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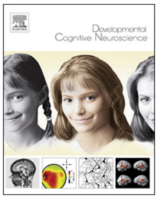

Abnormal alpha modulation in response to human eye gaze predicts inattention severity in children with ADHD

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ABSTRACT

Attention-deficit/hyperactivity disorder (ADHD) is characterized by problems in directing and sustaining attention. Recent behavioral studies indicated that children with ADHD are more likely to fail to show the orienting effect in response to human eye gaze. The present study aimed to identify the neurophysiological bases of attention deficits directed by social human eye gaze in children with ADHD, focusing on the relationship between alpha modulations and ADHD symptoms. The electroencephalography data were recorded from 8–13-year-old children (typically developing (TD): $n = 24$; ADHD: $n = 21$) while they performed a cued visuospatial covert attention task. The cues were designed as human eyes that might gaze to the left or right visual field. The results revealed that TD children showed a significant alpha lateralization in response to the gaze of human eyes, whereas children with ADHD showed an inverse pattern of alpha modulation in the left parieto-occipital area. Importantly, the abnormal alpha modulation in the left hemisphere predicted inattentive symptom severity and behavioral accuracy in children with ADHD. These results suggest that the dysfunction of alpha modulation in the left hemisphere in response to social cues might be a potential neurophysiologic marker of attention deficit in children with ADHD.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that is characterized by an inappropriate pattern of inattentiveness, hyperactivity and/or impulsivity causing impairment in multiple settings of life (American Psychiatric Association, 2013). It affects ˜5% of school-age children (Willcutt, 2012) and has a high probability of persisting into adulthood where the prevalence is ˜2.5% (Simon et al., 2009). The neuronal substrate of the disease is still relatively unknown. In laboratory studies, an experimental paradigm known as visual search (e.g., whether there is a unique circle-shaped item among numerous diamond-shaped items) has been used extensively to investigate the factors that govern attentional selection and distractor suppression. By using a visual search paradigm, previous behavioral studies have reported selective attention deficits in ADHD children (Mason et al., 2003; Huang-Pollock et al., 2005). Event-related potential (ERP) studies further indicated that children with ADHD showed abnormal components in target selection (Lopez et al., 2006; Cross-Villasana et al., 2015; Wang et al., 2016), distractor suppression (Wang et al., 2016), executive control (Wiersema and Roeyers, 2009; Johnstone and Galletta, 2013) and error monitoring (Liotti et al., 2005; van Meel et al., 2007) processes in visual attention tasks. These EEG/ERP results imply the occurrence of spatial attention impairments in ADHD.

Except for ERP components, increasing evidence has demonstrated that allocating spatial attention is associated with region-specific modulation of alpha oscillations in the posterior area (Worden et al., 2000; Thut et al., 2006; Doesburg et al., 2016). When covert attention is directed to one side of the visual field, alpha oscillations are more strongly suppressed over the hemisphere contralateral to the attended

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Table 1
Demographic information of subjects in the final sample.

	TD	ADHD	Statistics
Age (years)	10.10 ± 1.03	10.10 ± 1.32	t = -.008, *ns*
Sex (boys, girls)	15, 9	17, 4	χ^2 = 1.067, *ns*
WISC-III (*n*)	107.14 ± 14.52 (7)	103.00 ± 15.46 (10)	t = .557, *ns*
RSRT percentiles (*n*)	85.06 ± 10.13 (17)	78.55 ± 15.78 (11)	t = 1.335, *ns*
Inattention Score	16.63 ± 3.35	27.19 ± 3.87	t = -9.826, $p < .001$
Hyperactivity Score	14.33 ± 4.08	21.81 ± 5.98	t = -4.950, $p < .001$

Values are the mean ± SD, unless otherwise indicated; the value of χ^2 is corrected.
ADHD, attention-deficit/hyperactivity disorder; TD, typically developing; *ns*, not significant.

hemifield (Worden et al., 2000; Thut et al., 2006). The alpha oscillations were suggested to gate streams of information through a top-down control by means of functional inhibition (Jensen and Mazaheri, 2010; Klimesch, 2012; Sadaghiani and Kleinschmidt, 2016). Previous studies have shown that alpha synchronization is closely related to behavioral performance in visual attention tasks (Romei et al., 2010; Handel et al., 2011). For instance, anticipatory alpha lateralization could predict the performance of the experimental switch (Horschig et al., 2014).

