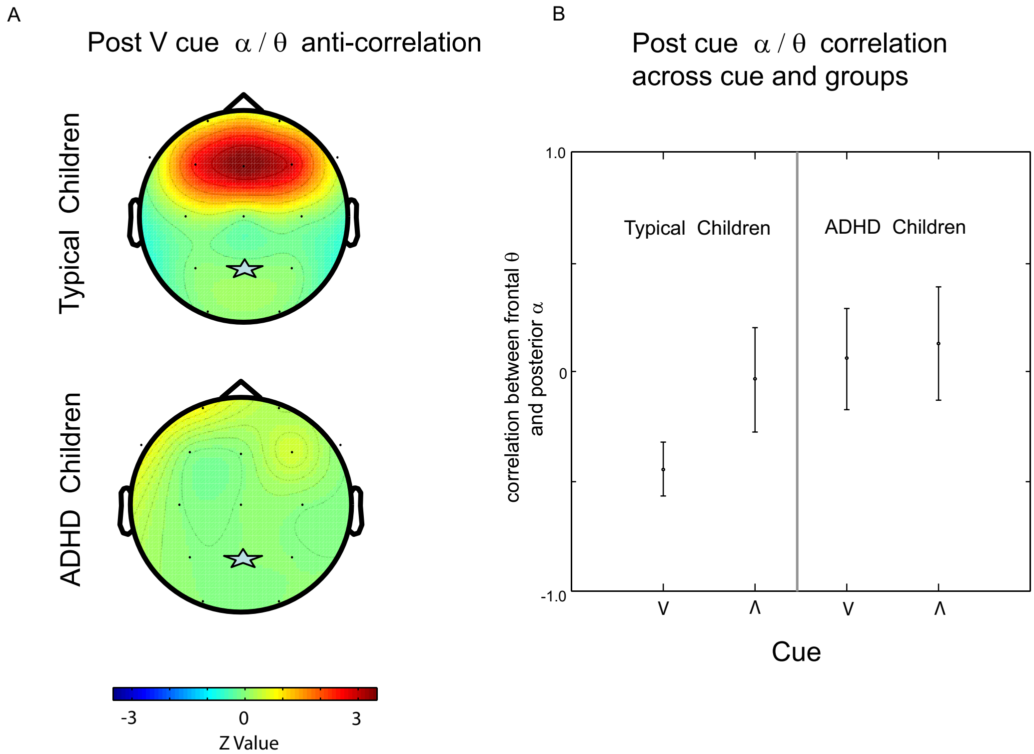


**Figure 5.** **(A)** The parieto-occipital channel (marked with a star) was used as a seed location for the correlation analysis. The correlations between alpha power in the reference electrode and theta power in all the other sensors were calculated on a trial-by-trial basis within subjects and converted to *t* values then *z* scores across subjects. For the typically developing children, there was a strong anticorrelation between parieto-occipital alpha and midline frontocentral theta power. No such correlation was observed in the children with attention-deficit/hyperactivity disorder (ADHD). **(B)** The mean frontal theta and posterior alpha correlations across cue and groups. Error bars represent the standard error of the mean.

present findings permit a specific mechanistic hypothesis about attentional control deficits in ADHD.

In summary, the present findings provide neurophysiological evidence for a specific deficit in top-down attentional control in children with ADHD. This deficit is likely due to a functional disconnection between frontal and occipital cortex during preparatory attention.

*This work was supported by National Institute of Mental Health Grant MH072958 and grants from the Perry Family Foundation, the Debber Family Foundation, and the Aristos Academy to BAC; National Institute of Mental Health Grant MH057714 to GRM; a Rubicon Fellowship from the Netherlands Organization for Scientific Research to AM; and a TALENT Fellowship from the Netherlands Organization for Scientific Research to EMB.*

*We are deeply grateful to the volunteers who participated in this study.*

*The authors reported no biomedical financial interests or potential conflicts of interest.*

*Supplementary material cited in this article is available online.*

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