As problems in sustaining directed attention is one of the most marked clinical features in ADHD patients, posterior alpha modulation is an important aspect in ADHD studies. By using variant Posner's paradigm (Posner, 1980), adults with ADHD were shown to have a shorter duration for sustaining alpha lateralization (ter Huurne et al., 2013), and boys with ADHD were shown to have a decreased alpha lateralization (Vollebregt et al., 2016). However, a similar, adult-like pattern of alpha modulation is already present in 7–10-year-old typically developing (TD) children (Vollebregt et al., 2015). These findings partly explained the poor behavioral performance in ADHD patients.

In the domain of visual-spatial attention, the human eye gaze is considered a special kind of cue. Some studies have indicated that the eye gaze cues show a stable cue effect on the target located at the eye gaze position even if the target is more likely to appear in the opposite visual field, while arrow cues do not trigger this reflexive attention shift (Friesen et al., 2004). In addition, eye gaze cues generate a later inhibition of return than exogenous cues (Frischen et al., 2007). Humans can generate sensitivity to eye gaze direction in the early infant years (Farroni et al., 2002; Vernetti et al., 2018), and this effect can be distinctly reflected by ERPs (Farroni et al., 2004; Hoehl et al., 2008) and oscillation responses (Hoehl et al., 2014; Michel et al., 2015). In early human life, the ability to capture the eye gaze of other individuals plays important roles in the development of visuospatial attention (Kylliainen and Hietanen, 2004), social communication (Striano and Stahl, 2005) and language learning (Brooks and Meltzoff, 2005). From childhood to adulthood, the social meaning of eye gaze direction continues to develop (Neath et al., 2013) and serves as a strong predictor of social competence in adulthood (Klin et al., 2002). Recent behavioral studies have indicated that children with ADHD fail to show the orienting effect of social eye gaze cues (Marotta et al., 2014) and the interference effect from eye-gaze distractors (Marotta et al., 2017), but they show stable effects on nonsocial indicators. These results reflect an attentional impairment in ADHD children in attending to socially relevant information and that social cues, such as human eye gaze, may have stronger indicative effects in ADHD recognition compared with nonsocial cues.

To the best of our knowledge, the alpha modulation directed by the social cues of human eye gaze has not been studied in children with ADHD. The gaze of cartoon fish eyes has been used as the cue in two recent EEG studies (Vollebregt et al., 2015, 2016); however, compared with real human eyes (or faces), the eyes of other species (Itier et al., 2010) and the abstract sketches of human faces (Schindler et al., 2017) would elicit weaker electroencephalic responses. Therefore, the alpha activities induced by the cue of human eyes may be different from those of cartoon fish eyes. Thus, through a covert attention task, the present study aimed to investigate (1) whether children with ADHD would show abnormal alpha modulation when they see the cue of human eye gaze and (2) if so, whether attention problems in ADHD children could be explained by abnormal alpha modulations.

2. Methods

2.1. Participants

A total of 63 right-handed children aged 8–13 years were recruited in this study, including 31 ADHD children (25 boys, 6 girls) and 32 TD children (19 boys, 13 girls, see Table S1 for details). Written consent was obtained from all of the children's parents, and verbal assent was obtained from the participants. The study was approved by the Ethics Committee of Beijing Normal University according to the Declaration of Helsinki. TD children were determined to be free from ADHD using the ADHD DSM-IV Rating Scale completed by their parents. There was no history of neurological or psychiatric disorders in the TD children. Children with ADHD were drug-naive and assessed by professional psychologists based on the DSM-IV criteria, and subjects with comorbid psychiatric or neurological disorders were excluded. All children had normal or corrected-to-normal vision. The intelligence quotient (IQ) was estimated with the Wechsler Intelligence Scale (WISC-III) or the Raven Standard Reasoning Test (RSRT), and subjects with low IQ levels (below 80 for the WISC-III, below 25% for the RSRT) were excluded. In each group, children with poor behavioral performance (accuracy lower than 75% or reaction time (RT) longer than two times the standard deviation of the mean) were also excluded (2 TD children; 2 ADHD children). EEG data with a high ratio of noise, muscle artifacts, or eye movement ($>$ 60% of trials, see details below) were also excluded from further analysis (6 TD children; 8 ADHD children). Therefore, 24 TD (15 boys, 9 girls) and 21 ADHD children (17 boys, 4 girls) were included in the EEG and behavioral analysis. There was no significant difference between the two groups in age and sex ratio or IQs (see Table 1).

2.2. Attention task

We used the gaze direction of human eyes as the cue stimulus (see Fig. 1A). Each trial started with a cue presented for 200 ms. The cue was a pair of human eyes gazing towards the left or right (with a width of 2° visual angle, randomized with equal probability), which was predictive (with 70% validity) for the side where the following target would appear. Following a 1000–1500 ms interstimulus interval, a visual search array was presented for 200 ms. The search array consisted of a circle (target) and 11 diamonds arranged into a circle with a visual angle of 5° from the center. The target might appear at 2, 4, 8 or 10 o'clock. The participants were instructed to maintain their gaze at the central cross and indicate the position of the target circle in the upper or lower visual field by pressing a button with the right middle or index finger. Different from the design in two recent studies (Vollebregt et al., 2016; Marotta et al., 2017), in which the response of target position was consistent with the direction of the cues, this design prevents the participants from preparing to make a response according to the cue's

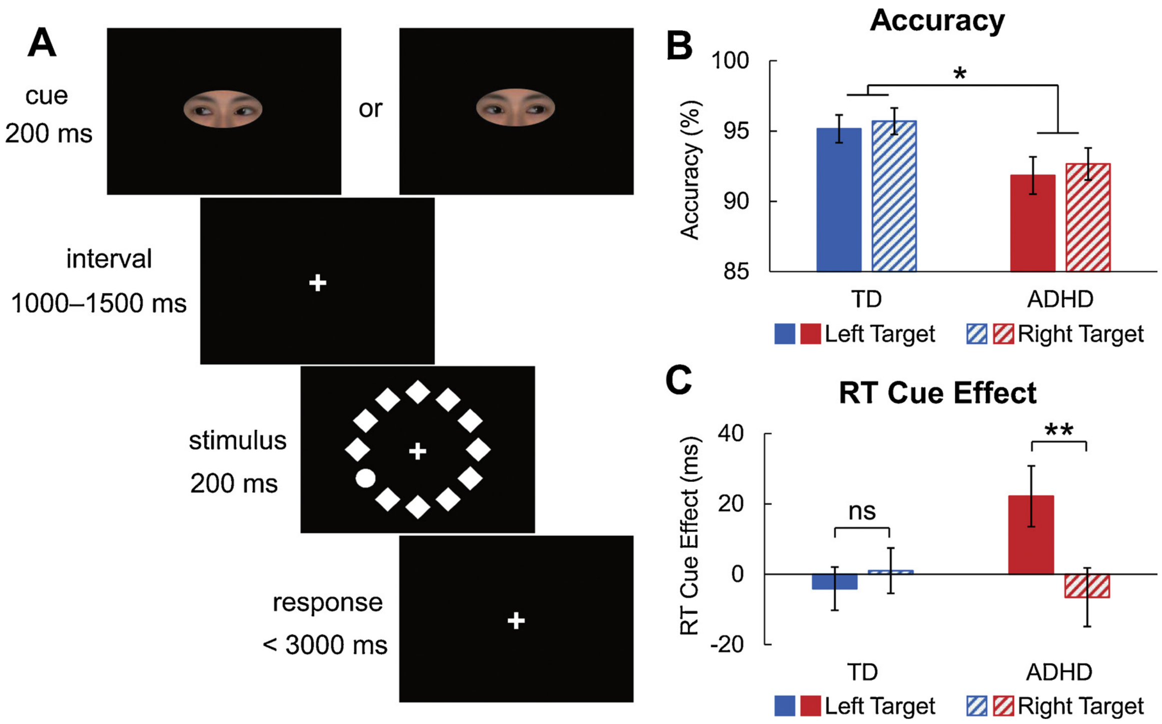

Fig. 1. Experimental paradigm and behavioral results. A. Experimental paradigm. B. Behavioral results of accuracies, $*p < .05$. C. Behavioral results of the RT cue effect, $**p < .01$.

direction before the target appears and thus avoids ERPs (Kranczioch et al., 2009; Krummenacher et al., 2014) or spectral perturbations, such as the mu rhythm (Pfurtscheller et al., 2006; ter Huurne et al., 2017), related to response preparation. The intervals between trials were jittered between 1000 and 1200 ms. There were 12 blocks of 30 trials in the experiment.

2.3. EEG recording and processing

The EEG data were acquired from a 128-channel system (HydroCel Geodesic Sensor Net, Electrical Geodesics, Inc., Eugene, OR). Cz was used as the online reference, and the impedances of all electrodes were kept below 50 kΩ during data acquisition. The EEG data were amplified with a bandpass filtering range of 0.01–400 Hz and digitized at 1000 Hz.

EEG processing was performed with the EEGLAB software package in the MATLAB environment (Delorme and Makeig, 2004). Because it is difficult for ADHD children to maintain a long-term motionless state like adults, and the outermost electrodes are quite susceptible to eye, face and head movements during EEG recording, data from the 34 outermost channels were excluded due to the low signal-to-noise ratio (Figure S1). This method was also used in a recent EEG study (Debnath et al., 2019). Then, the EEG data were downsampled to 200 Hz followed by a 1–30 Hz bandpass filter. The data were referenced to the average of all electrodes after interpolating the electrodes with bad signals (< 10% for each subject). Epochs were extracted from 0.7 s before the cue to 1.5 s after the cue. Epochs with overt eye blinks or movements were excluded using the step function provided by the ERPLAB toolbox (Lopez-Calderon and Luck, 2014). The eye movements were detected from the horizontal electrooculogram signal (difference between F9 and F10) with a window length of 100 ms, step size of 50 ms, and threshold of 50 μV during a time window from -50 to 1050 ms around the cue onset. Eye blinks were detected from the vertical electrooculogram signal (average of Fp1 and Fp2) around the cue display (-100–300 ms) with a window length of 200 ms, a step size of 100 ms and a threshold of 75 μV. Then, an independent component analysis was used to detect and remove component(s) with electrooculographic origins (Jung et al., 2000; Delorme and Makeig, 2004). Epochs with overt artifacts were detected in a semiautomatic way. A simple voltage threshold function was used to examine the absolute voltage value of all channels, with a threshold of 100 μV from -200 to 1000 ms around cue onset.

2.4. Spectral analysis of the EEG data

Spectral analysis of EEG data was performed with custom-written MATLAB scripts and the Fieldtrip software package (http://fieldtrip.fcdonders.nl). Because the time-frequency power might be disturbed by the ERP in oscillatory signals (Yeung et al., 2007; van Driel et al., 2017), the trial-averaged activity was subtracted from the raw EEG signal of each trial. The time-frequency representation of EEG data was calculated using continuous wavelet transformation. For each epoch, data were convolved with a set of Morlet wavelets (time window of five cycles) at frequencies ranging from 5 to 20 Hz with a step of 1 Hz and a time resolution of 0.01 s. The time interval of time-frequency power was -200–1000 ms around the cue onset. In each time-frequency interval, the modulation index (MI) and combined MI were computed using the following formulas:

$$MI = \frac{Power_{Left\ Cue} - Power_{Right\ Cue}}{\frac{1}{2}(Power_{Left\ Cue} + Power_{Right\ Cue})}$$

$$Combined\ MI = MI_{Left\ hemisphere} - MI_{Right\ hemisphere}$$

Fourteen parietal and occipital electrodes (left hemisphere: 59, 60 (P1), 65 (PO7), 66, 67 (PO3), 70 (O1), 71; right hemisphere: 76, 77 (PO4), 83 (O2), 84, 85 (P2), 90 (PO8), 91; Figure S1) were selected for MI analysis. To identify the frequency ranges in which the MI were significantly different between two hemispheres, a permutation test (2000 iterations) was performed based on cluster correction in the 5–20 Hz range within the time window of -200–1000 ms. This method controls multiple comparisons by identifying significant time-frequency clusters rather than independent points (Maris and Oostenveld, 2007), so it is widely used in time-frequency and time sequence analyses

(Vollebregt et al., 2015, 2016; Proskovec et al., 2018).

According to the time-frequency analysis, we averaged the MI in 8–13 Hz (alpha band) for the time domain analysis. A cluster-based permutation test (2000 iterations) was further performed to identify time clusters for which the left MI differed significantly from the right MI in the time period of -200–1000 ms. The longest significant time cluster was used for statistical analyses.

2.5. Statistical analysis

We used repeated measures analysis of covariance (ANCOVA) to compare the alpha MI difference between the two hemispheres (left, right) with the group (TD, ADHD) as a between-subject factor. To control the developmental effect within the sample, age was controlled as a covariate. A simple effect analysis was performed if the results showed an interaction effect. We used partial correlation analyses to explore whether the alpha MI was correlated with behavioral performance (accuracy, RT) and clinical assessments with age controlled in the models. Through a naive Bayes classifier, we performed classification analyses using the alpha MI and age as features. The false positive rate and true positive rate were employed as the indexes for comparing the diagnostic ability of the alpha MI in each hemisphere.

3. Results

3.1. Behavioral data

In each condition, the trials with error responses or RT outliers (deviation from the mean more than 2 standard deviations) were rejected from averaging the individual RTs. A repeated measures ANCOVA was performed for both accuracies and RTs with target location (left vs. right) and cue validity (valid vs. invalid) as within-subject factors and age as a covariate.

For accuracy, the results showed a significant main effect of group, suggesting that the response accuracy of the ADHD group was lower than that of the TD group ($F_{1,42} = 4.841$, $p = .033$, $\eta_p^2 = .103$; Fig. 1B). For RT (Table S2), there was a significant three-way interaction of group × target location × validity ($F_{1,42} = 6.646$, $p = .014$; $\eta_p^2 = .137$). Simple effect analysis showed that in the ADHD group, there was a significant interaction of location × validity ($p = .004$), and the RT of the valid cue was significantly shorter than the invalid cue for left target locations ($p = .005$), whereas there was no effect of validity for right target locations ($p = .389$). There was also no significant interaction of location × validity in the TD group ($p = .601$).

3.2. Modulation in the alpha band

We calculated the MI for each hemisphere that indicated the relatively higher power of the left versus right cues. The results of the time-frequency analysis showed the strongest modulation at 8–13 Hz in the TD group (Fig. 2A), and the topographic maps revealed that the distinct extremum of MI was focused on the posterior area (Fig. 2C). In TD children, the time cluster permutation test indicated a significant cluster 350–710 ms after cue onset, but ADHD children did not show any significant cluster of time (Fig. 2B, D).

Thus, we selected the alpha MI in 350–710 ms for repeated measures ANCOVA (Table S3). The results showed a main effect of group ($F_{1,42} = 9.352$, $p = .004$; $\eta_p^2 = .182$) and a significant interaction of group × hemisphere ($F_{1,42} = 5.925$, $p = .019$; $\eta_p^2 = .124$). Simple effect analysis showed that for the TD group, the alpha MI in the left hemisphere was significantly higher than that in the right hemisphere ($p < .001$), whereas this effect was absent in the ADHD group ($p = .711$). That is, the children with ADHD showed a similar alpha MI in the right hemisphere ($p = .230$). However, the alpha MI for the ADHD group was significantly lower than that for the TD group in the left hemisphere ($p < .001$).

The following one-sample *t*-test confirmed the abovementioned results. In both TD and ADHD children, the alpha MI in the right hemisphere was significantly lower than zero (TD: $t = -2.035$, $p = .054$, $d = .415$; ADHD: $t = -3.401$, $p = .003$, $d = .742$). In the left hemisphere, the alpha MI was significantly higher than zero for the TD group (TD: $t = 2.751$, $p = .011$, $d = .562$) but was significantly lower than zero for the ADHD group ($t = -2.591$, $p = .017$, $d = .565$). The difference in alpha MI between the two groups indicated the dysfunction of alpha modulation in the left posterior area in children with ADHD.

3.3. Alpha MI correlation with behavior and symptoms

Compared with the TD group, children with ADHD displayed poorer behavioral performance and abnormal alpha modulation in the left hemisphere. We further investigated whether there were relationships between the alpha MI and behavioral performance (accuracy, RT). The results showed that for the ADHD group, the mean accuracy had a significant positive correlation with the alpha MI in the left hemisphere ($r = .460$, $p = .041$; Fig. 3A), but the correlation was not significant in the right hemisphere ($r = .083$; $p = .729$). In the TD group, the alpha MI did not show any significant correlation with accuracy or RT (*ps* > .364). These results indicated that a lower level of alpha modulation in the left hemisphere was related to the poorer behavioral accuracy in children with ADHD.

To verify whether the attentional problems could be explained by the abnormal alpha modulation, we performed partial correlation analysis between the alpha MI and the scores of the ADHD rating scales (inattention subscale and hyperactivity/impulsivity subscale). As shown in Fig. 3B, the alpha MI in the left hemisphere was negatively correlated with the symptom severity on the inattention subscale ($r = -.500$, $p = .025$) but not on the hyperactivity/impulsivity subscale ($r = -.228$, $p = .334$). The alpha MI in the right hemisphere did not show any correlation with the symptom score from any subscale (*ps* > .151). These results indicated that ADHD children with lower alpha MI in the left hemisphere showed more attention deficiency.

3.4. Recognition capability of alpha MI

To compare the recognition capability of the alpha MI between the two hemispheres, through a naive Bayes classifier, we performed 20,000 iterated classification tests between the two groups in a three-fold cross-validation procedure for each hemisphere. In each iteration, the data from 2/3 of the participants (16 for the TD group; 14 for the ADHD group) were selected at random to train the classifier, and data from the remaining 1/3 of the participants were used to assess the classifier's performance. We used the false positive rate and the true positive rate to estimate the classification property. For each index, the difference between the left and right hemispheres was estimated using a Monte Carlo method. In each iteration, the index difference between the two hemisphere conditions was computed, and the 20,000 iterations led to a distribution of index differences. Then, the 95% confidence interval was computed (alpha = .05). The index difference between the two hemisphere conditions was considered significant if the 95% confidence interval did not include zero. The results showed that the true positive rate of the alpha MI in the left hemisphere was significantly higher than that of the right alpha MI (percentile of zero: $p = .019$; confidence interval: [.080, .389]; Fig. 4A, B). In addition, the false positive rate difference between the two hemispheres was not significant (percentile of zero: $p = .905$; confidence interval: [-.345, .055]; Fig. 4C, D). This result suggested that relative to the alpha MI in the right hemisphere, the alpha MI in the left hemisphere has a stronger capability to recognize ADHD.

4. Discussion

In the current study, we compared the posterior alpha modulations

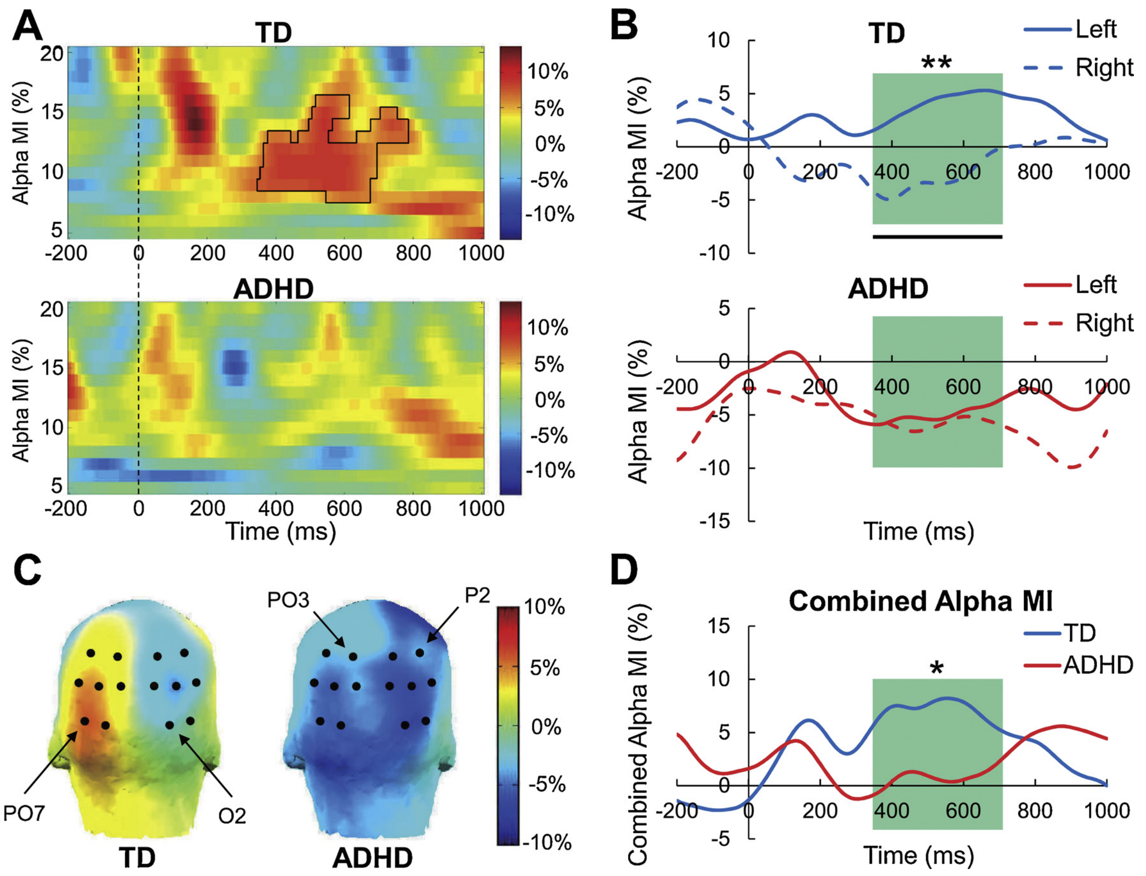

Fig. 2. The modulation of alpha power in response to the cue. A. Time-frequency representation of the combined alpha MI for left and right parieto-occipital electrodes. The black solid line indicates the significant cluster between the left and right MI ($p < .025$). B. Time course of the alpha MI (8–13 Hz) in the parieto-occipital electrodes. The green square indicates the time period (350–710 ms) used for statistical analysis, $^{**}p < .01$. C. Topographic representation of the alpha MI. The solid dots indicate the electrodes used for further analyses. D. Time course of the combined alpha MI averaged over the parieto-occipital electrodes, $^{*}p < .05$.

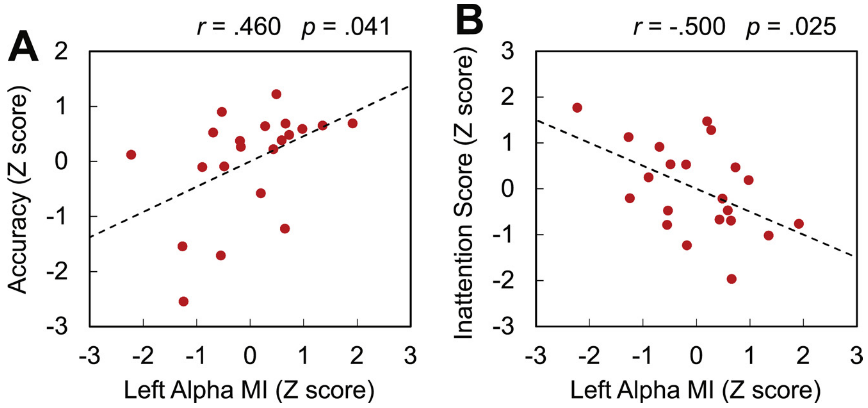

Fig. 3. Results of the correlation analysis. A. Significant correlation between the left alpha MI and mean accuracies in children with ADHD. B. Significant correlation between the left alpha MI and inattention scores in the ADHD rating scale.

between TD and ADHD children when they performed a covert visual attention task directed by the social cues of human eye gaze. We found a similar, adult-like pattern of alpha modulation in 8–13-year-old TD children, and children with ADHD showed decreased alpha lateralization in response to the human eye gaze. Such aberrant alpha modulation in the ADHD group was mainly manifested in the left hemisphere but not in the right hemisphere. More importantly, the aberrant left hemisphere modulation of alpha waves had a close relationship with poor behavioral performance and inattention severity in children with ADHD. The classification analyses confirmed that relative to the right alpha hemisphere, the alpha modulation in the left hemisphere had a higher ability to recognize ADHD children. These results suggested that in the attentional process of human eye gaze, the function of the alpha oscillations in two hemispheres may be different from each other, and the abnormal modulation of alpha power in the left hemisphere might be related to some neurophysiologic substrates of ADHD.

In contrast to studies involving nonsocial cues (ter Huurne et al., 2013; Vollebregt et al., 2016), we found an asymmetric dysfunction of alpha modulation in children with ADHD in the current study. This finding established a relationship between alpha modulation in the left hemisphere and the visual attention process of social cues in children with ADHD. These results are consistent with a previous study in which

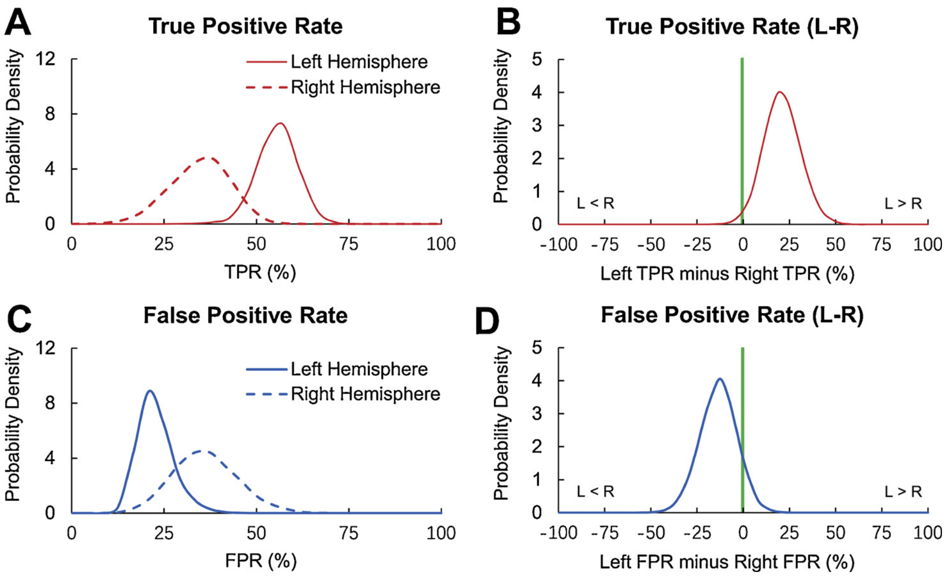

Fig. 4. Probability density of classification accuracies between the TD and ADHD groups. A. Probability density of the true positive rate (TPR) of the alpha MI for the two hemispheres. B. Probability density of the interhemispheric difference of the TPR for the two hemispheres. C. Probability density of the false positive rate (FPR) of the alpha MI for the two hemispheres. D. Probability density of the interhemispheric difference of the FPR for the two hemispheres.

the alpha desynchronization difference between cases with and without joint attention is mainly located in the left posterior area (Lachat et al., 2012). Because combined EEG-functional magnetic resonance imaging (fMRI) studies have proved that the posterior alpha power is robustly correlated with the BOLD signal in the occipital cortex (Feige et al., 2005; Mizuhara, 2012), and MEG studies also provided direct evidence for the lateralized alpha modulation generated in the occipital and parietal cortices (Marshall et al., 2015a, 2015b), we suggest that the alpha modulations here are mainly located in the parieto-occipital cortices. A comparison study of human eye gaze and arrow cues suggested that the attention orienting by the two cues is supported by different cortical networks, and the activated foci for gaze-cued orienting are mainly located in the occipital cortex (Hietanen et al., 2006). In addition, both ERP and fMRI studies showed that the occipital cortex can be induced in different degrees of activation to different emotional valences of social cues (Pourtois and Vuilleumier, 2006; Engell and Haxby, 2007). These studies indicated that the occipital cortex plays an important role in social cognition. Compared with TD children, children with ADHD showed reduced regional homogeneity, gray matter volume, white matter volume and functional responses in the left occipital cortex (Durston et al., 2004; Valera et al., 2010; Shang et al., 2018). Therefore, we speculated that the abnormal alpha modulation in children with ADHD reflected the attenuated social function in their left occipital cortex.

The abnormal alpha modulation in the left hemisphere proved to be correlated with behavioral performance on the task and inattention severity in children with ADHD. It should be noted that the correlation between the posterior alpha modulation and symptom severity has not been found before (ter Huurne et al., 2013; Vollebregt et al., 2016). This indicates that the abnormal left alpha modulation in ADHD children not only reflects the behavioral impairment in the experiment time but also is closely related to the daily life function associated with ADHD. Some studies have indicated that children with ADHD show impaired social cognition (Mary et al., 2016; Lugo-Candelas et al., 2017) and may make them more inappropriate in social responses (King et al., 2009). The present results built a bridge between ADHD symptoms and the underlying neural activity in visual attention with social information. Therefore, the left hemisphere alpha oscillations directed by the social cue of human eye gaze could serve as a neurophysiologic marker of ADHD.

The cue-directed shifts of attention are thought to be promoted by the dorsal attentional network that includes the intraparietal sulcus (IPS) and frontal eye field (FEF) (Corbetta and Shulman, 2002). The bilateral FEF and IPS were found to be causally involved in the attentional top-down control of alpha oscillations in the occipital cortex (Capotosto et al., 2009; Marshall et al., 2015b), which was consistent with the suggestion that the alpha modulation in the posterior area was affected by the top-down control of the dorsal attentional network (Jensen and Mazaheri, 2010; Marshall et al., 2015b; Sadaghiani and Kleinschmidt, 2016). Further studies are needed to investigate whether top-down attentional control from the dorsal attentional network influences left hemisphere alpha modulation in children with ADHD (Mulligan et al., 2011).

In the present experiment, it was unexpected that the RT cueing effect in TD children was absent, whereas the children with ADHD showed a significant RT cueing effect for the left visual field response. The absence of a cue effect may be due to the special button design in the present study. Instead of detecting the target position consistent with the cue directions, we told children to discriminate the target position orthogonal to the cue directions. This design prevented the children from getting their response hand ready to press a button as soon as the cue appears, which could also reduce the cueing RT effect.

5. Conclusions

The experiment provides novel neurophysiological evidence that the attentional problems in children with ADHD are at least in part related to poor covert visuospatial attention guided by the social cue of human eye gaze, mainly arising from the deficit in the left hemisphere alpha oscillations. The correlation between alpha lateralization and ADHD severity implies that the left hemisphere alpha oscillations directed by the social cue of human eye gaze could provide a potential neurophysiological marker of ADHD.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.dcn.2019.100671.

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